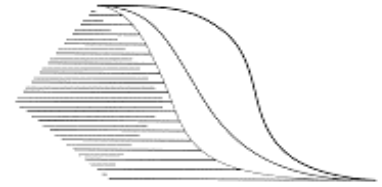


**Centre for Health Services
and Policy Research**



**Triple-Marker Screening
in British Columbia:
Current Practice, Future Options**

Final Report
made to
The Minister's Advisory Council on Women's Health

BCOHTA 00:14T

July 2000

British Columbia Office of Health Technology Assessment



THE UNIVERSITY OF BRITISH COLUMBIA

Triple-Marker Screening in British Columbia: Current Practice, Future Options

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The Minister's Advisory Council on Women's Health

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Foreword

The British Columbia Office of Health Technology Assessment (BCOHTA) was established on 1 December 1990 by a grant to the University of British Columbia from the Province, to promote and encourage the use of assessment research in policy, planning and utilization decisions by government, health care executives, and practitioners. The Office does not participate in policy development for a requesting agency; its role is confined to appraisal of the scientific evidence.

Assessments are performed in response to requests from the public sector such as hospitals, physicians, professional associations, health regions, and government; private sector groups such as manufacturers; and members of the general public. One or more of the following criteria are used to determine the priority of an assessment and the level of analysis: (1) number of users and potential change in quality of life; (2) acquisition and operating costs to the health care system; (3) potential to influence provider and consumer behaviour as a result of a review; and (4) the availability of accurate information and appropriate research skills.

Health Technology Assessment projects are conducted by faculty and staff (including medical consultants) who are expert in systematic review methodology. Electronic bibliographic databases and fugitive literature (that is, literature not indexed or distributed publicly) are searched using predefined inclusion and exclusion criteria based on a specific search strategy. The critical appraisal of retrieved evidence includes the formulation of logical and defensible conclusions about the technology under study.

Reports are reviewed internally, and then sent for external review to experts from a variety of academic or clinical disciplines. All comments and suggestions are considered before a final document is produced. Completed reports are available for public distribution, by request from the Office or through inclusion on the mailing list.

The strength of BCOHTA's method of systematic review lies in the process of explicitly detailing the methodology and criteria used to evaluate the research evidence, which is the sole basis for report recommendations. This transparent and reproducible assessment process allows other investigators to review the evidence objectively for themselves.

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EXECUTIVE SUMMARY

The purpose of this review is to examine maternal serum triple-marker screening (TMS) for fetuses with Down syndrome, other chromosomal abnormalities, and spina bifida, in the British Columbia context. Evaluation is both qualitative, addressing the personal and social significance of TMS, and quantitative, assessing effectiveness and cost.

The review is organized around the evaluation of four possible options for funding TMS. The first three options are in essence variations on current TMS practice in the province. A fourth option adds co-ordination of TMS, that is, provision, standardization, evaluation, and education throughout the province. In the interest of clarity, the options are discussed as much as possible in relation to Down syndrome, the most common condition traced through TMS.

The review has been conducted with particular attention to the interests of groups who may in some respects be seen as vulnerable, women during pregnancy and members of the Down syndrome community; and also to the concerns of TMS providers. The issues examined are those relevant to large-scale population screening of women considered at low pre-test risk of carrying an affected fetus. Not addressed are issues of particular relevance to women identified as being at high pre-test risk owing to individual or family history of affected births.

I. Findings

1. Recent provincial health policy has strongly supported the right of individual women to choose prenatal testing such as amniocentesis and abortion services on demand, a policy reflecting the principles of individual autonomy and informed consent enshrined in the Canadian Charter of Rights and Freedoms. But while the right to individual autonomy and informed consent has remained paramount in relation to prenatal screening, there is a growing need to examine the social implications of this type of testing for, and selective abortion of, fetuses with viable genetic conditions, such as Down syndrome.
2. Provincial health policy can neither promote nor discourage TMS use. The former could lead to criticism that the province is supporting eugenics, while the latter could be criticised as denying women their right to individual autonomy. In the absence of directive health policy, TMS utilization will in all likelihood continue to reflect a complex combination of social norms, women's expectations, and professional standards and anxieties. Furthermore, in the absence of provincial program status, quality of TMS program provision will remain uncertain, and access is likely to vary depending on locality.

3. The Genes, Elements, Metabolism (GEM) program at BC Children's and Women's Hospital currently analyses all TMS tests in the province. GEM data show that TMS utilization has approached 25% of live births in fiscal year 1998/99. In the third quarter of 1999/2000, utilization increased a further 75% (from 700 to 1200 per month) compared with the same period for the previous year. Virtually all health professionals, administrators, and policy-makers interviewed for this review agreed that TMS is well on the way to becoming a standard component of obstetric care.
4. TMS is effective if used prior to amniocentesis because it improves upon several features of using amniocentesis alone, an approach offered to women age 35 years and older in BC. Most notably, in any age group, the use of TMS increases the detection rate per amniocentesis performed. This results in a reduction in the number of unaffected fetuses lost due to amniocentesis for each fetus with Down syndrome detected.
5. Although an improvement on amniocentesis alone, in terms of the ratio of amniocentesis induced fetal loss to Down syndrome detected, TMS remains less than ideal as a screening test, owing to an initial false-positive rate for Down syndrome of 8.7% (in BC), and an overall detection rate of 60%-70% (false-negative rate of 30% - 40%). Amniocentesis alone is not associated with false-positive or false-negative results.
6. Similar to the prenatal screening tests which preceded it, cost-benefit analysis of TMS has found that the excess health-cost of caring for children with Down syndrome or neural tube disorders is so great that it easily exceeds the cost of providing these prenatal screening programs. This circumstance has been identified in the published literature since the late 1970s, and validated in a series of more recent economic analyses. The cost of providing TMS therefore is not a valid argument against its implementation.
7. A further argument that TMS ought to be provided because it will reduce health costs, is properly considered unethical. In fact, current interest in prenatal screening in general, and TMS in particular, does not derive from the inclination to make savings by eliminating the cost of caring for children with Down syndrome or other detectable conditions. Nor has this argument ever been sufficient in the province to justify prenatal screening.
8. The current health-policy issue therefore does not seem to derive from the question of whether TMS ought or ought not to be provided, or whether TMS will increase or decrease health care costs. Instead, the policy question is how to provide TMS equitably and efficiently across the province, assuming that the initial serum test will be offered to women, whether paid for publicly or purchased privately. Policy-makers are faced with significant imbalances in most regions of the province between ready access to the serum blood test, and relatively poor access to diagnostic, counselling and abortion services.
9. The realities of geography and population distribution in BC mean that the development of health policies supporting equitable regional access to diagnostic amniocentesis, genetic counselling and abortion services, will, as with the majority of health services, remain highly challenging. In the absence of a specific policy requiring regional centres or distribution of funds to regions for the purchase of services, prenatal diagnostic and counselling services are likely to remain centralized in Vancouver and Victoria.

10. Currently, no provincial group is assigned either responsibility or funding to set standards regarding the provision of prenatal testing across various regions of the province, such as would ensure informed choice, provider and patient education, and culturally appropriate methods of counselling. It should be understood that this status quo implies a level of risk of harm to populations affected by TMS testing. Now that the province has accepted some role in providing TMS services to women, if policy-makers wish to move forward, balancing costs and benefits necessarily implies an evaluative process able to balance provision with need.

II. Option-specific Conclusions

In terms of the four options considered by this review, we draw the following conclusions:

- **Option 1. Current practice of *ad hoc* funding.**

The TMS blood test is currently funded for women of all ages. There is no program funding for co-ordination, systematic quality control, or provider or patient education. This form of funding is termed '*ad hoc*' by geneticists and proponents of comprehensive program funding because individual clinicians, institutions and regions, as opposed to a centralized authority, are left to determine whether TMS is integrated into diagnostic and counselling services in their area. Local and international experience recognizes that to pay for TMS without adequately funding infrastructure support for quality assurance and education as well as diagnostic and abortion services, risks unnecessary harm to women who lack ready access to adequately informed clinicians or diagnostic facilities.

- **Option 2. TMS funding for women over age 35.**

Offering TMS on the basis of maternal age would seem to provide a way to integrate TMS into clinical practice without fundamental change to existing social understandings of pregnancy and disability, especially the awareness of an accelerating risk of Down syndrome with advancing maternal age. However, this approach would detect, at most, 30% of affected fetuses. Moreover, women over age 35 may find the false-negative rate associated with TMS unacceptable, and opt for amniocentesis regardless of negative TMS result.

It is of significant concern that much of the literature on women's experiences with prenatal screening suggests that the primary determinants of 'appropriateness' of this type of testing are women's perceptions of risk, not actual risk, and women's perceptions of disability, not actual disability. It is therefore difficult to justify assigning an age cut-off level using pre-determined population-based features such as a detection rate or maximum cost per affected fetus detected. Despite the acknowledged age-dependent prevalence of relevant conditions, from the perspective of the individuals concerned, TMS could be appropriate for as many women under an arbitrary screen-eligible age level as over it.

- **Option 3. No public TMS funding.**

A decision to withhold government funding for TMS would send a positive message to the Down syndrome and disability-rights community. However, although this community would appreciate the broad-level support, they also recognize that TMS would inevitably continue through private funding, and necessarily with much less opportunity for them to influence the educational messages provided to physicians and women. The privatization of TMS and the subsequent difficulty low-income women and couples would be likely to experience in obtaining TMS risk further marginalization of disadvantaged groups.

- **Option 4. Co-ordinated TMS funding.**

Co-ordinated TMS funding refers to the cost of maintaining TMS standards, independent of the actual utilization level. Informed opinion and focus groups interviewed during the data-gathering phase of the review gave this option the widest degree of support. The consensus was that TMS needs to be provided as part of a co-ordinated prenatal screening service in order to minimize the potential for harm and to provide equitable access. Since TMS is likely to increase in response to a complex combination of factors influencing clinical care, this option is also the most challenging: to provide TMS as part of a co-ordinated prenatal screening service in northern and isolated regions of the province will require an active government role in achieving an unprecedented level of decentralization for those diagnostic and counselling services currently concentrated in Vancouver.

A summary of the population and economic impact analyses for each option is given in **Table A**.

Table A: Population and economic impact of four alternative funding options (10,000 TMS tests)

	Option 1: Current practice (<i>ad hoc</i> TMS funding)		Option 2: TMS funding limited to women age 35 and over	Option 3: No public TMS funding. Amniocentesis for women age 35 and over	Option 4: Co-ordinated TMS funding for women of all ages	
POPULATION	AGE < 35	AGE ≥ 35	AGE ≥ 35	AGE ≥ 35	AGE < 35	AGE ≥ 35
Eligible	37,150	7,221	7,221	7,221	37,150	7,221
Tested	7,471	2,574	2,574	----	7,471	2,574
UTILIZATION						
Screen positive	397	578	578	----	397	578
Follow-up amniocentesis	278	347	347	3074 screening amniocenteses	278	347
DETECTION RATE						
Down syndrome correctly identified by TMS	7/13	16/20	16/20	----	7/13	16/20
False-negative rate	6/13	4/20	4/20	0	6/13	4/20
Down syndrome confirmed by amniocentesis	5/7	10/16	10/16	24 (amniocentesis accuracy 100%)	5/7	10/16
POPULATION IMPACT						
False-positive TMS tests	390	558	558	----	390	558
Therapeutic abortions	5-7	8-10	8-10	19 - 24	5-7	8-10
Normal fetuses lost through amniocentesis	3	4	4	31	3	4
Down syndrome births with negative TMS	6	4	4	----	6	4
Ratio of induced miscarriages following amniocentesis to Down syndrome fetuses detected	1 to 1.7	1 to 2.5	1 to 2.5	1 to 1.3	1 to 1.7	1 to 2.5
ECONOMIC IMPACT						
Cost per case detected	\$101,000		\$50,000	\$82,000		\$114,000
TMS cost	\$900,000		\$230,000	----		\$900,000
TMS-related genetic counselling	\$220,000		\$55,000	----		\$220,000
Amniocentesis costs	\$397,000		\$220,000	\$1,953,000		\$397,000
Follow-up care: amniocentesis induced abortion	\$1,500		\$700	\$6,500		\$1,500
CO-ORDINATION COSTS						\$186,000
TOTAL ANNUAL COST		\$1,619,500	\$555,700	\$2,041,500		\$1,818,500

PART I • CONTEXT OF REVIEW

INTRODUCTION

British Columbia is deliberating whether to implement its first prenatal screening program: testing for a fetus with Down syndrome, other rarer chromosomal abnormalities, and non-genetic open neural-tube disorders.

The primary impetus for the provincial Health Ministry to consider a programmatic approach to prenatal testing is a transition in clinical obstetrics away from offering amniocentesis testing of older women, and towards mass application of the triple-marker screening (TMS) test. The outlined program therefore includes both targeted testing of older ‘high risk’ women, and mass or universal screening of younger ‘low risk’ women.

Prenatal testing for Down syndrome and open neural-tube disorders has been provided to women in the province for almost two decades. However, while medical procedures and genetic counselling have hitherto been funded as individual fee items, prenatal testing has not received program funding or achieved program status (that is, funding for a co-ordinated prenatal screening service, at any level of utilization and everywhere that it is offered in the province).

Anticipated service components include overseeing technical and logistical details of all prenatal screening and diagnostic services, evaluating prenatal testing performance, such as initial false-positive and false-negative rates, as well as addressing regional disparities in amniocentesis and abortion rates for screen-positive women.

Establishing this kind of provincial prenatal testing program is a very considerable undertaking, requiring re-organization of institutional roles, regionalization of professional responsibilities, and restructuring of funding mechanisms. The effects are likely to be significant for clinical-care providers, for administrators and for society at large. Equally significant however, and central in any evaluation, are the costs and benefits likely to emerge for individual women.

Review mandate

In 1998, The British Columbia (BC) Ministry of Health & Ministry Responsible for Seniors asked The Minister’s Advisory Council on Women’s Health to assist in developing a comprehensive, province-wide approach to prenatal screening.

A principal objective of this mandate was to provide provincial policy makers with context-specific data from BC. At the same time, the Ministry wished consideration to be given to existing problems of access in remote regions of the province; and to anticipated problems such as the increasing scarcity of abortion services.

The Minister’s Advisory Council has hitherto strongly supported women’s autonomy and the right to chose all forms of reproductive care, including prenatal testing and abortion. In the instance of TMS, however, the Council found itself considerably troubled by a number of issues arising from the proposals, and uncertain how to proceed.

Issues of concern

The first concern of the Advisory Council was the substantial scale of proposed TMS screening, a program potentially applicable to all pregnant women in the province. Established forms of testing were formerly offered either to women aged 35 years and older, or to those younger women considered at elevated individual or familial risk. But in BC, as elsewhere in Canada and throughout the industrialized world, the advent of TMS has meant significantly greater availability of prenatal screening, and accelerating utilization.

This availability of TMS has itself given rise to a second concern for the Council, namely the number of healthy women who will incorrectly test positive to TMS and subsequently undergo unnecessary invasive diagnostic testing, with associated loss of unaffected fetuses. The Council asked whether a benefit to relatively few women warranted so much risk and related expense.

The Council was further concerned with a sharply developing imbalance in the provision of services. They noted that over the past two years, physicians and midwives providing obstetrical care had become greatly more inclined to offer TMS to all pregnant women. This has arisen in part because TMS can be initiated with a simple blood test, collectable at any laboratory or medical clinic in BC. Since, however, women who test TMS positive will require counselling, diagnostic testing and, in a few cases abortion in either Vancouver or Victoria, a discrepancy has developed in the utilization and the overall quality of TMS program performance, favouring women living in the urban south-west of the province.

The Council was also aware that a funding decision related to TMS was pending at the BC Ministry of Health. As a result of all these concerns, the Council asked for the review so that it could at minimum obtain a summary of what was known about TMS, its utilization in BC, and how it compared to other types of population-wide prenatal screening.

BCOHTA review

The British Columbia Office of Health Technology Assessment (BCOHTA), funded in part to conduct these types of reviews, recognized the importance of TMS to the population and has been able to apply its resources to compiling this report. The agreed-upon goal was to arrive at an understanding of TMS in the BC context.

During the course of its investigations, however, BCOHTA significantly developed the original study terms of reference. While retaining a strict focus on TMS and the issue of provincial program status, the investigators have seen it as a primary task to compile the most comprehensive data possible, reflecting the views of all interested groups in the province. These include pregnant women, individuals with Down syndrome or spina bifida, parents and other care-givers of children with Down syndrome or spina bifida, and health-care professionals (geneticists and genetic counsellors, obstetricians and general practitioners, laboratory technicians and pathologists).

In addition, in the light of the virtual explosion of genetic testing capability both pre- and post-natally, the scope of inquiry was expanded to examine critically the broader social, ethical and economic implications of TMS programmatic development. Incorporating all these elements has required a much wider qualitative and quantitative review than that originally envisaged.

Methods

BCOHTA conducted both original research, using quantitative and qualitative methods, as well as reviewing systematically-gathered secondary research findings from published and unpublished literature. A general outline of the original and secondary research is provided in this Introduction. More detailed description is provided with the reported findings.

The documentary search has been carried out with electronic searching via Medline, the Web of Science, and others, together with extensive non-electronic searches for materials. The library resources of the BC Office of Health Technology Assessment were used extensively. Gathered material includes government reports and other documents, the reports and documents of other agencies, information on the bio-technology industry and media reports.

TMS effectiveness

A formal protocol was adopted so as to identify recent syntheses of evidence on TMS efficacy, effectiveness and safety, as well as the impact of TMS on geographical populations and costs to the health care system. The full protocol is detailed in **Appendix A**.

TMS utilization

British Columbia utilization and cost data were gathered from the Genes, Elements, Metabolism (GEM) Program at BC Women's and Children's Hospital. Administrative payment data were obtained from the Medical Services Commission of the BC Ministry of Health.

Women's experiences

The report utilizes both primary and secondary data on women's experiences of prenatal screening. Some primary data on women's experiences with TMS were gathered opportunistically from concurrent research with women caring for children with Down syndrome. Time and resource limitations of this TMS review have, however, necessarily required reliance on previously-published literature. The literature review is not intended as exhaustive, but only as sufficient to emphasize that TMS cannot be adequately understood outside the lives of the women, families and communities in which it occurs.

Genetic counsellors

Data regarding genetic counsellors and counselling were collected through a questionnaire and at a focus group among geneticists and genetic counsellors within the Department of Medical Genetics at Children's and Women's Health Centre of BC. Research on genetic counselling was facilitated by the relatively small number of counsellors and their concentration in Vancouver and Victoria.

Primary-care providers

Two major sources of data were used. First, literature relating to practitioners' knowledge and practice of TMS was surveyed and summarized. Wherever possible, data on Canadian practitioners were included. Second, interviews were carried out with professionals who, in different capacities and at a variety of sites, provide and interpret TMS. This exercise was not intended as an exhaustive or even representative survey of BC providers' attitudes. Rather the interviews were carried out with individuals identified as key informants of practice and policy issues in TMS and clinical care.

Model of population impact and cost

A simulation-planning model was used to estimate the population impact of various TMS program options. The model was developed in two stages.

The first step was to estimate the number of pregnant women for each year of age in British Columbia¹ and to estimate the number of fetuses with Down syndrome in each age group.² The number of fetuses with Down syndrome was estimated for the 2nd trimester, the time of TMS testing (as opposed to live births). The spontaneous abortion rate for fetuses with Down syndrome between the 2nd trimester and term is taken as 23%.

The second stage was to estimate the effect of applying TMS to the modelled 2nd trimester population. TMS test characteristics are known to vary according to maternal age, that is the sensitivity (detection rate) of the test increases as the prevalence increases with advancing maternal age. Because data from BC regarding TMS test characteristics³ have been reported, for the purposes of this analysis women are divided into two groups, those over and those under 35 years of age. The model allows for estimates of the detection rate, the false-positive rate, the false-negative rate, and of costs for each sub-population and for the total population.

CHAPTER 1: IMPLICATIONS OF PROGRAMMATIC TESTING

Who is affected?

Those likely to be affected by the introduction of a prenatal testing program fall into two main groups of women, with their partners and families.

The **first** group are those most *directly* affected. This includes three distinct sub-sets of women already pregnant or contemplating pregnancy and therefore candidates for pre-natal screening:

- (i) The first sub-set are those women, who, given the option, will want TMS. This is likely to be the majority. Utilization of earlier forms of maternal screening with AFP alone⁴ by the majority of women has been found in Canadian jurisdictions⁵⁻⁷ and suggested as likely in large population surveys conducted for the Royal Commission on Reproductive Technologies and reported in its summary:

“The vast majority of those surveyed would be prepared either to use PND (prenatal diagnosis) themselves (79 percent) or to allow others that option (81 percent). About 18 percent were opposed to either personal use or wider availability of PND services.

A marked majority of those surveyed also support the availability of the option to terminate a pregnancy after PND, with only 16 percent opposed in all circumstances. The level of support depends on the severity of the disorder. For example, 73 percent of people surveyed strongly supported the availability of abortion if a disorder that is fatal early in life is diagnosed in the fetus. Approximately 60 percent supported the availability of abortion for disorders that make it almost certain that independent living will not be possible.”⁸

- (ii) The first group further includes women who, *given the option*, do not want the test. They may decline because (among other reasons) either they are willing to accept the possibility that their baby may be disabled, or because they are unwilling to contemplate the possibility of follow-up tests and ultimately abortion if the fetus is found to be affected. Although they may not proceed to the testing stage, these women are nevertheless likely to find the decision process significantly demanding, perhaps disturbing, in itself.
- (iii) This group must also include women who would want the test, but who are *not* given the option. They or their primary care provider may simply be unaware of the existence, or applicability of TMS; or they may be denied access because they live outside the Lower Mainland where anything beyond the primary laboratory test is all but unavailable.

Some women in this last sub-set may come to feel that failure to provide the service - and therefore the option of ending the pregnancy - represents a violation of their rights, entitling them to pursue a case for damages before the courts in what is termed a ‘wrongful birth’ lawsuit. **Chapter 8** examines this issue, and its implications for laboratory biochemists and clinicians.

Of those women who subsequently have a baby with one of the relevant disorders, many will accept the challenges of raising their child, usually with the guidance of the one of the provincial support groups. **Chapter 7** provides insights into the perspective of this group of women and families.

For this first group, however, TMS, accepted or declined, has the potential for a direct effect on the outcome of their pregnancy. The implications of TMS in obstetrical and medical care are summarized in **Chapter 9**.

The **second** main group are *indirectly* affected by the test, those women, families and individuals already living with a relevant disability.

It may seem paradoxical to consider those for whom (except for subsequent children) the test would seem to serve no purpose. It is however fundamental to the ethical issues raised in this review that their voices be heard, individually, or as expressed through the main support associations (**Appendix B**).

The principal concern emerging from within this group is that any testing procedure seeking to identify a disorder such as Down syndrome has a eugenic purpose, namely to cleanse the population of imperfection. This they regard as not merely bad for society, diminishing both its genetic and moral base, but also as likely to perpetuate discriminatory attitudes towards individuals with Down syndrome as being ‘unworthy’ to live as equal citizens.

Several respected authors have collectively raised concerns about the eugenic context of testing, the importance of non-directive counselling, the problems women face regarding guilt and blame, and the uncritical drive to standardize these prenatal testing programs without adequate public debate.⁹⁻¹⁴ An overview of the published literature on women’s attitudes and experiences with TMS, other forms of serum screening and prenatal testing with amniocentesis is provided in **Chapter 5**.

In raising these issues in relation to TMS, the clear expectation of this group however, is that the ethical questions must be addressed not just by individuals, but at the policy-making level. They assert, for example, that it is unjust to channel public funds almost exclusively towards TMS and diagnostic services, instead of providing social support for affected individuals and families. The inadequacy of such support, they argue, is a major inducement for women to take the screening option.

The ethical and economic implications of a testing program are complex and even contradictory. A short outline of some of the arguments at issue follows here.

Economics or ethics?

As part of the economic dimension, this report seeks to provide costing estimates for various TMS option possibilities. These estimates are to some extent based on current data, and to a further extent substantially speculative. A central problem facing policy-makers, however, is not their level of accuracy, but whether they are material to policy considerations at all.

This issue is no unforeseen and unwelcome baggage of the new technology. The question was first asked in the province almost 20 years ago,¹⁵⁻¹⁶ and has been, it must be admitted, largely side-stepped since that time. Raised again in current conditions, it still goes to the heart of the matters under review.

Simply put, if the utility of TMS is to be measured only by financial savings, then a full program should be introduced without delay. Allowing for even a broad degree of uncertainty in costing

estimates, introduction of TMS with its corollary, the termination of affected pregnancies, will undoubtedly secure substantial savings in public expenditure.

Several generally accepted reports have estimated the more quantifiable health (as opposed to social) costs associated with Down syndrome. One of the more widely-cited appraisals, derived in part from primary data from children in BC with Down syndrome, estimated that, in 1997 dollars, the excess cost of health care for a person born with Down syndrome is \$350,000 (assuming 75% inflation since 1981).¹⁶ A similar estimate, after adjusting for inflation, puts the net present value (in 1987) of the excess cost to society of a child with Down's syndrome at around \$300,000.¹⁷

These estimates of excess health care costs for children with Down syndrome, although crude, support the generally-accepted conclusion that even for younger women at lowest pretest risk, prenatal screening for Down syndrome is cost-beneficial to society.¹⁸ The maximum estimate for the cost of TMS per detected fetus with Down syndrome in the younger age groups is \$100,000, resulting in a minimum cost-savings ratio of 3:1.

Even the much lower lifetime excess health costs associated with a child with spina bifida are estimated at \$150,000 (assuming 75% inflation since 1983).¹⁵ A cost-benefit analysis of prenatal detection of Down syndrome and neural tube defects in older mothers is sufficient alone to make TMS screening cost-saving.

Given these figures, why was a comprehensive screening policy not adopted 20 years ago? It is, simply, because the value of a life, disabled or otherwise, is not to be calculated in the columns of credit and debit. The ethical questions, that is, the human questions, are not usefully illuminated by bare arithmetic.

In this respect, far from providing a route forward, the new technology has only deepened the problems for the present generation. It has, in effect, created two opposing lines of ethical claim.

The first is voiced most often by clinicians. The new technology has made the search for the relevant conditions so easy and free of risk that providers now say: we must offer this test procedure to women because it is the standard of care, and because we expose ourselves to risk of malpractice litigation if we do not.

The second is the counter claim, mentioned above, of the disability-rights groups and of humanitarian concerns generally, that to identify the targeted conditions as unworthy of existence is to adopt a policy of eugenics more suited to the Nazi era than to the Canada of today. Our supreme commitment, they argue, must be to humanitarianism and the Charter of Rights.

Until now, the apparent resolution of these claims has been to pass the question off to individual women, under the guise of freedom of choice. But this freedom has proved largely illusory, only truly available to those advantaged women living in the Lower Mainland, where a bare laboratory test result can be given the full range of follow-up support: ultrasound, amniocentesis, counselling and abortion facilities.

In summary, if the question for policy makers were simply whether to meet the financial cost of extending these services throughout the province, it would be an easy calculation to make. The ethical dilemma, on the other hand, is not so easily weighed, and it is this that any future policy proposals must confront.

Informed choice: individual and collective

In relation to this field and its ethical dilemmas, the assertion that ‘society must decide’ is not an equivocation.

The principle of individual informed choice and consent is well established in medicine, law and ethics. Facilitating informed choice in regard to TMS by as many as 30,000 individual women a year is a very considerable challenge in itself, and the task will in all probability fall on primary care givers, almost exclusively general practitioners and obstetricians, whose formal training in genetic knowledge and counselling varies widely.

A second relevant principle, however, is that of collective informed choice, which in relation to prenatal screening means population-wide understanding of and support for a genetic testing program that could lead to selective abortion. This notion remains far less developed and without an institutional, professional, or political home. The question to be addressed is: does society support a universal prenatal genetic screening option, and if so, for which conditions, and with what testing accuracy?

The literature contains several well-described examples of this aspect of collective informed choice. The most often-cited instance¹⁹ is the support given to genetic screening for Tay-Sacks disease, a rare but distressing condition resulting in early infant death. Several Jewish communities in large American cities collectively agreed that funding of this genetic testing program was warranted. Although a test of prospective parents for recessive gene carrier status, not a test during pregnancy, it provides an example of how collective consent may in practice be achieved.

The Final Report of Royal Commission on New Reproductive Technologies does in fact provide evidence of broad public support across Canada for the availability of prenatal testing to detect conditions such as Down syndrome and neural tube disorders:

“A substantial majority (about three-quarters) say that if the fetus has a severe anomaly, the parents should have the option to terminate the pregnancy.”²⁰

Knowing that women would seek this service or think it ought to be made available is, however, merely the starting point for consideration. Another question might be: would women rather allocate scarce resources to other programs, known to prevent congenital disorders (for example, programs to reduce neural tube disorders through folic acid supplements or to reduce toxic injuries to the fetus by supporting drug and alcohol addiction programs for women) ?

At this interface between the broad social issues and resource allocation, significant questions emerge as to where TMS and requests for program support might fit within government. The issues are not only of spending priorities, important though these are, but also of how TMS is to be evaluated and prioritized, and who its champions should be.

Population-wide prenatal screening requests

How should policy-makers respond to the present demand for a TMS program? The provincial government is clearly in no position to arbitrate on the ethics and either promote or restrict prenatal testing. In the modern context, to aim at the former risks accusations of eugenics, while favouring the latter might be interpreted as acting to limit women’s rights.

This inevitably points to the conclusion that it must be for individual women to make their own choices. But even here, the provincial government is not in an especially strong position to disseminate awareness of TMS and its ethical aspects to individual women in the province. Even without commercial advertisement or widespread promotion of the test, the growth of TMS use will doubtless continue, driven by complex individual, social and professional pressures.

It should be noted that while provincial programs and the policy process develop in discrete stages, clinical care does not. Clinical management evolves continuously from doctor to doctor, clinic to clinic, hospital to hospital. Growth of clinical care utilization inevitably pressures policy change, but it neither directly determines nor reflects the public policy process. Indeed, as this report documents, clinical care has increasingly adopted mass prenatal screening for Down syndrome in the virtual absence of, and to some extent in defiance of, public policy.

Other jurisdictions

TMS programs are not universal nor are they uniformly applied in the United States,²¹ Canada,⁵ the United Kingdom,²² or other European nations.²³ In the European Union, for example, three of fifteen countries had national serum screening strategies, while three others had locally determined screening programs.²³ A recent systematic review of the literature on prenatal screening²⁴ concluded that “the differences have been explained in terms of political choices, available resources, and the strong influence of university hospitals”. In her study of the diffusion of prenatal screening across Europe, Reid concluded that within these political environments, “the key people in diffusion are members of the medical profession”.²⁵

In Canada, a province-wide TMS program in Ontario was initiated as a two-year pilot project in 1993.²⁶ Alpha fetoprotein screening was established in Manitoba in 1985,²⁷ and more recently has been expanded to include additional serum markers.

It is important to bear in mind, however, that even with the current variation in programs across populations of wide cultural and economic diversity and dispersed over very large geographical areas, substantial common ground exists in Canada, likely to have significant implications for provincial policy-making.

For example, Canadian jurisdictions have approximately the same incidence of affected pregnancies. Moreover, all parts of Canada are served by the same health-care system, based on the principles of universal access to services, under exclusive government funding with self-regulating health professions. Provinces also share the same legal and regulatory system, providing principles of patient autonomy and informed choice under the Charter of Rights and Freedoms.

Furthermore, all jurisdictions face similar challenges in relating a program with the complexity of TMS (involving local clinicians, diagnostic imaging and provincial laboratories) to established government funding and policy structures. In responding to these challenges, there is equivalent access to clinical trial and epidemiological evidence, and to cost-benefit analyses where these are helpful.

This review acknowledges both the broad similarities and the context-specific differences between TMS programs within and outside Canada. A central theme in this review is how these similarities and differences have emerged in the BC context over the past decade.

The role of government

Recent years have seen a virtual explosion of genetic testing possibilities, increasing federal regulatory and patent protection favouring commercial over social interests, and far more vocal and effective anti-abortion and disability-rights movements. The challenge is to recognize that within this unpredictable milieu, prenatal genetic testing technologies are here to stay, and will inevitably have an accelerating influence.

The role of government in this area, while limited, seems relatively clear. It has the responsibility to maintain equal access to pre-natal screening as to any other health service. It can influence the conditions under which the test is provided and conditions for controlling the quality of testing procedures. In addition, government is in a position to facilitate broad public input, and perhaps debate, on the implications of pre-natal testing in general and of TMS in particular.

To summarize, government and publicly-funded institutions facing this tide of technology must address practical policy questions. While few easy answers are in prospect, far less long-term policy commitments, if it is to balance its obligations to the community at large, to caregivers, to practitioners, and most particularly to affected individuals, government must inevitably become more engaged with these issues, and will require the best available information if it is to do so effectively.

Clearly, the application of prenatal testing is set to affect not only the lives of today's parents and children, but the future of generations unborn. The ultimate aim must be to understand and direct the flow of the new technologies in ways that are, if not universally beneficial, then at least directed to cause least potential for harm.

CHAPTER 2: POLICY HISTORY

This chapter aims to situate TMS in BC policy history, and to explain why a prenatal screening program was not established in the 1980s (and hence why there is now no governmental ‘home’ for prenatal screening requests and relevant issues).

The roles, relationships, and decisions surrounding the development of alpha-feto protein (AFP) screening which began two decades ago is of considerable importance in understanding the more recent development of TMS in maternal screening. One decision taken at that time, namely that a provincial health program of AFP testing should not be established in BC, has fundamentally influenced current TMS policy questions. Other provinces, such as Ontario and Manitoba which elected to establish AFP programs in the 1980s, today face quite different policy options.

Prenatal serum screening and provincial health policy

AFP screening for neural tube disorders, while not strictly genetic screening, is closely analogous to the newer technology. It involves an initial simple serum test offered by primary care physicians to pregnant women of all ages; test interpretation requires an accurate estimate of gestational age, usually involving ultrasound measurements; and the process depends on a tight referral system between primary, intermediate, and tertiary care facilities.

Provincial funding of maternal serum screening for fetal congenital disorders began in the British Columbia in 1981-82, when the Medical Services Plan (MSP) established an AFP laboratory fee item. This meant that, on a physician’s request, laboratories were able to bill a standard fee for reimbursement from the MSP.* The primary care physicians who ordered and interpreted the test were not (and are not) paid a specific fee. They were and continue to be paid more general fees for providing prenatal care.

From the time of its initiation in the province, genetic services associated with AFP testing, such as counselling and geneticist consultation, were funded by the government through a block payment to the Provincial Medical Genetics Program.† The Program was in turn expected to provide appropriate services to pregnant women out of this general revenue. Provincial funding therefore reflected overall demands of the Program, rather than need associated with specific forms of testing, such as AFP screening.‡

* MSP fee items, and their level of reimbursement (in this instance to laboratories) resulted from complex negotiations between the BC Medical Association, through its Tariff Subcommittee, and representatives of the ministry responsible for the MSP. Decisions regarding MSP fee items also reflected the opinions of Provincial Medical Advisory Committees, established by the Ministry of Health to obtain technical advice and expert clinical opinion on a wide range of new and established tests and treatments. Expert Advisory Committees, including the Medical Genetics Committee, were primarily appointed by the Government, but membership also reflected established positions. For example, the Medical Genetics Advisory Committee included the director of the Provincial Medical Genetics Program.

† Medical Genetics is a small, highly specialized unit, until recently centralized in Vancouver. A second Medical Genetics Department, involving one geneticist, began in Victoria in 1993.

‡ Assigning resources within the Medical Genetics Program for AFP testing and, at times selective abortion, has not however been without difficulty. For example, provincial funding to the Medical Genetics Program between 1982 and 1988 was channelled through the Salvation Army Grace Hospital, the institution where the program was physically located. The Salvation Army takes a strict pro-life approach to abortion.

The MSP provided additional technical and professional funding for the tests and procedures, such as ultrasound and amniocentesis, offered to women who were AFP screen ‘positive’. In the case of amniocentesis, direct funding included procedural fees to the obstetrician and the institution providing the procedure. Funding for biochemical and cytogenetic laboratory tests on the amniotic fluid and cultured cells were paid to the provincial laboratory facilities on a fee-for-service basis.

Paying for tests, not establishing a program

A full provincial AFP testing program would properly have included funds specifically designated for general physician and patient education, designated geneticist and genetic counsellor activities, and a communication and referral infrastructure. Such an infrastructure would set standards and establish practical means to deal with patient notification, as well as subsequent testing and transfer of patients to referral centres from remote areas of the province.

In BC, however, provincial funding for maternal serum screening never moved beyond funding AFP laboratory costs. That is, AFP screening and subsequent diagnostic testing did not expand beyond simple test funding to become a formal AFP testing program.

Instead of specific funding, the Ministry of Health decided on the overall level of funding to the Provincial Medical Genetics Program. It did not direct the internal distribution of funds within the Program. One executive-level medical consultant at the Ministry has stated that an implicit part of government policy was not to call for screening for any congenital condition, particularly conditions such as neural tube disorders that could result in women seeking a medically-induced abortion.

The fear on the part of government was not so much the controversy surrounding abortion. Rather, the concern was that to call for specific genetic testing programs, such as a serum AFP screening, could be seen as a negative value-judgment on people born with this condition. In advice to the present authors, the consultant cautioned:

“Be very careful when you are writing your report. Do not call any Provincial Medical Genetic activity a "program" other than the overall institution itself. The Ministry has not funded, nor does it wish it to be seen as funding programs to eliminate certain individuals. Be particularly careful when you describe prenatal screening for Down syndrome in women over age 35. This is not a program. It is a service provided by some obstetricians and helped in part by the Provincial Medical Genetics Program, but its existence reflects the request of women and their physicians, not the desires of the Ministry of Health.”²⁸

Establishing a provincial AFP testing program would have implicitly and explicitly recommended this testing as part of routine prenatal care. That is, doctors would have been expected to offer this test to all pregnant women. As established, however, government policy wished AFP utilization to reflect the requests of individual patients and professionals, not the programmatic expectations of government.

Herein lay the dilemma for AFP program proponents and provincial policy makers. Policy makers did not wish to fund this form of testing unless it was clear that women or their physicians were asking for these services. But without some sort of programmatic effort to establish a service, most doctors and women would not become aware of this type of testing, or familiar with its capabilities.

This dilemma is not peculiar to AFP testing. Congenital conditions are generally regarded as one of the most difficult areas of medicine in which to develop appropriate clinical practices and associated health policy, for several reasons:

- congenital conditions, including those of genetic origin, are poorly understood by the public and professionals, including physicians;
- risk is difficult to understand and to interpret in relation to populations versus individuals;
- congenital conditions, while in total occurring in 1 to 3% of births, individually remain too rare for general experience or knowledge.

The funding-demand dilemma (funding being dependent on proven patient demand, while patient demand is dependent on prior programmatic and educational funding) has continued to affect maternal serum screening to the present.

Committees, contexts, and choices *

Before launching an AFP program, the Medical Genetics Program called for program funding to upgrade regional prenatal testing facilities and expertise, as well as improving technology such as ultrasound. The Program Director at the time argued that in the absence of these programmatic and infra-structural developments in many areas of the province, an AFP screening program would, on balance, do more harm than good.¹⁵

Throughout the 1980s, a group of geneticists, obstetricians, and pathologists associated with the Medical Genetics Program put forward proposals for the development of a Provincial AFP Program. Submissions were made to both the Provincial Medical Genetics Advisory Committee and the Continuing Advisory Sub-Committee on Screening; two of the various Medical Advisory Committees established to inform the Ministry of Health regarding new tests, techniques, and technologies. The proposals justified the need for a Provincial Program because AFP testing had become “a normal standard of obstetrical practice” (particularly in some American states) and because “AFP testing is being done by an increasing number of British Columbia physicians. Problems result from the lack of education and facilities to interpret results, and to deal with abnormal results.”²⁹

In the event, the decision not to promote widespread AFP testing in the absence of program funding did not appear to be greatly challenged by physicians or women. A provincial AFP screening program, although clearly supported by some members of the Medical Genetics Department and several obstetricians and physicians routinely ordering the test, did not receive wide support among physicians or women throughout the province. Neither general practitioners and obstetricians providing primary obstetrical care nor women receiving it came forward in significant numbers to ask the Medical Genetics department to develop a provincial neural tube disorder screening program. Some of this lack of support may be accounted for by ignorance of the test.

* Features of the AFP era are presented here primarily through the recollections of the Director of the Provincial Medical Genetics Program at the time. She acted as a consultant to and was interviewed for this HTA report.

The former Director of the Provincial Medical Genetics Program Director argued that unilaterally to introduce an AFP program was outside her power. She had funds within the Provincial Medical Genetics Program allocated toward supporting prenatal testing. For example, from the late 1970s, the Medical Genetics Program had been allocating increasing resources to women over age 35 considering or actually undergoing amniocentesis. However, while provincial funding was expanding to the Provincial Medical Genetics Program which was, in turn, directing increasing support to prenatal testing, the Program Directors protested that there was no funding to develop the service beyond university-affiliated hospitals and health institutions based in Vancouver.

From the government's perspective, by contrast, funding for a provincial AFP service was already being provided as part of the global budget to the Provincial Medical Genetics Program; in its view, if such a service were warranted, it should be provided from this budget. A funding impasse resulted that has not been resolved to the present.

Despite the absence of Provincial Program funding, utilization of AFP testing grew steadily throughout the decade, albeit at a low level, reaching 1000 tests per year by 1990 (3% of live births).²⁹ In addition, some of the referral pattern and patient care infra-structure became established both for women under age 35 having serum AFP testing and women over age 35 having amniocentesis or CVS. Although not formally studied, utilization seemed dominated by women living within or within a few hours drive of the major metropolitan areas of the province.

Summary

In summary, from its initiation, the policy process relating to maternal serum screening has hinged on demand, need or general interest in this form of testing. Policy-makers, of necessity, have been obliged to interpret the level of demand for maternal serum screening in the province as sole indicator of whether or not women or primary care physicians support a maternal screening program.

Until very recently, maternal serum screening utilization remained limited to a relatively small nucleus of obstetric and genetic specialists centred in the large south-western metropolitan regions of the province. Based on the utilization rate, health policy-makers decided that maternal serum screening had not been demanded by a sufficient number of primary-care physicians or women; nor by a sufficiently vocal set of their political representatives. Advocacy and public-policy developments have become caught in a circular argument: program funding requires popular use, but popular use cannot occur without the educational strategies that accompany program funding.

PART II • PRENATAL SCREENING

CHAPTER 3: AMNIOCENTESIS & TMS

This report is not primarily designed for a specialist audience, and its mandate reaches beyond discussion of specific prenatal testing techniques. Accordingly, the technical material on amniocentesis and TMS has been kept to a minimum. Some degree of technical detail is, however, necessary for understanding current issues relevant to prenatal screening options, and this follows here and more specifically in **Appendix C**. Subsequent chapters will focus on general issues raised by moving to a publicly-funded mass prenatal screening program.

This chapter looks at two competing diagnostic strategies currently considered for program status in BC. They are: amniocentesis alone; and TMS as the primary test with amniocentesis as a secondary confirming test. Both approaches are designed to detect fetuses with Down syndrome, other rarer chromosomal abnormalities or open neural tube disorders. Each has strengths and weaknesses for individual women, clinical care providers, and population health.

Identified conditions

A brief summary follows of the conditions that pre-natal screening aims to detect.

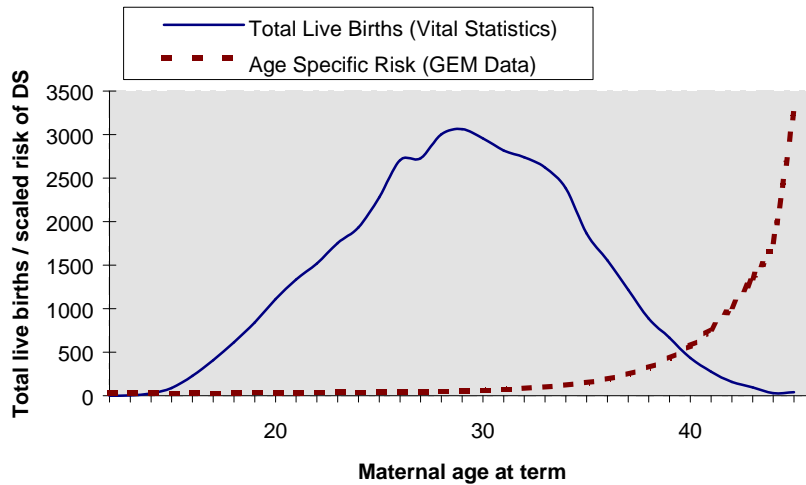
Down syndrome

In the medical and genetics literature, Down syndrome is usually reduced to prevalence statistics, live birth rates, percentage of heart and gastro-intestinal defects and life expectancy, some of which follow here. But this implicitly negative presentation belies much of the reality of individual women, families and communities living with Down syndrome, which many regard as an altogether richer experience. This perspective has been considerably developed in recent time, and it is therefore with an appropriate caution that Down syndrome is discussed in this section.

Down syndrome, also known as trisomy 21, is the most commonly occurring chromosomal disorder. In most instances, fertilization resulted in each cell having three copies of chromosome 21, instead of the normal two. The problem is estimated to occur with an incidence of about 1 in 600 to 700 births in BC (60-70 births per year).^{2,30} Down syndrome is associated with mental retardation, congenital heart disease and various additional physical manifestations. **Figure 1** illustrates the distribution of fetuses in a population of women. Note that most pregnant women are under the age at which prevalence of Down syndrome is highest.

TMS is also used to identify women at increased risk for carrying a fetus with other rarer, usually fatal chromosomal disorders such as trisomy 18.

Figure 1. Distribution of live births by age and risk of Down syndrome



Open neural tube disorders

Open neural tube disorders, serious abnormalities of the brain and spine. The latter group occur with an estimated incidence of 1.3/1000 live births (40-50 births per year in BC)^{1,31}

Closed, or skin covered defects, which constitute 5%-10% of all neural tube disorders, will not be detected. Open neural tube disorders consist of anencephaly and spina bifida in about equal percentage. Anencephaly, which results in a seven-fold rise in the median maternal serum AFP level, has little overlap with unaffected pregnancies, and therefore is not considered part of the routine screening parameters. Instead, neural tube disorder screening parameters, such as false-positive and detection rates are discussed in terms of open neural tube disorders.

Open neural tube disorders, in contrast to Down syndrome, occurs independent of maternal age. Detection of open neural tube disorders, therefore is a direct function of the overall percentage of women undergoing prenatal testing.

Other congenital disorders

It is important to note that amniocentesis, with or without TMS, detects only a very small percentage of the major physical and mental disorders found in newborns. Congenital disorders are estimated at between 3% and 5% of all births.³² Thus, although TMS can lead to detection of the majority of fetuses with two of the most common congenital conditions, Down syndrome and neural tube disorders, taken together these conditions account for less than 10% (0.1% of all births) of the major disorders found at birth.

Ethnicity as a factor in relevant disorders

Several cohort studies have looked for associations between ethnicity and TMS marker levels as indicators of the risk of having a child with Down syndrome or neural tube disorder.³³⁻³⁶ The overall conclusion is that while ethnicity should be considered in TMS testing, no link exists between Down syndrome incidence and a definable ethnic group.

Despite the absence of an association between Down syndrome and an ethnic group, it is important to question what impact ethnicity could have on TMS; whether, for example, decisions about giving birth to a child with a disability may make women in ethnic groups already discriminated against even more vulnerable to discrimination by the dominant cultural group. More subtly, membership of a visible minority may also make women vulnerable to discriminatory practices based on ethnic stereotypes regarding use and purpose of reproductive technology.

A cautionary example from the United States of how prenatal screening can be discriminatory against a particular ethnic group is cited by Bradby.³⁷ The Sickle Cell Anemia program was not intended as a racist policy, but as a useful way of addressing health care issues deemed relevant for individuals of African-American descent. The program targeted individuals considered to be at a higher risk of the sickle cell anemia genotype, but eventually paved the way towards a form of anti-black eugenics.³⁸ Genetic carriers of the trait were discriminated against in the form of employment loss, higher insurance premiums, and in receiving particular types of medical treatment.³⁹

This example of the dangers of a screening program illustrates the fine line between encouraging individual choice, and introducing a tool that furthers discriminatory practices.

Clinical manoeuvres: mass screening* and targeted testing for Down syndrome

Amniocentesis as the primary test

Amniocentesis is a technique whereby amniotic fluid is obtained from a woman during pregnancy by inserting an ultrasonographically-guided needle trans-abdominally into the amniotic sack. Fluid is aspirated and fetal cells are separated. These cells are cultured and analysed for chromosomal patterns, a process that takes approximately 2-3 weeks.

* Population screening in relation to prenatal care is defined as “the identification, among apparently healthy individuals, of those who are sufficiently at risk of a specific disorder to justify a subsequent diagnostic test or procedure.”¹⁷² It is to be noted that women who undergo screening and are identified as screen-positive do not necessarily have a fetus with a specific disorder. Rather, they are members of a group that has a higher incidence of the disorder than the screen-negative group. It is also the case that a few screen-negative women will carry a fetus with a disorder. However, the percentage of such cases is lower than the percentage of affected fetuses in the screen-positive population.

The most common tests conducted are:

- fetal cell karyotyping *
- alpha feto-protein (acetylcholinesterase, if elevated AFP)
- other bio-chemical analyses; DNA testing.

Women receiving amniocentesis are also incidentally screened for neural tube defects, although the incidence of these disorders does not increase with maternal age.

Amniocentesis for fetal karyotyping can be performed in the first three months of pregnancy, but it is usually conducted in the second three months of pregnancy when the amniotic sac is much larger.

Fetal loss

The virtue of amniocentesis is its ability to discriminate between a positive and negative diagnosis for conditions such as Down syndrome. This power is, however, materially mitigated by significant numbers (approximately 1%) of spontaneous abortions resulting from the procedure. The UK Health Technology Assessment report concluded that second trimester amniocentesis is safest in terms of fetal loss, and the method most likely to be efficacious in obtaining useful amniotic fluid and cell samples.⁴⁰

The best estimate of fetal loss comes from a randomized controlled trial of screening, which reported a procedure related risk of 0.9% (mid-range estimate 15-75 percentile of 0.6-1.2) of pregnancies.⁴¹ This study was conducted in the 1980s and may over-estimate loss. Techniques have since improved.

Amniocentesis over age 35 years

Hitherto, this procedure has been offered in BC only to pregnant women above age thirty-five. In various Canadian and US jurisdictions, this has been rationalized as the cut-off point because over this age, the risk of having a child with a genetic disorder was considered to be greater than the risk of an abortion as the result of CVS or amniocentesis.^{42, 43}

Most younger women (and therefore most women in pregnancy) have generally been considered to be both at too low a risk for detectable congenital[†] abnormalities and at too high a risk of fetal loss from the testing procedures, specifically amniocentesis, for testing to be justified.

Chorionic villous sampling

It may be noted that Down syndrome can also be diagnosed prenatally by determining the karyotype of fetal cell samples obtained by chorionic villous sampling. Chorionic villous sampling is used early in pregnancy, between 10 and 12 weeks, and is an uncommon alternative to amniocentesis for women over age 35. It is not directly relevant to the main issues addressed in this report, and will only be considered in the economic analysis, **Part V**.

* Karyotype means the chromosomal element typical of a cell, arranged according to the Denver classification and drawn in their true proportions, based on the average of measurements determined in the number of cells.

† Congenital disorder means a disorder present at birth.

Triple-marker screening (TMS)

The benefit to harm ratio associated with TMS is to a large extent dependent on the logistics of its provision in any setting. As the chapter following indicates, women having TMS need ready access to diagnostic and counselling services, especially those living in more remote areas of the province.

The simplicity of the TMS blood test, completed in a matter of seconds in any laboratory or medical facility, therefore belies the complexity of the context in which women choose TMS as part of their obstetrical care. In fact, a series of choices confronts each woman. Instrumental in this process is the knowledge, skill and attitude of the professional who provides the technical information on which these decisions will be based.

TMS comprises several technical components:

- 1) Biochemical testing and analysis of maternal serum (*see Appendix C*)
- 2) Dating ultrasound (*see Appendix C*)
- 3) Amniocentesis (*see p25*)
- 4) Cytogenetic testing of amniotic fluid cells (*see Appendix C*)
- 5) Second trimester abortion (*see p26*)

False-positive

TMS, similar to other screening tests, provides a collection of true-positive, as well as false-positive and false-negative results. Between 8% and 10% of the women who have TMS will test positive. Only a small percentage of these women, however, will actually have an affected fetus (1 to 2% of those testing positive).

False-negative

TMS also results in false-negative results, so that some women carrying a fetus with Down syndrome will be falsely reassured that their fetus is unaffected. False-negative results are of greatest significance to approximately 15% of women over age 35 who may elect not to have a definitive diagnosis with amniocentesis.

Detection rates

Population-wide, as opposed to age-specific, TMS could detect 60%-70% of fetuses with Down syndrome, and 80% of those with neural tube disorders. Population-wide TMS is recommended because most cases of Down syndrome and neural tube disorders occur to women considered at low risk for conceiving a fetus with these disorders. It is possible to obtain higher percentages of Down syndrome positives with TMS, but this is associated with higher rates of false-positives (requiring confirming amniocentesis) and induced abortions. Prevalence of Down syndrome is directly related to maternal age, increasing for older cohorts of women (see **Figure 1**).

Ultrasound

TMS is considerably dependent on ultrasound scanning during pregnancy. **Figure 2** provides an example (after the Ontario Ministry of Health) of a decision tree which locates ultrasound in a TMS service. It includes the timing and type of test and their decision paths.

Initial TMS-positive women who have not had dating ultrasound are asked to have a scan to confirm dates. If the ultrasound date estimate is greater than 10 days' difference from non-ultrasound estimates, the TMS risk estimate must be recalculated.

TMS can be provided at any time between 15 and 18 weeks' gestation, but the actual gestation must be known for accurate test interpretation. Gestational dating almost always requires an ultrasound scan. An ultrasound scan also assists TMS interpretation by determining fetal viability and gestational number if there is more than one fetus.

There is increasing use of sophisticated ultrasound testing during pregnancy, particularly in the second trimester.^{44,45} Ultrasound itself is a screening tool for detecting congenital disorders, primarily structural abnormalities, some of which are associated with genetic conditions such as Down syndrome. Prior ultrasound testing may also have an impact on TMS by conferring an elevated risk status on some women who are subsequently offered serum testing.

Although estimates of the effects of ultrasound dates are not possible from actual BC data, it is reasonable to assume the effect would be similar to that found in the world literature. Wald shows the effect of ultrasound dates on screening test performance. TMS detection rates rise from 59% without dating ultrasound, to 69% with these scans.^{22,46}

Summary

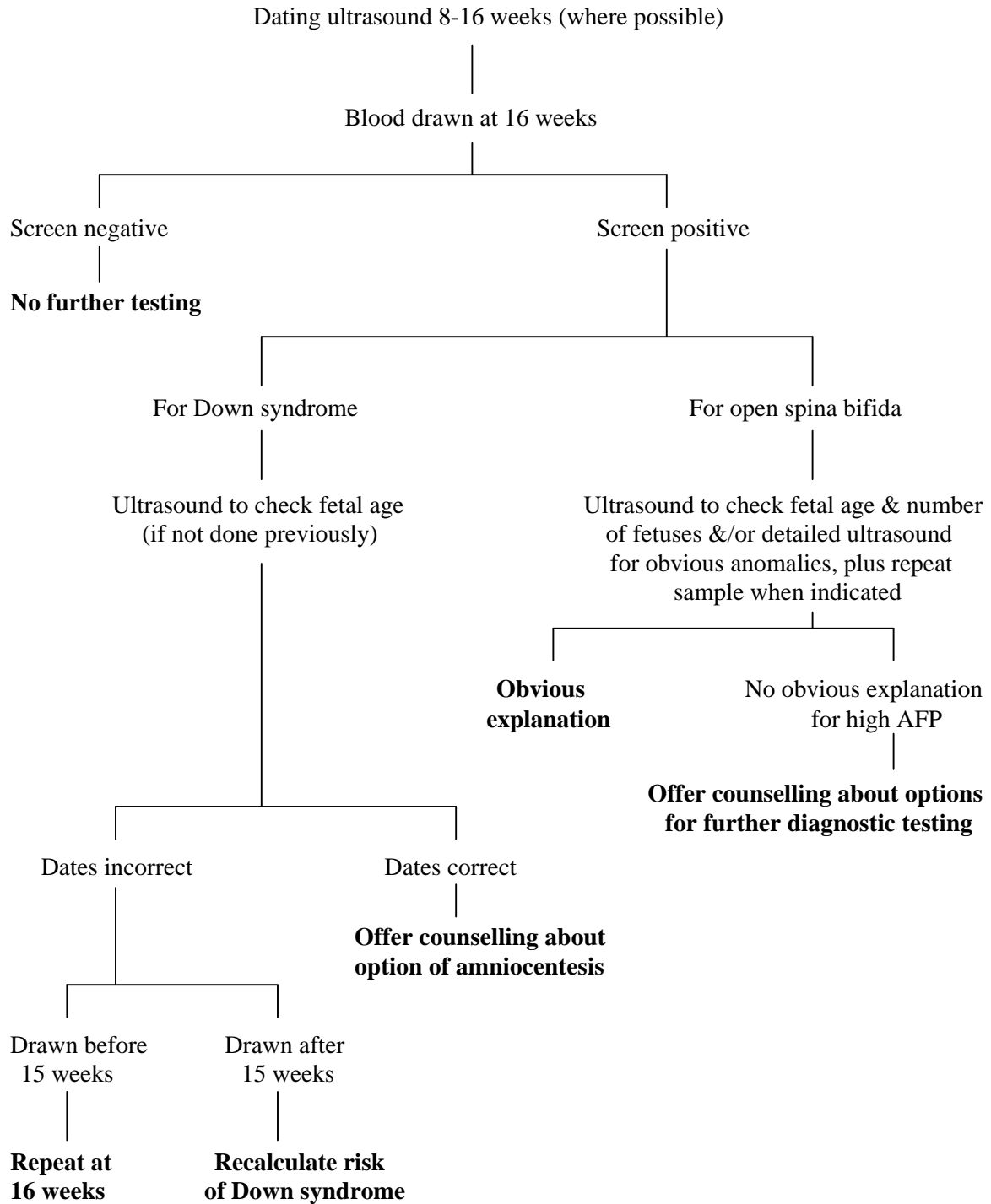
TMS followed by amniocentesis, and amniocentesis alone are obstetrical care services both designed to identify those women with a fetus affected by Down syndrome, neural tube disorders, or rarer chromosomal abnormalities.

Each has strengths and weaknesses. The primary advantage of amniocentesis alone is that it leads directly to cytogenetic analysis with virtually no false-positive or false-negative results, so that pre-test counselling by obstetrical care providers remains relatively easy. The primary disadvantage of amniocentesis alone is the 1% risk of fetal loss due to amniocentesis itself. As a result, it has been limited to the 15% to 17% of pregnant women over age 35 in Canada at sufficiently high *a priori* risk for carrying a fetus with Down syndrome to justify the risk of healthy fetal loss. The maximum number of fetuses with Down syndrome that can be detected remains limited to about 25%, the number that occurs in women over age 35.

The primary advantage of a TMS service is that it applies to women of any age, thus increasing the potential detection rate to 60% to 70% of affected fetuses. For women under age 35, it can identify a subset of women at sufficiently increased risk of carrying a fetus with Down syndrome to justify the risk of amniocentesis. For women over age 35, it can identify a subset of women at sufficiently low risk that amniocentesis may not be recommended.

The primary problem with TMS in any age group is that, in contrast to amniocentesis, it is associated with false-positive and false-negative results. Pre-test counselling is therefore much more difficult for obstetrical care providers. In addition, TMS requires several steps, including detailed ultrasound, which may be logistically difficult for women living in rural or remote regions of any jurisdiction.

Figure 2: Maternal Serum Screening Protocol *



* After Ontario Ministry of Health. *Maternal Serum Screening*. Health Care Providers' Reference Pamphlet. Jul 1993:4

CHAPTER 4: TMS UTILIZATION TRENDS, REGIONAL DISTRIBUTION, SERVICE PERFORMANCE

In the province of BC, TMS, primary and tertiary obstetrical care, medical genetics, amniocentesis, abortion services, and laboratory medicine have all developed separately, reflecting independent professional, economic and social processes. For the most part these clinical care activities involve different professional groups, and are funded through different mechanisms within different departments and institutions, all of which have at least somewhat different agendas, demands and priorities. Rather than a single entity, TMS in BC might therefore more appropriately be regarded as a loose association between virtually independent clinical services.

This chapter seeks to explain how in the mid-1990s, laboratory services developed much faster throughout the province than associated diagnostic, counselling and abortion services. The result is that major challenges of regional disparities in access to genetic counselling and diagnostic services such as amniocentesis now face TMS development in the BC. A second aim is to understand the widespread use of ultrasound scanning, itself a prenatal screening test for congenital disorders including Down syndrome, and its impact on prenatal obstetrical care in general and TMS in particular.

Maternal serum screening and laboratory medicine

Maternal serum screening for Down syndrome * became increasingly important to laboratory pathologists (clinical biochemists) during the late 1980s. Along with local geneticists, the obstetricians and pathologists associated with the Medical Genetics Departments became aware that the AFP tests ordered to assess the risk of neural-tube disorders (NTDs) could also be used to interpret the risk of Down syndrome: elevated AFP associated with increased risk of NTDs, and decreased AFP associated with increased risk of Down syndrome. As a result, women having an AFP for NTDs, could equally well have a Down syndrome risk assessment.

Prior to the advent of TMS, an ethical dilemma arose for laboratory pathologists in regard to reporting low alpha protein results. The issue (discussed in **Chapter 8** below) has largely been resolved by the introduction of triple-markers.

With the expanded possibilities for maternal serum testing for genetics disorders and the failure of NTD program development, formal proposals for the development of a provincial maternal serum screening program switched in 1990/91 to requests for a maternal serum genetic screening program. The program proponents faced a problem, however. AFP tests were paid for as a provincial benefit under the Medical Services Plan as described above. The two additional serum markers needed for genetic risk assessment, human chorionic gonadotropin (hCG) and unconjugated estriol, were not.

Laboratories were already funded and capable of performing two components of the triple screen test, independently, for other indications. Serum alpha-fetal-protein (AFP) levels, as mentioned,

* Other, rarer genetic conditions (usually by a factor of 10), which serum screening may also provide a risk assessment are not specifically considered in this discussion.

were used as a test for neural tube disorders. HCG assays were used for, among other things, early diagnosis of pregnancy. The type of serum estriol that needs measurement requires specific additional testing capability. Program development therefore needed expanded indications for each of these established tests.

The proposals accordingly provided a number of justifications for provincial funding of laboratory TMS testing:

- To fund laboratory marker measurement and risk calculation would increase the options for interested women, particularly women already seeking AFP testing.
- Triple-marker measurements would allow an additional risk assessment for women over age 35 interested in diagnostic testing via amniocentesis. These women could forego amniocentesis if their risk assessment situated them at levels found in much younger age groups.
- It would largely relieve the dilemma laboratory pathologists faced when finding a low AFP result.
- The tests had been proven effective in large, sophisticated clinical trials;
- The proposals also noted that TMS was offered or about to be offered in two other Canadian provinces.

Beyond seeking provincial funding of laboratory tests, the initial proposals requested establishment of one or two urban-centred pilot projects. That is, while envisioning the ultimate development of a province-wide maternal serum screening program, they initially sought limited funding to develop a model for and to evaluate options for integrated service-delivery beyond the serum TMS test.

Introduction of population-based TMS

The laboratory-led proposals for a TMS program in BC, similar to prior proposals in the early 1990s and 1980s, did not receive provincial funding. In the event, the Genes, Elements and Metabolism Program, at BC Children's and Women's Hospital began participation in an international research project on TMS, fortuitous in that it largely resolved the problem faced by laboratory physicians in relation to reporting low AFP results.

Conducted from 1995 to 1997, the GEM study was designed to determine which serum markers were best for prenatal screening. In addition, the researchers were interested in the impact of TMS on the amniocentesis rate for women aged 35 years and older. They hypothesised that TMS use by women in this older age group would reduce the use of amniocentesis, thereby reducing the associated risk of loss of unaffected fetuses.

The women in the study had TMS substituted for single-marker screening with AFP. The resulting risk assessment based on three markers represents the innovation associated with TMS, providing a more accurate risk assessment for Down syndrome than AFP alone. Therefore, while designed to assess the relative merits of alternate serum screening strategies, the study resulted in the first large scale introduction into the province of a serum screening program.

Although not published in the medical literature, several newsletters were circulated to all provincial physicians, and the study introduced TMS to many practitioners. Seventy-five percent of the women were under age 35 (in compliance with the initial study design).

Since one of the objectives was to examine TMS introduction in three different contexts (BC, Ontario, and Quebec) this research study was in part intended as a pilot project.⁴⁷ Further aspects of the project are discussed in **Chapter 8** in relation to wrongful birth lawsuits and in **Appendix C** in relation to laboratory services in BC.

TMS trends

The GEM study in 1995 began the replacement of AFP testing with TMS as the maternal serum screening test used in British Columbia. Only AFP appears as a fee item in the BC Medical Services administrative database. Since, however, AFP is one of the three markers which make up the triple screen, it provides a rough estimation of the trend in maternal serum screening use.*

In 1996/7, 25% of eligible women received an AFP (and by assumption a TMS) test during their pregnancy. The proportion of tests for women under 35 was 54% of all tests in 1991/92, 47% in 1994/95, and 56% in 1996/97. The potential for expansion of service provision is in the category of women under age 35. 83% of live births occurred in this age group, with only 17% of potentially eligible women receiving serum testing to date. TMS testing rates were obtained directly from the GEM program (**Figure 3**).

Ultrasound trends

The volume and cost of prenatal ultrasounds at 14 weeks' gestation and over has also been reasonably stable over time. The fee-for-service price of prenatal ultrasound after 14 weeks is \$90.63. Ultrasound examination will be considered in **Appendix D** on TMS effectiveness.

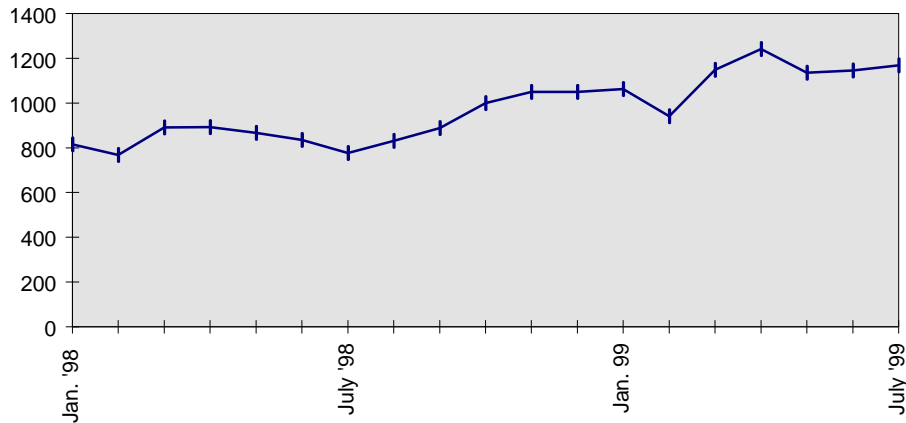
The volume and cost of prenatal ultrasound at less than 14 weeks has been reasonably stable during the 1990s: 28,476 test at a cost of \$1,820,924 in 1991/92; 28,966 tests at a cost of \$1,960,014 in 1994/95 and 26,990 tests at a cost of \$1,844,963 in 1996/97. The fee-for-service price of prenatal ultrasound before 14 weeks is \$68.00.

Routine dating ultrasound prior to TMS has been recommended in BC.⁴⁸ However, because of limited access to ultrasound in several regions of the province, prior dating ultrasound has not become a requirement for TMS testing.

Although more prenatal ultrasound testing is occurring in the province each year, less pre-TMS dating ultrasound may be occurring. This is because the current provincial recommendation by the Council on Clinical Practice Guidelines, in keeping with the Society of Obstetricians and Gynecologists of Canada, is for a single ultrasound scan at 18 weeks' gestation.⁴⁹ This gestation was selected as a compromise between dating (which is optimal earlier) and detection of fetal anomalies (which is optimal later, as structures develop). The timing of dating ultrasound is therefore too late for many women having TMS starting at 15 weeks' gestation.

* A proportion of the AFP tests included in these totals were not conducted on maternal serum but amniotic fluid. This accounted for approximately 35% of all AFP tests reimbursed in 1996/97.

Figure 3: Number of TMS tests per month, Jan. 1998 to July 1999



Source: GEM data

Amniocentesis

Genetic counselling, chorionic villous sampling (CVS) or amniocentesis, and fetal karyotyping has been offered to women over age 35 in British Columbia since the late 1970s.

For complex social and historical reasons (not least of which is their characterization as ‘elderly’ with respect to their reproductive capability),⁵⁰ approximately sixty percent of women over age thirty-five (and to a much lesser extent women under this age) have sought these services.⁵¹

Amniocentesis rates were not obtained directly from the Medical Services Plan administrative database because it does not distinguish between amniocentesis for prenatal testing and other indications (**Appendix E**). Instead, amniocentesis utilization for genetic testing is assumed from the number of cytogenetic analyses. Each amniocentesis produces only one sample for cytogenetic analysis. The volume of cytogenetic analysis of amniocentesis fluid increased steadily from 2,826 tests in 1991/92 to 3,433 in 1994/95 and 3,871 in 1996/97 (**Appendix E, Tables 14-16**).

Amniocentesis rates for advanced maternal age in 1996/1997 were provided in the Amniocentesis Business Plan for 1998,⁵² which included regional data. Amniocentesis services have remained centralized in Vancouver and Victoria, and as a result have favoured women in these areas (70% versus 40% in other regions).⁵²

Medical services payments for AFP (TMS) compared with other prenatal tests

The cost of AFP (TMS) was compared to the costs of amniocentesis and prenatal ultrasound. As **Figures 4 & 5** demonstrate, the cost of prenatal ultrasound exceeded \$7 million in 1996/97, compared with about \$400,000 for AFP and \$49,000 for amniocentesis.

As noted above, much of the cost of amniocentesis and TMS is from alternative payments and therefore not included in this database. Nevertheless, the cost of ultrasound far exceeds costs associated with other prenatal screening and diagnostic tests.

Abortion

Province-wide TMS will almost certainly increase the demand for second trimester abortion services in BC. Present access to abortion services in rural, isolated and northern communities is somewhat limited.⁵³ In addition, growing anti-abortion violence in BC and elsewhere has led to noticeably diminished numbers of practitioners willing to offer abortion services in any geographical area. There is, not surprisingly, a growing reluctance on the part of graduating medical students to learn and practise the procedure.

The problems associated with providing abortion services in the province are well known to the Ministry of Health and to the Minister's Advisory Council requesting this review. Therefore, although some details follow regarding abortion services and the provincially-sponsored Abortion Working Group, abortion services will remain essentially outside the scope of the present review.

Abortion rates

According to provincial Ministry of Health data, approximately 15,000 medically-induced abortions are conducted annually in the province: about 14,000 prior to 14 weeks' gestation and 1,200 after 14 weeks. Of those occurring after 14 weeks, approximately 100 arise from the detection of a significant fetal congenital or chromosomal anomaly.

The US Task Force summarizes the morbidity evidence following first trimester abortion, including infection, haemorrhage, and injury, at 2%-3% of procedures, although serious morbidity is rare. In one series reporting on 170,000 cases, for example, the hospitalization rate was 0.07% and no reported deaths.^{54,55} The US Task Force reports higher morbidity from second trimester abortions, but mortality remains rare. They estimate the case-fatality rate for legally-induced abortions at 0.4/100,000 procedures. This is contrasted with a pregnancy-related mortality rate of 8-9/100,000.⁵⁴

While they are limited to well under 1% of the total abortions performed in the province, abortions in BC requested because of prenatal diagnosis are significant because they occur late in the second trimester of pregnancy and are technically difficult. Most late second trimester abortions are currently provided by the Comprehensive Abortion and Reproductive Education (CARE) program at BC Women's Hospital. A small number are conducted in three additional regional hospitals.

Figure 4: Total payments for amniocentesis and AFP over three time periods
 Source: MSP data

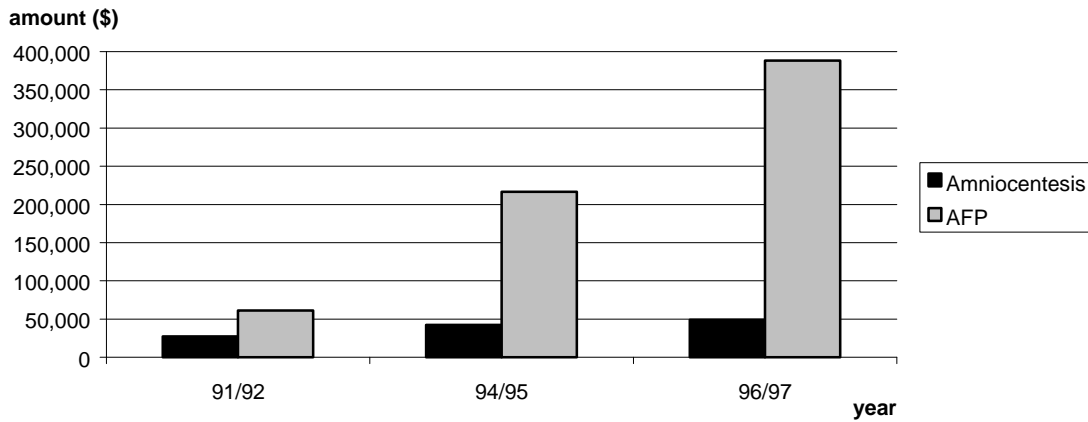
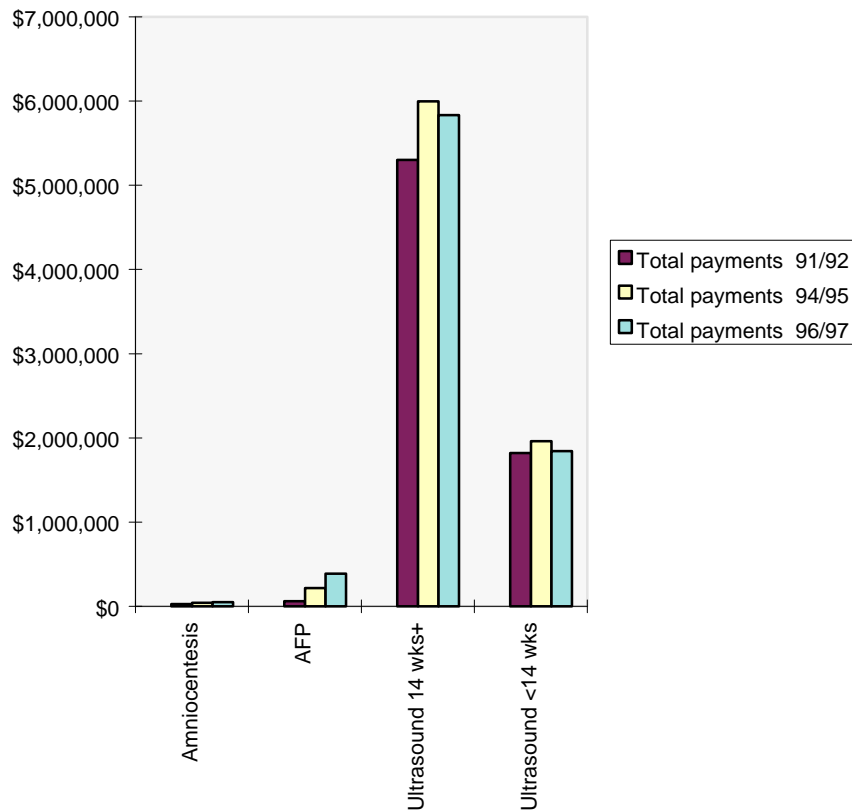


Figure 5: Total payments for prenatal screening tests over three time periods
 Source: MSP data



The rate of abortion following positive amniocentesis is unknown for BC; estimates are available in the literature.⁵⁶⁻⁵⁸ The rate of induced abortion as an adverse effect following amniocentesis is similarly not known for BC. Estimates from randomized trials are also available in the literature.⁴¹

The Ministry of Health has established an Abortion Services Working Group which is addressing the ongoing issues of access to services in some areas of the province, aspects of provider and patient safety, and the particular problems associated with providing late second trimester abortions, such as those arising from prenatal screening.

The Abortion Services Working Group recently commissioned a province-wide survey⁵³ that describes wide disparity in access to services outside Vancouver and Victoria. The Working Group continues to support initiatives aimed at promoting local services and reducing out-of-province referrals.

The Abortion Services Working Group is also addressing the major issue of physician supply. They note that a decreasing number of physicians are providing an increasing proportion of abortions in the province, and at a time when these physicians approach retirement and new obstetricians are reluctant to include abortions in their practices. The Comprehensive Abortion and Reproductive Education (CARE) program at BC Women's Hospital is working to increase the number of well-trained providers by offering optional medical student and obstetrical resident education.

Regional diversity

Limited awareness of cultural diversity

This review includes an examination of regional utilization of TMS and diagnostic services, as well as considering the range of clinical care approaches to TMS across the province.

In the multi-cultural context found in BC, however, the diversity of experience within and between communities is a separate and most important consideration. Neither the published literature, nor current research in the province helps in understanding culture-specific perception of TMS, neural tube disorders, and Down syndrome.

While representing only a preliminary examination of this complex issue, some questions of cultural diversity are raised through interviews with members of the Vancouver South Asian community (**Appendix F**).

Regionalization of administration

BC is currently devolving centralized authority from the Ministry of Health to Health Regions of the province. Within this evolving system, administration and management of TMS components may become central issues: is TMS to be designated a core service required of all regions by the Ministry, or will individual regions be left to consider what place TMS testing and counselling should have within their own program priorities? A larger question was highlighted by the Royal Commission on New Reproductive Technology: how can public policy ensure equal access to all forms of prenatal testing and abortion services?⁸

Distribution of prenatal testing

Although access is in theory universal, in practice TMS utilization is dominated by patients living in or close to the major urban centres in the south-western corner of the province. All the laboratories responsible for karyotyping and two departments responsible for genetic counselling are located within this area.

Regional disparity is exacerbated by the imposition on initial screen-positive women of excess travel costs. The case illustrations below show the typical problem. The issue of provision for travel to centralized sites as an alternative to regionalization of amniocentesis services is addressed in the provincial report on the provision of amniocentesis services.⁵²

The use of prenatal tests has steadily increased over the time period in most regions (**Appendix E**). The highest use of TMS testing occurred in Vancouver, South Fraser Valley, North Shore, Simon Fraser and Capital health regions, as indicated by both medical services commission and GEM data. The GEM program provided data on the regional distribution of physicians who have ever ordered or received the results of a triple-marker screening test (**Appendix E, Table 13**).

The pattern of amniocentesis use also follows this pattern. **Tables 16 & 17 (Appendix E)** present total services and payment data from the BC Medical Services Commission administrative database on alpha fetoprotein serum testing, cytogenetic analysis of amniotic fluid, transabdominal amniocentesis and ultrasonic guidance of amniocentesis for fiscal years 1991/92, 1994/95 and 1996/97. These time periods were chosen to illustrate general trends.

Diversity of service provision: Case illustrations

As part of this project research, interviews were conducted with physicians currently practising in the province. Based on what they describe, the following represent typical TMS scenarios in urban and rural primary care settings.

Scenario 1. Westside Vancouver

Woman A, age 28, in the 12th week of her first pregnancy, returns to her general practitioner's office for a routine prenatal visit.

Her doctor, trained in Canada, had practised obstetrics in this urban setting for almost 20 years. In keeping with her routine practice, she'd provided this woman with various documents and pamphlets regarding nutrition and birth-place options, and had included material describing TMS, obtained from the GEM Program, BC Children's and Women's Hospital. The doctor was familiar with the GEM Program because she'd routinely offered alpha fetoprotein testing to all her patients since the late 1980s.

The physical examination, considered normal, was completed quickly. By contrast, the discussion of various tests including TMS continued much longer than the planned 15-minute appointment. The woman evidently understood that TMS was a screening test for Down syndrome, but seemed reluctant to accept that, at her age, she was at risk of carrying a fetus with this condition. She assumed only older women were at risk.

Nevertheless, she agreed that the test would probably be a good idea as she didn't want a baby with Down syndrome. However, she asked why she had to wait until so late in her pregnancy to have the blood test. Her doctor explained that the best time for an accurate test was after 15 weeks.

Pre-test counselling for TMS continued at the next prenatal visit at 16 weeks' gestation. The patient hadn't yet had serum drawn for TMS, but agreed to have it done the following day. Consequential on the initial decision to have TMS, the woman, her partner and family faced several potential outcomes (see **Figure 2**).

TMS negative (95% of women under age 35)

The laboratory report would follow about three days later as 'negative', that is, the risk of Down syndrome was found to be less than 1:385 (the pre-test risk of a woman 35.5 years old) at term. The risk of open spina bifida was estimated to be less than 1:1000, the assumed pre-test risk for women in BC, regardless of age.

TMS positive

Several sequences are possible:

Measurement error:

The initial report was 'positive', but an ultrasound examination the following day estimated that her gestational age was wrong (over or under by more than 10 days) or that she had a twin pregnancy; the test result was revised to 'negative'. A repeat TMS was recommended at 15 weeks if, for example, her gestational age was under-estimated at 12 weeks by ultrasound.

Amniocentesis and abortion:

The laboratory report was 'positive' and remained positive despite an ultrasound scan. The woman was then referred to the Department of Medical Genetics at BC Children's and Women's Hospital later the same week, where she was counselled regarding the risk of carrying a fetus with Down syndrome, and informed that she was eligible to have a diagnostic amniocentesis. The woman was also advised of the risk of abortion due to the amniocentesis procedure itself. She then chooses to have or not to have amniocentesis. The amniocentesis procedure requires an additional appointment with the prenatal screening program at BC Children's and Women's Hospital. The results of the amniocentesis take an additional 10 days to 2 weeks. The cytogenetic studies show Down syndrome in about 1-2% of women who test TMS positive. If carrying a fetus with Down syndrome, the woman must decide whether to have an abortion. An abortion at this stage of pregnancy would almost certainly be performed at the BC Children's and Women's Hospital in Vancouver.

Scenario 2. East Kootenays

Woman B, age 28, in the 12th week of her first pregnancy, returns to her general practitioner's office for a routine prenatal visit.

Her doctor, medically trained in Canada, had practised obstetrics in this rural setting for almost 20 years. Consistent with his routine practice, he hadn't provided this woman with any written material describing TMS, and was not aware of the TMS material available from the GEMS program at BC Children's and Women's Hospital. Moreover, neither he nor his four local GP colleagues routinely offered AFP testing to their patients, since it was more than a hundred kilometers to the nearest obstetrical specialist and almost 300 kilometers to the nearest genetic counsellor in Calgary. Prenatal serum testing either with alpha fetoprotein or TMS were rarely requested by women in this community.

In keeping with the recommendations of the Society of Obstetricians and Gynecologists of Canada and the provincial Council for Clinical Practice Guidelines, the doctor recommended routine ultrasound testing at 18 weeks' gestation to all of his patients. He made this recommendation, not because ultrasound could detect fetal anomalies, but to assist with obstetrical care. Most women in his practice expected, and about two-thirds obtained, a routine obstetrical ultrasound examination.

Although not routinely offering prenatal serum screening, he was nevertheless in the process of changing his practice. This was in part because of a Continuing Medical Education course earlier in 1999 which had discussed the new forms of screening such as TMS; and in part because he had read an account of a wrongful birth lawsuit in Chilliwack (a community in the lower Fraser Valley). He was alarmed to note that the College of Physicians and Surgeons bulletin recommended that he should offer TMS to all pregnant women in his practice. Of greatest immediate concern was how to arrange for women in his practice to obtain amniocentesis. He discusses the situation with his patient, and she agrees to have the initial blood test.

Several courses are again possible:

TMS negative

As in approximately 95% of cases, the laboratory report followed three days later as 'negative'.

TMS positive

The laboratory report came back 'positive', and in order to have an ultrasound scan, this woman needed to travel 120 kilometers to an intermediate level care hospital. The scan could revise the estimated gestational age and result in a negative test finding, or if a fetal anatomical abnormality was found the woman would have to travel 300 kms in the opposite direction for detailed ultrasound examination.

The report remained positive despite ultrasound. The woman was then referred to the Medical Genetics Department in Vancouver. She may or may not be able to obtain sufficient time off work or have sufficient funds for travel. If undertaken, the counselling and amniocentesis would probably be arranged for the same day. Abortion, if indicated and requested, would require a second journey to Vancouver about 2 weeks later.

Summary

The provision of TMS in the BC context depends on several key variables:

1. TMS utilization is growing rapidly, but not for all age groups. As shown by GEM data (**Appendix G, Table 6**), TMS utilization, at least in this initial phase, is strongly identified with women over age 30 and close to age 35, the established eligible age for amniocentesis without prior TMS. Also taken from the GEM experience, 50% of women age 35 and older who opt for prenatal testing continue to select amniocentesis first, rather than TMS. In other words, for the population 35 years and older, the GEM data suggest that at least half the women who would have chosen amniocentesis in the past will continue to choose amniocentesis, despite the availability of TMS.
2. The actual role of TMS in obstetrical care is very sensitive to women's decisions following TMS: whether or not to have amniocentesis after a TMS positive result, and whether or not to have an abortion if Down syndrome is confirmed by cytogenetics. Amniocentesis rates are known to depend on access to services, which in BC favours women in Vancouver and Victoria.⁵² Amniocentesis utilization also varies with age, with the highest utilization in the younger age groups.
3. Although the quality of laboratory and post-test counselling services are not in issue, the degree of training or specific expertise of individual physicians and midwives providing pre-test counselling has not been assessed. Significant program adjustments are likely to prove necessary as obstetrical care providers either assume or decline this professional role.
4. Commercial interests have not had a significant impact on TMS. TMS has not to date been actively promoted by the drug or device industry. As a result, it has received relatively little public and professional attention as compared with other tests promoted through manufacturer-subsidised lectures, conferences, and publications. With an increasing number of genetic conditions detectable through prenatal testing, however, this may change, and commercial interests may ultimately play a key role. In one disquieting development, for example, US companies have announced preparedness to offer 'mail-order' genetic testing, in which a privately-funded local facility would gather blood samples and mail them to a centrally-located laboratory. Test results would be mailed directly to women, leaving local geneticists and counsellors to interpret results and provide any necessary additional services.

PART III • PATTERNS OF EXPERIENCE

This section of the review considers TMS in the lives of ordinary women and their families.

The primary difficulty in this policy area (and the primary deficit in this study) is that while research has reported on TMS utilization and cost, almost nothing is known about the impact of (population-wide) TMS on women, who are likely to know little about issues of genetic and congenital risk.

Consequently, it is apparent that if any policy in this difficult area is to prove sustainable, it will be essential to bring forward the concerns of women and the disabled and to consider the patterns of their experience.

The authors of this report regard critically claims that TMS provides reassurance. Most informants in the data-gathering phase themselves questioned whether reassurance is needed at all. One focus group participant stated: “I think that by offering the test you’re making the fear,” and another mother reasoned “As we remove old medical fears, we replace them with other medical fears that might be less life-threatening but take up the space left by the previous fear.”

Not all those whose views are considered here have encountered TMS directly, but even indirect effects are significant. This section explores individual and family experience with TMS, counselling, and the perspective of families caring for children with Down syndrome.

Chapter 5 summarizes some of the published and unpublished literature on women’s experiences with prenatal screening in general and serum screening in particular. The ensuing **Chapter 6** examines genetic counselling efforts aimed at assisting women to understand and manage a TMS positive test result. Finally, **Chapter 7** provides a perspective from women and families raising children with Down syndrome, a largely self-confident viewpoint focussing on children, often forgotten amid technical discussions of screening parameters and economics. Social issues of disability-rights and selective abortion of viable conditions are examined in **Part VI**.

CHAPTER 5: WOMEN AND PRENATAL SCREENING

The goal of this chapter is to incorporate current knowledge of women’s experiences into prenatal screening policy development, and to highlight the need for additional research investment in this area.

Some primary data on women’s experiences with TMS were gathered opportunistically from concurrent research with women caring for children with Down syndrome. For the most part, however, time and resource limitations of this TMS review required reliance on previously-published literature on women’s experiences with TMS and other prenatal screening technologies. The literature review is not intended as exhaustive, but as sufficient to emphasize that TMS cannot be adequately understood outside the lives of the women, families and communities in which it might operate.

Overview of literature

Most studies of women's experiences with maternal serum screening use standardized scales to assess the psychological impacts, or effects of these tests.

Some research focusses on explaining variations in emotional and psychological responses to maternal serum screening in terms of women's lack of proper information about it. A few studies have examined women's experiences of maternal serum screening along multiple dimensions, including attitudes towards disability, feelings of being 'at risk', and attitudes towards abortion. While such assessments may explore the psychological-emotional dimensions of maternal serum screening in some detail, the entire experience in which women make sense of and negotiate prenatal genetic technology is intricate, certainly less easy to investigate than simple assessment of what women know about serum screening or about detectable conditions.

Asking 'what women know' addresses whether women understand the medical meanings and rationale for the test. By contrast, to ask 'how women make serum screening meaningful' reminds us that women make sense of new technologies in ways that reflect existing cultural frameworks, social relationships of family and community, financial circumstances, and individual histories.

Ethnographic studies of women's experiences with prenatal screening and diagnosis include maternal serum alpha fetoprotein in California,^{59,60} amniocentesis in New York City,^{12,61} amniocentesis in Manitoba,²⁷ and ultrasound fetal imaging in Quebec.⁶² A number of studies to be published shortly examine women's experiences, for example, with the detection of Down syndrome in BC,⁶³ with ultrasound-detected anomalies in BC,⁶⁴ and with amniocentesis in Quebec.¹⁰

These studies specifically address how women's experiences are shaped by the social and cultural configurations of their lives, and how women come to refuse or undergo prenatal diagnosis. Unfortunately, while richly detailed, none of these ethnographies specifically addresses TMS, and most examine prenatal screening in the United States, rather than in Canada.

Deciding for or against maternal serum testing

Lee noted⁶⁵ during the early stages of the TMS pilot in BC that the broader social and cultural contexts within which women make decisions is complex, bound with issues of religious persuasion, ethical concerns about the rights of the disabled, and cultural pressures from family and community.

When an anomaly is detected following TMS, amniocentesis or ultrasound, all that can be offered is termination of pregnancy. Objection to abortion is generally assumed to be the primary reason why women refuse maternal serum screening or prenatal diagnosis. Yet ethnographic research among women undergoing and refusing prenatal diagnosis indicates that attitudes about abortion and religious affiliation are not static traits either of individuals or of groups. Rather, they are flexible resources which women and couples use in diverse ways to address the issues arising from a fetal anomaly.

There is evidence that women who are opposed to abortion are less likely to have prenatal genetic testing. More than one third of the Manitoba women refusing MSAFP screening in a 1981-82 study felt that pregnancy termination was unwarranted under any circumstances.⁶⁶

In their California study, Press and Browner⁶⁰ found women who had never terminated a pregnancy, Spanish-speaking Latina women, and women who described themselves as ‘religious’ were more likely to refuse AFP screening.

Nonetheless, the relationships among ethnicity, religion, and test refusal is complex. The same study found that membership of a particular religion or cultural community does not necessarily predict refusal of maternal serum screening. Neither the presence or absence of a male partner nor personally knowing someone with a disability was a predictor of the test decision. Furthermore, the study found no significant association between a woman’s current age, age at first pregnancy, number of previous pregnancies, number of miscarriages, or number of live births and a women’s decision whether or not to have AFP testing.⁶⁰

It is worth noting that for most women, the decision to refuse maternal serum screening does not appear to be made quickly. Test refusers in the California study were significantly more likely than those who accepted to say that their decision had been reached only after a lot of thought, and after talking with others.⁶⁰ More than 60% of test refusers said they might terminate a pregnancy if a disabling condition was detected, and less than 15% of women who accepted maternal serum screening said they would have terminated if an anomaly had been detected.⁶⁰

Therefore, although a negative attitude toward abortion may be an important predictor of refusal, one cannot conversely assume that acceptance means a positive attitude toward pregnancy termination.⁶⁰

Perception of 'risk'

The direct impact of prenatal screening on a woman’s experiences of pregnancy has been explored in some literature. Rothman⁶⁷ concludes that the first half of pregnancy can easily be overshadowed by concern for what may happen in the second half. Classifying a woman as ‘high risk’ or ‘low risk’ for having a child with Down syndrome or some other neural tube defect or anomaly, has a profound effect on the way a pregnancy is viewed.

“Genetic information, like all fortune telling, works in probabilities, possibilities, and potentials. Women anguish over the decision to terminate a pregnancy after a diagnosis of Down syndrome; after all, who can tell what degree of retardation the baby might have? Who can tell what physical problems it might have? Women now will be given the bits, dribs and drabs of partial information genetic decoding will offer—an increased chance of this, risk of that, probability of the other. Based on this information they will be asked to decide whether to terminate a pregnancy.”⁶⁷

Reproduction and pregnancy in Canada today are often talked about and experienced in terms of ‘risk’ and ‘anxiety’.^{65,68} Women, even low risk women, may be extremely anxious during pregnancy; indeed, it is not uncommon for them to be told it is natural to worry about their baby.

This is not to imply that all women or all authors writing about pregnancy see it as negative or entailing risk. Searle⁶⁹ for example points out that pregnancy in the 1990s is generally regarded as a joyful experience; low congenital abnormalities and rare maternal deaths lead pregnant women to feel generally confident.

Some authors have noted, however, that perception of risk is increasing among women. Searle found in her quantitative and qualitative study that anxiety about an abnormal baby was not associated with health insurance status, education level, occupational level, or age, but that it was universal.^{13,69,70} Goel and colleagues' ⁷¹ study of TMS found that for many of the 1741 Ontario women studied, anxiety increased between 15 and 24 weeks of pregnancy regardless of their maternal serum screening status.

In attempting to explore the origin of such fears, Searle ⁶⁹ found that some women reported a fear of being 'blamed', a few discussed the role of societal expectations, and many felt that society was not yet accepting of people with disability and feared the impact this would have on them as carers for their children.

Maternal responsibility for the outcome of pregnancy has a long history in European-descended cultures.⁷² This sense of responsibility is reinforced for contemporary Canadian women through advertisements warning them not to drink or smoke during pregnancy, guides to pregnancy which discuss only risks brought about through the mother's actions, and media coverage of legal battles over the rights of pregnant women who continue to use drugs. This has also been noted in the United States.⁷³⁻⁷⁵

Disability and normality

A society's values regarding normality and abnormality greatly influence a woman's beliefs and feelings. Perspectives about disability give rise to fear and anxiety. For example, without full and non-discriminatory support for people with disabilities, the 'choice' in prenatal screening and diagnosis is weighted against continuing a pregnancy with an affected child.

Although largely unstudied, the ideas women hold about 'disability' and 'normality' may significantly shape their acceptance and refusal of TMS and other prenatal genetic tests, and also how they interpret any test results.

A Finnish study found that women, particularly women who had not completed high school and women under 24 years old, underestimated the occurrence of Down syndrome.²⁴ Rapp ¹² among others found differences in how American women of different cultural backgrounds view disability. While women of Anglo-European descent, especially educated women, are particularly anxious about mental retardation, women of Puerto Rican and Dominican background define abnormality primarily in terms of visible malformations.

Buddhist women in Tudiver's Manitoba study ²⁷ replaced questions about 'abnormality' with commentaries about 'respect for life'. A British study ⁷⁶ in a multi-ethnic inner city health district has shown that screening programmes for Down syndrome have not yet resulted in substantial reduction in the number of affected babies. Only four women out of 15 cases of Down syndrome identified terminated their pregnancies.

The high proportion of ethnic minorities may have been unrepresentative of the country as a whole, but it demonstrates that screening ethnic minorities provide additional challenges despite similar detection rates of the test. The study concluded that improved provision of screening services and ante-natal care should be instituted, and optimal understanding of the implications of the test ensured. As Rapp ¹² points out, notions of normal and abnormal have "specific, local meanings and evocations".

One of the unpublished studies noted above is currently looking at the experiences of women and couples in British Columbia who have received an ultrasound diagnosis of anomaly, which may help to identify the configurations of risk, responsibility, disability, and normality to be found in the province.⁶⁵

Psychological aspects of maternal serum screening

A number of studies indicate the psychological dimensions of having TMS within a framework of choice and individual responsibility for decision-making. In general, while numerous studies have reported on the psychological effects of alpha fetoprotein screening, there is little consensus about what these effects are.

The same mixed results appear with regard to TMS. The psychological products of prenatal diagnosis include fear of revealing an abnormal pregnancy, fear of having to face a decision about pregnancy continuation, and fear of a complication resulting from the procedure.⁷

Screen-negative results

Negative TMS results appear to have a reassuring effect on women.⁷¹ That reassurance appears to persist into the third trimester.⁵ There are differences in anxiety levels between women who have serum screening and those who do not, although the extent and source of the differences is unclear.

Two British studies found a slight difference in general anxiety between screened and unscreened women.^{9,77} Untested women had a lower anxiety level than women who were tested and this difference existed before the test was offered.

As Green¹³ suggests, one conclusion may be that “the test was not causing higher anxiety, but was being accepted by those who were more anxious initially”. Anxiety may also be linked to lack of knowledge about the test and why it is performed. In Manitoba, women who were unaware of neural tube disorders before screening were more likely to report anxiety about screening than women who had some knowledge of neural tube disorders.²⁷

In a Finnish study, women who had not participated in serum screening were less often worried about Down syndrome than the women undergoing serum screening (14% vs. 23%).²⁴ Not surprisingly, women who have had a previous pregnancy or birth involving an anomaly are particularly anxious about prenatal screening and diagnosis in subsequent pregnancies.⁷⁸

It has been argued that to offer TMS among women over 35 should mean fewer women would be subject to risks from and anxieties surrounding amniocentesis. However, in a study of 200 women in the Netherlands, women eligible for amniocentesis for advanced maternal age welcomed the addition of maternal serum screening for neural tube defects and for Down syndrome, but did not intend to decline amniocentesis even if the serum screening results were negative.⁷⁹

Screen-positive results

About 8% of women having TMS in BC will have a positive test result, that is, their test will be interpreted as showing an increased risk of Down syndrome, neural tube defects, or trisomy.⁴⁷ Similar results have been reported for Ontario.⁵ About 6% of the test results will be positive for

Down syndrome and about 1-2% will be positive for neural tube disorders. Receiving a positive test result is widely experienced by women as distressing and anxiety-producing,^{9,80-82} even though TMS does not diagnose the presence of any of these conditions.

The anxiety women may experience when they receive a positive test outcome is considerable, higher, as one author suggests, than the worry experienced by patients on the eve of major surgery.⁸³ The anxiety women feel may also be accompanied by negative attitudes towards their pregnancies and towards the baby.⁸⁴

Women having maternal serum screening and subsequently referred for amniocentesis may feel more anxious than those women undergoing amniocentesis simply because of their age.^{66,80} Similar findings were made by Hunter et al⁸⁵ who studied reactions to ultrasound in women with raised alpha fetoprotein. Although both groups demonstrated a reduction in anxiety following a normal ultrasound, the women with increased alpha fetoprotein were significantly more anxious before the scan.

Since only 1% to 2% of the 6% of women receiving initial screen-positive TMS test results are carrying an affected fetus, several studies have investigated the anxiety arising from false-positives. In Ontario, Goel and colleagues⁷¹ investigated whether women receiving initial screen-positive results had higher levels of anxiety and depression than women who had either initial screen-negative results or did not have TMS at all. In that study, depression scores did not differ between women with false-positives and women with true-negatives, and differences in anxiety scores between the two groups were small and non-significant.

Rather different findings emerged from a British prospective study of women with initial screen-positive results (most of whom are ultimately shown to be false-positive) involving measurements at seven points between pre-test and 6 weeks post-partum.⁸⁴ Women who received an abnormal test result had both more anxiety as well as more negative attitudes towards their pregnancies and towards the baby than did women who received normal test results.

Some research suggests that women receiving a positive alpha fetoprotein test result have anxiety levels which remain elevated until normal results are obtained through subsequent testing.⁷ However, the British study found increased anxiety and negative attitudes persisted, even when subsequent tests indicated normal results.⁸⁴ In the same study, women who had amniocentesis following an abnormal TMS result were significantly less worried at 28 weeks and immediately after the birth than those women who did not have a subsequent amniocentesis.

Summary

Prenatal genetic testing is, as Green⁸⁶ points out, “a process ... [and] not a question of undergoing a single test which will magically reveal that the baby is normal”. Offered as a way to detect anomalies, prenatal screening test results are inherently ambiguous and uncertain, providing probabilities and risk statistics rather than definitive answers.

Many of the detectable conditions have an uncertain prognosis and no ‘treatment’, other than pregnancy termination. Thus, the ‘choices’ which a technology such as TMS offers are fraught with uncertainty, and place women in a unique position. Women in particular have become “moral pioneers”¹² faced with the complexity and ambiguity of clinical information, moral dilemmas, and conflicting cultural and social meanings of normality, disability, abortion, parenting, fetal and maternal rights.

CHAPTER 6: COUNSELLING TMS POSITIVE WOMEN

In the pre-natal screening process, women will encounter a number of laboratory technicians for non-invasive tests, and specialists and sub-specialists for invasive diagnostic tests. In the least favourable situation, women may come to these procedures largely uninformed, and remain passive participants in the testing. In fact, many will gain a practical sense of the implications of TMS only if they are part of the relatively small proportion of women who go on to receive counselling. It is consequently in this particular arena that the volatile debate within Canada over the meanings of prenatal testing, ‘choice’, and disability rights is most sharply focussed.

At present, genetic counsellors are few in number and work closely with geneticists, all of whom are located in Vancouver and Victoria. Accordingly, almost all BC pre-screen counselling (arguably the most complex) is provided by physicians and midwives scattered throughout the province.

The allocation within and between professional groupings of responsibility for counselling involves professional and public policy issues beyond the mandate of this TMS review. But while the division of practice is outside the scope, the issue of counselling itself is central to it.

Virtually all interested parties, legal experts, women’s advocacy groups and the disability-rights movement share an intense interest in defining what ought, and ought not, to be said to women in relation to prenatal screening. Given this collective interest, remarkably little is known about what is actually said to women during counselling, and how much women ultimately understand.

Obtaining data

Data for the present review were collected through a questionnaire (**Appendix H-1**) and at a focus group among geneticists and genetic counsellors within the Department of Medical Genetics at Children's and Women's Health Centre of BC. In contrast to pre-screening endeavours of physicians and midwives scattered across the province, the relatively small number of counsellors, their specialty training and their concentration in Vancouver and Victoria has made it easier to characterize accurately the post-screening counselling they offer.

Genetic counselling

In 1975, the American Society of Human Genetics (ASHG) defined genetic counselling as:

“a communication process which deals with the human problems associated with the occurrence or risk of occurrence of a genetic disorder in a family. The process involves an attempt by one or more appropriately trained persons to help the individual or family to: (1) comprehend the medical facts including the diagnosis, probable course of the disorder, and the available management, (2) appreciate the way heredity contributes to the disorder and the risk of recurrence in specified relatives, (3) understand the alternatives for dealing with the risk of recurrence, (4) choose a course of action which seems to them appropriate in view of their risk, their family goals, and their ethical and religious standards and act in accordance with that decision, and (5) to make the best possible adjustment to the disorder in the affected family member and/or to the risk of recurrence of that disorder.”⁸⁷

Since, this definition was proposed, the scope of genetic counselling has expanded to include conditions that are not entirely genetic.⁸⁸

The phrase “appropriately-trained persons” implies that genetic counselling requires special knowledge and skills distinct from those needed in other medical and counselling interactions.⁸⁸ The term “communication process” serves to emphasize that genetic counsellors are more interested in the actual process of educating a family about their options than with the outcome of their decision-making. In other words, it serves to emphasize the non-directive nature of the counselling.

Genetic counselling is based on the principles that:

- utilization of the service be voluntary;
- genetic services be equally accessible to all;
- client education is essential;
- all relevant information be disclosed to the client;
- counselling be non-directive;
- counselling needs to address psycho-social issues;
- counselling must respect an individual’s confidentiality and privacy.

In Canada, it is generally accepted that information should be made available and tests offered when appropriate, but that ultimately patients and families should have the right to make decisions free from pressure that a particular course of action is economically or socially irresponsible.⁸⁸

It is important to remember two points (**Chapter 5** above and **Chapter 8**): first that some patients who have made no specific request are nevertheless referred for genetic services, either because of providers’ litigation fears, or because they have been identified through a screening program about which they may not be adequately educated; and second, that a family’s decision is often influenced by financial or other concerns which supersede decisions based on personal preferences or moral views.⁸⁸

Today, there are more than 1500 genetic counsellors practising in the US and Canada, including 17 who practise in BC. The Children’s and Women’s Health Centre of BC, the major genetic counselling referral centre in the province, employs 15 genetic counsellors and 11 clinical geneticists, though not all on a full-time basis.

TMS counselling practice

In BC, most women under 35 with a positive triple-screen result are referred to the Provincial Medical Genetic Counselling Program. Women over 35 with a positive screen result may or may not be referred to the Program, depending on the referring physician’s level of comfort counselling such women.

Geneticists and genetic counsellors work as a team to provide a wide range of genetic counselling services. The geneticist, holding an MD and with specialized training in medical genetics, is primarily responsible for providing a diagnosis, for counselling in complex cases, and for a patient’s follow-up care.

The role of the genetic counsellor is to aid the geneticist in making a diagnosis, to provide patients with informative and supportive counselling, and to co-ordinate follow-up services and testing. Prenatal diagnosis and screening has become the primary focus of most genetic counsellors, and approximately 80% of genetic counsellor appointments arise from prenatal concerns. In contrast, the majority of clinical genetics appointments are for general care.

At the Children's and Women's Health Care Centre of BC, the greater part of a genetic counsellor's workload involves counselling couples about a positive screen result for Down syndrome or trisomy 18. Approximately 40% of all genetic counsellor prenatal appointments are for a positive TMS result, with an overwhelming majority of those (88%) being screen-positive for Down syndrome.

When combining the referrals for positive screens for Down syndrome & trisomy 18 with referrals for positive ultrasound screen (soft-markers), the combined group comprises 64% of all prenatal genetic counsellor appointments, and 52% of total genetic counsellor appointments (prenatal and general appointments).⁸⁹

An appointment with a genetic counsellor for a positive screen result is scheduled for one hour. Within that hour, the genetic counsellor aims to establish whether the couple understand the reason for their referral, what information has been previously given them by their referring physician, and their personal reactions to any results.

The counsellor will then give the couple an opportunity to ask questions, resolve any misunderstandings, and explore any further psycho-social issues involved. Often, the counsellor will offer an understanding of the condition for which they have tested positive, and if necessary explain the difference between a screening test, and a diagnostic test. Any appropriate information regarding amniocentesis is also provided.

The genetic counsellor is required during the session to take a detailed family history and to review the woman's pregnancy history. If additional concerns are identified, such as increased risk of an additional genetic condition, the counsellor is obligated to discuss this information with a geneticist and, where appropriate, to explain the relevance to the patient and offer appropriate testing.

Women with a positive TMS result often have a detailed ultrasound performed prior to their appointment with Medical Genetics, in order to screen for ultrasound markers for aneuploidy as well as for any structural anomalies. If any ultrasound marker is identified, the 'triple-screen risk' may be modified for the patient. It should be noted that when a patient appointment is scheduled with a genetic counsellor following a positive TMS result, an appointment for amniocentesis is also arranged so as to provide the couple with that option as soon as possible.

If the couple decide to pursue amniocentesis, arrangements are made for disclosure of results. After review of the results by a geneticist, it is often the genetic counsellor who will communicate the results of the amniocentesis to both patient and referring physician. A letter is sent to the referring physician outlining the information discussed during the session, the genetic assessment of the family history and pregnancy history, what further testing has been offered or arranged, the recommended follow up, and how results will be disclosed.

In the event of an abnormal amniocentesis result, the patient is offered an appointment to discuss further options. In this follow-up session, the couple are assisted in exploring their feelings regarding the various options: preparing for the birth of a child with special needs, making plans for adoption, or having an abortion. If the couple have decided to plan for the birth of their child, the counsellor or geneticist may put them in touch with similarly-situated parents for their experience and support. Alternatively, if the couple decide to place the child for adoption or terminate the pregnancy, suitable arrangements are made.

Genetic counsellors and TMS

This section is extracted from a study conducted by Lee and Sroka between 1997-1999, funded under the auspices of the BC Centre of Excellence for Women's Health (BCCEWH) through a Health Canada seed grant. The report of the study "The Missing Voices in the BC Experience of Maternal Serum Screening for Down Syndrome" will be submitted to BCCEWH for subsequent publication. For this portion of the study, qualitative methods were used to develop, circulate and analyze a questionnaire and focus group data collected from the genetic counsellors working at the Children's and Women's Health Centre of BC.

These findings, similar to those derived from targeted interviews with physicians and midwives, are not intended as representative, nor are the conclusions considered relevant for the determination of public policy, except in the most general sense of directing further definitive research. The original material collected from interviews is combined, whenever possible with published and unpublished research material.

Explaining TMS

Genetic counsellors are familiar with the complex issues of providing both pre-screening and post-screening prenatal counselling, although most of their daily work in BC deals with the latter.

An important issue in developing a standard of care relating to TMS is consideration of not only the content of the TMS message, but the time taken to deliver it. The genetic counsellors collectively consider that it takes between 15 and 30 minutes to explain the triple-screen to a patient, depending on the patient involved. A recent BC study, aimed at evaluating the triple-screen information received by patients, demonstrated that satisfaction with the information received depends on the amount of time the health care provider spent explaining the test.⁹⁰

This study found that 61% of participants (42/69) felt that their health care provider (those outside genetic centres) spent less than 6 minutes explaining the screen; and that most (29/42) of these women were dissatisfied with the information given. One participant expressed the view that patients should receive more detailed information about tests, and interpretation of ultrasound, but that that doctors seemed unable or unwilling to invest the time required.

All the counsellors interviewed stated that they drew on different kinds of resources to help patients understand Down syndrome or spina bifida. In addition, all stated that certain types of information (for example, using ultrasound to screen for chromosomal aneuploidy) would prove too confusing if provided in pamphlet form.

Common misconceptions

In the genetic counsellors' experience, they found that a widespread misconception among patients is to regard a positive screen result as signifying the presence of an anomaly. Increasing women's understanding of the significance of a positive screen may well serve to decrease patients' anxieties following a positive screen result.

There is evidence that couples may not fully understand the clinical options following a positive diagnosis. In a recent Ontario study,⁹¹ only 48.9% of individuals receiving the triple screen information package understood that if amniocentesis shows Down syndrome, the options are either to have a baby with Down syndrome or to terminate the pregnancy.

Three respondents felt it was important to make clear to couples that there is no cure for the detectable conditions; and that TMS results will only signal that families should either prepare for the birth of a child with special needs or take steps to end the pregnancy. The third respondent suggested that it would be sufficient to point out that there is no cure.

Screening programs have been criticized for failing to make clear that women may be faced with a decision about pregnancy termination. In some contexts, it is clear that this omission serves to enhance patient uptake of screening.⁶⁰ Genetic counsellors in BC clearly share the same concern, emphasizing that the most important thing couples need to consider before testing is that the screen may give them information they do not want.

Value of TMS

A potential benefit of TMS is being able to know the diagnosis prior to birth, which can prepare a family for a child with special needs. In the questionnaire to genetic counsellors, two agreed with this view, pointing to the medical benefits of preparation as well as reduction in stress surrounding the delivery. Another suggested it enables parents to get more information, to talk to other affected couples, and receive emotional support. The remaining counsellor remained more cautious, responding that this is a personal decision.

Two of the responses to the question of whether it was possible to educate families about the benefits of raising a child with special needs were, while remaining non-directive, almost identical. For two respondents, this was possible "by providing an equal amount of the information regarding the hardships and medical attention that may be required". A third respondent answered very differently: "No. If you haven't experienced something personally one cannot give a couple the true picture. Everyone is different as well." The fourth respondent stated:

"I think this would be very difficult, but could be raised in the context that every family views disability (differently) and that decisions regarding prenatal diagnosis and termination of pregnancy are individual and very personal. One could also raise the issue that there is much more social acceptance of children with differences and that every experience people have is perceived differently."

Recommendations of counsellors

During the course of the interviews, focus group, and questionnaires, the following recommendations were made by genetic counsellors regarding TMS in BC:

- the wording of the results form should be changed to replace the terms “positive” and “negative” with “increased risk” and “decreased risk”;
- TMS false-positives could be reduced by instituting an early low-cost dating scan;
- enhanced education of patients and physicians would facilitate informed choice;
- an educational pamphlet about screening tests and TMS for women and their partners is needed (not all providers interviewed were aware of the pamphlet from BC Children’s and Women’s Hospital);
- TMS should be available only with the necessary support services (amniocentesis, counselling, termination);
- a program for maternal serum screening, rather than TMS, should be put in place, since there are new biochemical markers under development that BC may consider in future; ideally, these new screening technologies should be assessed without repeating the entire evaluation process;
- additional funding should be available for children with special needs, to help ensure women have true ‘choice’;
- public debate should be encouraged, with a view to determining whether public funds should be spent on population prenatal screening;
- prevention of Down syndrome and spina bifida should not be the goal of prenatal screening.

Summary

Among this sample of counsellors there was general support for TMS as representing an improvement over screening based on age alone. However, the counsellors had significant concerns about its current use in BC. In particular, the present situation was described as an inefficient use of resources and inadequate with regard both to access to this screening tool, and to the availability of patient and provider education about it.

CHAPTER 7: DOWN SYNDROME CAREGIVERS

This chapter summarises the attitudes and perspectives of mothers of children with Down syndrome, and professionals who work with affected families. It investigates the culture of Down syndrome from within, and also seeks to explore personal experiences: what it is to confront a technology designed selectively to abort a fetus with the disability that is part of one's life - raising and loving a person with Down syndrome.

The data are based on a qualitative research project by Lee and Sroka conducted between 1997 and 1999.⁶³ The goal of this research, supported by the Down Syndrome Research Foundation, was to develop a pamphlet describing Down syndrome, suitable for distribution to women during pregnancy, physicians and midwives, as well as the general public.

Important ideas emerging argue the importance of individual women being able to give balanced, informed consent; and of society being conscious of the dangers of selective abortion of viable conditions.

A description of the major BC support groups is presented in **Appendix B**. In summary, the two major groups assert that reproductive technologies are predominantly a woman's issue; that they can only be considered positive if they support and enhance women's right to control their own bodies and make meaningful choices about when and whether to give birth; and that in general, reproductive technologies do not support and enhance the equality of either non-disabled women or disabled people.

An issue for women

Issues of gender equality and disability are intrinsically linked. It is women who predominantly care for persons with Down syndrome. As Peters points out:

“At the centre of this debate (fears and concerns about reproductive technologies) are the interests of women's gender equality and disability rights. Issues of reproduction are pre-eminently women's issues, as it is their bodies and their foetuses which are the targets of scientific research and experimentation. It is essential to examine women's experiences in relation to the evolution of reproductive technology. In addition, the quest for the perfect baby and the expanded use of prenatal testing and prenatal screening raises the issues of disability and how it is perceived by society.”⁹²

The overwhelmingly female gender of caregivers emerges elsewhere in this review. Geneticists and genetic counsellors are predominantly women, and the care of children with Down syndrome falls mainly on the mother.

Therefore, while the study material on which this chapter is based has not sought to eliminate the views of fathers, other male caregivers or professionals, it necessarily offers a gendered perspective. Only women (mothers and professionals) participated in the focus group conducted with members of the Down syndrome community; and opinions were sought from women who are administrators of the two organizations providing support services.

Perceptions of TMS in the Down syndrome community

Methodology

The data for this section are based on analysis of a questionnaire and a focus group circulated to members of the Down syndrome community, and on interviews with representatives of both Down Syndrome Research Foundation (DSRF) and the Lower Mainland Down Syndrome Society (LMDSS). The questionnaire was constructed and piloted with delegates attending the 1st Biennial Conference on Down Syndrome held in Vancouver April 1-4 1998.⁶³

Some respondents to the questionnaires expressed interest in participating in the later phases of the research. The questionnaire was also made available to the Down syndrome community on a national basis through advertisement in “Hand in Hand”, the quarterly newsletter of the DSRF and through their website.

The questionnaire itself (**Appendix H-II**) was devised by posing general questions allowing for a range of responses. Participants were encouraged to explain their perceptions of what Down syndrome meant to them and to explain why women might undergo prenatal screening. Questions explored whether women should be offered or recommended testing; and whether there are positive or negative, and individual or societal effects from screening for Down syndrome.

Concerns about giving birth to a Down syndrome infant and the adequacy of social, economic, financial, and educational support were examined. Finally participants were asked whether triple-marker screening should be made readily available in BC, and if and why it should be provincially funded.

Fifteen questionnaires were analyzed for recurrent themes. Nine respondents were mothers of children or adults with Down syndrome; two were speech therapists – one male and one female; two were female professionals and one was a female friend and support person.

The respondents raised many of the same issues in different ways. Eight themes emerged from the analysis of the questionnaires that were used to formulate the focus group session sponsored by the DSRF. Subsequently the experiences generated from the first focus group were refined to create another questionnaire and focus group devised specifically for genetic counsellors.

Themes emerging from the questionnaire were:

- the positive aspects of raising a child with Down syndrome;
- the need for better and more counselling;
- the fear of the unknown;
- the ideal of the ‘perfect’ baby;
- preparing for the birth of a baby with Down syndrome;
- the availability of screening as a signifier of its importance;
- the idea of ‘choice’;
- use of prenatal diagnosis to prepare for the birth of a child with Down syndrome;
- the importance of reassurance, particularly for older mothers.

These themes were modified in order to construct ten guiding questions for discussion in a focus group. In this report, particular attention was given to responses to the question: “Why do you think women undergo testing?”

The first focus group was held on March 1st 1999 at Sunny Hill Health Centre. It was composed of ten women, some of whom had expressed interest in further phases of the research after completing the questionnaire, as well as representatives from the DSRF, the Provincial Infant Development Programme, and other recommended participants. The focus group was audiotaped and the tapes were transcribed for analysis. Some of the participants were subsequently contacted for further comments.

Positive aspects of raising a child with Down syndrome

The focus group participants emphasized the positive aspects of raising a child with Down syndrome. The women who decided to birth and raise a child with Down syndrome learned to be positive and to discount negative views encountered from, among others, health-care providers and other social and hospital support services. The following focus group comments about the negative responses at the arrival of their infant attests to this phenomenon:

“... inside the delivery room, how they make you feel – they looked like there was a funeral going on when my daughter was born.”

“I had a woman from the Salvation Army come in at Women’s and Children’s and she said to me “oh my gosh, I’m so sorry” and of all the people my minister did the same thing. To me that is just appalling”.

Reflecting on the horrified responses she had received from health-care providers in the delivery room, one mother expressed how within a month she had learned to dispel the negative aspects and look on the positive side:

“it’s like this is the best blessing ... she’s our life, along with our son and it’s heartbreaking the lack and the misinformation out there and it’s draining. And you want to say ‘come live at my house for a week, and see if this is not a happy family, a family ... I hate the word disability, and I’m not in denial, I know my daughter has Down syndrome and I love her for it. I look at her beautiful little face and I love her and I wouldn’t change a thing in our lives or her life, nothing. I know there’s probably going to be bumps along the road, with my son too, with all of us in life”.

Parents of children with Down syndrome work hard to promote the abilities of their offspring, arguing, as did one participant that

“the general perception I think in the public is that Down syndrome must be really bad because they screen for it. And because they screen for it we don’t want to have Down syndrome in our family, because, look, nobody wants it.”

Reassurance and information as ‘positive’ aspects of screening

The focus group was generally critical of the notion that TMS provided reassurance, and whether indeed reassurance is needed at all. One focus group participant went as far as to state: “I think that by offering the test you’re making the fear”. In reference to the danger of childbirth in the past, another mother reasoned “As we remove old medical fears, we replace them with other medical fears that might be less life threatening but take up the space left by the previous fear.”

When women receive screen negative results their fears are usually allayed, although the anxiety may persist through other fears about the second half of the pregnancy, an aspect which some studies have addressed.

Some of the focus group participants expressed support for maternal serum screening, provided it was accompanied by increased education about both screening and the Down syndrome condition.

“For me, it was acquiring as much information as possible. I know, I don’t think that any of us really think we’re going to have a child with Down syndrome. It could be fear ... but I just wanted information.

The way in which information was imparted was considered significant. When delivered too briefly or in an ambiguous way, it could lead to anxiety or compliance in the patient. A busy family practitioner’s office may not always be able to provide careful, time-consuming counselling to explain sensitively all the ramifications.

Press and Downer’s California study⁶⁰ of women’s uptake of maternal serum alpha fetoprotein echoed these concerns when they discovered that patients were rarely counselled for more than two minutes, and often had the test represented to them as just another blood test requiring no deliberation. There was concern in the focus group that prenatal screening could easily come to be regarded as routine prenatal care, and that expectant women would not be aware of the decision-making implications for them in the event of a screen-positive result.

The focus group saw that women are increasingly challenged to feel in control of and positive about their pregnancies. Some felt in greater control by researching all aspects of pregnancy from a broad spectrum of literature, both medical and lay.

“So, the more knowledge you have, the greater the fear such that you need to keep it under control if you are going to go through anything [the pregnancy] at all”.

But while for some participants the knowledge gained from screening results is empowerment, for others it creates fear owing to lack of understanding.

“So it’s interesting how you can have two ends of the spectrum, and certainly (at) both be mother of a child with Down syndrome. ... There’s no pat answers to so much of this, which concerns me ... because I think there’s so many people that have limited understanding and they are making decisions, big decisions, with very little knowledge.”

Reassurance and autonomy is the reason most often expressed by women for undergoing screening. Yet, as Lippman points out,¹⁰ reassurance would not be needed if women had not been defined as ‘at risk’ in the first place. She goes on to point out that, as the pregnancy experience is restructured, dependency on the technological fix leads to medicalization, increased supervision and finally disempowerment of women.

Lippman further argues that it is the very availability of technology that leads to propagation of fear and the need for reassurance. Nevertheless, many women state that they participate in screening for reassurance,⁹³ under the illusion that they are enhancing their pregnancy outcome and doing the very best they can for their future child.

Ambiguities of the screening results and the changed pregnancy experience

When the predictive values of testing were explained with a visual chart during the focus group session, participants responded in terms of the emotional stress placed on the pregnancy experience. One woman stated:

“What a waste of money, and time and energy on being frustrated and thinking that you’re going to have something in the end you don’t end up having - its an emotional situation”.

Green similarly pointed out⁸⁶ how the process of screening with a number of tests and assessing the results they produce is inherently ambiguous, often providing an uncertain prognosis.

The anxiety that women may experience when they test positive may be reflected in negative attitudes towards not only their pregnancy but toward the expected child (similarly Marteau et al⁹). Another mother reported:

“... pregnancy is not so much a physical condition for women, it’s an emotional condition, and ... for all those women [who test false-positive] their emotional health is damaged throughout the pregnancy. And whether with ongoing tests which will take about three weeks, and then the negative result, could you re-establish that positive emotional feeling that we all feel during our pregnancies?”

One mother of an infant with Down syndrome felt she had benefitted from not undergoing screening. Retrospectively she appreciated the normality of her pregnancy experience:

“We did not know that our daughter had Down syndrome until she was born. I was actually quite relieved or quite grateful that we didn’t have to spend the pregnancy being worried about it ... I thought I would have spent most of my pregnancy just in a great worry, and ... I felt that I avoided that. And when our daughter was born, it was far more easy in my mind to accept her with Down syndrome and all, when she was already in my arms.”

Santalathi’s Finnish study²⁴ reported that women who had not undergone serum marker screening were less likely to be anxious about Down syndrome than those who had been screened.

Pressure to abort following a positive screen

It is interesting that in this select focus group of mothers with children with Down syndrome, some women stated that the pressure to have a termination of pregnancy following a positive screen did not come explicitly from health care providers but from close family members. Associated with this was the tendency to blame a woman for refusing to undergo further testing such as amniocentesis with a view to aborting.

“I did the serum after our daughter with Down syndrome was born and we were having another baby. My parents were quite horrified that we weren’t going for amniocentesis, and I was 35, just after J. was born with Down syndrome. And we had determined before I got pregnant that we would just take the odds and ... I eventually did do the maternal serum ... But I did it more for my parents than I did it for me ...”

“ ‘Cause I had the [positive] diagnosis, my parents reamed me out to have an abortion, so it’s a good argument for not testing”

“I am sure my family would have {pressured me to abort) if that had happened in my situation ... and I find it frightening, because you are so emotionally overwrought with this decision, or this new information, and you don’t know how you feel about it anyway, because really who is educated until you’ve been there.”

The executive director of DSRF pointed out that women often contact the office for advice, having just had the news that they tested screen-positive. The director added,

“It is extremely common for family, spouse, everybody around them, particularly health professionals, as they perceive it anyway, to put pressure on them to terminate the pregnancy, often when they’re not wanting to do that, and don’t have sufficient information. That is certainly where my concern as an organization has come from. I feel we have to look as a community about how we get the information out if this test is going to be available for people, which it is.”

Ironically, one mother expressed her view that most people have a warped idea about Down syndrome, seeing it as solely undesirable. Women begin to see the incongruities only when they have been exposed to Down syndrome in the family.

“We learned the most about Down syndrome after our child was born. And not only that, but the families that kind of pressured people towards having an abortion, once that child is there, they are advocating for and loving that child the same as any other child in the family.”

Another mother stated that although her doctor knew she did not want to be screened, the doctor was very relieved when she agreed to the screening because it lessened the doctor’s concern about her own medical-legal liability.

“I think that as a medical doctor she’s concerned about you know, I guess, there’s always a liability issue in any medical office. And I think that there’s a big problem because they have to cover their butts, and ... I have great rapport with my doctor and she’s been nothing but supportive. But I know she was relieved when I said I am going for the triple screen ... I would say that the medical profession is probably the first stop to the pressure and then after that the family and that’s just as intense if not more. I think doctors feel they really need to be sure that the women know what their options are, because they don’t want to be accountable”.

Fear of the unknown as a reason to screen

Fear of the unknown was a repetitive theme that emerged from the questionnaire and was pursued through the focus group encounter. One “geriatric mother”, as she describes herself, was eager to learn as much as possible about the status of her fetus at the time of her pregnancy. Later, she came to believe that the medical profession was telling her only about the negative outcomes, such that she not only feared for the viability of the pregnancy from spontaneous abortion but was also preparing herself to give birth to a severely handicapped, sub-human being.

“I was glad to have the time to research and prepare because I thought I was about to bear a severely handicapped almost non-human being. In retrospect, it would have been better to find out after I held her and could see that she was overwhelmingly human and

typical and minimally different. Knowing beforehand engenders fear of every possible health problem associated with Down syndrome. Knowing afterwards allows you to deal with the fraction of problems that occur in each individual case ... This type of testing also engenders fear in prospective parents about their ability to raise a child with Down syndrome. It certainly did in my case even though now I have a hard time remembering the reason why I was so anxious and stressed about having I. two years ago. Children are a lot of work and a long-term commitment. Period.”

Dick similarly notes⁷ that psychological effects include “fear of revealing an abnormal pregnancy”.

Blaming women for bearing a disabled child

“Being a ‘geriatric’ mother (43 years) I was asked by colleagues, co-workers and family whether I was going to be tested. Afterwards knowing the result was positive for Down syndrome, these people either implicitly or explicitly held me responsible for bearing a child with Down syndrome. A pregnant mother to be is not the appropriate person to be making eugenic-type decisions for the “good of society” out of a fear of blame. Society as a whole has yet to decide upon the acceptability of aborting fetuses based on the potential lower IQ limit which justifies abortion. There does not yet exist a test for most handicaps so the testing for spina bifida and Down syndrome, resulting in abortion, is the front line of selecting the next generation based on attributes preferred by the customer. This is not to be confused with the mother’s right to choose, which is a separate and in my mind a valid issue. The issue here is the right of society to encourage women to abort because of physical or mental limitations in their prospective child through the advocacy of testing”.

Adoption

According to a parent advocate with LMSS (telephone interview May 10th 1999) families that have already had positive experience with family members with Down syndrome and who wish to adopt are also more likely to request a baby with Down syndrome. Some women who have tested positive for Down syndrome and know they will be unable to care for a disabled child, but who oppose abortion, may continue with the pregnancy and then give the baby up for adoption.

The researcher was provided with one account of a woman, having given birth to a baby with Down syndrome who subsequently died, decided to adopt another child with Down syndrome from a couple, one partner of whom refused to accept the baby. The second mother had agreed to give the baby up for adoption rather than risk ending her marriage and becoming a single mother of a disabled child.

In some countries, particularly those that have strongly-developed religious societies or strong cultural mores around abortion, adoption of infants with Down syndrome is condoned. Dumaret *et al* reported⁹⁴ that in France, professionals have noticed an increase in newborns being placed for adoption, while in Britain, 8-10% of infants born with Down syndrome between 1970 and 1975 were abandoned in the maternity ward and by school age, 8-17% were not raised by their families.

A recent follow up study in two British regions reported a 7% adoption rate.⁹⁵ In Israel in 1986, it was noted that 40% of babies with Down syndrome were abandoned in hospitals and that 95% died in the first year.⁹⁶ In the French study it was noted that socio-cultural attitudes

played a part in family decisions about adoption. It also found that Parisian obstetricians, who were more likely to use new medical technologies, were also more often in favour of terminating pregnancies where a fetus with Down syndrome was identified, than obstetricians in other regions.⁹⁷ In a predominantly Catholic country, abortion would be a less likely option than adoption.

A Tennessee study showed that severity of neural tube disorders appeared to influence the decision to continue or terminate an affected pregnancy. All the women carrying a fetus with anencephaly elected to abort, whereas of the 27 women carrying fetuses with spina bifida, 21 elected to terminate the pregnancy.⁹⁸ It is unclear whether the parents understood the nature of spina bifida and the possibility for corrective surgery. Saxton, herself a survivor of spina bifida, discusses misperceptions about the condition.⁹⁹

A similar question arises whether infants with Down syndrome who need corrective surgery are more likely to be rejected by their parents. Information about the prognosis for people with Down syndrome and spina bifida is in urgent need of development.

Fostering is an alternative to adoption. The Provincial Advisor of the BC Infant Development Program recalled in the focus group session, that in the late 1970s and early 1980s she noticed that most Down syndrome children living in a specific community, were being placed in foster care. At this time Woodlands Hospital was no longer taking infants with Down syndrome. After conducting a survey, she found that the local social work department in the birth hospital believed that the biological family could not handle the 'burden' of raising a child with Down syndrome. Since institutional care was not an option, many of these infants were being placed in foster homes.

Conclusion

The original data collected from mothers of people with Down syndrome, other caregivers and professionals working with and advocating on their behalf indicate opposition to screening, because it targets Down syndrome for the express purpose of eliminating 'defective fetuses'.

This does not necessarily mean that there is no recognition of some of the 'positive' values of prenatal screening. But these groups certainly call for more balanced information about the costs and benefits of prenatal screening, and about the conditions the screening is designed to detect.

These issues include understanding what it means to be explicitly identified with a condition that is a 'target'; what utilization of prenatal screening technology means to pregnant women, whether they are considered able-bodied or disabled; and what it means to raise, live with and love a child or an adult with Down syndrome.

PART IV • PROVISION OF CLINICAL CARE

This Part aims to situate TMS in the context of clinical obstetrical care in BC.

Prenatal screening during obstetrical care reflects complex historical, social, and economic factors which to date have had little direction from provincial health policy. It may be argued, however, that the health-policy decision not to fund directly a provincial prenatal screening program had a significant effect on clinical obstetrical care, a phenomenon noted by authors in other instances.^{15,16}

Recent developments in clinical obstetrical care are important to this discussion. Rapid increases in TMS utilization and growing standardization have resulted in significant pressure on the provincial government to develop health policies in relation to the provision of prenatal screening. In this instance, policy-makers are not asked either to promote or inhibit TMS growth. Instead, they are pressured to set standards in which TMS is provided in all regions of the province.

The goal of this section is not to provide an exhaustive account of TMS during clinical obstetrical care, but rather to demonstrate that clinical care develops and clinicians act in relation to forces and factors quite distinct from those of policy-makers, or women experiencing the tests.

CHAPTER 8: TMS IN A LEGAL AND REGULATORY FRAMEWORK

Legal and regulatory controls of TMS have developed in the convergence of three processes: defensive medical fears of practitioners; disciplinary action by professional regulatory Colleges; and adoption of clinical practice guidelines from the Society of Obstetricians and Gynecologists of Canada.

It should be noted that it is beyond the scope of this report to examine the legal responsibilities that may fall on state agencies in the provision of this technology, other than to note that, in the era following ‘tainted blood’ and similar investigations, such questions might arise and affect policy significantly. The present review is limited to consideration of legal factors which have operated to increase TMS use during routine obstetrical care.

Serum screening ambiguity and negligence actions for wrongful birth

Legal action for wrongful birth may be brought by parents of a child with a congenital illness or abnormality against the physician or midwife who has allegedly failed to provide appropriate prenatal counselling or information. In a typical claim, parents assert they were given no adequate warning of a potential problem in their child, and that the lack of timely information prevented them from obtaining an abortion. Their consequential claim is for damages for themselves and support for the care of their child.

Widely accepted in many US jurisdictions for at least two decades,¹⁰⁰ the first Canadian wrongful birth action occurred in Manitoba in 1994, in which a physician and his wife sued Manitoba doctors and laboratories for not satisfactorily reporting the results of an alpha fetoprotein test.

As described above (**Chapter 4**), an alpha fetoprotein test is generally used to screen populations for neural tube disorders. Elevated alpha fetoprotein results are associated with an increased risk of neural tube disorders. Low alpha fetoprotein results can be used to gauge, albeit with unreliable accuracy, the risk of Down syndrome.

The problem for the laboratories and physicians before the advent of TMS was how to report low alpha fetoprotein results. The option for pathologists was either simply to report the alpha fetoprotein values and risk-assessment as requested for neural tube disorders, and to ignore the Down syndrome result; or to report the Down syndrome result both to the physician (who might or might not know anything about alpha fetoprotein assessments) and to the patient (who in all likelihood had not given informed consent for Down syndrome testing).

The laboratory and physician in Winnipeg chose the former option and did not inform the doctor and his wife, whose lawsuit followed the birth of a baby with Down syndrome. The case was settled relatively quickly out of court, but not before considerable publicity had raised awareness of the issue.¹⁰¹

Geneticists, obstetricians, and laboratory pathologists associated with the University of BC were among those acutely aware of the implications of this legal action. They recognized that approximately 5000 women per year who were having alpha fetoprotein in the province could also be given a Down syndrome risk assessment. Laboratory pathologists were particularly concerned that possessing, but not reporting, Down syndrome risk assessment placed them in a difficult and legally vulnerable position.

Provincial laboratory pathologists solved their dilemma by verbally reporting, usually by telephone, elevated and decreased alpha fetoprotein results to physicians ordering the test. Genetic consultation, counselling and further diagnostic tests were offered in both instances. This verbal reporting approach, while time-consuming and unsustainable for large numbers of tests, was possible for the small number of abnormal levels among the relatively small number of alpha fetoprotein tests ordered in the province (12%; 5,000 of 43,000 live births).

The pathologists collectively assumed that reporting low alpha fetoprotein and Down syndrome risk to women choosing alpha fetoprotein tests for neural tube disorders would not violate their right to informed choice. This assumption may or may not have been well-founded. As far as the authors of this report have been able to ascertain, the assumption has not been challenged in either the literature or the courts.

In any event, failure to properly inform patients of a low alpha fetoprotein result is in itself no longer an issue in the province, since alpha fetoprotein was incorporated into TMS and used to assess Down syndrome risk along with two other serum markers discussed below.

But with the availability of TMS, a new and larger concern began to develop, namely the possibility of a wrongful birth lawsuit founded on withholding actual prenatal screening tests such as TMS, which have increasingly been adopted as part of standard prenatal obstetrical care.

TMS, clinical standards and wrongful birth

Where threat of legal action follows advances in medical capability such as TMS, this will inevitably prompt development of explicit practice standards. These in turn provide the norms by which negligence actions are judged.

A Vancouver lawyer who successfully represented parents in a wrongful birth suit, argued that “The law goes hand in hand with these tests. Before the tests, we couldn’t have a legitimate case. But if the tests are available and accurate and considered standard protocol, they should be offered.”¹⁰²

Clinical standards form a central issue in malpractice lawsuits. Such actions depend on proving negligence, in other words, that health professionals or institutions failed to provide an adequate standard of care, and that this failure resulted in patient injury.

The primary task of a negligence action therefore is to establish what constitutes an adequate standard of care, which usually requires testimony from clinical experts. A key issue at trial is the relationship between standard care and the care received by the plaintiff patient.

Regardless of ultimate patient outcome, it is a complete defence to demonstrate that an adequate standard of care was provided. In their practices, therefore, clinicians are powerfully motivated to act according to appropriate standards, especially if case records may subsequently provide a means of reconstructing clinical events crucial to a successful negligence action.

One other important aspect should be noted. In all medical negligence cases, the plaintiff bears the burden of proving that failure to adhere to the standard of care resulted in patient injury. In the case of wrongful births, however, it is usually the parents who claim injury. This is arguably the most problematic aspect of wrongful birth claims. As Botkin and Mehlman explain, the claim rests on the controversial notion that “the harm be, in fact, the birth of a child with impairments”.¹⁰⁰

Medical standards and the law

Medicine and the law work co-operatively in establishing medical standards, as physicians work directly with lawyers, seek legal counsel or, at minimum, act in relation to real or anticipated legal rulings. In turn, law helps to formalize and make explicit the judgments based on those clinical standards.

The rapid growth of explicit clinical standards is well described in the medical¹⁰³ and legal¹⁰⁴ literature. Their growth has been particularly rapid in obstetrics.

In keeping with this trend, the Society of Obstetricians and Gynecologists of Canada has published guidelines for the Prenatal Diagnosis of Genetic Disorders in general; and for Down syndrome and neural tube disorders in particular.^{105,106} This includes a specific recommendation to offer TMS at 16 weeks’ gestation.

Wrongful birth and publicity: Disseminating defensive medicine

Noted above was the publicity given the Manitoba case in the public press. In February 1999, a front page report of the BC Province newspaper publicized an action for wrongful birth brought in the BC Supreme Court against a family doctor who had failed to book an appointment for ultrasound until his patient was more than nineteen weeks' pregnant. Following the birth of a child with spina bifida, accountability was placed on the physician.¹⁰⁷

The same newspaper article reported that in another wrongful birth case of December 1997, which had gone largely unnoticed in the media, parents of a child born with Down syndrome were awarded \$500,000.¹⁰⁷

Regardless of the actual effect on litigation risk of a test such as TMS, however, the noteworthy issue is the degree to which clinicians are influenced by press accounts of trials. Such reports give veracity to the prospect of substantial professional or financial losses.

The legal literature has recorded how an actual or perceived lawsuit has been known to precipitate rapid change in clinical practice by solidifying a particular practice pattern as the established standard of care.¹⁰⁸ A recent Ontario study¹⁰⁹ on the medical-legal risks of TMS concluded similarly that having a prenatal test available in a climate of wrongful birth lawsuits inevitably leads to widespread use.

The study showed, however, that the primary legal concerns of practicing physicians and midwives do not rest with whether to offer TMS, but with problems associated with informing women about the test. The authors conclude that in interactions with patients, it is crucial that providers be well-educated about the complex issues involved, and that there is clear and effective communication about them.

Formal recognition of standards in BC

The College of Physicians and Surgeons of BC.

The College of Physicians and Surgeon of BC has become increasingly involved in setting and supporting standards of care. In 1996, the College's Clinical Practice Guideline Committee, mandated to identify and disseminate scientifically-valid clinical practice guidelines to physicians in the province, considered a request from a consortium of geneticists, pathologists and obstetricians at BC Children's and Women's Hospital to provide a guideline on TMS.

The Committee decided not to offer such a guideline, primarily because of concern that without physician education and an established and efficient referral system, to recommend TMS would be premature and could do more harm than good.

The Committee was also concerned about the growing problem of establishing medical standards of care in response to a significant malpractice threat. In their view, this would not only have set an undesirable precedent, but would also have precluded adequate public consultation on a change in standards that, once introduced, would prove all but immovable.

As a result of these concerns, the College has not included specific recommendations regarding prenatal screening in its Policy Manual. Instead, prenatal screening is viewed as a specific example of the more general admonition to proper conduct relative to non-directive care and securing informed consent.

In the instance of prenatal screening, the College requires physicians to be sufficiently aware of the test parameters and diagnostic testing options, and to provide accurate and timely information to patients, directing them neither toward or away from these testing options.

Although it did not form a Guideline Committee to consider the issue, the College nevertheless produced an information bulletin in its *College Quarterly*¹¹⁰ which stated that “pregnant women of all ages should be offered triple-marker screening as part of their routine prenatal care”. It includes a directive that physicians opposed to abortion on moral grounds and therefore under difficulties in counselling their patients about screening, have an ethical obligation to refer their pregnant patients to a colleague.

The emphasis here is on the right of women to be informed about and to obtain triple-marker screening as a standard of prenatal care. Since all physicians in BC are members of the College and receive the bulletin, it seems reasonable to assume that physicians in the province will see these statements as directing them to inform, or to arrange for informing all pregnant women in their practice about TMS.

The concerns of the College Guideline committee nevertheless remain. To recommend province-wide use may be, at minimum, premature in many areas of BC without adequately informed physicians or a properly developed referral infrastructure.

Nevertheless, the College is finding itself obliged to deal with TMS in a more traditional way, in relation to complaints by patients. In an interview for this review, a Deputy Registrar explained that the College does in fact deal with TMS primarily in relation to complaints by patients, although the actual number is not available since the College does not keep statistics. Complaints typically fall into one of two opposing categories: physicians either neglect to inform patients of available tests; or they are overly directive toward obtaining an abortion following detection of certain fetal abnormalities.

If a complaint is registered with the College, physicians are informed by letter of the nature of the complaint. They are also informed of the College’s expectations regarding informed consent and non-directive care, in particular that physicians unable to meet the standards owing to their personal beliefs or values are advised to refer patients to colleagues. In general, the complaints to and responses from the College regarding serum prenatal screening were described as typical of the types of complaints received for several years in relation to amniocentesis screening and to medically-induced abortions.

The Canadian Medical Protective Association

Although mass media coverage of wrongful birth cases is growing, the Canadian Medical Protective Association, which provides legal representation for most physicians in Canada, has remained officially silent. In particular it has not published, nor does it report any plan to publish, official statements on wrongful birth issues.¹¹¹ The Association does not make any direct recommendations regarding clinical practice, such as clinical practice guidelines.

However, the Association alerts physicians to legal issues through illustrative case examples in newsletter format. Taken together with media reports of wrongful birth trials, case illustration through such publications are likely to consolidate widespread TMS use.

Summary

TMS has become part of the vigorous current trend toward standardization of clinical care in general and obstetrical care in particular. Its adoption is encouraged both by professional litigation fears, and by the emerging stance of the College regulatory body that the appropriate standard of care is to offer TMS.

It should be pointed out, however, that while increasing legal and regulatory control can be seen as effective in supporting the right of women to informed choice, it has so far failed to demonstrate equal concern for disability rights or for the broader issue of eugenic potential.

CHAPTER 9: TMS PRIMARY CARE PROVIDERS

In undergoing TMS, a series of choices confronts each woman. She must begin by deciding whether to engage with TMS, which is likely to depend on her situation within probability ratios. If pursued, she must ultimately relate TMS to her individual experience, family expectations and cultural norms.

Instrumental in this process will be the knowledge, skill and attitude of the professional who provides the technical information on which these decisions are to be based.

Data sources

In assessing the role of primary care givers, two major sources of data were used:

- i) Literature relating to practitioners' knowledge and practice of TMS was surveyed and summarized. Wherever possible, data on Canadian practitioners were included.
- ii) Interviews were carried out with professionals who, in different capacities and at a variety of sites, provide and interpret TMS. The interviews were not intended as an exhaustive or even representative survey of BC providers' attitudes. Rather they were conducted with individuals identified as key informants of practice and policy issues in TMS and clinical care. Interview questions are given in **Appendix H-III**. A further opportunity to hear BC providers discuss maternal serum screening was offered during Grand Rounds at the Victoria General Hospital (April 23, 1999).

Literature on providing TMS

While it is beyond the resources of the present review to survey the practices and knowledge of BC providers relating to TMS, relevant data are available from Ontario and Manitoba. Ontario has had a province-wide TMS program in place since 1993. In Manitoba, a maternal serum screening program using alpha fetoprotein has been in operation since 1985.

In a study of 778 family physicians, 273 obstetricians, and 46 midwives in Ontario, Carroll and colleagues⁵ found that 97% of providers were offering TMS to pregnant women in their practices. Eighty-eight per cent of the total group were routinely offering it to all pregnant women (100% of the midwives, 90% of the obstetricians and 87% of the family physicians).

In Manitoba, a survey of 289 obstetricians and family physicians found that 60% provided this test to all their patients.⁴ However, only 38% did so by providing it with consent, while 41.5% conducted alpha fetoprotein testing "automatically, either without seeking consent or unless the patient specifically declines".

The Ontario survey found no significant differences between the three types of providers in knowledge about maternal serum screening. While respondents generally knew the percentage of women who would have an initial positive TMS result, 30% of providers over-estimated the true-positive rate by a factor of ten.⁵ Moreover, between 30% and 38% of respondents did not answer these questions, indicating the level of lack of knowledge may in fact be significantly greater.

Some indication of provider satisfaction and concern with TMS in Ontario is shown by the finding that, although 50% of respondents felt the program should be maintained, 22% said the program should be discontinued.⁵ Providers' opinions on abortion are influential here: while only 18% of those providers who would refer a woman for abortion following detection of anomaly wanted to abandon the TMS program, a full 47% of those who would not refer wished to do so.

Interviews with BC providers regarding TMS practice and policy

This section is based on interviews conducted with a small number of health-care providers. The providers include four obstetricians, ten family physicians and two medical geneticists involved in educating obstetrical caregivers. All the interviews (either in person or by telephone) were guided by a series of open-ended questions intended to elicit providers' views about TMS. In addition, providers were asked for their comments on each of the proposed options for funding TMS in BC.

The interviews indicated general agreement on two substantive points relevant to this review. First, although providers viewed TMS as an improvement over screening based on age alone, all had significant concerns about the current use of TMS in BC. Second, providers felt that TMS should nevertheless be available in BC. There were, however, marked differences in opinions about the most appropriate way to provide TMS to women in the province.

It is important to note that this review focusses on the broad concerns of providers, and not their satisfaction with aspects of the screening program. In fact, all providers shared confidence in the laboratory system to obtain, accurately measure, and rapidly report serum findings. Similarly, they had no concern with the accuracy of ultrasound dating, and they had generally high praise for the follow-up services available for screen-positive women, including counselling and diagnostic testing and second-trimester abortion services.

It should also be noted that obstetrical care providers do not share the same orientation as other providers in the TMS program, who deal only with women who have 'chosen' the test and are then managing the outcome. For the latter group, standards for performing the relevant tasks are clearly established. Obstetrical care providers on the other hand generally offer this test to healthy women, many of whom have not even heard of it. They require standards that bear on if, when, and how to offer TMS, issues considerably more complex and difficult to evaluate, both objectively and subjectively.

Concerns:

Providers' concerns about TMS centred on four main issues:

1. the lack of a standard of practice in BC;
2. the cost-benefit of TMS;
3. the social meanings of offering TMS; and
4. the lack of education for women and providers.

Lack of standard of care and practice

When asked about current TMS practice, nearly all providers expressed concern about the absence of a standard of practice in BC. In referring to the current situation, several providers used terms such as “chaos”, “confusing”, and “anxiety-producing”. One of the geneticists involved in teaching family physicians and obstetricians refers to TMS as “triple-scream”, since its current use in BC is causing anxiety and dissatisfaction among women, as well as primary care and specialist providers.

“I think there are a fair number of doctors who aren't quite sure if this is supposed to be a quote ‘standard of care’ for a prenatal patient, and some, you know, obstetricians will say ‘yes it is,’ and others will say ‘no,’ and so I think the family doctor is kinda caught.”

Similar concerns about the lack of standard of practice were voiced by primary care providers attending Grand Rounds on TMS at the Victoria General Hospital in April 1999. By way of introduction to Grand Rounds, a recently published article in the BC College Quarterly was quoted:

“A British Columbia trial of Triple Marker screening (TMS) for Down syndrome, trisomy 18 and open neural tube defect completed in April 1997 confirmed results from studies in other countries, that TMS could decrease the need for amniocentesis in women older than 35 and that the 3 markers were more efficient than alpha fetoprotein alone in screening for fetal trisomy 21. In response to this evidence, the Ministry of Health provided block funding on an annual basis to continue the screening program for women of any age in British Columbia. **Pregnant women of all ages should be offered Triple Marker Screening as part of their routine prenatal care.**” (emphasis in original)¹¹⁰

At the Grand Rounds and during interviews, concern was expressed that a mixed and confusing message was being sent to providers. On one hand, providers heard during Grand Rounds that current funding provides for only 10,000 TMS tests each year (roughly 25% of all births). Yet, with this article, the College seemed to be saying that the standard of practice was to offer tests to all pregnant women.

Many subsequent questions to presenters indicated anxiety among providers that in the light of this implicit standard of care, failure to offer TMS routinely to all pregnant women could precipitate a negligence lawsuit if a child was born with a prenatally-detectable condition.

The general practitioners interviewed, in particular, sought clarity on the standard of care issue, saying that by themselves they would not offer it to all pregnant women. Instead, they would offer it to older women at increased pre-test risk of Down syndrome, and younger women who sought it for any personal, familial or cultural reason. If they felt they had to offer it, however, they would offer TMS to all women, regardless of age and attitude.

In contrast, the obstetricians interviewed said that it was reasonable to assume that most obstetricians were less concerned about developing provincial standards because offering TMS had already become a standard component of ‘specialist’ care.

The uncertainty of these general practitioners regarding TMS, and their individual indisposition to offer the test without provincial direction, seems to fit with the history of maternal serum screening in the province. Despite being available since the early 1980s, general practitioners

did not embrace alpha fetoprotein serum screening for neural tube disorders. In fact, despite similar performance as a screening test for neural tube disorders as TMS for Down syndrome, its utilization remained limited to 6000 tests per year (13% of live births) at the time TMS began in the province (See **Appendix E**).

Cost-benefits

The providers interviewed shared several perceptions about the benefits and costs of TMS.

There was general agreement that TMS might reduce anxiety among women over 35, so long as the screen results were negative. Another benefit voiced by nearly all providers was that TMS among women over 35 exposes fewer pregnancies to the risk of amniocentesis. Although the perception exists that TMS will result in fewer amniocenteses being carried out, several providers expressed uncertainty about whether this was true. “I’d like to think this is true,” remarked one provider.

In Victoria, questions about the impact of TMS have taken on a distinctive configuration. The genetics laboratory in Victoria has seen a sharp drop in the number of amniocenteses over the past year. One contributing factor may be that women over 35 who have negative TMS results are deciding not to go on for amniocentesis. However, actual age- and city-specific TMS and amniocentesis utilization was not conducted for this review.

The use of TMS among younger women generated two primary concerns. First, several providers commented that screening younger women simply created unnecessary anxiety in a low-risk population. Second, the potential harm to a pregnancy by screening among younger women was also discussed. Given that the risk of Down syndrome is very low in women under 30, providers expressed concern that TMS exposes them to the risk of an invasive procedure, since a positive screen test may be followed by amniocentesis. “All that to detect one Down syndrome baby and you might be risking a normal baby at the same time.”

The economic dimensions of screening young women were called into question: “it would be a lot of money spent searching for one Down syndrome baby.” Some discussed the costs of TMS in terms of opportunity costs:

“Instead of spending \$300,000 to screen ... a group of 21 year old women at very low risk of Down syndrome, instead of spending that much money on one Down syndrome, maybe we should spend that money on a bone-marrow transplant that a two-year-old is waiting [for] because of leukemia or something else.”

Social meanings of TMS

Discussion of the cost-benefit of TMS was closely linked to a third area of concern: the social meanings of TMS. The current connection between TMS, abortion, and disability rights in BC is conflicted, ambiguous, and volatile. Several providers expressed uncertainty and discomfort surrounding the use of cost-benefit analysis to make decisions about prenatal screening and diagnosis.

While it may have been appropriate in the past to speak about the saving to society by detecting and terminating pregnancies involving anomalies, perceptions of disability have changed. This concern was particularly keenly felt with regard to Down syndrome.

As evidence of this shift, several providers noted the existence of better social support for and the existence of more positive images of people with Down syndrome. At the same time, the language used when discussing prenatal testing such as TMS is heavily weighted with terms like ‘prevention’, ‘savings to society by picking up Down syndrome’, and ‘reducing the risk of Down syndrome’.

Within this context, some providers ask whether it is appropriate to be offering tests like TMS which may lead to the prenatal detection of conditions such as Down syndrome. For several of the interviewed providers, the central issue is the lack of social consensus surrounding the meanings of disability and prenatal screening. For them, decisions about whether or not to be offering TMS are ‘societal decisions.’

“... that’s the kind of societal choice that we need to make. How much money should we invest to screen for some Down’s syndrome? Because people say well, what you are doing mostly is we’re trying to assure the public. And that’s true and that’s a very important goal to assure people, that make them have an easier pregnancy by giving them negative results of different screening tests. But there’s the other side of the equation which is, you know, ‘search and destroy.’ And that’s a tough question. How bad is a Down syndrome to be sought so aggressively and destroyed. I don’t know what the answer to that is and I think that’s the ethical issue. No, I don’t think it’s a medical answer, it’s society making choices. But you cannot avoid that kind of question, it [is] part of the picture.”

For some providers, the primary value of TMS is as a tool for reassurance, rather than as a technology to detect anomalies.

“One of the things I always think is very important when we talk about any form of genetic screening or genetic testing is that we really put on the table what it is that we’re trying to do here. Because most people think that prenatal diagnosis is search and destroy, and it’s actually the complete opposite. What it is, is that it provides reassurance and so that, because that reassurance can be provided, either by a diagnostic test or by a screening test, patients will carry on with pregnancies where, if they’re not able to give that reassurance, they may not want to take that risk. So actually prenatal diagnosis, whether its invasive or whether it’s screening, actually prevents termination of pregnancy, rather than promotes it.”

“One thing I can’t seem to get out of anybody on the policy side is, they ask me, you know, ‘what bang do I get for my buck?’ Well, I think you have to tell us what ‘bang’ you’re looking for. What is the purpose of doing it? Is it a selective screening test for spina bifida and chromosomal abnormalities, to give women advanced knowledge of choice? Or, is there some other agenda here that stems from previous cost-benefit studies which show, time and time again, that amniocentesis was cost beneficial and that’s what sold amniocentesis to policy makers. But I say things have changed now, so I don’t know what kind of ‘bang’ they’re looking for. That’s why I say I see triple screen and prenatal diagnosis as for reassurance, because 95% of those women are going to go away reassured.”

Not all providers interviewed were persuaded to view TMS as a means of reassurance. As one pointed out, that reassurance is hard to give when the results are imprecise - it is a screening tool and there will be false-negatives. Another felt that this rationale was relevant only among women over 35.

“We are screening to pick up abnormal more than anything else. Otherwise why offer it to women under thirty-five?”

Another provider commented:

“It’s a misconception to think that we are going to prevent more Downs by targeting the thirty-five or more. There’s more Downs born in the young mothers, so we should offer them the screen.”

Later in the interview, the same provider added the following:

“... there needs to be a decision made because we are now in the worst time, and every family with a baby with Down syndrome is asking why they weren’t screened. And they’re not saying that they would necessarily have terminated their child with Downs, they’re saying that they had a right to know - that the technology is there, that it’s being offered in a lot of other places, that in fact, at the moment if they had just chosen a different GP, they might have been screened. So I think we’re in a very uncomfortable, and really, untenable position, and there needs to be some very clear decisions made so that ... family physicians aren’t caught in between.

Evident within these remarks is the tension within Canadian society about whether the goal of prenatal screening is to prevent the birth of children with Down syndrome or to provide women with ‘choice’. And providers are aware that to make TMS routine may in itself structure women's choices.

“I think [with] medical tests, that just happens. Once you have a standard of care that involves offer[ing] something to everybody, it becomes harder for women to say ‘no, that’s not something I want you to test for’ ... I would hope that we live in a society where we accept and support women that say ‘this should be entirely a matter of choice’, test is a choice, and if the test is offered to a woman in that pregnancy that she should not feel compelled to take it. And she should not be blamed if she has a child with a problem.”

Marteau⁹ found that in the three countries she surveyed, Germany, Portugal and the UK, and across all study groups, screening history of the mother was the single most important factor influencing attributions of control and blame following the birth of a child with Down syndrome. Thus, a mother who had declined screening was seen as having control over the outcome and was, in part, blamed for it.

The Canadian Down Syndrome Society and the Down Syndrome Research Foundation support the view that women should have the right to choose to have prenatal screening. However, they argue that the purpose of screening and diagnosis should not be aimed at reducing the number of individuals born with Down syndrome.

As one provider commented, “if you put all your resources into the triple screen, and none of your resources into supporting children with handicaps then it certainly looks like public policy is dictating prevention rather than support.” The concerns expressed by the interviewed providers illustrate very clearly the difficulties of providing ‘choice’ without the language of ‘prevention’.

Lack of issue awareness for women and for GPs

A fourth area of concern identified by providers is the lack of education in this field for women and for primary care providers.

There were three main points raised in this connection.

First, emphasis was placed on the lack of public and provider understanding about the difference between screening tests and diagnostic tests. Second, many practitioners providing TMS are not specially trained in either general or TMS-specific counselling, although consideration of risk assessment for cancer and cardiovascular disease has become an increasingly important dimension of clinical medical care. Third, providers and the public are perceived to be relatively unfamiliar with screening tests and so often interpret a screen-positive result to mean the anomaly is present.

“The way things are currently set up, a result will come back “screened positive for Down syndrome”, which to the uninitiated is equivalent to a diagnosis, and that usually gets conveyed to the patient as well as her provider, and that is almost impossible to remove from consciousness, that screen-positive”.

There is a strongly felt need to educate both women and primary care providers as to the most likely causes for a positive screen result (for example, twins, incorrect gestational dates, diabetes).

“I think it’s just a question of having the program properly funded so that we are embarking on this for the long-term. That there is real publicity and education of physicians and then the public. At this point it’s gone from research to service, but service with parameters that say only so many, and don’t publicize it almost. And therefore, there’s never been proper dissemination of the information.”

To increase patient understanding of TMS as a screening tool was also perceived as a means to reduce women’s anxiety. However, one provider noted that patients do not expect to be offered the choice of a test. This is particularly noteworthy since, as remarked earlier in this review, there is evidence that women may not actively be making decisions about whether to have prenatal screening.

The desire for publicity about TMS and patient education is tempered by concern over the possibility of contributing to public perception of pregnancy as a dangerous condition.

“I would say on a given day in my experience ... ninety per cent of patients come to see me with a vastly, vastly overrated sense of risk, blown out of proportion by the public perception that all pregnancies have this dreadful risk associated with them. It’s sort of working pregnancy almost into a disease.”

The second issue of concern underscored by providers was that, although TMS does not provide a diagnosis, it is important to discuss with women the implications of using this screening test.

“This is not just an over-and-done test,” said one provider. Another said, “You are setting a series of interventions into play. Step one leads to step two, and it may lead to termination, to step three ... People need to know what the implications are.”

Another provider believes that it is important to try to determine what people will do with the information from TMS: “If they are absolutely adamant that they won’t have a termination or don’t want amniocentesis, then I try to get them to see that maternal serum screening is not for them.”

As suggested during Grand Rounds at the Victoria General Hospital and by several of the interviewed providers, one way to reduce ambiguity about TMS is to view it as “a screening test for amniocentesis”. The providers' comments on the relationship between TMS, ultrasound, and amniocentesis are in this respect revealing. When asked about how the triple screen fits in with other tests such as ultrasound, amniocentesis and CVS, one provider stated:

“... [it] fits right next to ultrasound. I view them as very similar. Really, the response to a positive triple screen is no different to the response to the positive ultrasound, and nobody is hesitating about recommending an ultrasound, so I don’t know why there’s been so much hesitation about recommending triple screen. I think that those two are very much at the same level, CVS and the amnio are different. They are a procedure that has a risk and on the other hand, it is a procedure that gives you a diagnosis rather than the screen, so it’s very, very different. I think that with time it will make sense that we use triple screen and ultrasound to assess women’s risk of having a child with a chromosomal abnormality, or fetal anomaly, and to decide who qualifies for an amnio.”

A third issue for providers was that of informed consent.

“I’m not sure how much of it is done under informed consent, truly informed ... Not just kind of ‘this will help us to screen your pregnancy’. I mean there are some women who, anecdotally, it seems never really wanted their pregnancy screened. And ... if it comes up positive, now they’re placed in a position which they would rather not be in.”

None of the providers felt that written informed consent for TMS was necessary, and several felt that obtaining written consent would be far too time-consuming and would ‘open the floodgates’, leading to written consent for all tests. Instead, providers emphasized that physicians need sufficient time to discuss TMS with patients, and women need sufficient time to decide whether to have the test. Several physicians raised the possibility of a billable category specifically for discussing different forms of prenatal screening and diagnosis.

This was not an issue for the midwives interviewed since their MSP reimbursement is different. Three providers felt that TMS counselling could be done at less cost by non-physicians, for example, by genetic counsellors.

Clearly providers in BC have concerns regarding the current lack of knowledge of women undergoing testing. Indeed, several studies which have endeavoured to evaluate the information women receive about TMS have universally concluded that TMS is commonly misunderstood. Further, they have concluded that improving patient education is important in reducing the anxiety of having a ‘positive’ result and ensuring informed consent.^{9,112-114}

Summary

The issues raised by obstetrical care providers in BC seem typical of the range of issues raised in the published literature. Providers recognize that TMS involves a complex balance between reassuring the majority and investigating a minority of women. The challenge is how to present it equally to women of all ages with differing pre-test risks for Down syndrome.

Obstetrical care providers also raised issues particular to the BC context. The most important issue is that, in the absence of a pre-existing routine serum screening test using alpha fetoprotein, there is a strong need to establish a standard of care in the province.

Most general practitioners interviewed were considering prenatal screening of women under age 35 for the first time. As a result they were looking for a clear direction that this ought to be done, as well as educational material on how to do it. The tone of general practitioners' responses also suggested that they considered themselves burdened with responsibility for providing all the services associated with pregnancy and birth; and some saw TMS as a weighty addition to that burden.

The obstetrical care providers largely assumed, incorrectly, that TMS would increase overall health-care costs. They did not consider the savings associated with not having to provide services and support for children with Down syndrome or neural tube disorders.

While each felt TMS should be available in BC, there was no consensus on how best to provide it to women in the province.

PART V • CHOICE, RIGHTS, AND POLICY LIMITS

It was asserted at the beginning of this review that the powerful emerging technologies, of which TMS is one example, cannot expect to operate independently of the core values of society. In this part of the discussion, program options are situated in the broader context of individual and disability rights. The aim is to understand what factors affect the demand for and against the use of TMS.

The first chapter examines how an individual woman making decisions about pregnancy may come to consider she needs this technology. **Chapter 11** explores the competing claims driving current controversy over TMS use. The concluding chapter seeks to identify some of the implications for policy-making.

CHAPTER 10: TMS IN A FRAMEWORK OF INDIVIDUAL CHOICE

Within Canada and the United States, TMS and other forms of prenatal screening and testing are often described as tools which give women and couples ‘choice’ and, thus, some degree of control over pregnancy and reproduction. From this perspective, the central choices of TMS and other forms of prenatal genetic testing are whether to have the test; and subsequently whether to continue a pregnancy in which an anomaly is detected.

As part of this discourse, it is generally agreed among providers and women that access to information is the route to making better choices. Indeed, a central goal of prenatal counselling is ‘informed choice’. Given the cultural value many Canadians and Americans place on freedom of choice, individualism, self-determination, and tolerance of diversity, this discourse of choice is powerful and persuasive.

While the notion of choice may resonate strongly with many Canadians, the reality of the circumstances in which women become pregnant, encounter TMS, and then elect to have or decline this test will structure their experiences in distinctive ways.

The shaping of choice

A multiplicity of social circumstances condition choice. Some women may undergo testing not by their own wish, but at the insistence of their husband or other influential family member.¹²

A family’s decision is often influenced by financial concerns: even with universal health care in BC, the choices available to a family without financial security are not comparable with those open to a financially stable family. Thus, it is unrealistic to assume that families make voluntary decisions about utilizing prenatal screening or diagnosis or about reproduction based solely on their own preferences, personal goals, and moral views.¹¹⁵

Other factors which may condition prenatal genetic testing choice derive from the circumstances in which TMS is encountered. For example, some women may not themselves have chosen TMS, but find themselves referred because of their providers’ fear of litigation, or because they have been identified through a screening program about which they may know very little.

Although women and couples are largely dependent upon health care providers for information about, access to, and interpretations of TMS, there has been virtually no examination of how the presentation of maternal serum screening to women may influence their understanding.

Press and Browner's^{59,73} study of maternal serum alpha fetoprotein (MSAFP) in California study found that women's decisions were determined more by how they were informed about the test and the kind of information they were given than by their ethnic or social class background. According to California public policy, all women must be offered alpha fetoprotein testing, and their consent or refusal to testing must be voluntary.

Yet the California study found that the way in which MSAFP was presented obscured the need for choice on the part of the pregnant woman.⁷³ Specifically, the test was usually raised in the context of routine blood tests, providers spent generally no more than about 2 minutes discussing AFP testing, frequently told women the test was recommended, and then assumed patient consent unless a woman specifically said she did not want it.

“In the case of MSAFP, it would appear that broad patient acceptance has been accomplished through the absorption of this new form of prenatal screening under the rubric of an older, and non-controversial, medical practice--routine prenatal care. When MSAFP screening becomes just another blood test, it ceases to be something about which a deliberate patient decision needs to be made.”⁷³

A recently published survey of 200 women in France who received a positive a triple-marker screen test underscores the importance of providing women with information. The study found that 57.5% of the women's providers referred them for TMS without giving any opportunity to refuse.¹¹² After testing positive, nearly 68% of the women did not know there might be false-negative results, and 21.5% of the women believed their risk of a Down syndrome fetus was 50%.¹¹² Sixty percent of the women did not know until after screening positive that amniocentesis might be a subsequent test.¹¹²

Data from a recent BC study demonstrated that women's or couples' satisfaction with the information they received about TMS is dependent on the amount of time the health care provider spent explaining the test.⁹⁰ Sixty-one per cent of study participants (42/69) felt that their health care provider spent less than 6 minutes explaining the screen and most (29/42) were dissatisfied with the information given. An Ontario study found that women who received an educational pamphlet on TMS benefitted from reading it. However, women who did not speak English at home and women under 25 did not benefit.⁹¹

Inadequate time spent discussing TMS, the lack of language and culturally-appropriate educational materials, and the lack of opportunity to ask questions about TMS clearly shape not only women's and couples' experiences of TMS, but also their choices about it. Significantly, when serum screening is provided as if it were just another blood test not needing discussion or consent, its meanings for women are transformed.⁶⁰

Choice may be constructed and experienced by women in particular ways. For example, women may associate serum screening with the provision of information, emotional reassurance, and the prevention of fetal and maternal harm, and tend to diminish its connection with abortion and the detection of anomalies.⁷³ What is at stake for them may not be the presence of anomalies, or whether to have TMS, but simply having routine prenatal care.⁷³

This point is significant, since two studies have found that women may have TMS without actively deciding to do so.⁹³ Equating TMS with other routine blood or urine tests and trusting that if TMS is offered it must be in their best interests, nearly three-quarters of women in a Finnish study underwent TMS without going through any active decision-making process.

In their study of AFP screening in California, Press and Browner found that 85% of the women who agreed to testing said they did not deliberate much before deciding. Moreover, many women did not know precisely why they decided to have or to refuse prenatal genetic testing.⁷³

For most Canadians knowledge is prized, and being ‘left in the dark’ correspondingly unwelcome. Knowledge is inevitably value laden, however, and embedded in particular social configurations of power. Within the present context, for example, prenatal screening technologies have a distinct cultural weight or imperative.

First, as with amniocentesis and ultrasound, the fact that TMS is technologically and medically derived knowledge about the fetus may make it particularly compelling and persuasive to women. Second, there is high cultural value placed by many Canadians on ‘taking the initiative’ rather than ‘leaving things to chance’. Third, to have prenatal tests, to read about pregnancy, and to seek knowledge about the fetus are widely perceived in Canada as the signs of being a good mother. These cultural imperatives are highly likely to condition women’s and couples’ choices.¹¹⁶

The cultural emphasis on individual choice is allied with the notion that individuals, rather than community or family, are responsible for the outcome of pregnancy. Women who come for testing and who seek medical care are said to be ‘doing what’s best’ and not ‘leaving things to chance.’⁷⁴ In this light, as Press and Browner suggest, prenatal testing, including maternal serum screening, “is women’s only culturally approved means of reassuring themselves and others, that they are doing ‘all that can be done’ to ensure a healthy pregnancy.”⁷³

Given this cultural weighting of medical and technologically derived knowledge, TMS testing may be perceived as empowering regardless of the test outcome. The ‘knowledge’ offered by TMS may indeed be reassuring (as in a negative result); or helpful, since it may assist some women prepare for a child with a disability, and others to prepare for abortion.

Several studies have documented that women associate serum screening with Down syndrome⁹³ and that women know that ultrasound, amniocentesis and CVS will be offered following a positive test result.⁷³ Women have described AFP testing as desirable since they want to know everything. Some women may also see the test as an agent for the *creation* of a better pregnancy outcome.⁷³

In other words, maternal serum screening is perceived by some women as a test that would not only assure but also insure their baby’s health.⁵⁹ Similarly, some women may believe, incorrectly, that TMS will detect all cases of Down syndrome.⁹³

‘Choice’ may also be shaped by that fact that certain forms of prenatal testing are perceived by women and couples not as a test to detect anomalies, but as a means of seeing if the baby is healthy. Ultrasound fetal imaging in particular is widely viewed in this way^{62,93} and the same meanings may be true of TMS, especially where it is offered to all pregnant women.

A different perception of TMS is evident in a Finnish study comparing ideas held by two groups of women about serum screening and of ultrasound screening.⁹³ While ultrasound was generally discussed in terms of reassurance about the health of the fetus, gestational age, and ability to rule out twins, serum screening was much more often discussed as a means of finding abnormalities. The same study, also found that termination of pregnancy was much more likely to be discussed by women in connection with serum screening than with ultrasound screening.

“Even if the screening is organised to detect diseases, an individual uses it as assurance that everything is as it should be. This makes it understandable why many women are very surprised and feel unprepared to receive positive screening results ... Because of this it is unlikely that increasing women’s knowledge alone would solve the problem of the anxiety that women experience when receiving positive screening results.”⁹³

CHAPTER 11: TMS IN A DISABILITY RIGHTS FRAMEWORK

This chapter seeks to understand how TMS is regarded from the perspective of disability rights, and the significance of arguments for and against its funding.

Although voiced primarily by disability-rights groups, the issues go beyond narrow sectional interest. In fact, the principal argument is one of accelerating importance within what we properly regard as a free society. At base, it asserts that where the interests of society as a whole are affected, simply because the technology exists to enable a choice does not mean a person should necessarily be obliged, or even entitled, to make it.

The practical significance of this issue can hardly be over-emphasized, since the revolution in health care promised by genetics will have far reaching consequences for humanity in the next century, likely to challenge our understanding of what it means to be human. The application of genetic knowledge is certain to result in completely new paradigms of the individual and health; and in re-drawn boundaries, widening those that have until now confined the disciplines of health care.

Within this framework, the World Health Organization is currently developing guidelines on bio-ethics surrounding medical genetics and public-health related bio-technologies. The authors of the draft guidelines caution that the new era of profound changes in traditional health care,

“... will challenge our ability to develop societal guidelines and to provide relevant, accurate, timely, and coordinated information only to the public and to politicians, policy-makers and legislators ... We should develop strategies now, to be able to anticipate and manage the long-term public health implications of this revolution, coordinate our efforts, and harmonize standards and practices at an international level.”¹¹⁷

However, international-level policy creation relating to new genetics seldom involves even provincial policy-makers, far less the representatives of community organizations serving disadvantaged groups. Although the disabled have perhaps the most poignant perspective on the nascent technologies exemplified by triple-marker screening, and experiences which should be central to discussion of the ethics, risks and benefits in the field, they remain voices at the margin.

The equality perspective on disability issues

In 1996 the federal government task force report on disability issues *Equal Citizenship for Canadians with Disabilities*¹¹⁸ advised that the federal government adopt a disability policy framework to help achieve its objective of an inclusive society, guided by the equality guarantees under the Canadian Charter of Rights and Freedoms. The task force urged the federal government to involve provinces in building disability considerations into mainstream policies and programs.

It is critical to this process that gender inequality be seen as conceptually allied with issues of disability, since in the TMS debate, women's gender equality and disability rights are both highly salient. In screening for Down syndrome, women are the recipients of prenatal screening technologies and are expected to make 'choices' whether to resist or accept technical

interventions in their pregnancies. They may bear guilt, either for terminating a pregnancy or giving birth to a disabled infant who may then be given up for adoption. Moreover, since women are the primary caregivers for family members with disabilities throughout the life span, it is women rather than men who are most affected by the needs of the disabled.

In the 1980s and early 1990s an abundance of feminist literature detailed the forces which undermine sexual equality by depriving women of reproductive freedom. They raised issues of reproductive choice, the right to abortion, contraceptive and conceptive technologies, of maternal over fetal rights, and ways in which women's autonomy and control and the safety of their bodies had been compromised by drugs and devices.

Over the last decade, however, the rhetoric surrounding questions of choice has gradually shifted from the radical feminist critiques into vernacular biomedical discourse. More 'choices' are offered in prenatal health care delivery – a variety of prenatal techniques to monitor pregnancy (blood tests, ultrasonography, CVS and amniocentesis), choice of service provider for delivery (midwife, general practitioner, specialist) and place of birth (home or hospital).

This proliferation of options has been seen as improving the situation of women. It has not, however, operated to enhance the context within which option choices are made.

The spectre of neo-eugenics: genetics as population control

A major feature of the context is that prenatal screening and diagnostic technologies are becoming standard components of clinical care during pregnancy. Burgeoning information technology and knowledge generation leads us to the belief we can and should know everything that can be determined about life issues.

But while many Canadians would argue it is beneficial to know as much about the status of the invisible fetus as possible so that the pregnancy will be 'under control,' from the point of view of the disability-rights movement these developments are viewed with alarm.

From this perspective, the focus of screening is not about individual choices but about population control, and as such, reminiscent of the eugenic policies in the early part of this century. Even in Canada, it is important to remember, certain populations were formerly identified as less worthy of existence than others. The danger of this new set of determinants is that they direct women to consider using prenatal screening technologies for the express purpose of identifying 'defective' fetuses, and once identified, to abort them.

The British Council of Disabled People (BCDP) has produced a discussion document on the new genetics and disabled people.¹¹⁹ As a representative voice of disabled people's organizations in Britain, the Council has raised alarm about many recent developments in both genetics research and clinical practice, and the ill-informed presentation of these developments.

The Council also argues that both popular ideas and professional opinion about the ability of genetic technologies to provide 'cures' for disability has unleashed a new genetic determinism with strong eugenic overtones. Given the historic and continued links between genetics and eugenics, the dangers are posed not only to the disabled, but to us all.

The BCDP asserts that the value of life is far too important to leave to geneticists:

“[Eugenics overtones] constitute a serious threat to disabled people, for we are not disabled by our genes or our impairment but by societies which actively and passively discriminate against us. Our disability is a socio-political not a medical problem. Therefore, far from helping us, the new genetics and the cultural and political ideology which informs it threatens to foster a more negative image of disability and is likely to lead to increased discrimination against disabled people.”¹¹⁹

While it unequivocally respects a woman’s right to choose within the unique circumstances of her pregnancy, the BCDP contends that the choice to continue pregnancy must be secure in the knowledge that all children will be brought into a society which does not discriminate against disabled people. The present climate in which prenatal screening has exacerbated prejudice against and a fear of disabled people has exerted a powerful negative influence over women’s choices. Thus rather than expanding choice, prenatal screening and prejudice against disability have combined to limit women’s options.

Canadian popular understanding of Down syndrome has benefitted very little from the experience of those who appreciate the complexities of living with disabilities. Scarce resources too have limited discussion in Canada of prenatal screening from a disability rights’ perspective.

BC support groups

In BC, there are currently two principal support groups which have endeavoured to focus attention on these issues: the Down Syndrome Research Foundation and Resource Centre (DSRF); and the Lower Mainland Down Syndrome Society (LMDSS). **Appendix D** provides a summary account of the foundation and aims of active associations.

Both main organisations have formulated and published a statement on maternal serum screening, which raise several central concerns about its use and the lack of information available to those affected. In particular, they caution that balanced information about both the predictive value of the test and about Down syndrome should be made available, ensuring that positive aspects of having a child with Down syndrome are balanced against the negative impact of testing.

The Foundation takes the position that the primary goal of prenatal testing should be to improve health care, not to reduce the birth prevalence of Down syndrome: “If the test is only used to identify and abort fetuses with Down syndrome, we feel it will adversely affect the quality of life for people with Down syndrome in our community, since there is the assumption that Down syndrome should be eradicated.” (position statement below)

The Lower Mainland Down Syndrome Society (LMDSS), affiliated to the Canadian Down Syndrome Society, provides support, information, network opportunities and development for individuals with Down syndrome, their families and professionals working with them. The mission of the LMDSS is to facilitate positive change so that individuals with Down syndrome become full members of society.

The statements of these groups on prenatal genetic testing and maternal serum screening follow on the next two pages.

CANADIAN DOWN SYNDROME SOCIETY

Position Statement on Prenatal Genetic Testing

With this Position Statement on Prenatal Genetic Testing, the aim of the Canadian Down Syndrome Society (CDSS) is to foster a climate of understanding and mutual respect for the dignity, worth and equal rights for all people, regardless of handicap or disability. All people, including those with Down syndrome, are a part of their local communities, and shall be recognized as having a rich contribution to make in the development and well being of the human community. The mission of the Canadian Down Syndrome Society is to enhance the quality of life for all individuals who have Down syndrome.

The Maternal Serum Screening Test establishes the probability of a pregnant woman having a child with Down syndrome or spina bifida and other neural tube defects. The Society wishes to address screening in relationship to Down syndrome. We believe that the widespread use of genetic screening for the purpose of identification and abortion of fetuses with Down syndrome may adversely affect the quality of life for all persons with Down syndrome in our community. This adverse effect could potentially reduce funding and support services to individuals with Down syndrome and may encourage negative attitudes of society towards persons with Down syndrome.

The following statements are in reference to prenatal genetic testing.

Where used in the foregoing statements, and in any other CDSS publications, the term “prenatal genetic testing” is intended to include maternal serum screening.

1. We believe the primary goal of prenatal genetic testing should not be to reduce the birth prevalence of Down syndrome in the population. Its use should be directed towards the provision of improved health care.
2. Prenatal genetic testing should be voluntary. The woman or couple should receive counselling that is comprehensive and provided in a language that is easily understood by them. Prior to any consent for prenatal genetic testing, the couple should be given accurate and up-to-date information on all relevant issues surrounding prenatal genetic testing and Down syndrome. This information should be provided in a balanced manner. Each woman or couple should be allowed to decide whether prenatal genetic testing is appropriate for them, based on informed choice. An appropriate period of time should be allowed between receiving the information and deciding, with written consent, whether or not to proceed with the test.
3. Following a test result which implies that the fetus may have a probability of a chromosome abnormality such as Down syndrome, the woman or couple should be provided with detailed, balanced information regarding the options available to them. This information should be provided by a knowledgeable and qualified health care provider such as those found in accredited genetic centres. Balanced information should be so recorded for the woman or couple to review at their leisure. Opportunities to have the woman or couple speak to parents of children with Down syndrome should be offered.

THE DOWN SYNDROME RESEARCH FOUNDATION & RESOURCE CENTRE

Statement Concerning Maternal Serum Screening

The Down Syndrome Research Foundation (DSRF) has several concerns about the pre-natal screening tests available for families, relating to the way in which they are being used and the lack of information provided for those affected by the tests.

The DRSF feels that families must be provided with effective information to counter-balance the negative impact of the test. Careful preparation and timing, with accessible information at each stage, is important to insure an informed choice is possible and to diminish parental anxiety.

Written information about Down syndrome, especially when more than ten years old, can give an unnecessarily negative view. The information given should be balanced by written and audio-visual material depicting the more positive reality of having a child with Down syndrome.

The blood test for maternal serum screening is a screening test and does not give a confirmed diagnosis. Further tests are necessary to establish a diagnosis. Some prospective parents do not understand this process when they take the maternal serum-screening test.

The maternal serum screening test can raise or lower prospective parents' anxiety tremendously. It may engender fear in the prospective parents about their ability to raise a child with Down syndrome. Research shows that the majority of families have more joy than suffering and regrets.

The primary goal of pre-natal testing is to improve health care, not to reduce the birth prevalence of Down syndrome.

If the test is only used to identify and abort fetuses with Down syndrome we feel it will adversely affect the quality of life for people with Down syndrome in our community, since there is the assumption that Down syndrome should be eradicated. Maternal serum screening and other pre-natal testing provide useful information regarding the pregnancy. The Foundation recognizes the challenges of having a child with Down syndrome but feels that prospective parents should not feel it is a reason for termination of a pregnancy.

The Mandate of the Foundation is to improve the independence of people with Down syndrome through education, information, research and clinical services. As an organization providing information and educational services on Down syndrome, we are prepared to assist in ensuring that the professionals providing the screening have current information about Down syndrome. We will help ensure that suitable materials and counselling are available to all families.

We urge you to work with us to ensure appropriate, 'up-to-date' and balanced counselling is available in the Province of British Columbia.

Social determinants of disability

The deterministic view of disability as a biologically-actuated ‘defect’ fails to consider that disability may, in some senses, be a social construct. The narrow view is to individualize disability. As Hubbard points out, characterizing disability as an exclusively biological issue ignores for example, the environmental causes of disability which are largely preventable given the political will to do so.

“... the interactions between genes and the environment are enormously complex. It moves our focus from the environmental causes of disabilities – which are terrifying and increasing daily – to individual genetic ones.”¹²⁰

In reality the experience of many people with disabilities “is that the disability itself is a minimal barrier – the real problems come from the discriminatory attitudes and thoughtless behaviour of the non-disabled majority.”¹²¹

Hearing the voices of experience

In preparing this review, therefore, it has been seen as important to integrate the comments of women who also represent the disabled community as both self-advocates and activists. While this research has been unable to document the full meaning, particularly for women, of living with the condition of Down syndrome, it has examined allied experiences: what it means to live with some form of disability, and what it means to be responsible for deciding to give birth to an infant with Down syndrome or to be directly responsible for the care of a person with Down syndrome.

Pacific DisAbled Women’s Network (DAWN), formed in the early 1990s, is presently mobilizing its members to become more active in determining and acting upon issues which directly affect them. It is involved in three research projects co-sponsored with BC Centre of Excellence for Women’s Health, which has given rise for the need for research guidelines. It calls for women with disabilities to be included in all research and for ethical guidelines to be agreed upon so that researchers can benefit from DAWN’s expert participation.

“Women with disabilities have unique perspectives and understandings which derive from our experiences in the largely inaccessible world in which we live. Research that has the experience of women with disabilities as its subject matter must reflect these perspectives and understandings.”¹²²

This stance addresses an important issue, that research related to minority groups should aim to be collaborative: that researchers ought not to speak simply for or about the disabled, but with them.

In the general critique of prenatal screening, what is missing is a sense of why Western society is preoccupied with ‘the perfect baby’ and of why so much money is put into emerging and expensive medical technologies, at the expense of providing services and funding to those already living with disability.

A disabled, self-advocate member of DAWN and People First makes a powerful case for the rights of the disabled and to show why, from her perspective, TMS makes little sense in a world where concepts of normality are slippery, and those of abnormality oddly perverse:

“I would think that everybody would want a so-called ‘normal’ child. And I think this test (triple-marker screen) is saying to me that your life isn’t as good when you have

Down syndrome. So if you are born with Down syndrome you can't help that, I mean, you are born that way ... So if you have a handicap that you can't see, like mine you can't see it really, but because it's [Down syndrome] facial, and I don't think that is fair. Like ... everybody's disabled in some way ... So to me, I feel that it's really making people feel less about themselves. Like, if you're going to say that with this test that a mother isn't going to have you because of your disability ... there's a lot of mothers that wouldn't want a child with a disability." (taped interview with disability rights' self-advocate 10th February 1999)

The self advocate points out that the percentage of children born with Down syndrome, compared with fetal alcohol syndrome or low birth weight infants is small. Yet heroic medical efforts are made to deliver these other infants at the optimum time and provide them with crucial intensive care, not only in the short term but throughout their lives.

Challenges in policy development

Once articulated, there still remains the problem of finding ways to integrate these lived experiences with public policy. Presently, the Working Group on Women and the New Genetics are exploring opinions about prenatal screening of some Canadian community groups, including the CDSS. This strategy was intended as a means of mapping key issues in women's health, the new genetics and the Canadian Biotechnology Strategy (CBS) from the perspective of community-based work.

In February 1999, a national network of community-based and academic women met in Winnipeg for a community consultation. Its aim was to prepare for a national strategic workshop on women's health and the Canadian biotechnology strategy, entitled "Women's Health: An Impact Assessment of the Canadian Biotechnology Strategy" planned for Toronto in February 2000.

The consultation was co-sponsored by the Working Group on Women's Health and the New Genetics, and funded by the National Network on Environments and Women's Health, a Centre of Excellence for Women's Health, and the Prairie Women's Health Centre of Excellence and the Canadian Women's Health Network.

The goals of the consultation were threefold: to explore *experiences* by learning how communities face genetic knowledge; to identify *priorities* by learning what communities' key issues are and what policies, if any, community-based organizations have in relation to genetic knowledge; and then by considering experiences and priorities, to develop *strategies* so as to position community workers as effective operators, and to develop a greater women's health presence in the CBS and the new genetics.

Two difficult lessons emerged from the consultation: first, the reality that under-resourced organizations are not dealing with questions related to genetic biotechnology; and second, that forging new alliances outside the existing network of community-based women's health organizations will take considerable effort.

The consultation process did however show that for women's health advocates and disability-rights organizations, prenatal testing is the point at which genetic knowledge is most often encountered. Generally speaking, the majority of the workshop participants were much more conversant with prenatal diagnosis than with any other area. However, a range of perspectives were articulated:

“Significant issues and tensions emerged in discussions over these issues. On the one hand, some participants saw prenatal diagnosis as inherently eugenic, being based on biased understandings of the reality of life with a disability. Other participants suggested that this was not always the case and that, at least for families with known genetic diseases, encounters with prenatal diagnosis was not premised on ignorance. Continuing with this tension, some participants suggested that disability selection through prenatal diagnosis was equivalent to sex selection and that both should be banned. Other participants were less convinced of the equation, and felt that disability and diseases were experienced in different ways and different degrees and that this was unlike sex. Finally, while the issue of restricting prenatal diagnosis was a common concern, and the limitations of the language of “choice” were acknowledged, some participants warned about the actual mechanics of such interventions in the health system; be careful what you wish for, one participant suggested, drawing an analogy with the feminist debates over pornography and the homophobic backlash.”¹²³

The mobilization of such organizations is presently developing at local, national and international levels. But until workable strategies are fully developed, it is unlikely that the concerns and attitudes of the disabled about prenatal screening technologies will be recognized or given the attention they deserve at the policy levels of government.

From the disabled communities’ viewpoint, however, it is most important that the Canadian Equality Perspective on Disability Issues articulated by the federal government Task Force report¹¹⁸ be acted upon to guide the creation and review of public policies and laws. Their anxiety is that if the emerging views of disabled communities are not heeded by policy-makers at the provincial level, then constitutional imperatives will be no more than platitudes.

To reiterate, the report’s goal of equality for disabled people means that “self-determination, autonomy, dignity, respect, integration, participation and independent living must be the effect of all federal government programs, laws and activities”.

If it is to abide by the spirit of the federal directive, provincial mandates need to include ‘the missing voices’ of the disabled in its policy decisions. Nowhere is this more important than in the forum of the genetic revolution, and on the focal issue of prenatal screening technologies.

CHAPTER 12: CHOICE AND POLICY LIMITS

Public policy, legislation, and legal precedents currently uphold publicly-provided abortion services in Canada. This support includes funding hospitals and clinics to provide services, and applying sanctions against those seeking to deny the exercise of legal rights. Professional Colleges have sought consistency in this area by requiring all practising physicians, regardless of their personal moral convictions, to make women aware of abortion services.

The need for support has been particularly acute in relation to abortions which occur late in the second trimester, as is usual with TMS. At this point, the ethical and emotional issues for women and families, and health care providers too, are particularly complex and intense. Additional to them are the difficulties of providing women outside major metropolitan areas with access to abortion services.

Despite the practical and ethical challenges, public policy on prenatal diagnosis and selective abortion rests on a relatively solid ‘pro-choice’ legal and regulatory framework. However, public policy is facing significant issues, most notably how to set funding limits within and alongside changing definitions of disability, and while continuing to respect individual rights.

Setting Limits

Individual choice, unrestricted, would allow women to maximize their preferences in determining which screening tests to have and what level of risk should justify subsequent diagnostic tests or abortion. But in their discussion in this area, Hook and Waller show that any attempt to set public-funding limits, whether based on finances or prevalence rates, must inevitably restrict the scope of individual choice.¹²⁴

In the Canadian context at least, limits have been a routine part of prenatal testing and selective abortion. Most commonly, these limits have taken the form of ‘cut-off’ points, such as maternal age or serum biochemical levels, which women must pass to become eligible for screening or diagnostic testing.

Other limits are found in patterns of service provision. For example, more sophisticated, ‘detailed’ as opposed to ‘dating’, ultrasound has only been made available in regional centres, forcing triage among eligible patients.^{5,45} Limits are effectively also set if timely access to services such as amniocentesis and abortion cannot be provided in more remote regions of the province.

While limits are evident, the basis for policy in current prenatal testing limits has been particularly difficult to discern. Research has examined the more common cut-off levels such as age 35 as the age of amniocentesis eligibility.⁶ However, very little has been established about other prenatal tests such as routine ultrasound, its distribution, justification, or relationship to genetic counselling and informed choice, although the latter has been studied in some jurisdictions.¹²⁵

TMS in a context of limits

Prenatal screening with a simple serum screening test, in contrast to diagnostic screening with amniocentesis, makes particular demands on public policy. In BC, it was first noted in 1983 by Sadovnick and Baird¹⁵ that introducing a serum screening test (at that time AFP testing for neural tube disorders) could easily create a potentially harmful imbalance in prenatal services.

Sadovnick and Baird argued that such a test should *not* be made available without pre-established standards of pretest counselling, and referral networks able to provide efficient diagnostic facilities. They judged that from an overall program perspective, if all aspects of a screening process are not in place, harm will exceed benefit.

In BC, however, TMS has diffused into widespread use without meeting many conditions Sadovnick and Baird viewed as necessary. Public policy neither promoted nor discouraged this trend. Instead, diffusion has occurred incrementally, expanding within and between clinical practices. In consequence, while public policy has not been responsible for TMS utilization, it now faces what seems to be an unavoidable need to set the conditions in which TMS utilization occurs, since if such conditions are not set, problems may be regarded as inevitable. The potential risks associated with not having these necessary conditions in place have been reiterated recently in the Ontario,⁵ and the United Kingdom.¹²⁶

The need to establish conditions has been made more acute by the policy statement of the College of Physicians and Surgeons of BC. In keeping with its policy regarding individual patient autonomy and informed consent, the College has stated that practitioners must make women aware of TMS,¹¹⁰ notwithstanding any reservations about the practicability of offering TMS in isolated areas of the province.

Bearing in mind that all elements of a full programmatic service are simply not in place, this represents considerable pressure on the BC Ministry of Health, responsible for mandating services and service distribution in BC, to address the dilemma.

In the instance of maternal serum screening, public policy limits might take the form of necessary 'conditions' for serum screening introduction. For example, maternal serum screening could proceed if training in pre-test counselling, regional amniocentesis services, and second trimester abortion services are available and adequate in the province.

Qualifying factors

Although the need for public policy regarding TMS seems paramount, some additional factors should be borne in mind.

Cost-benefit analyses are not likely to provide much assistance in determining how to proceed. As Sheldon and Simpson argue,¹⁸ cost-benefit analyses can be useful if a health jurisdiction decides to provide prenatal screening for a condition such as Down syndrome, in that such analyses assign a cost figure to evaluate which prenatal program might provide a cost-benefit versus alternatives. However, cost-benefit analyses provide no assistance with the more difficult judgments of which conditions to test for, or what constitutes adequate testing accuracy.¹⁸

Furthermore, any mandated service provision may contradict the consumer movement for home testing (blood pressure, pregnancy and also genetic testing), claimed as a means for the individual to ‘take control’ of health. In this sense, to insist on genetic counselling may be seen as paternalistic and even authoritarian, particularly by disability-rights activists who are apt to view genetic counsellors with suspicion, and would wish to ensure the availability of independent counselling.

It should also be noted here that an emphasis on heredity and individual disease risks should not overwhelm significant and frequently over-looked environmental and social factors in many of these disabilities.

PART VI • POLICY OPTIONS

In broad consequence of the circumstances mentioned in previous chapters, the range of policy options open to government is relatively restricted. As part of the design of the present review, the investigators established a number of options that encompass the available possibilities, drawing upon the shared and context-specific features mentioned above.

Four TMS options were developed reflecting different configurations of TMS testing. The possibility of further options emerging during ensuing consultations was left open. The final chapter of the section provides a brief economic analysis of the option-specific findings.

It is important to note that these option-specific findings are offered as illustrations to inform the provincial policy-making process. They should not be regarded as definitive evaluations of TMS program performance in BC, since they are based as much on estimates as on actual data. For example, while TMS and amniocentesis rates are based on provincial data, birth rates of affected fetuses are estimated from the prevalence data of other jurisdictions.

There are other uncertainties associated with evaluating provision of TMS. Actual payments for laboratory components, for example, have included both fee-for-service and contract payments. Included in the laboratory contract payment is a portion designated for genetic counselling, a service provided under a different department, with a different group of specialists, and payment system.

Similarly, although amniocentesis is listed as a fee-for-service item that can be billed to the provincial payment plan by any obstetrician or radiologist, most amniocentesis is provided through a contract to BC Children's and Women's Hospital in Vancouver. The actual current cost of amniocentesis in the province, therefore, should reflect a yet-to-be-determined component of that contract, together with an estimate of utilization outside the contract from around the province.

The GEM program staff generously provided extensive data on TMS in the province for this review. In particular, they provided details from the pilot project study which enrolled a population between January 1st 1995 and March 31st 1997. This data set has the advantage of including the most complete follow-up of outcomes; that is, the incidence of Down syndrome and other chromosomal abnormalities were obtained not only from amniocentesis, but also from mail-out questionnaires to attending physicians post-delivery. This source is required in order to detect Down syndrome births missed by TMS testing (false-negatives).

CHAPTER 13

OPTION 1: CONTINUATION OF CURRENT PRACTICE

(component funding for *ad hoc* use of TMS by women of all ages, but not program funding)

The first Option reflects the current situation in BC. It is termed '*ad hoc*' by geneticists and proponents of comprehensive program funding because it is not a co-ordinated service applying provincial standards, referral structures or quality control. Funding for laboratory services, pre- and post-test counselling, amniocentesis and abortion are being found within different budgets. Although disfavoured by proponents of co-ordinated funding because of inconsistencies in service delivery, this Option is carefully weighed as to its costs and benefits.

To a significant extent, *ad hoc* use may reflect both the demand among women and the current capabilities of clinicians (in pre-test and post-test counselling for example), as well as the problems of co-ordinating services among historically-independent components of the health-care sector. Program proponents and government administrators may ultimately find themselves obliged to accommodate *ad hoc* utilization regardless of their recommendations and funding decisions, since the complex of social, institutional, and professional forces which have defined current use of serum screening will in all probability continue to be the effective determinants of this procedure.

One of the features of *ad hoc* service delivery, reflected in the analysis presented below, is that there is no central reservoir of comprehensive data. As result, a number of different sources and methods have been used to map out elements of current TMS utilization, population impact and cost.

All the TMS laboratory testing in the province is provided by the GEM program at Children's and Women's Hospital in Vancouver. The GEM program is not reimbursed for TMS by the Medical Services Commission (MSC), the provincial government payment agency, as a fee-for-service item similar to other laboratory tests. In fact, TMS does not appear as a fee item at all. One component of TMS, alpha fetoprotein (AFP), has been a payment item since 1982, and it has been used, in part and indirectly, to reimburse the GEM Program through payment to Children's and Women's Health Centre. A second component of TMS, human chorionic gonadotropin, although on the fee schedule for a variety of indications including serum pregnancy testing, is not reimbursed for prenatal testing.

The background incidence of births of children with Down syndrome in BC is not precisely known, and therefore the age-specific incidence was estimated using actual BC maternal age distribution and age-specific risk profile taken from a recently-published meta-analysis.² Sources and methodology are detailed in **Appendix G**.

This GEM study time-period was used for this analysis because it overlaps with the time-period for which maternal age distribution is available (1997). More recently, the GEM program provided important estimates of amniocentesis utilization rates by women with initial TMS positive results (**Appendix G, Table 18**). Outcome data of comparable reliability are not available after March 1997.

Provincial administrative databases provided additional information regarding trends in prenatal test utilization rates starting in 1991/92, and including alpha fetoprotein, amniocentesis, chorionic villus sampling and ultrasound scanning. **Appendix E** details the total services and payments by age and utilization, by health regions (**Tables 8-10, 14-17**). The 1996/97 fiscal year is the most recent complete year for which data were available and is therefore used for detailed analysis.

For the population impact estimates, data for 1997 have been used, as it is the most recent year for which the age distribution of BC women giving birth is available.

SUMMARY OF POPULATION IMPACT AND COST

Model of 10,045 TMS tests in 1997, which approximates actual utilization.

Total live births in 1997: 44, 371

Women under age 35

Subset of total live births 1997: 37,150 (BC Vital Statistics)

Tested population: 7,471 (20%); age profile skewed to women 30-35 (GEM data)

Down syndrome fetuses at the second trimester*: total population under age 35: 54;
tested population: 13

Utilization:

Using TMS parameters (sensitivity and specificity) obtained from the BC, TMS study:

- 397 women screen-positive (5.3%)
- 278 women subsequently undergo amniocentesis (70% from GEM 1998)

Detection rate:

- 7/13 DS correctly identified in screen-positive group (true-positives)
- 5/7 DS diagnosed through amniocentesis (70% uptake)

Population impact:

- 4 to 5 abortions would result (80-100% uptake of abortion; estimated from literature)
- 390 initial false-positive TMS results
- 3 normal fetuses lost due to amniocentesis induced abortion (assume 1% rate)
- 6 DS births would occur in TMS-negative population (false-negatives)
- Ratio of induced miscarriages following amniocentesis to DS fetuses detected is 1:1.7

Women age 35 and over

Subset of total live births 1997: 7,221 live births (BC Vital Statistics)

Tested population: 2574 (35%); modeled on age profiles report by GEM

DS fetuses at the second trimester: total population over 35: 58; tested population: 20

Utilization:

Using TMS parameters (sensitivity and specificity) obtained from the BC TMS study:

- 578 women screen-positive (23%)
- 347 women subsequently undergo amniocentesis (60% amniocentesis, GEM data 1998)

* Approximately 23% of Down syndrome fetuses abort spontaneously between the second trimester and birth.

Detection rate:

- 16/20 DS fetuses correctly identified in the screen-positive group (true-positives)
- 4/20 fetuses incorrectly identified (false-negatives)
- 10/16 diagnosed with a 60% amniocentesis uptake rate (GEM data 1998)

Population impact:

- 558 false-positive TMS test results
- 8 to 10 abortions (80-100% uptake after amniocentesis diagnosis)
- 4 normal fetuses lost due to amniocentesis (assume 1% fetal loss rate)
- 4 Down syndrome births would occur in TMS negative group testing (false-negatives)
- Ratio of induced abortions following amniocentesis to DS fetuses detected is 1:2.5

Note: 1537 additional women (21% of women age 35 and older) were assumed to continue to use amniocentesis as first screen. An additional 12 Down syndrome cases would be detected.

TABLE 1: Population Impact and Cost Option Option 1 (Current practice).

**Total cost and cost per case detected* for 10,000 TMS tests, all age groups
(amniocentesis rate: 70% for women under age 35 and 60% for women age 35 and over)**

Age and screening group	TMS costs	Amniocentesis costs	Follow-up care: amniocentesis-induced abortion	Cases detected	Average cost per case detected	TOTAL cost
<35 TMS	\$836,772	\$176,540	\$585	5	\$206,918	\$1,013,897
35+ TMS	\$286,685	\$220,232	\$730	10	\$49,769	\$507,647
TOTAL all ages	\$1,123,457	\$396,772	\$1,315	15	\$101,436	\$1,521,544

*** Explanatory Notes:**

- Current prices estimated using GEMS data and 1999 MSC fee schedule prices only
- Excludes capital overhead costs borne by health centres providing services
- TMS cost includes cost of prenatal counselling estimated at \$22.00 per TMS test
- Excludes costs of dating ultrasound. Although a dating ultrasound is strongly recommended for TMS test interpretation, the majority of women in the province are currently receiving this service for other reasons as part of routine obstetrical care.

Costs were only estimated to the point of detection of Down syndrome or spina bifida; that is, they do not include costs associated with elective pregnancy termination, delivery or perinatal and ongoing costs of care associated with the management of Down syndrome or spina bifida whether they accrue to the health care system, families or society as a whole.

Comments on Option 1: Current practice: *ad hoc* funding for TMS

Nearly all individuals interviewed for this report, or who have provided a written opinion on TMS in BC, concluded consistently that: 1) the current *ad hoc* system is an inefficient use of resources and 2) the system is unacceptable since there is no prevailing standard of practice. Two medical care providers, for example, said that if the current situation was the only choice, then it was better not to have TMS at all.

“[Continuing in this way is] just refusing to attack the problem and address it properly. That's the way it has been introduced, though, through the back door and very inadequately through a pilot (project) that has been expanded. In the end, everyone ends up the loser except for a very small fragment of the population ... lucky enough that the doctor is knowledgeable and knows how to use the triple screen, how to interpret and how to explain the triple screen.

I think that politically the government's fine the way they are doing it right now, because they provide amniocentesis for those who want it, they provide triple screen for those who want it, but they're not really looking at the public good. They're not really looking at what is an appropriate public choice - effective health care ... We can do a better job.”

“It shouldn't be this half-way measure that satisfies the minority of pregnant women who happen to be conveniently geographically situated.”

Among this sample of counsellors there was general support for TMS as representing an improvement over screening based on age alone. However, the counsellors had significant concerns about its current use in BC. In particular, the present situation was described as an inefficient use of resources and inadequate with regard both to access to screening, and to the availability of patient and provider education about it.

During the course of the interviews, focus group, and questionnaires, the following recommendations were made by genetic counsellors regarding TMS in BC:

- the wording of the results form should be changed to replace the terms “positive” and “negative” with “increased risk” and “decreased risk”;
- TMS false-positives could be reduced by instituting an early low-cost dating scan;
- enhanced education of patients and physicians would facilitate informed choice;
- an educational pamphlet about screening tests and TMS for women and their partners is needed (Not all providers interviewed were aware of the pamphlet from BC Children's and Women's Hospital);
- TMS should be available only with the necessary support services (amniocentesis, counselling, termination);
- a program for maternal serum screening, rather than TMS, should be put in place, since there are new biochemical markers under development that BC may consider in future. Ideally, these new screening technologies should be assessed without repeating the entire evaluation process;
- additional funding should be available for children with special needs, to help ensure women have true ‘choice’;
- public debate should be encouraged, with a view to determining whether public funds should be spent on population prenatal screening;
- prevention of Down syndrome and spina bifida should not be the goal of prenatal screening.

CHAPTER 14

OPTION 2: FUNDING A TMS PROGRAM FOR WOMEN AGE 35 AND OLDER

TMS can be offered to women over the age of 35 prior to amniocentesis so as to revise their age-based risk assessment for carrying a fetus with Down syndrome. Provided with this adjusted risk level, women may be sufficiently reassured that they will subsequently decline amniocentesis. They may still choose amniocentesis, however, because it has virtually a 100% detection rate, in contrast to the lower TMS detection rate associated with women in this age group of 88%-90%.

Some women over age 35 who have no intention of having an amniocentesis or abortion may still elect to have TMS so as to assess their risk status. This option has been studied in BC during a pilot project from January 1995 to April 1997.⁴⁷ The research was designed to ask, in part, whether TMS reduced the number of women over age 35 who chose amniocentesis.

Insofar as it represents TMS funding for women age 35 and older, Option 2 is a subset of Option 1. Some material presented below is therefore a re-iteration of the previous Option. The overview of population impact and cost during 1997 is repeated here for ease of reference.

However, although Option 2 considers public funding for a much smaller population than Option 1, it is somewhat more complex because of the historical use of diagnostic-screening with amniocentesis in this sub-population. Women in BC age 35 years or older have been offered diagnostic-screening with second trimester amniocentesis or less frequently chorionic villous sampling (CVS), since the late 1970s and mid 1980s, respectively.

The policy is based on the rationale that the risk for Down syndrome rises so steeply in this age-group that the benefits of detection outweigh the risks of invasive diagnostic procedures. Amniocentesis also includes diagnostic testing for open neural tube disorders using intra-amniotic alpha fetoprotein and acetylcholinesterase levels. The incidence of open neural tube disorders, in contrast to Down syndrome, is independent of maternal age.

The GEM research project found that about 21% of women still choose amniocentesis as the first screen because, in contrast to the 100% detection rate associated with amniocentesis, the detection rate associated with TMS is 80% (GEM data).

It may be noted that women under age 35 could privately purchase TMS. An analysis of the population impact and cost of private purchase of TMS is considered in Option 3.

Women age 35 and over

Subset of total live births 1997: 7,221 live births (BC Vital Statistics)

Tested population: 2574 (35%); modelled on age profiles report by GEM

DS fetuses at the second trimester: total population over 35: 58; tested population: 20

Utilization:

Using TMS parameters (sensitivity and specificity) obtained from the BC TMS study:

- 578 women screen-positive (23%)
- 347 women subsequently undergo amniocentesis (60% amniocentesis, GEM data 1998)

Detection rate:

- 16/20 DS fetuses correctly identified in the screen positive group (true-positives)
- 4/20 fetuses incorrectly identified (false-negatives)
- 10/16 diagnosed with a 60% amniocentesis uptake rate (GEM data 1998)

Population impact:

- 558 false-positive TMS test results
- 8 to 10 abortions (80-100% uptake after amniocentesis diagnosis)
- 4 normal fetuses lost due to amniocentesis (assume 1% fetal loss rate)
- 4 Down syndrome births would occur in TMS-negative group testing (false-negatives)
- Ratio of induced abortions following amniocentesis to DS fetuses detected is 1:2.5

Notes: 1537 additional women (21% of women age 35 and older) were assumed to continue to use amniocentesis as first screen. An additional 12 Down syndrome cases would be detected.

TABLE 2: Population Impact and Cost Option 2 (Limiting TMS funding to women age 35 and over)

Total cost and cost per case detected* for approximately 2,500 TMS tests per annum for women age 35 and over (amniocentesis uptake rate for women with positive screens of 60%)

Age and screening group	TMS costs	Amniocentesis costs	Follow-up care: amniocentesis-induced abortion	Cases detected	Average cost per case detected	TOTAL cost
35+ TMS	\$286,685	\$220,232	\$730	10	\$49,769	\$507,647

*** Explanatory Notes:**

- i) Current prices estimated using GEM data and 1999 MSC fee schedule prices only
- ii) Excludes capital overhead costs borne by health centres providing services
- iii) TMS cost includes cost of prenatal counselling estimated at \$22.00 per TMS test
- iv) Excludes costs of dating ultrasound. Although a dating ultrasound is strongly recommended for TMS test interpretation, the majority of women in the province are currently receiving this service for other reasons as part of routine obstetrical care.

Cost were only estimated to the point of detection of Down syndrome or spina bifida; that is, they do not include costs associated with elective pregnancy termination, delivery or perinatal and ongoing costs of care associated with the management of Down syndrome or spina bifida whether they accrue to the health care system, families or society as a whole.

Opinions regarding Option 2: Funding TMS for women 35 and older.

There were mixed views on this option. Reasons given to reject it also varied. One medical care provider considered that this option was a duplication of existing services: “we have an acceptable process right now which has been working for the over thirty-five year old.” Another provider expressed a similar view, “we know that this pathology [Down syndrome] happens most commonly in women under thirty-five, it’s just that the risk increases with age.”

Yet another provider raised the spectre of legal challenges under the Canadian Charter of Rights: “someone could challenge that, I think, saying ‘you’re discriminating against me on the basis of age, and age alone.’” The view was also expressed that, since TMS carries no risk to the pregnancy (unlike amniocentesis), there is no reason to limit it only to women over 35.

“... I think it would be wrong just offer it to the [advanced maternal age] population. I mean, why try to use that test to reduce someone’s risk, instead of saying this is a good screening test and we’ll use it to assess everyone’s risk. So I think [for] the women who are young, [and] don’t qualify for amnio, we’re using ultrasound to modify their risk. Why not use ultrasound and triple screen? And there’s a justification for that. I mean, there are women who we find on ultrasound, a soft marker and we use triple screen to prevent them from having an amnio. If we don’t offer them triple screen, they may well go directly the route of the amnio. So, I think that triple screen should be offered in conjunction with the detailed ultrasound to all women.”

Four providers supported the argument of offering TMS to women over a certain age, but only if that age threshold were lowered from 35, as three others suggested, to age 30. One provider felt that to lower the bar to 30 years would probably generate controversy about cost-benefits, but that the benefit of reassuring women in the slightly higher risk group was justified.

“Instead of using a cut-off of 35 and older, let’s define who need it the most and then lets try to define that group who need it the most. And yes 35 and older would be part of that group, but maybe another group should be 33 and older or patients who have other reasons, high risk factors or ultrasound markers, or other things. Even if they are 22 but there is something wrong with their pregnancy they have an increased risk for whatever reason. Then the risk is equivalent of a 35 year old ... It’s like it would be available to women who have a risk equivalent to a 35 year old or I think even lower than that, a 32 year old or a 30 year old.”

CHAPTER 15

OPTION 3: NO PUBLIC FUNDING FOR TMS

Description

Option 3 considers ending public funding of TMS, while at the same time recognizing that, in the absence of public funding, private purchase of TMS is likely to occur. The level of private purchase, however, is unknown and unpredictable from available data sources.

Continuing the long-standing public funding for alpha fetoprotein screening, in the absence of the additional two markers comprising TMS, is considered problematic. While elevated levels of alpha fetoprotein are considered a reasonable screening test for neural tube disorders, low alpha fetoprotein results are considered a poor screening test for Down syndrome. Although not considered in this report, a possible policy option would be to fund TMS in cases with unexplained low alpha fetoprotein results.

The policy of providing second trimester diagnostic-screening with amniocentesis and CVS is assumed to remain in place. The population impact and cost analysis therefore examines use of these invasive tests for women age 35 and older. In the interest of clarity, and because CVS utilization has decreased dramatically to less than 100 per year in the province, this analysis will focus on amniocentesis alone.

Women age 35 and over

Subset of total live births 1997: 7,221 live births (BC Vital Statistics)

Tested population: 2574 (35%); modelled on age profiles report by GEM

DS fetuses at the second trimester: total population over 35: 58; tested population: 20

Utilization:

- 3074 amniocentesis (42%) would be expected among the 7,221 live births in 1997 (from BC utilization data, 1995/96 - Amniocentesis Business Plan⁵²)

Detection rate:

- 24 Down syndrome fetuses would be correctly identified (100% amniocentesis accuracy)
- no Down syndrome fetuses incorrectly identified (no false-negatives)

Population impact:

- 19 to 24 abortions (80-100% uptake following positive amniocentesis)
- 31 normal fetuses lost due to amniocentesis-induced abortion (assume 1% rate)
- 8 spontaneous abortions, and 26 Down syndrome births would occur in the non-tested population
- Ratio of induced miscarriages following amniocentesis to Down syndrome fetuses detected is 1:1.3

AND in the absence of private purchase of TMS:

- 13 Down syndrome spontaneous abortions and 41 Down syndrome births would occur to women under age 35 in the absence of TMS testing

Note: the number of Down syndrome fetuses born would decrease in proportion to age and percentage of the population purchasing TMS

TABLE 3: Population Impact and Cost Option 3 (Amniocentesis funding for women age 35 and over).

Amniocentesis total cost and cost per case detected* (approximately 3,074 amniocentesis per annum for women age 35 and over, based on current 42% amniocentesis uptake rate)

Age and screening group	TMS costs	Amniocentesis costs	Follow-up care: amniocentesis-induced abortion	Cases detected	Cost per case detected	TOTAL cost
35+ no TMS	Not Applicable	\$1,952,591	\$6469	24	\$81,628	\$1,959,060

* Current prices estimated using GEMS data and 1999 MSC fee schedule prices only (i.e. excludes capital and overhead costs borne by health centres providing services.)

Opinions on Option 3: No public funding for TMS

An option which would not provide public funding for TMS was rejected by most providers interviewed for this research (**Chapter 9**). In part, this was because all of the providers interviewed felt that TMS should be available in BC as it is a better screening tool than age alone. In addition, the lack of support for this option reflected the view that once a technology is introduced, it cannot be retracted - even if it were possible it would appear 'foolish'.

“I think it would be very hard for the government to not offer triple screen at all, to cut the funding back completely. Because there are people out there that know about it and will request it and it's standard of care in so many other places.”

Furthermore, to withdraw all public funding for TMS was felt to be unacceptable insofar as privatization conflicts with the Canadian health care principle of universality. Even among three who felt that TMS might be offered privately, none felt this was an ideal solution.

“... I don't mind if the government wants to say, we've looked at this and ... it's just something we can't afford. But we will allow you to have this as an unfunded option. That if you want to go out and put together a package ... of all of the things that you think are right, and you want to charge the patient for it, as you do for circumcision, etc, you go ahead. I'm quite happy to do that. I believe there is a certain amount of ... entrepreneurial health care that is appropriate ... But for pregnancies, I think its different. I just don't think its right.”

“I guess I'd still say, it's hard to know whether offering a little bit is better than not offering at all, but ... I guess I wouldn't really like to see it not available at all, I just think it's not as it should be right now. I mean if public funding is available for something as expensive as amnio and CVS, you know ... who's making these decisions that these are worth spending the money on versus the blood test that doesn't cost very much?”

CHAPTER 16

OPTION 4: CO-ORDINATED TMS FUNDING FOR WOMEN OF ALL AGES

Description

In contrast to Options 1, 2 and 3 which to some extent present actual population impact and cost measurements of TMS in BC, Option 4 is almost completely model-based. Two models are presented.

- The first provides an estimate of the cost of co-ordinating TMS with other prenatal screening tests, genetic counselling and fetal diagnostic services in all regions of the province.
- The second model estimates the population impact and cost analysis, based on a hypothetical scenario expanding TMS testing from 10,000 tests per annum, approximating current practice (Option 1), to 30,000 tests per annum, approximating the maximal expected uptake of 67% of current live births in the province). Additional cost estimates for intermediate utilization levels (12,000 through 25,000 tests) are summarized in **Appendix J**.

Option 4 maintains the assumption that TMS would be offered to women of all ages. Further, it makes no assumption that amniocentesis testing would be limited to those women over age 35 who screen positive on TMS. A decision to limit access to amniocentesis for women over age 35 who have traditionally been eligible without TMS, is beyond the scope of this review, although the benefits of this policy to population parameters have been mentioned earlier.

Co-ordinated service-funding model

An accurate estimate of the cost of co-ordinating TMS services for the province would require substantial additional program evaluation research beyond that conducted for this review. In this respect, TMS would need to be situated in relation to relevant prenatal services such as ultrasound scanning, genetic counselling, amniocentesis and abortion in all regions of the province.

Some information has been derived from recent program evaluations of abortion services and, in particular, the Amniocentesis Business Plan.⁵² The Plan provides detailed information derived from meetings with individuals providing prenatal diagnostic services in most health districts in the province. This document was the most recent and comprehensive estimate of the costs of co-ordinating a regional network of prenatal services.

These are applicable because TMS relies on amniocentesis for diagnosis and amniocentesis is best delivered closest to where women live. TMS as well as other fluid and tissue samples may continue to be analyzed centrally. It is assumed, therefore, that the cost of adding TMS-specific information to this co-ordination effort would be relatively small if it is integrated into this overall regionalization effort. Additional costs, such as those required to develop abortion services have not been included.

It also provides seemingly reasonable estimates of the resources needed to create regional amniocentesis centres and a provincial co-ordinating centre at BC Children’s and Women’s Hospital in Vancouver. Therefore its estimates will be used as a starting point for discussion around this component of TMS funding. It should be noted that co-ordinating regional amniocentesis services would result in significant overlap with co-ordination of TMS services.

Table 4: Start up & operating costs of co-ordination

START-UP COSTS	\$
Regional centres	130,000
Co-ordinating centre	69,100
Provincial steering committee	45,000
Database requirements	130,000
Total	374,100

ANNUAL OPERATING COSTS	\$
Subsidy of 3 regional centres	30,000
Maintenance of skills	10,320
Provincial steering committee meetings	30,000
Database requirements	66,000
Annual general meeting	6,000
Total	142,320

Population impact and cost model: (30,000 TMS test per annum)

TMS test parameters: data from the BC context

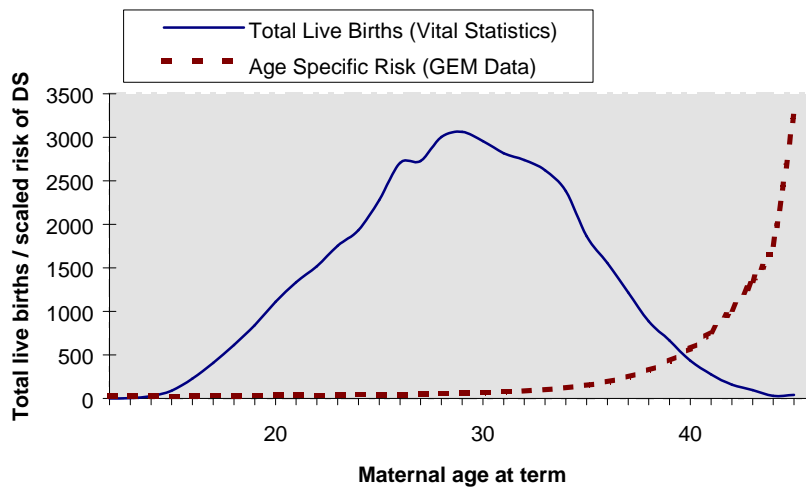
The GEM program provided local test parameters for TMS. Because the ability of the TMS test to detect a fetus with Down syndrome is dependent on the prevalence of Down syndrome in the population tested and because this prevalence is age dependent, these test parameters are influenced by the age distribution of the test population.

As **Figure 1** (repeated below for convenience) demonstrates, the age distribution of the population tested to date within the GEM program differs markedly from the maternal age profile in BC. This means that test parameters from the GEM program cannot reliably be extrapolated to the larger population. They must instead be adjusted to sensitivities and specificities that reflect the larger, and much younger, test population. (See **Appendix E, Table 10**).

Population impact parameters

Total eligible population in 1997: 44, 371 live births

[Figure 1: Distribution of live births by age and risk of Down syndrome]



Women under age 35

Subset of total live births 1997: 37,150 (BC Vital Statistics)

Tested population: 24,800 (66%); based on GEM data age profiles

DS fetuses at the second trimester*: total population under age 35: 54; tested population 37

Utilization:

Using TMS parameters obtained from the GEM study:

- 1,065 women TMS-positive (4.3 %)
- 745 women subsequently undergo amniocentesis (70% uptake rate from GEM 1998)

Detection rate:

- 17/37 Down syndrome correctly identified in screen-positive group (true-positives)
- 20/37 fetuses with Down syndrome incorrectly identified (false-negatives)
- 11/17 Down syndrome diagnosed through amniocentesis (70% uptake)

Population impact:

- 9 to 11 abortions would result (80-100% uptake of abortion; literature estimate)
- 1,048 initial false-positive TMS results
- 7 normal fetuses lost due to amniocentesis induced abortion (assume 1% rate)
- 9 Down syndrome births would occur in TMS-negative population (false-negatives)
- Ratio of induced miscarriages following amniocentesis to Down syndrome fetuses detected is 1:1.6

Women age 35 and over

Subset of total live births 1997: 7,221 live births (BC Vital Statistics)

Tested population: 5,186 (72%); modelled on age profiles report by GEM)

DS fetuses at the second trimester: total population over 35: 58; tested population: 41

Utilization:

Using TMS parameters obtained from the BC TMS study:

- 1,176 women screen-positive (23%)
- 705 (60%) undergo amniocentesis (uptake rate; 1998 GEM data)

Detection rate:

- 34/41 Down syndrome correctly identified in screen-positive group (true-positives)
- 7/41 fetuses with Down syndrome incorrectly identified (false-negatives)
- 20/34 Down syndrome diagnosed through amniocentesis (60% uptake)

* Approximately 23% of Down syndrome fetuses abort spontaneously between the second trimester and birth.

Population impact:

- 1,159 false-positive TMS tests
- 16 to 20 abortions (80-100% uptake following positive amniocentesis)
- 7 normal fetuses lost due to amniocentesis-induced abortion
- 2 Down syndrome spontaneous abortions, 5 Down syndrome births would occur in TMS-negative group (false-negatives)
- Ratio of normal fetal loss to Down syndrome fetuses detected is 1:2.9

Note: 1,537 women would likely use amniocentesis as a first screen detecting an additional 12 Down syndrome cases, while inducing the loss of 15 normal fetuses.

TABLE 5: Population Impact and Cost Option 4 (Co-ordinated program funding for all ages)

Total cost and cost per case detected* for 30,000 TMS tests per annum, all age groups (amniocentesis for women with positive screens at a rate of 70% for women under age 35 and 60% for women age 35 and over)

Age and screening group	TMS costs	Amniocentesis costs	Follow-up care: amniocentesis-induced abortion	Cases detected	Cost per case detected	TOTAL cost
<35 TMS	\$2,781,737	\$473,390	\$1,568	12	\$273,672	\$3,256,696
35+ TMS	\$585,451	\$447,972	\$1,484	20	\$50,731	\$1,034,907
TOTAL ALL AGES	\$3,367,188	\$921,362	\$3,052	32	\$134,113	\$4,291,603

*** Explanatory Notes:**

- Current prices estimated using GEM data and 1999 MSC fee schedule prices only
- Excludes capital overhead costs borne by health centres providing services
- TMS cost includes cost of prenatal counselling estimated at \$22.00 per TMS test
- Excludes costs of dating ultrasound. Although a dating ultrasound is strongly recommended for TMS test interpretation, the majority of women in the province are currently receiving this service for other reasons as part of routine obstetrical care.

Cost were only estimated to the point of detection of Down syndrome or spina bifida; that is, they do not include costs associated with elective pregnancy termination, delivery or perinatal and ongoing costs of care associated with the management of Down syndrome or spina bifida whether they accrue to the health care system, families or society as a whole.

Opinions of Option 4: Offering TMS to all pregnant women (program funding)

Three medical care providers felt this option was unacceptable, saying either that routine and universal offering of TMS was not cost-effective, or that TMS is too confusing for women, giving the wrong message that women should be trying for the perfect baby. Five providers felt that this was the best option. However, each stated that although this was the option they would support, it was expensive and would likely take limited health care resources away from some other program.

“My first choice. That’s because ... it is the right choice when we’re dealing with obstetrics and health care. You know, equal access, I think it’s cost effective and a number of other things. It may not be anxiety effective, ‘cause that’s the one thing that everybody keeps harping back to, but I think ... if you could get the people to understand what it is they’re having, I think you’ll decrease that anxiety.”

One provider emphasized that this option would have to be voluntary screening, rather than population screening as rubella screening has become.

CHAPTER 17: SUMMARY OF POLICY OPTIONS

Economic analyses

The resources required to diagnose a fetus with Down syndrome depend on its prevalence in the population tested and the diagnostic methods used for its detection. Prevalence of Down syndrome is directly related to maternal age, increasing for older cohorts of women (**Figure 1** p98).

Two competing testing strategies are considered in this review:

- Amniocentesis as the primary test;
- TMS with amniocentesis as a secondary confirming test.

The power of amniocentesis is its ability to discriminate between a positive and negative diagnosis. This power is materially mitigated by significant numbers (approximately 1%) of spontaneous abortions resulting from the procedure.

The sensitivity of the TMS test is varied by maternal age to maintain a constant absolute risk for Down syndrome. Consequently, at any level of sensitivity for detecting a positive Down syndrome case, the TMS produces significant numbers of false-positive cases. To resolve the true-positives from the TMS-positive results, a confirming amniocentesis test is used.

TMS provides lower costs than amniocentesis for a population when the avoided costs of amniocentesis and induced abortions offset the additional TMS costs. In high prevalence populations therefore, where the false-positives relative to the true-positives are lower, TMS can be more cost-effective in detecting Down syndrome than amniocentesis.

The problem with cost per case detected is that it ignores the population detection rate. A population health perspective would ask “for a given detection rate in the population, what is the cost/case detected?” The answer varies according to the target detection rate. Thus, to detect only 30% of fetuses with Down syndrome, the least expensive alternative is to offer amniocentesis to women over age 35.¹⁸

In lower-prevalence populations, the false-positives relative to the true-positives can reverse the relationship. This is observed in the cost tables presented in the program options above. The TMS cost per positive detected case for women less than 35 year old is higher than amniocentesis, while the reverse is true for women 35 years and over.

This analysis is dependent on the selected sensitivity of the TMS for different age groups. It is possible to obtain higher percentages of Down-syndrome positives with TMS, but this is associated with higher rates of false-positives (requiring confirming amniocentesis) and induced abortions. Consequently, the chosen TMS test sensitivity will change the cases detected and costs, but is unlikely to change the relative efficiency related to prevalence.

At current test sensitivities, TMS can only resolve a relatively small number of Down syndrome cases in the under 35 age group compared to the 35 + age group. A question not answered here is the cost and population effects of altering TMS sensitivities.

The population and economic impact estimates for four funding options are summarised in **Table 6** following.

Option-specific interview material

The providers interviewed were generally unsupportive of Option 1 (the current situation) and Option 3 (no provincial funding for TMS). Option 2 (funding for age-based TMS) was supported so long as the age limit for routinely offering TMS was lowered to a younger age, although there was no consensus as to what that age should be or how it should be justified. Option 4 (offering TMS to all pregnant women) received most support, despite being widely and incorrectly considered an expensive option.

TABLE 6: Population and economic impact of four alternative funding options (10,000 TMS tests)

	Option 1: Current practice (<i>ad hoc</i> TMS funding)		Option 2: TMS funding limited to women age 35 and over	Option 3: No public TMS funding. Amniocentesis for women age 35 and over	Option 4: Co-ordinated TMS funding for women of all ages	
POPULATION	AGE < 35	AGE ≥ 35	AGE ≥ 35	AGE ≥ 35	AGE < 35	AGE ≥ 35
Eligible	37,150	7,221	7,221	7,221	37,150	7,221
Tested	7,471	2,574	2,574	----	7,471	2,574
UTILIZATION						
Screen positive	397	578	578	----	397	578
Follow-up amniocentesis	278	347	347	3074 screening amniocenteses	278	347
DETECTION RATE						
Down syndrome correctly identified by TMS	7/13	16/20	16/20	----	7/13	16/20
False-negative rate	6/13	4/20	4/20	0	6/13	4/20
Down syndrome confirmed by amniocentesis	5/7	10/16	10/16	24 (amniocentesis accuracy 100%)	5/7	10/16
POPULATION IMPACT						
False-positive TMS tests	390	558	558	----	390	558
Therapeutic abortions	5-7	8-10	8-10	19 - 24	5-7	8-10
Normal fetuses lost through amniocentesis	3	4	4	31	3	4
Down syndrome births with negative TMS	6	4	4	----	6	4
Ratio of induced miscarriages following amniocentesis to Down syndrome fetuses detected	1 to 1.7	1 to 2.5	1 to 2.5	1 to 1.3	1 to 1.7	1 to 2.5
ECONOMIC IMPACT						
Cost per case detected	\$101,000		\$450,000	\$82,000		\$114,000
TMS cost	\$900,000		\$230,000	----		\$900,000
TMS-related genetic counselling	\$220,000		\$55,000	----		\$220,000
Amniocentesis costs	\$397,000		\$220,000	\$1,953,000		\$397,000
Follow-up care: amniocentesis induced abortion	\$1,500		\$700	\$6,500		\$1,500
CO-ORDINATION COSTS						\$186,000
TOTAL ANNUAL COST	\$1,619,500		\$555,700	\$2,041,500		\$1,818,500

PART VII • FINDINGS & CONCLUSIONS

CHAPTER 18: SUMMARY OF FINDINGS

This chapter summarizes general and option-specific findings regarding TMS. The option-specific findings include a summary of the advantages and disadvantages of each option as perceived by different interest groups. Estimates of screening program performance and costs are also provided.

The first three options are in essence variations on current TMS practice in the province. The fourth option incorporates co-ordination, regulation, education, and evaluation of TMS at various utilization levels.

Notwithstanding consultation with all interested parties on the possibility, no further option emerged from the review.

I. General Prenatal Screening Findings

1. Provincial health policy has in recent time strongly supported the right of individual women to choose prenatal testing such as amniocentesis and consequent abortion services on demand, a policy reflecting the principle of individual autonomy enshrined in the Canadian Charter of Rights and Freedoms. But while the right to individual autonomy has remained paramount in relation to prenatal screening, there is a growing need to examine the social implications of this type of testing for, and selective abortion of, fetuses with viable genetic conditions, such as Down syndrome.
2. This TMS review and several other recent governmental and non-governmental studies have found that current access in the province to genetic counselling, diagnostic testing and abortion is unequal, favouring women in the Vancouver and Victoria regions.
3. Dissemination of genetic prenatal screening services has mainly occurred through passive transfer of responsibility to primary care physicians and obstetrical specialists around the province, rather than by any relocation of genetic specialists themselves. This responsibility transfer began with pre-test counselling of women over age 35 for amniocentesis, and is continuing with TMS.
4. There is currently no provincial group with the responsibility or funding to set standards for the provision of prenatal testing across various regions of the province, that is, with a mandate to evaluate and ensure the quality of informed choice, provider and patient education, and culturally-appropriate methods of counselling.
5. There is as yet no mechanism to provide individuals with disabilities, their families or representatives the opportunity to design educational materials, or provide social commentary on prenatal screening programs. Furthermore, although social support for these individuals has begun to develop in the province, there is as yet no formal means to balance the degree of public funding for prenatal detection with support for people living with disability; and no voice for these individuals or their representatives in designing or providing prenatal screening programs.

II. TMS Specific Findings

1. The Genes, Elements Metabolism (GEM) program analyses all TMS tests in the province. GEM data show that TMS utilization has approached 25% of live births in fiscal year 1998/99. Utilization has further increased 40% in the first quarter of 1999/2000 as compared with the same time period of the previous year.
2. Virtually all individuals interviewed for this review agreed that TMS is well on the way to becoming a standard component of obstetric care. This is probably the result of several factors, including: dissemination of professional knowledge of the test; growing awareness of the threat of wrongful birth lawsuits if TMS is not offered; and advice published by the College of Physicians and Surgeons of BC stating that TMS should be offered as part of routine prenatal care.
3. TMS prior to amniocentesis improves upon several features of using amniocentesis alone (an approach offered to women age 35 years and older in BC). Most notably, TMS increases the percentage of affected fetuses detected, reduces the initial false-positive rate, and reduces unaffected fetal loss due to amniocentesis, in any age group.
4. Although an improvement on amniocentesis alone, TMS remains less than ideal as a screening test, owing to an initial false-positive rate for Down syndrome of 8.7% (in BC), and an overall detection rate of 60%-70%. Although the detection rate increases to over 80% for women age 35 and older, the less than 100% detection rate associated with TMS may be of particular importance to women in this age group, at highest pre-test risk of carrying a fetus with Down syndrome, and who are eligible for amniocentesis.
5. Provincial health policy has supported a number of medical genetics services relevant to TMS, such as counselling, amniocentesis, and laboratory testing, but this has not extended to overall responsibility for co-ordinating a TMS service. A decision to fund a co-ordinated TMS service would therefore be a new initiative in the province.
6. The anticipated costs of co-ordinating TMS are small (approximately 10%) relative to current costs of providing TMS and associated services, regardless of whether the services are offered in a provincial centre or in various regional centres. Potential benefits of a co-ordinated service include provision more responsive to regional needs in physician education, counselling, diagnostic testing and abortion. The costs of providing quality services across all regions are not taken into account, however, and could be substantial. The cost of counselling alone, both in relation to positive TMS results and to abortion, could add significant costs to the health-care system.
7. Because of the lower prevalence of Down syndrome in women under 35 years old, the cost per fetus detected is significantly higher in this group than for women 35 years and older, \$268,700 and \$64,600 respectively. This is because, compared to the higher-prevalence population, many more younger women need to be screened for each affected fetus.

8. TMS will also result in the detection of open spina bifida, adding to the cost, but also the detection rate of the program. The cost will include an increase in the initial screen-positive rate by 1%-2%. The actual number of fetuses with open spina bifida detected remains difficult to predict owing to uncertainty regarding the prevalence of open spina bifida at 16-18 weeks' gestation. The prevalence is estimate at 1/1000 without, and 1/2000 with pre-screening with ultrasound. Using an 80% detection rate for TMS, 8 out of 10 cases would be identified as screen-positive per 10,000, for women who have not had pre-screening ultrasound. An estimated 4-5 women would have subsequent diagnostic amniocentesis. **Figure 6** illustrates expected outcome from 10,000 tests.
9. From a broader economic perspective, the cost of detecting a fetus with Down syndrome, rarer chromosomal or neural tube disorders has been weighed against the very significant cost of developing and providing health and social services for these children and families. Although cost estimates vary and do not include any estimate of the value of people with Down syndrome to society, virtually all cost-benefit analyses conclude that prenatal screening with TMS does not result in a net increase in public expenditure. However, these cost-benefit analyses do not take into account the value of people with these disabilities to their families and to society, and so the economic arguments for or against prenatal screening have not been given significant weight in this review.

III. Option-specific Findings and Comments

Option 1. Current Practice of 'ad hoc' funding

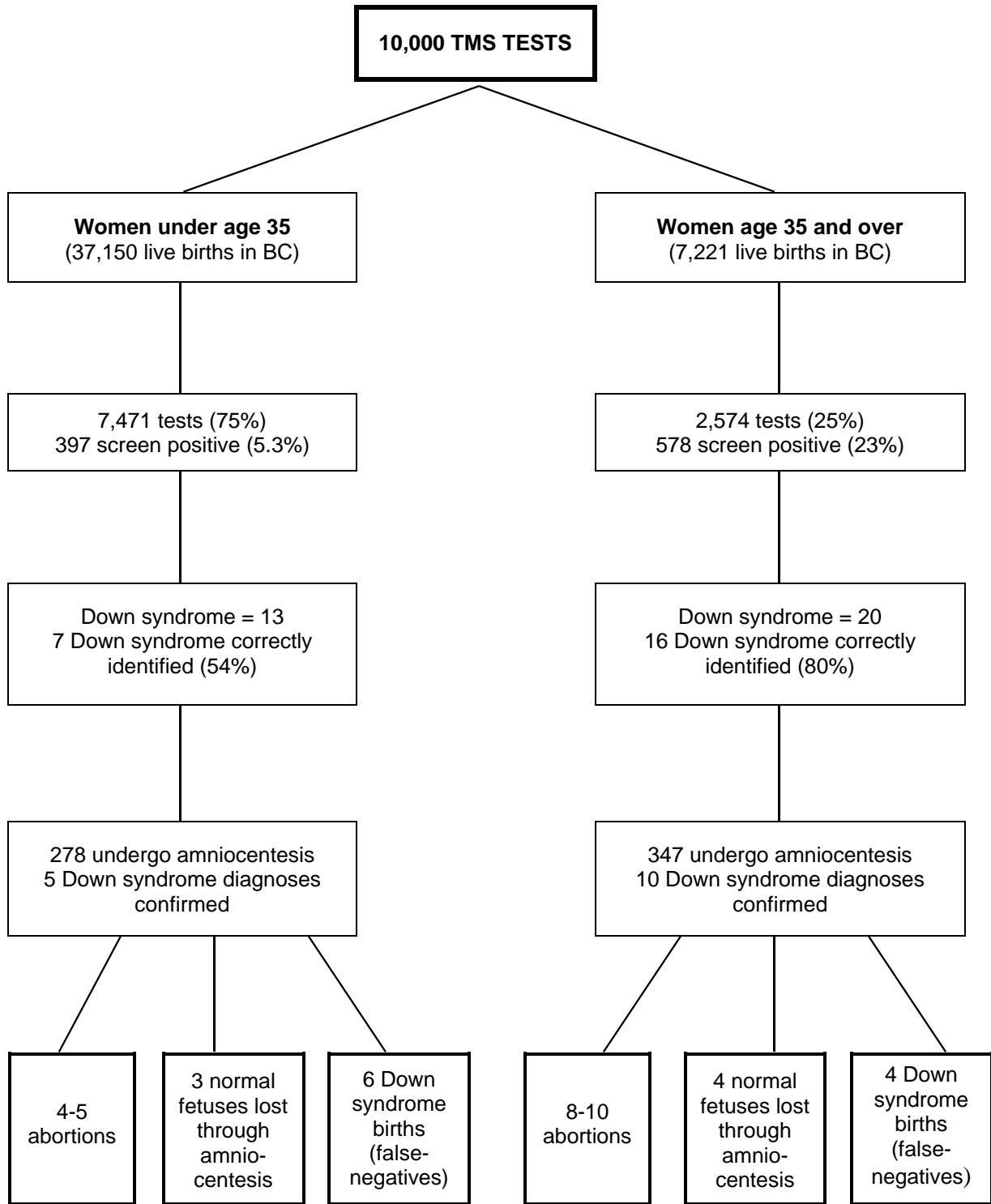
The TMS blood test is currently funded for women of all ages. There is no program funding for co-ordination, systematic quality control, or provider or patient education. This form of funding is termed '*ad hoc*' by geneticists and proponents of comprehensive program funding because individual clinicians, institutions and regions, as opposed to a centralized authority, are left to determine whether TMS is integrated into diagnostic and counselling services in their area.

Individual Rights / Autonomy Framework

When viewed within a framework of individual choice, access to TMS in the current system is a service available to women who live in the south-west of the province and who have either the initiative to ask for TMS or a provider who will offer it. Women over 35 may choose initial TMS instead of amniocentesis screening, and all women may choose TMS as a means of reassuring themselves about the health of the fetus.

Clearly, without extensive education and a commitment to consistent and province-wide practices, screening does not 'support or enhance' equality for women. Those better educated, living in urban areas or who have a well-informed physician enjoy a distinct advantage.

Figure 6: Expected impact of 10,000 TMS tests on Down syndrome detection



Disability Rights Framework

From the Down syndrome community and disability-rights perspective, this option is neither desirable nor acceptable. That is, while all forms of TMS are disturbing and frustrating from this perspective, an *ad hoc* system provides no opportunity for systematic education of women, health care providers, and the general public regarding Down syndrome and those affected by it. The lack of education about Down syndrome was articulated frequently by representatives of the Down syndrome community as being the most significant gap in the screening process.

Legal / Regulatory Framework

Among the providers interviewed, there was nearly unanimous agreement on the need for clear guidelines in the provision of TMS. Nearly all those interviewed expressed concern that the current system was both an inefficient use of resources, and unacceptable in having no standard of practice.

Providers generally did not support the argument that current *ad hoc* utilization reflects demand by women and willing providers. They explained that many women did not demand TMS during pregnancy (often because they were unaware of the test); and that many providers offered it, not because they supported the test, but from compelling malpractice concerns.

Health Management Framework: Utilization and Cost

In 1997, approximately 10,000 tests were performed (25% of total live births); 75% were women under age 35, 25% in women age 35 and older. The overall Down syndrome detection rate was approximately 45% (15 of 33) in the test population. The relatively low detection rate was primarily the result of only 60% of TMS-positive women electing to have amniocentesis. The immediate TMS program cost plus associated amniocentesis and cytogenetics totals approximately \$1,521,544.

Summary of Cost estimate: 10,000 TMS tests - all ages

Serum testing	\$900,000
Genetic counselling	\$220,000
Amniocentesis	\$397,000
Follow-up cases of amniocentesis-induced abortion	\$1,500
<hr/>	
<i>Total cost</i>	\$1,619,500

Option 2. TMS funding for women over age 35

Under this option, TMS would become an additional funded service, along with diagnostic amniocentesis and chorionic villous sampling (CVS), available to women 35 years of age or older. TMS, similar to amniocentesis, would not be a provincial program with program funding. TMS can be offered to women prior to amniocentesis so as to revise their age-based risk assessment for carrying a fetus with Down syndrome.

Women may be sufficiently reassured by a low age-adjusted risk level that they will subsequently decline amniocentesis, or they may still choose amniocentesis because they are aware that the detection rate with TMS, even if all initial screen-positive women elect to have amniocentesis, is about 60-70%. The illustrative example below shows that TMS use for women over age 35 decreases the amniocentesis rate and corresponding fetal loss, while at the same time increasing the detection rate, owing to the greater proportion of women having TMS than had amniocentesis screening in the past. Some women over age 35 who have no intention of having an amniocentesis or abortion, may still elect to have TMS so as to assess their risk status.

Individual Rights / Autonomy Framework

Within an individual-rights framework, this option may well be perceived as enlarging the choices available to women over 35 years of age. It will be familiar to many women in BC who already associate 'advanced' maternal age with increased risks during pregnancy and a need for increased medical surveillance. While this option fits within the framework of choice that is prevalent in Canada, it continues to medicalize pregnancy in older women, while withholding the choice of TMS from younger women.

Disability Rights Framework

From a disability-rights perspective, age-related screening, as with Option 1, continues what these groups consider the controversial practice of screening for Down syndrome.

Legal / Regulatory Framework

Among the providers interviewed for this review there were mixed views on this option. Many believed that, because TMS would be offered to women at highest pretest risk, this option would be the best use of limited funds. With one exception, the physicians interviewed were generally hesitant about supporting any option that would apply a specific age cut-off for funding. They noted that to avoid risk of either wrongful birth lawsuits or sub-standard clinical practice, they would feel compelled to offer TMS to women of all ages, despite an absence of public funding.

Health Management Framework: Utilization and Cost

As detailed in Option 1 above, in 1997, this option would have detected 10 cases of Down syndrome at an immediate cost to the Medical Services Commission of \$555,700. Additional cases of Down syndrome would have been detected for the 25%-30% of women who choose amniocentesis screening. Further costs could also arise if women under age 35 purchase TMS privately, then seek amniocentesis on the basis of a positive screen.

Note on test-performance: TMS reduces by half the number of amniocenteses needed to detect one fetus with Down syndrome. This in turn reduces by half the number of unaffected fetal losses.

Cost estimate: TMS funding for women age 35 and over (approximately 2500 tests at current level of 10,000)

Serum testing	\$230,000
Genetic counselling	\$55,000
Amniocentesis	\$220,000
Follow-up cases of amniocentesis-induced abortion	\$700
<hr/>	
<i>Total cost</i>	\$555,700

Option 3. Funding amniocentesis and CVS for women age 35 and over (No public TMS funding; possible private funding)

As with Option 2, this option continues a long-standing practice in BC of offering diagnostic screening with second trimester amniocentesis, or less frequently chorionic villous sampling (CVS), to women aged 35 years or older. In discussing this option, we recognize that the absence of provincial funding does not preclude private purchase of TMS.

Individual Rights / Autonomy Framework

This option seems to conflict with the framework of individual autonomy and choice in a number of ways. In particular, not offering TMS removes from women’s choice a non-invasive and, for that reason, potentially preferable method of assessing risk. The main concern is that, in the absence of provincial funding for TMS, private purchase is likely to occur, and thereby conflict with the principle of universality in health care and discriminate against low-income women and families.

Disability Rights Framework

Many, but not all, members of the Down syndrome community implicitly or explicitly support this option. In general, they expressed a high level of antipathy towards TMS and broadly considered that it should not be offered at all.

Noting that testing for Down syndrome implied the condition is ‘bad’, many members of the focus group felt this would be the message sent by government through any type of Down syndrome screening. Similarly, those who work daily with the Down syndrome community found it discouraging to see government dollars used to support genetic screening rather than providing resources for people with Down syndrome or promoting social programs aimed at changing cultural perceptions of disability.

However, the Down syndrome and disability rights communities shared concerns that privately-funded TMS would, if anything, represent a worsening of current problems associated with the *ad hoc* use of TMS.

Legal / Regulatory Framework

As with Option 2, providers stated that they are likely to continue to offer TMS to all women because of concern over malpractice lawsuits and because of peer pressure to offer it as a standard component of obstetrical care.

Health Management Framework: Utilization and Cost

Without public funding for TMS at any age group, women over age 35 may continue to utilize amniocentesis at current rates of about 42% of all live births in this age group. It is also possible that the private sector would offer TMS testing. TMS utilization rates and the age distribution of women who would privately purchase is speculative. It seems reasonable to assume that a majority of women purchasing this test would be in the older reproductive age-groups, that is, at higher pre-test risk. Women who purchase the TMS test privately and have a positive screen for Down syndrome may request amniocentesis and expect it to be paid for through public funds. The following estimate is probably an underestimate of demands on public funds, should funding for TMS be discontinued for all age groups.

Cost estimate: No public funding for TMS - Amniocentesis funding for women age 35 and over

Amniocentesis	\$1,953,000
Follow-up cases of amniocentesis-induced abortion	\$6,500
<i>Total cost</i>	<i>\$2,041,500</i>

Rationale: Without public funding for TMS, women over 35 in a high-risk age category may continue to use amniocentesis at the current provincial levels of 42% on average.

Option 4. Co-ordinated TMS funding for women of all ages

Under this option, TMS would not necessarily be either expanded or restricted. Rather, the emphasis would be on co-ordination of TMS and associated services in all regions of the province. Within the frameworks of choice, disability rights, and providers' concerns, this option has mixed but overall general support.

Individual Rights / Autonomy Framework

This option has the potential to provide equitable access to TMS and a standard of care. It would also provide the opportunity to ensure culturally-appropriate education and counselling aimed at discouraging the perception of pregnancy as risk-laden, reducing the impression that having TMS is 'mandatory', and supporting women and couples in discussing its implications. Making TMS available to women of all ages as a co-ordinated service aligns well with the social value placed on individual choice, and with the Canadian principle of universality in health care.

Disability Rights Framework

Systematic government support of TMS, even limited to co-ordination, is unacceptable from the perspective of disability rights. Such support may well be perceived as a sign that people with disabilities are undesirable and that their elimination is supported by government. At another level, however, people within the disability-rights and Down syndrome communities recognize this as a preferable option to the present *ad hoc* situation, as it at least encourages education, information and a standard of care. As noted by one mother of a child with Down syndrome, it is not the test itself that is problematic, but the pressures surrounding it, and the confusion and stress that accompany a hazy policy.

Legal / Regulatory Framework

Among the providers interviewed, there was general agreement that while this was the best option it was potentially expensive and would be likely to take limited health care resources away from other perhaps more needed prenatal programs. They acknowledged that, while the province would save money from care of people with disabilities, it cannot be assumed that such savings would not be directly used to reduce the pressure on competing prenatal services.

Health Management Framework: Utilization and Cost

At current levels of testing (10,000) with an average annual cost of regional co-ordination of \$186,435, the total cost to the Medical Services Commission would be \$1,708,000.

Assuming the demand for TMS reached 30,000 (66% of live birth population) and assuming a 60% amniocentesis rate by TMS positive women, the proportion of Down syndrome cases detected will increase proportionally, as will the cost. It is assumed that, similar to the estimates for 10,000 TMS cases, the Down syndrome detection rate will remain at about 50% and the directly measurable Medical Services costs will reach approximately \$4,000,000.

Cost estimate: Expansion model of 30,000 TMS tests - all ages

Serum testing	\$900,000
Genetic counselling	\$220,000
Amniocentesis	\$397,000
Follow-up cases of amniocentesis-induced abortion	\$1,500
Cost of regional co-ordination	\$186,000 (average of start-up and annual cost over 4 years)
<hr/>	
<i>Total cost</i>	\$1,818,500

CHAPTER 19: CONCLUSIONS

The following conclusions have emerged, in part from quantitative and qualitative context-specific data gathered in BC, and in part from published and unpublished accounts of TMS in other jurisdictions. Additional and more detailed conclusions may follow consultations planned with local clinical experts and health policy-makers.

I. General Conclusions

1. The current policy issue does not derive from the question of whether TMS ought or ought not to be provided, or whether TMS will increase or decrease health care costs. Instead, the policy questions are (i) how equitably to provide TMS across the province, assuming that TMS is and will be offered to women, whether the initial serum test is paid for publicly or purchased privately; and (ii) what degree of effort and resources will ensure that access is accompanied by high-quality support (for example in educational and counselling services). In particular, policy-makers are faced with a current imbalance in most regions of the province between ready access to the first step in TMS, the serum blood test, and relatively inaccessible diagnostic, counselling and abortion services.
2. TMS, similar to other prenatal screening tests before it, is cost-effective. That is, the excess health cost of caring for children with Down syndrome or neural tube disorders is so great that it easily exceeds the cost of providing these prenatal screening programs. This reality has been identified in the published literature since the late 1970s, and validated in a series of more recent economic analyses. The cost of providing TMS therefore cannot be used as an argument against its implementation.
3. The converse argument, that TMS ought to be provided because it will reduce health costs, is quite properly considered unethical. In fact, current interest in prenatal screening in general, and TMS in particular, does not derive from the inclination to make savings by eliminating the cost of caring for children with Down syndrome or other detectable conditions. Nor has this argument ever been sufficient in the province to justify prenatal screening. Instead, complex factors (technical, personal, social, and professional) have encouraged screening to proceed.
4. Local and international experience recognizes that to pay for TMS without adequately funding infrastructure support for quality assurance and education as well as diagnostic and abortion services, risks unnecessary harm to women who lack ready access to adequately informed clinicians or diagnostic facilities.
5. Acknowledging that 25% of pregnant women in the province are now having TMS, and regardless of whether utilization continues to rise in BC, there is a clear need for specific funding to a single group or institution to co-ordinate TMS along with other prenatal screening services in the province. Because of the technical difficulties associated with TMS and associated prenatal screening and diagnostic tests, the group co-ordinating TMS should include, but not be limited to, the current consortium of specialists providing prenatal

services: tertiary care, university-affiliated obstetricians, geneticists, and laboratory pathologists. Because of the difficulties associated with providing TMS in remote and isolated regions of the province, the group co-ordinating TMS should also include regional representatives, either clinical, administrative or both. These representatives may usefully recommend regionally-appropriate practice: who should offer TMS (primary care physicians, public health nurses), and in what location (doctor's office, public health unit).

The responsibilities of the prenatal screening co-ordination group in relation to TMS should include establishing a province-wide standard of care and disseminating accurate information about TMS among providers and potential users. In particular, that information should include, but not be limited to the following:

- in conjunction with disability rights and support groups, providing accurate, balanced information about care-giving for people with Down syndrome and open neural tube disorders, as much as possible derived from personal experience
- highlighting the difference between screening and diagnostic tests
- indicating the false-positive and false-negative rates for TMS, and other screening tests
- identifying the most common causes of false-positive outcomes, such as inaccurate dates, or twins
- encouraging women or couples to consider how they might respond to a TMS result
- providing a discussion of the clinical and social aspects of detectable conditions

In addition, there is clear need to establish a prenatal screening co-ordinator whose role would be to oversee technical and logistical details of TMS and other complex prenatal screening and diagnostic services. Such a co-ordinator would be responsible for evaluating prenatal testing performance, such as initial false-positive rates, as well as noting regional disparities in amniocentesis and abortion rates for serum screen- positive women.

6. There is a clear need for greater input from various concerned groups regarding prenatal screening in BC. A Provincial Prenatal Screening Advisory Committee made up of primary care physicians, midwives, public health professionals, and women's health and disability rights' representatives would provide an organised forum for discussion among the interest groups, and a platform for making recommendations to government and to the group responsible for co-ordinating prenatal screening services. (A similar group was recommended for a federal committee by the Royal Commission.⁸) Such an Advisory Committee would provide information regarding the technology and practices of prenatal screening and diagnosis in BC, with particular attention to changes that affect policy.

II. Option Specific Conclusions

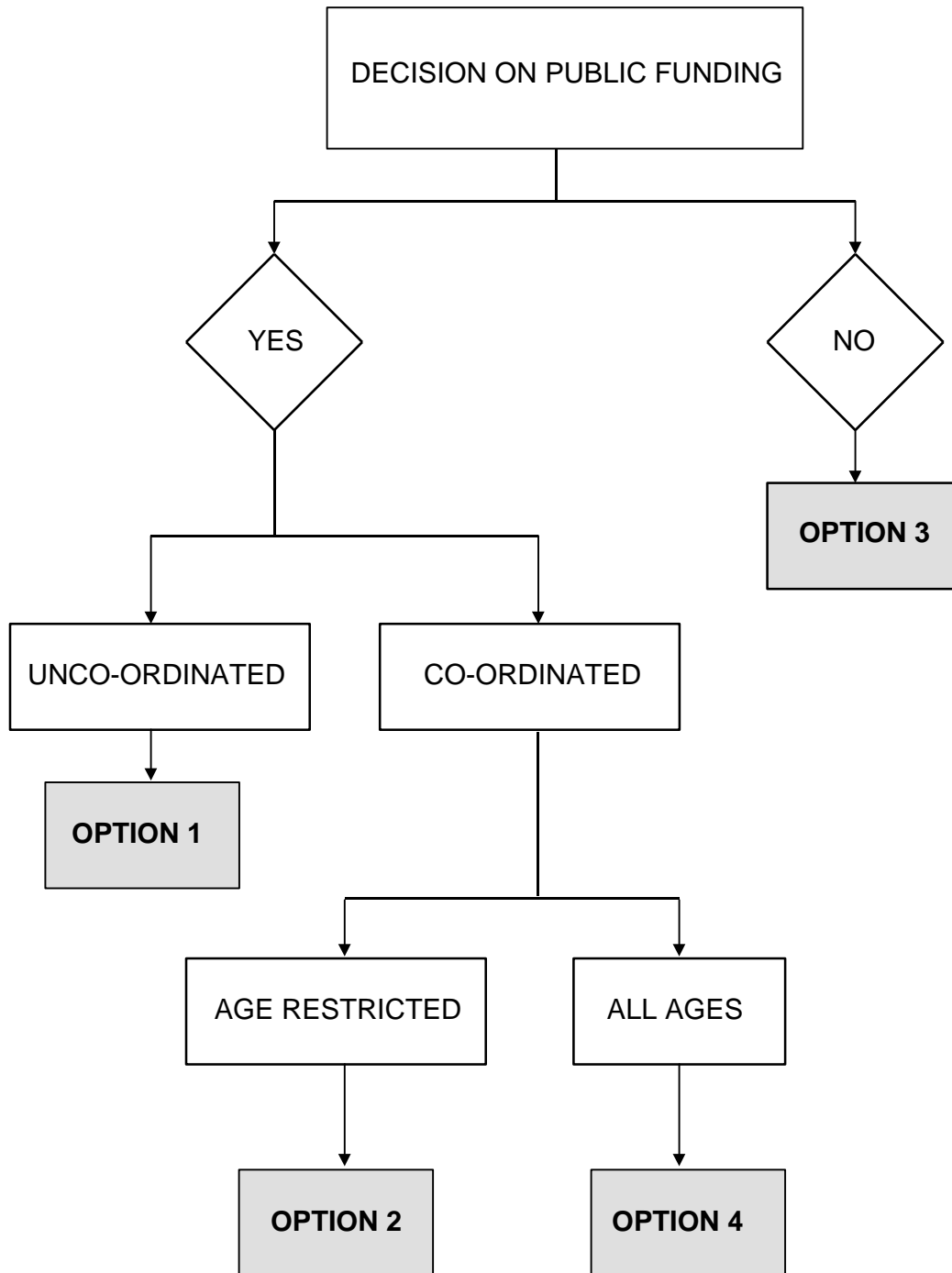
In terms of the four options considered by this review, we draw the following conclusions:

- **Option 1. *Ad hoc* funding:** *Ad hoc* or unco-ordinated provision of TMS received the least support of all the options.
- **Option 2. TMS funding over age 35:** Offering TMS on the basis of advanced (over age 35) maternal age would seem to provide a way to integrate TMS into clinical practice without fundamentally changing existing social understandings of pregnancy and disability, especially understanding of an accelerating risk of Down syndrome with advancing maternal age. However, virtually all the literature on women's experiences with prenatal screening strongly suggests that from a woman's perspective, the primary determinants of 'appropriateness' of this type of testing is her perception of risk, not actual risk, and her perception of disability, not actual disability. It is therefore difficult to justify assigning an age cut-off level using pre-determined population-based features such as a detection rate or maximum cost per affected fetus detected. Despite the acknowledged age-dependent prevalence, from the perspective of the individuals concerned, TMS could be appropriate for as many women under an arbitrary screen-eligible age level as over it.
- **Option 3. No TMS funding:** A decision to withhold government funding for TMS would send a positive message to the Down syndrome & disability rights community. However, although this community would appreciate the broad-level support, they also recognize that TMS would inevitably continue through private funding, and necessarily with much less opportunity for them to influence the educational messages provided to physicians and women. Moreover, from the reviewers' perspective, the privatization of TMS and the subsequent difficulty low-income women and couples would be likely to experience in obtaining TMS risks further marginalization of disadvantaged groups.
- **Option 4. Full co-ordinated TMS funding:** This option received the widest support among the groups interviewed for this review. It was agreed that TMS needs to be provided as part of a co-ordinated prenatal screening service, at any level of utilization and everywhere that it is offered in the province. In this sense, 'full' TMS funding refers to the full cost of providing TMS within a co-ordinated service, independent of the actual utilization level. Use of TMS is likely to increase in response to a complex combination of social and professional expectations and fears.

It should be borne in mind that provincial policy is not in a position either to promote or discourage TMS use. The former could lead to criticism that it is practising eugenics, while the latter could be criticised as denying women their individual rights. Providing TMS as part of a co-ordinated prenatal screening service to various northern and isolated regions of the province will require an active government role to achieve an unprecedented decentralization of pre-natal diagnostic and genetic counselling services currently concentrated in Vancouver.

Based on the conclusions of the review, **Figure 7** indicates the decision-making sequence appropriate to Option selection.

Figure 7: Decision diagram appropriate to Option selection



III. Future Policy Conditions

The foregoing findings and conclusions are derived from the most current information, but their applicability is inevitably finite.

In the era of rapid technological development (for example, with the introduction of maternal serum screening innovations already proven more accurate than TMS,¹²⁷ or alternate prenatal programs with ultrasound as the primary prenatal screening manoeuvre,¹²⁸) it is probable that the parameters of policy-making will change appreciably in the relatively near future. Further ahead, policy challenges are likely to shift again, as questions on the utilization of any given test turn to questions of how many conditions should be tested for. Asche¹²⁹ discusses this in the US context:

“ Given that more than 50 million people in the US population have disabling traits and that prenatal tests may become increasingly available to detect more of them, we are confronting the fact that tests may soon be available for characteristics that we have until now considered inevitable facts of human life, such as heart disease.”

The obligation for public policy actively to support individuals born with disabilities must therefore accompany the growth of prenatal testing and selective abortion. In Asche’s argument,

“... our clinical and policy establishments must communicate that it is as acceptable to live with a disability as it is to live without one and that society will support and appreciate everyone with the inevitable variety of traits ... When our professions can envision such communication and the reality of incorporation and appreciation of people with disabilities, prenatal technology can help people to make decisions without implying that only one decision is right.”¹²⁹

The tension between ethical questions and policy constraints, even considered academically as in **Part V** above, is complex. Decision-makers need to find ‘real-life’ solutions. The suggestion was therefore made in **Chapter 1** of this review that future policy might ideally be developed with the benefit of broad public input.

But policy developed with public support still has practical confines which should be borne in mind. For example, while relatively strong influences operate to limit prenatal testing for socially unacceptable reasons such as sex selection, to ban sex selection and selective abortion of female fetuses may not prevent infanticide, or improve social conditions which discriminate against female children.

Despite the diversity of preferences in our pluralistic society, it is clear that limits (whether based on ethics and rights, or economics) have been set by individuals and committees working for government, and equally clear that this kind of decision-making will continue.

However formulated, it appears from our present perspective that some established policy will be necessary to limit the conditions under which pre-natal testing is either publicly-funded or permissible outside the publicly-funded system. In the shifting sands of modern conditions, policy-makers seeking a firm foundation on which to base policy may usefully be guided by principles of utility and equity, that is, the most good for the greatest number of people.

APPENDICES

APPENDIX A: SYSTEMATIC LITERATURE REVIEW PROTOCOL

The following provides an outline of the specific protocol used to identify recent syntheses of evidence on TMS efficacy, effectiveness and safety, as well as the impact of TMS on geographical populations and costs to the health care system.

Objectives

The objective of the systematic review of the literature was to identify evidence on serum, triple-marker screening (TMS) programs to detect Down syndrome, other rarer chromosomal anomalies and neural tube disorders as well as alternate prenatal screening programs using amniocentesis or chorionic villous sampling. Specifically, this review was designed to identify:

- integrative analyses such as technology assessment reports, systematic reviews, meta-analyses, decision analyses, population impact analyses, utilization analyses, and economic analyses;
- the most recent primary data on test parameters and program effectiveness.

Search strategy

Computerised bibliographic databases searched included the Cochrane Library, Medline and Embase. The equivalent database-specific subject headings were used in the other databases searched. Text words only were used in Current Contents, as no subject headings are applied in this database.

Search terms were as follows:

“Amniocentesis”, “Karyotyping”, “Chorionic Villus Sampling”, “*CVS”, “*Biochemical Screening”, “*Antenatal Screening”, “Prenatal Diagnosis”, “*Prenatal Screening”, “*Prenatal Testing”, “Genetic Screening”, “Mass Screening”, “*Triple Marker Screening”, “*Fetal Abnormalities”, “*Fetal Malformations”, “*Congenital Malformations”, “Congenital Abnormalities”, “*Fetal Loss”, “*Fetal Outcomes”, “Pregnancy Outcomes”, “Miscarriage”, “Abortion—Etiology”, “*Preterm Deliveries”, “*Antenatal Complications”, “Genetic Diseases”, “Fetal Diseases—Diagnosis”, “Fetal Death—Etiology”, “Pregnancy”, “Pregnancy- Trimester-First”, “Pregnancy-Trimester-Second”, “*Infant Mortality”, “Risk Factors”, “Abnormalities—Diagnosis”, “Abnormalities—Ultrasonography”, “Diagnostic Tests, Routine”, “Chromosome—Abnormalities”, “Prenatal Care”, “Down Syndrome”, “Ultrasonography, Prenatal”, “Maternal Age 35 and over”, “Maternal Age”, “Gestational Age”, “alpha-Fetoproteins”, “Gonadotropins, Chorionic”, “Estriol”, “Biological Markers”, “Amniotic Fluid”, “False Positive Reactions”, “Sensitivity and Specificity”, “Cost-Benefit Analysis”, “Chromosome Aberrations”, “Chromosome Abnormalities”, “Trisomy”, “Neural Tube Defects”.

The following Medical Subject Headings (MeSH) were used in the Medline and HealthStar searches:

“Guidelines”; “Clinical Protocols”; “Consensus Development Conferences”; “Physicians’ Practice Patterns”; “Metaanalysis”; “Evidence-based Medicine”; “Decision Making”; “Decision Making, Computer-assisted”; “Technology Assessment, Biomedical”; “Quality Assurance, Health Care”; and “Quality of Health Care”. In addition, searches were limited to the following document types in Medline: “Consensus Development Conference”; “Consensus Development Conference, NIH”; “Guideline”; “Practice Guideline”; and “Metaanalysis”. The following text words (keywords) were used: “clinical, medical, practice or practise, performance, treatment*, planning, or care” and “guideline*, standard*, protocol*, recommendation*, statement*, criteri*, parameter*, policy or policies, option*, intervention* or review*”; “position” “paper* or statement*”; “guideline*”; “flowchart* or flow chart*”; “consensus”; “management” “plan or plans”; “practice or practise pattern*”; “clinical or medical” “necessit* or indicator*”; “reference standard*”; “appropriate” “care or evaluat*”; “clinical or critical” “pathway*”; “metaanalys* or meta analys* or overview*”; “evidence-based”; “expert panel*”; “care map*”; “algorithm*”; “systematic or critical” “review* or appraisal*”; “cochrane” “collaboration or collaborative”; “prediction* or decision*” “rule*”; “technology assess*”; “quality of care”; “quality” “assurance or standard*”; “datta”; “diagnostic therapeutic technology”.

References were obtained from citations identified in published reviews, clinical trials, conference abstracts and bibliographies.

Selection criteria

All integrative analyses that met one or more of the following criteria:

- reported on programs for identifying Down syndrome, other rarer chromosomal abnormalities and open neural tube defects;
- reported on programs which use any of the following prenatal screening tests: triple-marker, alpha fetoprotein, chorionic villus sampling, amniocentesis;
- reported at least one outcome measure relating to the following parameters:
 - ◊ fetal loss
 - ◊ abortion
 - ◊ detection rates for Down syndrome, other rarer chromosomal abnormalities or open neural-tube defects
 - ◊ test parameters, i.e. sensitivity, specificity, false-positives and negatives
- reported on costs, utilization rates;
- in participants of any age group;
- with a minimum observational period of two years.

Exclusion criteria

Research was excluded that:

- was conducted on animals;
- reported physiological or laboratory parameters.

Fugitive Search

A fugitive search was conducted to identify current and ongoing projects in the area of TMS. The following databases and sources were searched using the terminology outlined in the search strategy:

OCLC (Online Computer Library Center) Article1st Database

The OCLC provides references to over 13, 000 periodicals in the area of science, technology, medicine, social science, business, the humanities, and popular culture. It is offered through the University of British Columbia.

HTA Database (INAHTA Member Projects)

The HTA database contains information on health-care technology assessments and is produced in collaboration with the secretariat of the International Association of Health Technology Assessment (INAHTA).

BCOHTA In-House Library Catalogue

The BCOHTA Library Catalogue contains over 9,000 items including books, reports, newsletters, industry reports, policy statements, conference proceedings and article reprints.

TRIP (Turning Research Into Practice) Database

This database is a collection of evidence-based reports, systematic reviews and meta-analyses. It is maintained by the NHS Gwent Health Authority in the United Kingdom.

APPENDIX B: SUPPORT SERVICES IN BC

Among the organizations in BC, the BC Down Syndrome Research Foundation (DSRF) and the Lower Mainland Down Syndrome Society (LMDSS) provide services for families who are caring for children and adults with Down syndrome, and support services, education and networking to the Down syndrome community. DSRF is research based with a well-developed resource centre and active research arm, whereas the LMDSS is more support-service oriented. Policy Statements by each group are provided in **Chapter 11** of the review.

1. The Down Syndrome Research Foundation and Resource Centre (DSRF)

3580 Slocan St. Vancouver BC V5M 3E8

(604) 431-9694

Prior to the establishment of the Centre, concerned parents and professionals had articulated a need for medical services and educational opportunities for families and their children with Down syndrome, and one group was actively working for a clinic in BC. In 1993, a questionnaire was circulated to BC families by Sunny Hill Health Centre and the Down syndrome community to find out what co-ordinated services were required. The results demonstrated access to information about Down syndrome was extremely limited, and it was decided to develop a web page and Internet communications links with international groups.

With a view to basing the CDSS in BC, the executive director had previously moved from Alberta to open an office in Surrey. In the winter of 1994, the CDSS Board decided the main office should return to Calgary.

New beginnings were therefore envisaged in BC so as to provide access to clear, co-ordinated information about the latest research and recommended programs for children and adults with Down syndrome. Building upon this premise, a joint initiative between local parent groups in BC and Sunny Hill Health Centre for Children and supported by Simon Fraser University, resulted in the creation of DSRF, registered under the BC Society Act in March 1995. DSRF and its Resource Centre opened a research office on May 1st 1995 at the University.

With considerable volunteer support, a permanent resource centre for families and professionals was set up in a trailer on the grounds of Sunny Hill Health Centre in September 1995. A reference library was incorporated at the centre, as a source of information on Down syndrome. Donations provided the means to research several projects, and to offer educational conferences and video-conferences to assist people with Down syndrome and their families. The web page and Internet connection were established with the CDSS, thereby developing a national affiliation with Toronto and Calgary. Rather than adopting a role in advocacy, the focus developed along research and education lines.

In the early stages, only two people worked at the Centre, paid part-time and volunteering as needed. A part-time librarian was replaced by a part-time web-master, or 'virtual librarian', with the support of another person overseeing library resources. DSRF started educational programs through conferences and video conferences. A trial summer school program was undertaken, while the most ambitious and successful initiative to date has been the 1st Biennial Scientific Conference held in Vancouver in April 1998, which brought together international professionals and experts in Down syndrome, as well as local participants. The conference proceedings were published.

In the first nine months of the DSRF, the executive director raised \$100,000, and by the end of the following year that figure had “more than doubled, ... then the following year ... we raised \$400,000 plus ... and last year it was somewhere between \$500,000 and \$600,000” (interview with Executive Director March 22nd 1999). This funding has supported specific projects, such as the Adult Employment Program, and the Teen Social Program, which led to a summer school.

These significant projects led in turn to support to the Foundation from the financial community. Three companies in 1999 have each given \$20,000 to have their names on the logo. Among the most imaginative fund-raising events have been stock-market dinners, which have taken place in Vancouver, Toronto and Calgary. By 1999, the society was financially self-sustaining, with corporate financing, a strongly developing research arm, and a resource centre for the Down syndrome community.

Currently, funding has been directed towards employing a research development co-ordinator and to developing a list serve concentrating on reviewing Canadian research papers. It is hoped that this may lead to a research journal. The broad aim is to disseminate information about Canadian research both nationally and internationally. One of the purposes of the 1st Biennial Conference on Down Syndrome was to try to give Canadian research a higher profile. In time, DSRF hopes to fund and support research of its own, perhaps incorporating a student position. The Foundation recognizes that research has continually to be evaluated, if it is to receive continuing funding. The Executive Director maintains the importance of self-generated funds:

“I don’t think the government is going to be able to fund everything we want to do. And I think that more and more things are going to have to be self-supporting ... whether it is fee for service, or people doing things to raise funds to support it ... I don’t anticipate the running of the new building being dependent upon government funding, because I think we would be wasting out time if we did ... Whereas if you start getting people aware that ... this is a service which brings benefits, but it costs this much, they start contributing.” (interview with Executive Director March 22nd 1999)

In 1999, DSRF received permission to purchase property and build new premises. With present funding, it is hoped that this goal may be completed in the next few years. In addition to housing administrative offices, a resource centre and other facilities, the new building will facilitate research into Down syndrome. It is anticipated that it will include a laboratory established by Simon Fraser University, Department of Kinesiology.

Foundation response to maternal serum screening

As part of the ongoing dialogue raised by Lee and Sroka’s research initiatives, which have been supported and funded by DSRC, the Foundation formulated and published a statement about maternal serum screening (**Chapter 11** above). It raised several concerns about maternal serum screening in regard to the ways in which it is being used and to the lack of information for those affected by the test. The statement cautions that balanced information both about the predictive value of the test and about Down syndrome should be made available, ensuring that positive aspects of having a child with Down syndrome should be balanced against the negative impact of testing. The Foundation takes the position that the primary goal of prenatal testing should be to improve health care, not to reduce the birth prevalence of Down syndrome:

“If the test is only used to identify and abort fetuses with Down syndrome, we feel it will adversely affect the quality of life for people with Down syndrome in our community, since there is the assumption that Down syndrome should be eradicated”
(Position statement)

2. The Lower Mainland Down Syndrome Society (LMDSS)

14740 - 89A Ave. Surrey BC V3R 7Z9

(604) 930-1113

The Lower Mainland Down Syndrome Society (LMDSS), formerly affiliated to the Canadian Down Syndrome Society, provides support, information, network opportunities and development in issues of concern for individuals with Down syndrome, their families and professionals working with them. The mission statement of the LMDSS is to facilitate positive change so that individuals with Down syndrome become full members of society.

LMDSS was established in 1989 and currently has over two hundred members comprised of parents, self-advocates and professionals. The Society provides accurate and current information about Down syndrome, meetings with professional guest speakers, social family events, quarterly newsletters, new parent packages, resource referrals, family support through networking needs and concerns, groups advocacy, information on research projects and cross-cultural information. It maintains a resource library on Down syndrome. One of its main functions is to disseminate information packages in order to increase awareness about Down syndrome. The Society is self-sustaining through membership fees, independent fund-raising efforts and donations.

Based on interview data from an active member of CDSS, two issues were identified, religious affiliation and adoption, which have been poorly explored to date in relation to the use of triple-marker screening. They have a direct impact on many women's attitude towards screening. Certain religious convictions preclude the uptake of triple-marker testing or an abortion to terminate a pregnancy when a fetus with Down syndrome has been identified. Often, if one or other expectant parent feels abortion is morally wrong and therefore has no intention of terminating the pregnancy, there may be no wish to engage in the process of screening and diagnosis. This does not mean that the couple might not consider adoption of their infant on discovering the baby is disabled. Other couples, however, might consider using the screen in order to determine the status of the fetus and in the event of a positive screen, prepare to give birth to a disabled child and to make the necessary arrangements to care for their child. Again, this may provide the time necessary to consider and arrange for an adoption.

Another concern for the Society has been the effect of the information bulletin in the BC College of Physicians and Surgeons' *College Quarterly*¹¹⁰ (see **Chapter 8**), and its emphasis on the right of women to be informed about and to obtain triple-marker screening as a standard of prenatal care. Since all physicians in BC are members of the College and receive the bulletin, the Society feels that physicians are being pressured to provide screening, notwithstanding the absence of any provincial guideline. In their view the College's stance equates certain religious or ethical convictions with poor patient management. It is arguably a short step from withholding a technology which becomes routine just because it is available, to physicians being held liable for 'wrongful births'. The Ontario study¹⁰⁹ of health care providers and the medico-legal risks of maternal serum screening concluded that it is most important that providers be well-educated as to the complexities, and that in interactions with patients, there is clear, effective communication about them.

3. Spina Bifida Association of BC
9460 - 140th St. Surrey BC V3V 5Z4
(604) 521-2454

The Spina Bifida Association of BC is a support group for individuals with spina bifida or hydrocephalus and their families. The structure of the Association comprises a membership of approximately 400 parents, individuals and caregivers, with a volunteer board of directors. One half-time staff member undertakes office support.

The Association provides information and advice on spina bifida conditions, and on the care of people with spina bifida. It is presently assisting the national association with the preparation of a prenatal kit aimed at supporting expectant families. Currently available are new parent kits, an educator's guide, a teen kit, and folic acid information. The Association is also able to offer financial assistance for equipment, and has some limited funding available for research support.

Prenatal screening

The Association has not issued any public statement regarding prenatal screening or triple-marker screening. Its current position is that individuals receiving a screening result indicating a fetus with a neural tube disorder are faced with a personal decision, and that resources should therefore be available to enable them to make informed choices.

APPENDIX C: MARKERS, MEASUREMENT, AND ANALYSIS

The data reproduced here and elsewhere in this review has been provided by the GEM staff and biochemistry experts at the BC Children's and Women's hospital, whose generous assistance is gratefully acknowledged. The information supplied has ensured this review is not wholly dependent on published literature.

This Appendix provides details of laboratory activities in BC. It includes descriptions of the laboratory components of TMS, the biochemical markers sampled in maternal serum and how the sample levels are analysed to determine an individual woman's risk profile.

1) Biochemical testing of maternal serum

The triple serum markers

Alpha-fetoprotein (AFP)

Alpha-fetoprotein is a glycoprotein with a molecular weight similar to albumin (67,000 - 70,000) and is synthesised by both the fetal liver and yolk sack. The function of AFP is not fully understood, although it seems to act as the precursor form of albumin, the most common, osmotically-active circulating protein. AFP levels increase with open (non-skin covered) neural tube disorders because fetal plasma in the area of the open disorder comes in close contact with amniotic fluid and transfer can occur. Maternal serum AFP levels are optimally measured between 15-20 weeks' gestation. During this time, AFP levels increase by approximately 12%-15% per week.¹³⁰

AFP levels rise most dramatically with anencephaly (approximately 50% of neural tube disorders) and less with open spina bifida. In 1984, researchers noted that low AFP levels were associated with Down syndrome.¹³¹

Human chorionic gonadotropin (hCG)

Human chorionic gonadotropin (hCG) is a glycoprotein hormone made from two protein subunits, the alpha and beta chains. Antibodies directed at the β -chain are used in assays of hCG, which is secreted by the chorion and placenta. It acts to maintain the corpus luteum necessary for the production of both progesterone and estrogen. Maternal serum hCG peaks at approximately 10 weeks' gestation. In early mid-trimester hCG levels fall, reaching the relatively low level maintained for the duration of pregnancy.

Bogart et al first noted that pregnancies with a fetus with Down syndrome have approximately twice the level of hCG that is found in non-affected pregnancies between 15-18 weeks' gestation.¹³² Because of the extent of the separation between affected and unaffected populations, hCG is to date the single best marker for population screening for Down syndrome.

Unconjugated estriol (uE3)

Unconjugated estriol (uE3) is produced by a complex fetal metabolic pathway that includes adrenal tissue, liver and finally the placenta. Essentially all the maternal unconjugated estriol is of fetal origin. Maternal serum uE3 is rising at a rate of about 20% per week during the second trimester.

In 1988, Canick et al reported that low uE3 was associated with Down syndrome. Affected pregnancies were at 0.79 times the unaffected control mean values.¹³³

Triple-marker samples

Triple-marker samples can be gathered at any public or private laboratory in the province using standard serum collection techniques and storage vials.

Samples are normally transported by regular courier services used by hospitals and private laboratories. In some areas of the province however, there are concerns about unpredictable delays in the regular system. One community, for example, uses Greyhound bus for transmitting samples. Another community freezes samples and ships them once a week.

Tubes occasionally break or leak in transport. Based on test cancellation reports at BC Children's hospital between March 31 1998 and April 1 1999, sample recollection was requested in the following cases:

Broken in transit	5
Leaking in transit	13
Leaked / broken in centrifuge	10
Delay in receipt / questionable condition	9
Insufficient sample	1
Requisitions without samples	2

In the case of a broken tube or otherwise compromised sample, the laboratory will telephone a request for a repeat sample. Correction for missing samples is dependent on the error being noticed, and a check by telephone of the laboratory record of shipment. Another sample may then be gathered. The number of samples totally lost (i.e. no requisition or sample) is unknown.

Quality assurance for triple-marker screening

Quality assessment, quality control

Quality assessment and quality control, for laboratory aspects of TMS, depend on two factors:

- 1) Calculation of median values for each marker for the BC population;
- 2) Reliable measurement of individual serum samples.

Calculation of median values for each marker for each week of gestation (weeks 15-20) require a minimum of 100 samples from women of Euro-American descent, and unaffected singleton pregnancies. Individual risk estimates, and ultimately individual patient-labelling as over or under the risk cut-off level of 1:365, depend on each of these medians.

TMS performance, measured as the false-positive and detection rates, depends directly on these median estimates. Several uE3 assays have, for example, been in use in BC. The original uE3 assay was replaced in November 1996, when uE3 became based on medians from local frozen samples.

In April 1997, the uE3 medians were recalculated based on actual patient data from the 5-month period. During the transition phase, the median was slightly higher than past levels. The analysis used 0.92-0.96 rather than 1.0 multiple of the median as the risk cut-off. As a result, it is possible that more women at that time were labelled as initial 'test-positive' owing to uE3 levels and offered amniocentesis, than in subsequent years.

The reliability of serum marker testing in BC is also assured through regular laboratory accreditation and sample testing. For example, the laboratory subscribes to an FBC/CAP maternal screening survey. The survey provides unknown serum to numerous laboratories for analysis and risk estimation. The results are then compiled and the local findings of marker levels are compared to other laboratories included in the system.

Quality assurance protocols

Setting

Triple-marker screening is run in the Pediatric and Obstetric Laboratory located in the BC Children's and Women's Hospital in Vancouver to whom the authors are indebted for the following data. This clinical diagnostic laboratory is subject to accreditation by the BC Diagnostic Accreditation Program for Clinical Laboratories. Quality assurance procedures are in accordance with their general guidelines, with some features specific to the screening program.

Instrumentation

Triple-marker screens are run on the Autodelphia (Wallac Oy, Finland). A single analyzer handles the current workload. Downtimes for preventative maintenance are currently scheduled between assays. As workload increases, a second analyzer is likely to be required to accommodate both scheduled and unexpected downtime.

Quality assurance related to instrumentation includes maintaining an up-to-date method manual, instrument problem and troubleshooting logs, and maintenance logs.

Reagents

General quality assurance for reagents includes documenting condition on receipt, ensuring good reagent dating, appropriate storage and use, documenting refrigerator temperatures, monitoring calibration curve-drift within and between reagent lots, and running quality control samples.

Internal (daily) quality control

Assay performance is monitored on a day-to-day basis using quality control materials. Three quality control (QC) materials are used for each test, to monitor test performance at three levels within the analytical range. Each material is run twice in one assay (total 6 controls per assay). Controls are placed at the beginning, middle and end of each plate. This allows monitoring of within-assay variability, as well as between-assay variability calculated from results over time.

Two of the controls are made from large pools of serum from pregnant women. One pool has levels consistent with about 15-16 weeks' gestation, the other with 18-19 weeks' gestation. The third control for each assay is a commercially available lyophilized material (one for uE3, another for AFP and hCG). (**Table 7**)

Mean and standard deviation for QC data are set for each test on each material based on historical performance according to usual laboratory methods. During a run, QC results are compared with the allowable ranges set in the analyzer. Results greater than 2SD from the mean are reviewed to determine whether the run can be reported. Trends in internal QC data (Levy-Jennings charts) are reviewed monthly and also with reagent lot changes or if there are outliers.

Table 7: Assay performance on quality control materials (target mean (CV%) and a recent actual mean (CV%)):

Quality Control	Target/Actual	AFP ug/L	uE3 nmol/L	hCG kIU/L
Serum pool 1	Target	35.9 (1.3%)	2.47 (7.7%)	36.4 (2.5%)
	Actual	36.1 (1.3%)	2.69 (7.7%)	36.3 (2.1%)
Serum pool 2	Target	53.2 (1.2%)	4.52 (6.4%)	23.9 (3.5%)
	Actual	54.0 (1.7%)	4.86 (5.7%)	23.6 (2.7%)
Lyophilized	Target	228 (5.3%)	4.64 (6.0%)	193 (4.7%)
	Actual	230 (2.2%)	4.87 (4.6%)	186 (2.8%)

External proficiency testing

External proficiency testing is a way to compare laboratory performance with other laboratories undertaking testing. Samples with unknown results are sent from a commercial provider and the Pediatric and Obstetric Laboratory results are submitted back to them. A report is received that compares our results with those of other laboratories. Unacceptable results (usually more than 2 SD from the target mean) are followed up, and processes modified, as applicable, to improve performance.

The laboratory participates in three external proficiency testing programs:

College of American Pathologists (CAP)

Foundation for Blood Research Maternal Screening Program

Tests AFP, hCG and uE3 in serum, AFP in amniotic fluid.

Report assesses analytical performance (analyte results), clerical transcription accuracy, validity of medians (MOMs compared), risk calculation, interpretation and follow-up protocols. Patterns of practice questions are often included. Reports often contain an educational article.

Frequency: 3 sets (5 sera and 2 amniotic fluids each set) per year.

Murex Immunoassay Program

Tests AFP, hCG, uE3 in lyophilized serum.

Primarily assesses analytical performance. Same samples recur on a random basis through the cycle to assess precision.

Frequency: 1 sample every two weeks.

Ontario LPTP Maternal Serum Screening Program

Tests AFP, hCG, uE3 in serum.

Report assesses analytical performance (analyte results), clerical transcription accuracy, risk calculation, interpretation. Patterns of practice surveys are sent periodically. Some samples recur, often with modified clinical information, to assess precision.

Program was designed primarily for Ontario MSS labs: only 8 labs total participate.

Frequency: 5 sets (4 samples) per year.

Other quality assurance parameters

Mean multiple of the median (MOM) is monitored monthly. Deviation from a mean MOM of 1.0 may signify a change in method since the gestation-specific medians were set. If the mean MOM drifts significantly and troubleshooting does not identify and correct the problem, consideration is given to resetting the medians.

Screen positive rate is monitored monthly. It assesses whether changes such as MOM drift have a significant effect on interpretations.

Turn-around time (TAT) is monitored during sign-out. Delayed reports are faxed. Computerized TAT reports are not currently available. The goal is to have results signed within 1 week of collection.

Triple-marker measurement

All serum samples collected in BC for Triple-Marker testing are analysed in one biochemistry laboratory, the Pediatric and Obstetric Laboratory, located in the BC Children's and Women's Hospital in Vancouver.

The Children's Hospital laboratory measures the serum levels of AFP, uE, and total hCG using automated analysers. The analyser is calibrated every month using standardized samples to prevent assay drift.

The software program at Children's and Women's Hospital laboratory, known as AFP Expert (Benetech Medical Systems, Toronto) includes a Median Calculation utility that allows calculation of median values. It also allows extrapolation from known serum values to estimate values at the extreme gestational ages (20 weeks) when serum samples are much less commonly obtained.

Serum marker levels are reported using both mass units (ug/L) and multiples of the median values for the local population. The median value is defined as the value which divides a population in half.

The local median values are established for each marker, for each week (from 15-20 weeks) of gestation, from a minimum of one hundred local samples. The median value data must be from a homogeneous population of unaffected 'Caucasian', non-diabetic patients with singleton pregnancies.

A patient's serum level is divided by the median to establish her level as 'multiples of the median.' Multiples of the median units, as opposed to mean values in mass units, are used for reporting because:

- i) fewer observations are required to establish a median, compared to a normal range based on the mean and standard deviation;
- ii) the normal limits or screening cut-off can be described with a minimum of numbers that apply to all circumstances;
- iii) the results of different laboratories can be pooled, regardless of the source of standard, assay methodology or variance in precision.¹³⁴

Analysis of triple-marker measurements

The serum marker measurements are analysed using AFP Expert V5.00. The calculation of Down syndrome risk used in AFP Expert V5.00 explicitly follows from the work of Wald et al¹³⁵ and Cuckle.¹³¹

In 1988, Wald et al established that log values of the three serum markers follow Gaussian curves ('normal' bell-shaped curves) for affected and unaffected populations. It was therefore possible to use the mean and standard deviations that describe these curves to establish likelihood ratios for each marker.

Likelihood ratios are calculated from combining the separate likelihoods of a patient being part of the affected and unaffected patient populations. The separate likelihoods depend on where the individual's serum marker value (expressed as multiples of the mean) is placed relative to the

median value. In other words, the likelihood ratio is the height of one curve (i.e. affected) divided by the other curve (unaffected) at the patient's multiple of the mean value. A likelihood ratio forms the basis of the probability, or risk, estimate for each patient.

Down syndrome risk calculation

Down syndrome risk is calculated by multiplying the likelihood ratios for each marker, at a certain gestational age, by a women's prior risk. Prior risk depends on maternal age. Maternal age is estimated in days from the date of the start of the last menstrual period. Although gestational age is also estimated in terms of the number of completed weeks, this method is not used for risk estimates based on multiple serum markers.

Because the three markers are not completely independent assessments of risk, correlation coefficients must be calculated between each pair of markers. The correlation coefficients, originally published by Wald et al,¹³⁵ are used to adjust the final risk estimate. The actual calculation of individual risk involves complex mathematics not of relevance here. The correlation coefficients have been validated by three different research groups with the largest number of Down syndrome cases, all of whom considered all of the serum parameters in the same data set.¹³⁶

The risk calculation used at BC Children's Hospital has the advantage of building on risk assessments for open spina bifida, and it can be adapted to include or exclude specific markers. It also has been subjected to empirical validation.¹³⁶

The laboratory reports risk at term, not at the time of sample collection. The standard projection is that approximately 20% of Down syndrome pregnancies are spontaneously lost between the second trimester and term (48% between the first trimester and term).¹³⁷

Correction factors

A patient's risk estimate is based on gestational age, serum marker levels and the selected median. In addition, risk estimate is adjusted according to weight, whether the patient is of African-American origin, or if she has diabetes mellitus.

Weight adjustment

The effect of maternal weight on TMS performance has been shown to be slight.^{138,139} Nevertheless, the overall volume of circulating maternal plasma affects the concentration of the circulating markers, which in turn reduces the multiple of the mean levels for all three markers. However, while the reduced circulating levels will decrease the risk based on AFP and uE3, it will increase the risk estimate based on hCG. The converse applies in small women. Weight correction, therefore, is more important if only two markers are used, particularly for AFP and uE3.

The AFP Expert program used at BC Children's hospital applies minor weight correction factors based on the results of Palomaki.¹³⁹

African-American descent and diabetes mellitus

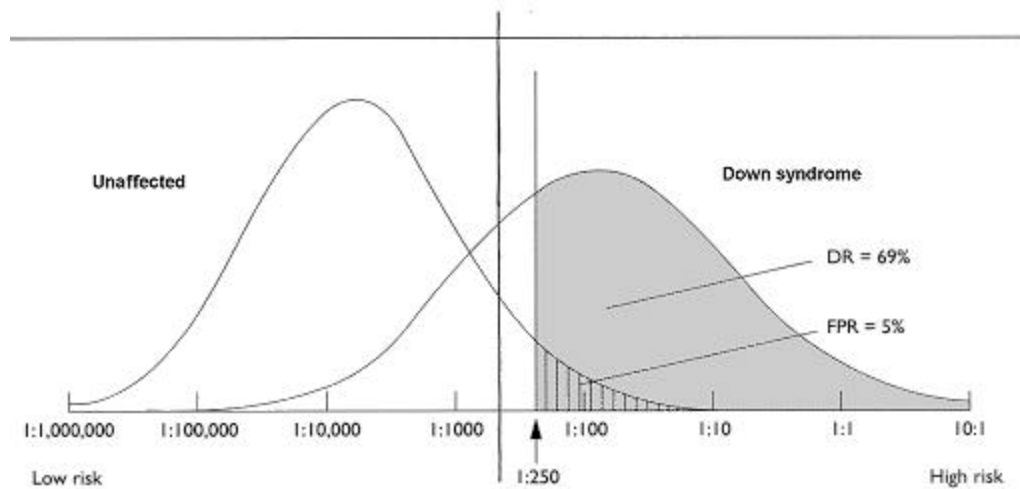
Maternal serum and amniotic fluid AFP levels have been shown to be higher in women of African-American origin.¹⁴⁰

Women with insulin-dependent diabetes mellitus are known to have lower AFP medians than the non-diabetic population.¹⁴¹

Median correction factors which are adjustable are built into the AFP Expert program. The correction factor is 1.10 for women of African-American descent and 0.80 for women with diabetes mellitus.

Figure 8 after Wald et al,¹⁴² shows the distribution of Down syndrome pregnancy in affected and unaffected pregnancies.

Figure 8: Distribution of the risk of having a Down syndrome pregnancy in affected and unaffected pregnancies using maternal age with AfP, uE₃ and hCG gestational age estimated by scan and marker levels adjusted for maternal weight) (DR, detection rate; FPR, false-positive rate). (After Wald et al¹⁴²)*



Reporting

The biochemistry laboratory at BC Children's Hospital processes serum samples and reports risk estimates to physicians usually within 2 - 3 days and in a maximum of 1 week.

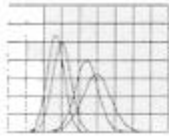
Typical positive and negative results reports are given in **Figures 9 & 10**.

If the initial screen result is positive, the physician is telephoned. If the physician is unavailable, the laboratory staff confirms with the doctor's office whether a report can be sent by fax. Physicians contacted by telephone are also asked if they will accept a faxed report, and most do.

Negative reports are generally transmitted by inter-hospital or regular mail depending on office location. Negative reports may, if requested, be phoned or faxed. Reports significantly delayed by an incomplete laboratory requisition or shipping problems may be faxed or phoned without a specific request. Mailed reports follow all faxed or telephoned reports.

* Reproduced by permission of the Controller of Her Majesty's Stationery Office

Figure 9: Sample TMS negative report



B.C.'S CHILDREN'S and WOMEN'S HOSPITAL
GEM (Genes, Elements, Metabolism) Program
Department of Pathology

MATERNAL SERUM PRENATAL SCREENING

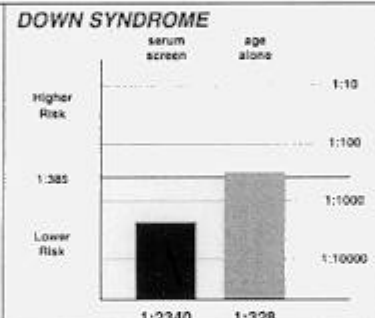
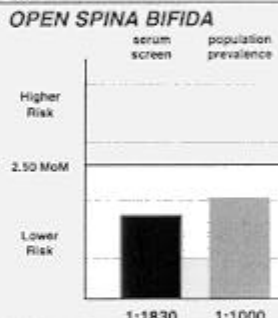
PATIENT INFORMATION
 NAME: - - - - -
 PATIENT CODE: MS - - - - -
 DOB: - - - - -
 LMP: 16.10.98
 LOCATION: LPTP - - - - -
 PHYSICIAN: (not specified)

Physician

CLINICAL INFORMATION
 GESTATIONAL AGE: 15 weeks 3 days
 estimated by LMP date
 MATERNAL AGE AT TERM: 36.2 years
 MATERNAL WEIGHT: 60.0 kg
 MATERNAL RACE: Caucasian
 MATERNAL IDDM: No
 GESTATION: Singleton
 Initial sample

SPECIMEN
 SPECIMEN CODE: S788235
 COLLECTION DATE: 01.02.99

RECEIVED: 02.02.99
 REFERRING LAB #: 99R-128511
 REPORTED: 04.02.99

CLINICAL RESULTS			DOWN SYNDROME		OPEN SPINA BIFIDA	
	Actual Value	MoM	serum screen	age alone	serum screen	population prevalence
AFP	56.6 ug/L	1.65				
uE3	2.59 nmol/L	1.18				
hCG	51.4 kIU/L	1.42				
Risk Assessment (at term)						
OSB:		1:1830				
Down Syndrome:		1:2340				
Age Alone:		1:328				
Equivalent Age Risk:		< 15.0				

Interpretation*

DOWN SYNDROME

Screen Negative

The risk of Down syndrome is LESS than the screening cut-off. The serum screen has indicated a SUBSTANTIALLY REDUCED risk from that based on maternal age alone, sufficient to place this patient BELOW the screening cut-off. Accuracy of gestational age dating is required for valid interpretation. A negative screening result does not exclude Down Syndrome. It indicates that the risk is not high.

OPEN SPINA BIFIDA

Screen Negative

The maternal serum AFP result is NOT elevated for a pregnancy of this gestational age. The risk of an open neural tube defect is less than the screening cut-off. Accurate gestational age dating is required for valid interpretation.

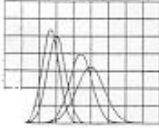
Dr. C. Halstead, MD, FRCPC (875-2918)

Dr. T. Mock, PhD, FCACB (875-2254)

* Accurate estimation of gestational age is essential for valid interpretation.

Reprinted 11:03 am 24 09 99

Figure 10: Sample TMS positive report



B.C.'S CHILDREN'S and WOMEN'S HOSPITAL
GEM (Genes, Elements, Metabolism) Program
 Department of Pathology

MATERNAL SERUM PRENATAL SCREENING

8.8 mL ALIQUOT Reprint
 LPTP, S9811-1 MSSP
 -CH 70/01/24 F
 CTL COMPLEX CHEMISTRY
 Sp-000655214 98/11/02
 98R-353746 (C)
 RMQ MHQ UED

FAXED
 Nov 12 1998

PATIENT INFORMATION
 NAME: [REDACTED]
 PATIENT CODE: [REDACTED]
 DOB: [REDACTED]
 LMP: [REDACTED]
 LOCATION: LPTP
 PHYSICIAN: UNKNOWN

UNKNOWN

SPECIMEN
 SPECIMEN CODE: S855214
 COLLECTION DATE: 02.11.98

RECEIVED: 03.11.98
 REFERRING LAB #: 98R-353746
 REPORTED: 04.11.98

CLINICAL INFORMATION
 GESTATIONAL AGE: 17 weeks 1 day
 estimated by LMP date
 MATERNAL AGE AT TERM: 29.2 years
 MATERNAL WEIGHT: 156 lbs.
 MATERNAL RACE: Caucasian
 MATERNAL IDDM: No
 GESTATION: Singleton
 Initial sample

CLINICAL RESULTS			DOWN SYNDROME		OPEN SPINA BIFIDA	
	Actual Value	MoM	serum screen	age alone	serum screen	population prevalence
AFP	536.5 ug/L	13.65	~ 1:50000	1:1050	Higher Risk	Higher Risk
uE3	1.08 nmol/L	0.35			2.50 MoM	
hCG	10.3 kIU/L	0.45			Lower Risk	Lower Risk
Risk Assessment (at term)						
OSB:		> 1:5				
Down Syndrome:		~ 1:50000				
Age Alone:		1:1050				
Equivalent Age Risk:		< 15.0				
Trisomy 18:		~ 1:80				

Interpretation*

DOWN SYNDROME

If ultrasound dating changes gestational age by >7 days, please call (604) 875-2331 for reinterpretation.

Screen Negative

The risk of Down syndrome is LESS than the screening cut-off. The serum screen has indicated a substantially REDUCED risk compared to that based on maternal age alone. Accuracy of gestational age dating is essential for valid interpretation. A negative screen result does not exclude Down Syndrome but indicates that the risk is low.

OPEN SPINA BIFIDA

SCREEN POSITIVE

The maternal serum AFP result is EXCEPTIONALLY HIGH, indicating a substantially elevated risk of an open neural tube defect. A LEVEL II ultrasound combined with AMNIOCENTESIS is suggested, followed by the definitive tests of amniotic fluid AFP concentration and acetylcholinesterase (AChE) typing.

TRISOMY 18

SCREEN POSITIVE

Concurrent LOW levels of serum AFP, estriol and hCG indicate an increased risk of TRISOMY-18. Counselling for amniocentesis is suggested. (Extremely low hCG levels could indicate non-pregnancy.)

Dr. C. BALION, PhD (875-2254)

Dr. J. TAI, PhD (875-2457)

* Accurate estimation of gestational age is essential for valid interpretation.

Printed 1:58 pm, 04.11.98

Trisomy 18

Trisomy 18, although considered a generally fatal malformation, is screened for along with Down syndrome, in part because it has no additional testing or analysis requirements other than an addition to the computer software program. Detection is justified for women since it may avoid the risk of unnecessary cesarean section operations in undiagnosed cases.

Using fixed cut-off rates, between 40% and 60% of affected fetuses can be identified. Maternal weight and ethnic origin are not relevant. BC reports use a risk cut-off method, with 1:100 and a false-positive rate of 0.2%.

Open neural tube disorders

Maternal serum AFP measurements taken between 15-18 weeks' gestation are also used to screen for open neural tube defects. Closed, or skin covered defects, which constitute 5%-10% of all neural tube disorders, will not be detected. Open neural tube disorders consist of anencephaly and spina bifida in about equal percentage.

Anencephaly, which results in a seven-fold rise in the median maternal serum AFP level, has little overlap with unaffected pregnancies, and therefore is not considered part of the routine screening parameters. Instead, neural tube disorder screening parameters, such as false-positive and detection rates are discussed in terms of open spina bifida cases.

As with other markers, the most common causes of elevated AFP are not the target conditions of neural tube disorders. Reasons can include under-estimation of gestational age, low maternal weight, ethnic origin, diabetes mellitus, multiple gestation, fetal blood contamination of amniocentesis sample, and other rarer fetal conditions such as gastroschisis that result in transfer of normal fetal AFP to the amniotic fluid.

Suppression of AFP is commonly the result of improper gestational dating. It can also be suppressed by the presence of Down syndrome.

The BC program to detect open spina bifida utilizes the same AFP expert software program, and assigns an initial, screen-positive cut-off level of 2.5 multiples of the median. With an assumed prevalence level of 1:1000 for a 'Caucasian population', the initial-positive rate is 2% and the detection rate is 70%-75%.

The initial screen positive rate for open spina bifida adds to the overall screen-positive rate for TMS. However, the actual amount of that increase is unknown, primarily because the more severe forms of open spina bifida and virtually all cases of anencephaly are detected by dating ultrasound, which often precedes serum screening. In fact, in BC, ultrasound detection of neural tube disorders now rivals that of serum AFP testing.

2) Dating ultrasound

Ultrasound scan estimates of gestational age, as against a women's own assessment, results in a narrower statistical range of serum markers in a TMS test population. This is represented statistically as a smaller standard deviation of the serum markers. The effect is greatest for markers whose concentrations change most with gestational age (notably uE3).¹⁴³

Although estimates of the effects of ultrasound dates are not possible from actual BC data, it is reasonable to assume the effect would be similar to that found in the world literature. Wald has shown the effect of ultrasound dates on screening test performance.¹⁴⁴ TMS detection rates rise from 59% without dating ultrasound, to 69% with these scans.

Cytogenetic laboratories

Cytogenetic analysis in BC is conducted at four laboratories: two in Vancouver (the Vancouver Hospital and Health Sciences Centre, and BC Children's and Women's Hospital); one in New Westminster (the Royal Columbian Hospital); and one in Victoria (the Victoria General Hospital).

The Director of the cytogenetics laboratory at BC Children's and Women's hospital, who was interviewed for this review, describes all four cytogenetic laboratories as following identical procedures to determine fetal karotype. In addition, she maintained that because of rapid improvements in computer imaging and enhancement programs, the capacity of the laboratories could expand to deal with the increased number of samples from a full provincial TMS program.

A randomized, controlled trial and several cohort studies have shown analysis of fetal cells obtained by amniocentesis to be an accurate and reliable method of prenatal diagnosis of Down syndrome and other chromosomal abnormalities, specifically trisomy 18.^{41,145,146}

APPENDIX D: EFFECTIVENESS OF TMS

This Appendix summarizes the clinical effectiveness evidence for TMS. It aims to address the clinical concerns mainly of physicians and counsellors, whose primary anxiety is whether TMS is able to provide pregnant women with sufficiently accurate data about the fetus to allow informed choices on termination of pregnancy or preparation for a child with trisomy or open spina bifida.

TMS effectiveness in terms of social and economic costs, as judged by health economists and policy analysts is examined in **Part VI**. The systematic literature review protocol used to identify the relevant literature is detailed in **Appendix A**.

Screening test performance

Screening test performance is assessed by two measurements:

1. the **detection rate** (the proportion of affected pregnancies with 'positive' results); and
2. the **false-positive rate** (the proportion of unaffected pregnancies with 'positive' results).

Before discussing TMS screening test performance data, a brief outline of TMS statistical models is presented to assist readers unfamiliar with this type of risk information and how it is provided to women during pregnancy.

Statistical models

TMS is used to provide individual woman with a risk estimate for carrying a fetus with Down syndrome. Because it is impractical to have sufficiently large databases to gather all the possible combinations of the various markers empirically, the risk estimate is based on a statistical model.¹³⁵ A known population is used to determine statistical parameters of several markers. These parameters are then combined with the age distribution of pregnancies, together with the age-specific risk for Down syndrome in order to develop a hypothetical population of affected and unaffected women.

After Wald et al,¹³⁵ the following features are considered necessary for valid risk-screening based on a model:

1. The statistical model used must be clearly specified.
2. The data used to construct the model must be published.
3. The limits over which the model is judged to be satisfactory must be defined.

The statistical parameters are defined in terms of the means and standard deviations for each marker in affected and unaffected pregnancies, and the correlation coefficient among all the markers. In addition, in this instance, the statistical models have been subjected to empirical validation.¹³⁶

Wald et al argue that serum marker values for affected and unaffected pregnancies used for the models are best obtained from the same patient population. They therefore support use of the Oxford-St. Bartholomew's Hospital Data as the most complete, noting that in addition to serum markers, this data set includes gestational estimates from both ultrasound and last menstrual period dates.¹⁴⁷

The statistical model used in BC is based on the Oxford-St. Bartholomew's Hospital Data set and the work of Cuckle et al.¹⁴⁸ Individual patient-risk estimates are primarily based on the regression relationship between age and serum markers. Additional factors known to affect the risk estimate, such as gestational age, maternal weight, ethnic origin, and diabetes mellitus, are considered separately and independently of the primary regression relationship. These were described in detail in the previous appendix.

Demonstration projects

Evidence on TMS effectiveness has been reported in the published literature since 1992. These reports, listed below, are all from interventional cohort studies using the same or very similar statistical models to determine individual risk.

The evaluation of TMS effectiveness presented in this review is based on the following four methodologically-sound secondary analyses of the primary cohort study evidence:

1. The Canadian Task Force on the Periodic Health Examination;*¹⁴⁹
2. The US Preventative Services Task Force;⁵⁴
3. The UK, Nation Health Service, Research and Development, Health Technology Assessment programme;²²
4. The Conde-Agudelo and Kafury-Goeta meta-analysis.¹⁵⁰

The findings from these reviews are summarized below. Because the 1996 Canadian and US Task Force reports considered essentially the same evidence on TMS, applied the same grading, and drew essentially the same conclusions, only the findings of the Canadian Task force are presented here, except where significant discrepancies occur.

1. The Canadian Task Force on the Periodic Health Examination

In its most recent update, the Canadian Task Force published a chapter on Prenatal Screening for and Diagnosis of Down Syndrome. Its recommendations regarding TMS were based on four prospective intervention studies, published to 1994, the cut-off date for inclusion in its literature search:

- Haddow et al¹⁵¹
- Phillips et al¹⁵² (< 35)
- Wald et al¹⁵³ (< 37)
- Cheng et al¹⁵⁴ (< 37)

The reported detection rate for TMS varied from 48 to 91% (mean 64.5%; CI 44-72%) and false-positive rate (after revision for ultrasound) of 3 to 10 %. The likelihood of Down syndrome, given an initial screen-positive result, ranged from 1.2 to 3.8% depending on the risk cut-off values used. The risk cut-offs ranged from 1/125 to 1/380. In Haddow et al,¹⁵¹ for example, of the women screened, 3.8% were offered amniocentesis (risk cut-off was 1:190).

* Now the Canadian Task Force on Preventive Health Care

The Canadian Task force raised one concern over study validity, regarding reported detection rates, (i.e. the proportion of fetuses with Down syndrome identified versus the total number of such Down syndrome fetuses in the screen population). They noted that, in most studies, determining the total number of Down syndrome cases is problematic owing to incomplete karyotype determination and incomplete diagnosis at birth. Most studies rely on indirect findings from independent surveillance systems to determine the number of Down syndrome babies born in the screened population.

The Canadian Task Force also noted that the detection rate varies with maternal age and between studies:

Wald et al ¹⁵³	39% among women younger than 37 years versus 71% among those 37 and older
Cheng et al ¹⁵⁴	67% among women younger than 30 versus 100% among those 30 to 39

They also noted that 21 to 31% of women with a positive initial screen did not have prenatal diagnosis using amniocentesis.

2. The UK, NHS, Health Technology Assessment programme

The UK, Health Technology Assessment Programme report on ante-natal screening for Down syndrome, published in 1998, added six prospective cohort studies to the four originally reviewed by the Canadian and US Task Forces. Four of the additional studies were published after the original search cut-off date used by the Task Forces:

- Piggot M et al ¹⁵⁵
- Goodburn SF et al ¹⁵⁶
- Mancini G et al ¹⁵⁷
- Kellner LH et al ¹⁵⁸

One prospective study seems to have been missed:

- Burton BK et al ¹⁵⁹

One was published in French:

- Prescia G et al ¹⁶⁰

Despite the additional data, the UK HTA group did not draw significantly different conclusions on TMS from those of the two Task Forces, that is, they found that variations in the TMS test performance features reflected differences in decisions on risk cut-off levels, and not any underlying flaw in the primary serum marker data used, or in the statistical model providing individual risk estimates.

The UK group reported a broader range of TMS test parameters, reflecting the wider range of program options selected. They summarize the following TMS features:¹⁵³

- a) screen uptake mean of 73% (reported in 3 studies)
- b) screen-positive rate the mean initial screen-positive rate was 7.5%, reducing to 5.7% after revision of gestational age using ultrasound scan among women with positive screening results
- c) amniocentesis uptake mean of 81% after screen-positive result
- d) abortion mean of 91% of affected pregnancies (from 6/10 studies)
- e) detection rate mean of 70% (adjusted to 64% owing to an estimated 23% fetal loss from spontaneous abortion)

3. Conde-Agudelo and Kafury-Goeta meta-analysis

The authors provide the most complete collection of TMS studies to date, reporting on a pooled analysis of the findings of 20 cohort studies involving 194,326 women, published to November 1996.¹⁵⁰

The validity of the meta-analysis was not formally evaluated for this TMS review, although the authors used standard methods for pooling and analysing individual study findings. Formal assessment of the meta-analysis would require retrieval of all studies, critical appraisal, and reconstruction of 'two by two' tables for each study.

The meta-analysis confirms the findings of the systematic reviews mention above. That is, the authors found detection rates (sensitivities) of 67%, 71%, and 73% for risk cut-offs of 1:190-200, 1:250-295, and 1:350-380, respectively. The median false-positive rates fluctuated between 4% and 8%.

The optimal risk cut-off rate suggested in this study will be of interest to those having to decide on an appropriate initial screen cut-off rate for TMS testing. The authors used the different point estimates of detection rates (sensitivity) and screen-positive rates to construct summary receiver-operating curves. The receiver-operating curves describe the relationship between detection rates and a screen-positive rates. Based on these curves, the authors suggest an optimal risk cut-off rate for testing of women of all ages as 1:190 (detection rate 67% with a 4% initial positive rate). Though not as comprehensive, similar analyses form the basis of deciding the appropriate cut-off rate for any population.

The screen-positive cut-off rate in BC is 1:365, the assumed pre-test risk of a women 35.5 years old at the time of birth. In contrast, the risk cut-off of 1:190 suggested by Conde-Agudelo and Kafury-Goeta is the pre-test risk for a women 38 to 39 years old.

Illustrations of program test performance evaluations

1. The number of amniocenteses to detect one fetus with Down syndrome

One way of illustrating screening-test performance is to consider the number of amniocenteses needed to identify one fetus with Down syndrome. Haddow et al, the largest of the studies, summaries the effectiveness of TMS in one US centre.¹⁵¹

They determined that in a relatively young population (5% >35 years) one case of Down syndrome was found for every 39 women considered screen positive (after ultrasound confirmation of gestational age). By contrast, they found that if women over 35 were given screening, for every case of Down syndrome identified, 140 women would have undergone amniocentesis.

The Canadian Task Force similarly considered TMS in relation to its predictive value, a numerical estimate of the number of positive tests, women actually having the condition of concern. They then compared TMS to the standard age-based screening of women over age 35.

2. Detection and false-positive rates

Wald et al¹⁶¹ argue that at high detection rates (over 60%) prenatal screening program performance should be compared in terms of their false-positive rates. That is, a detection rate should be set, for example at 60%, and the associated false-positive rates should be measured. Prenatal screening policy should favour the program with the lowest false-positive rate for a given detection rate.

3. Age-specific cost/effectiveness ratios

Cuckle¹⁶² and Torgerson¹⁶³ argue that screening policy should be informed by age-specific cost-effectiveness ratios. These are calculated as a cost per affected pregnancy detected for each year of maternal age. Based on this approach, Cuckle for example shows that using an age cut-off of 28 and a lower risk cut-off of 1:250 will result in the same detection rate.

4. Down syndrome birth rates

The rate of Down syndrome birth in a screened population depends both on the accuracy of the test results, and on the subsequent decision of the parents. In turn, the parents' decision will depend on their attitudes to induced abortion and towards Down syndrome. Induced abortion is currently sought by the majority of women whose prenatal diagnosis is Down syndrome or neural tube disorders.^{22,54} A study for the Royal Commission indicates a substantial majority of women in Canada have sought an abortion in these circumstances (76% for neural tube disorders and 83% for Down syndrome).¹⁶⁴

The US Task Force estimates that the prevalence of Down syndrome in women over age 35 offered amniocentesis ranges from 7.3%-29%.⁵⁴ The effect is low, owing to the relatively small number of a total population of pregnant women who are over age 35.

Limited data are available on the impact of TMS on the prevalence of Down syndrome. The US Task Force estimates the effect to range from 36% to 62%, depending on how many initial screen-positive women elect to have amniocentesis, and how many of these elect to have an abortion.⁵⁴

APPENDIX E: BRITISH COLUMBIA MEDICAL SERVICES COMMISSION ADMINISTRATIVE DATA

I. Analysis of cost and volume of prenatal test use in British Columbia

Maternal serum screening in BC: Alpha fetoprotein and TMS

1) Provincial payment data

Only a small proportion of the total cost of TMS is identified from provincial fee-for-service payment data. The fee-for-service plan currently reimburses TMS testing at a rate of \$28.24 per test. This is actually only the rate for the alpha fetoprotein (AFP) proportion of the TMS test. The other two markers which make up the triple-marker screen are covered from a contract grant to the Genes, Elements, Metabolism (GEM) Program at Children's and Women's Health Centre of BC through the Alternative Payments Division of the BC Medical Services Commission.

For example, the GEM program budget estimates that per 10,000 tests they have labour costs of \$381,502 and non-labour costs of \$373,500, giving a total cost of \$955,002 per 10,000 tests. This exceeds the Medical Services Commission payments of \$388,076 for 11,301 test by 2.5 times. Even so the GEM budget is an underestimate in that the budget does not account for capital and overhead costs which are born by the Children's and Women's Health Centre.

2) Trends

The total volume of AFP testing reimbursed by the BC Medical Services Commission increased from 1,872 tests in 1991/92 to 6,313 in 1994/95 and 11,301 in 1996/97 (**Tables 8-10**). Total payment increased to \$61,132, \$216,631 and \$388,076, respectively.

TMS began to replace AFP testing as the maternal serum screening test used in British Columbia in 1995. Only AFP appears as a fee item in the BC Medical Services administrative database. Since, however, AFP is one of the three markers which make up the triple-screen, it provides a rough estimation of the trend in maternal serum screening use.*

In 1996/7, 25% of eligible women received an AFP test during their pregnancy. The proportion of tests for women under 35 was 54% of all AFP tests in 1991/92, 47% in 1994/95 and 56% in 1996/97. The potential for expansion of service provision is in the category of women under age 35. 83% of live births occurred in this age group, with only 17% of potentially eligible women receiving serum testing to date. More recent data on TMS utilization were obtained directly from GEM (**Appendix G, Table 18**).

* A proportion of the AFP tests included in these totals were not conducted on maternal serum but amniotic fluid. This accounted for approximately 35% of all AFP tests reimbursed in 1996/97.

Table 8: Fee for Service Payments and Services, BC Physicians & Female BC patients, 1991-1992

Fee Item	Age Group at Date of Service									Total
	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	Other	
Payments										
00787 Amniocentesis, transabdominal	299.50	1,318.00	2,903.50	5,443.50	15,160.50	2,075.50	28.50	88.00	88.00	27,407.50
00794 Chorionic villus sampling	67.50	67.50	467.00	469.50	6,926.50	2,330.50	0.00	0.00	71.00	10,400.00
08651 Obs. - B-scan - 14 wks. or more	327,338.50	1,042,373.00	1,868,058.50	1,478,450.50	505,340.50	73,861.00	3,161.00	430.50	1,791.50	5,300,804.50
08654 Ultrasonic guidance for amniocentesis	601.00	2,546.00	8,308.50	17,233.00	70,695.50	7,510.50	0.00	0.00	260.80	107,154.50
08655 Obs. - B-scan - less than 14 wks.	130,931.50	358,284.00	572,991.50	455,417.00	252,402.50	48,426.00	1,401.50	254.50	816.50	1,820,924.50
08657 Ultrasonic guidance for chorionic villus sampling	84.00	605.50	1,114.50	2,503.50	22,827.00	9,331.00	177.00	0.00	0.00	36,642.00
09288 & 91120 Amniotic fluid examination	23.00	265.50	1,062.50	777.00	370.00	21.50	0.00	0.00	43.00	2,563.00
09480 & 91095 Alpha fetoprotein (R.I.A)	880.00	4,385.50	11,426.00	16,180.50	21,331.50	6,147.00	258.00	31.50	491.80	61,132.00
09542 & 93030 Cytogenetic analysis - amniotic fluid	3,660.50	6,451.50	27,550.50	115,379.50	856,786.50	146,377.50	1,232.00	0.00	0.00	1,157,437.50
Services										
00787 Amniocentesis, transabdominal	10	45	98	184	506	69	1	3	3	919
00794 Chorionic villus sampling	1	1	7	7	101	34	0	0	1	152
08651 Obs. - B-scan - 14 wks. or more	3,837	12,224	21,907	17,349	5,3935	867	37	5	21	62,182
08654 Ultrasonic guidance for amniocentesis	7	30	98	208	832	91	0	0	3	1,269
08655 Obs. - B-scan - less than 14 wks.	2,045	5,605	8,968	7,113	3,948	758	22	4	13	28,476
08657 Ultrasonic guidance for chorionic villus sampling	1	7	13	29	266	109	2	0	0	427
09288 & 91120 Amniotic fluid examination	1	12	48	36	17	1	0	0	2	117
09480 & 91095 Alpha fetoprotein (R.I.A)	27	134	349	495	654	189	8	1	15	1,872
09542 & 93030 Cytogenetic analysis - amniotic fluid	9	16	68	282	2,090	358	3	0	0	2,826

Table 9: Fee for Service Payments and Services, BC Physicians & Female BC patients, 1994-1995

Fee Item	Age Group at Date of Service									Total
	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	Other	
Payments										
00787 Amniocentesis, transabdominal	249.00	1,432.00	2,148.50	5,483.50	27,826.50	4,678.00	96.00	32.00	159.00	42,104.00
00794 Chorionic villus sampling	72.00	146.00	510.50	969.50	5,399.50	1,386.50	73.00	0.00	0.00	8,558.00
08651 Obs. - B-scan - 14 wks. or more	380,866.00	1,198,461.00	1,956,010.80	1,747,020.50	605,272.50	101,221.50	3,976.50	541.00	2,526.50	5,995,896.00
08654 Ultrasonic guidance for amniocentesis	725.50	3,454.25	4,814.50	16,335.50	83,068.00	14,161.00	363.50	0.00	181.50	123,192.00
08655 Obs. - B-scan - less than 14 wks.	164,043.50	381,893.50	534,665.00	499,094.00	308,766.00	66,673.50	3,523.00	609.50	745.50	1,960,013.50
08657 Ultrasonic guidance for chorionic villus sampling	0.00	181.50	635.00	1,361.50	8,167.50	2,360.00	91.00	91.00	0.00	12,887.00
09288 & 91120 Amniotic fluid examination	0.00	230.50	1,151.50	345.50	299.50	115.00	69.00	0.00	0.00	2,211.00
09480 & 91095 Alpha fetoprotein (R.I.A)	2,265.00	13,385.50	30,167.50	55,109.00	94,495.00	17,054.00	1,442.00	549.50	2,163.50	216,630.50
09542 & 93030 Cytogenetic analysis - amniotic fluid	3,440.00	14,636.00	17,637.50	154,588.00	1,090,254.50	194,909.50	3,884.00	0.00	432.00	1,479,781.50
Services										
00787 Amniocentesis, transabdominal	8	45	68	173	876	147	3	1	5	1,326
00794 Chorionic villus sampling	1	2	7	14	74	19	1	0	0	118
08651 Obs. - B-scan - 14 wks. or more	4,219	13,274	21,666	19,349	6,704	1,121	44	6	28	66,411
08654 Ultrasonic guidance for amniocentesis-	8	39	53	181	919	157	4	0	2	1,363
08655 Obs. - B-scan - less than 14 wks.	2,422	5,646	7,901	7,377	4,561	987	52	9	11	28,966
08657 Ultrasonic guidance for chorionic villus sampling	0	2	7	15	90	26	1	1	0	142
09288 & 91120 Amniotic fluid examination	0	10	50	15	13	5	3	0	0	96
09480 & 91095 Alpha fetoprotein (R.I.A)	66	390	879	1,606	2,754	497	42	16	63	6,313
09542 & 93030 Cytogenetic analysis - amniotic fluid	8	34	41	359	2,529	452	9	0	1	3,433

Table 10: Fee for Service Payments and Services, BC Physicians & Female BC patients, 1996-1997

Fee Item	Age Group at Date of Service									Total
	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	Other	
Payments										
00787 Amniocentesis, transabdominal	286.50	1,114.00	2,387.00	6,589.00	31,432.00	6,398.00	223.00	191.00	318.50	48,938.50
00794 Chorionic villus sampling	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
08651 Obs. - B-scan - 14 wks. or more	330,477.50	1,107,302.50	1,866,542.00	1,717,065.00	699,172.00	107,077.50	4,737.00	455.00	1,638.50	5,834,467.50
08654 Ultrasonic guidance for amniocentesis-	274.50	2,289.50	5,038.00	17,038.00	81,909.50	16,308.50	274.50	0.00	183.50	123,317.00
08655 Obs. - B-scan - less than 14 wks.	158,337.50	342,459.50	481,804.00	454,281.00	324,336.50	78,070.00	4,513.00	547.00	614.00	1,844,963.00
08657 Ultrasonic guidance for chorionic villus sampling	0.00	0.00	0.00	0.00	91.50	0.00	0.00	0.00	0.00	91.50
09288 & 91120 Amniotic fluid examination	0.00	161.00	530.00	576.00	184.00	115.00	0.00	0.00	0.00	1,566.00
09480 & 91095 Alpha fetoprotein (R.I.A)	6,318.50	27,746.50	70,465.50	116,584.50	129,118.50	24,690.50	3,949.00	2,369.50	6,834.00	388,076.00
09542 & 93030 Cytogenetic analysis - amniotic fluid	6,915.50	20,746.50	50,569.50	219,135.50	1,143,222.00	226,051.00	6,483.00	0.00	0.00	1,673,123.50
Services										
00787 Amniocentesis, transabdominal	9	35	75	207	992	202	7	6	10	1,543
00794 Chorionic villus sampling	0	0	0	0	0	0	0	0	0	0
08651 Obs. - B-scan - 14 wks. or more	3,627	12,152	20,483	18,842	7,672	1,175	52	5	18	64,026
08654 Ultrasonic guidance for amniocentesis-	3	25	55	186	894	178	3	0	2	1,346
08655 Obs. - B-scan - less than 14 wks.	2,316	5,010	7,048	6,647	4,744	1,142	66	8	9	26,990
08657 Ultrasonic guidance for chorionic villus sampling	0	0	0	0	1	0	0	0	0	1
09288 & 91120 Amniotic fluid examination	0	7	23	25	8	5	0	0	0	68
09480 & 91095 Alpha fetoprotein (R.I.A)	184	808	2,052	3,395	3,760	719	115	69	199	11,301
09542 & 93030 Cytogenetic analysis - amniotic fluid	16	48	117	507	2,645	523	15	0	0	3,871

TMS in combination with other prenatal tests

The Medical Services Commission database provides some data on the concurrent use of AFP, ultrasound and amniocentesis. In this analysis, AFP is considered as a surrogate for TMS use. **Table 11** shows that in 1997/98 AFP and ultrasound was used by approximately 7000 women; 1000 women used AFP, ultrasound and amniocentesis; and 100 women used only AFP and amniocentesis.

Ultrasound provides gestational age estimates needed for TMS test interpretation. It may also be used by some women as their only prenatal diagnostic test. Detailed ultrasound is required for definitive diagnosis of neural tube disorders. Amniocentesis is needed for definitive diagnosis of Down syndrome and other chromosomal anomalies.

Table 11: AFP use in combination with other prenatal tests, 1997/98, as a surrogate for TMS use.

Prenatal test combination	Total number of women	Services	Payments
AFP & amniocentesis	105	106	\$ 5621.50
AFP, ultrasound & amniocentesis	1056	3174	\$ 233,028.00
AFP & ultrasound	6931	12647	\$ 1,065,548.00

Source: BC Medical Services Plan, Fee-for-service payment statistics tapes

AFP = alpha fetoprotein = fee code 09480 (also includes some AFP testing of amniotic fluid);

Amniocentesis, transabdominal = fee code 00787;

Ultrasound = Obs. - B-scan - 14 wks. or more = fee code 08651;

Obs. - B-scan - less than 14 wks. fee code 08655

Medical services payments for AFP compared with other prenatal tests

The cost of AFP was compared to the costs of amniocentesis and prenatal ultrasound. As **Figures 8 & 9** demonstrate, the cost of prenatal ultrasound exceeded \$7 million in 1996/97 as compared to about \$400,000 for AFP and \$49,000 for amniocentesis. As noted above, much of the cost of amniocentesis and TMS is from alternative payments, and therefore not included in this database. Nevertheless, the cost of ultrasound far exceeds costs associated with other prenatal screening and diagnostic tests.

Amniocentesis and chorionic villus sampling (CVS)

1) Trends

Of the three Medical Services Commission amniocentesis fee codes, those for cytogenetic analysis of amniotic fluid (#09642 and #93030) most closely reflect the total volume because each amniocentesis produces only one sample for cytogenetic analysis. The volume of

cytogenetic analysis of amniocentesis fluid increased steadily from 2,826 tests in 1991/92 to 3,433 in 1994/95 and 3,871 in 1996/97, with costs of \$1,157,000, \$1,480,000 and \$1,673,000 respectively (**Table 14**).

2) Limitations

The two codes representing the procedure itself (#00787) and ultrasound guidance for the procedure (#08654) are incompletely represented in the Medical Services Commission administrative database (**Table 10**). This is because they (together with CVS) are also performed under global contracts to Children’s and Women’s Health Centre of BC Perinatal Program. If all items related to amniocentesis were reimbursed at 1999 fee-for-service prices, then the total cost to the Medical Services Commission would be \$2,795,907 for the volume of services conducted in 1996/97 (**Table 12**). This does not include the cost of genetic counselling.

TABLE 12: Potential amniocentesis fee for service costs using 1996/97 volume and 1999 prices

MSC fee items related to amniocentesis	1999 MSC fee schedule price	Price x 3871 (Volume of amniocentesis for 1996/97)
Transabdominal #04680	\$87.17	\$337,435
Ultrasound guidance #04680	\$57.53	\$222,699
Cytogenetic analysis #93030	\$402.20	\$1,556,916
OB Consult # 04010	\$88.20	\$341,422
TOTAL	\$635.10	\$2,795,907

CVS does not appear in the administrative database for 1996/97 because all procedures are now reimbursed under global contracts paid through alternative payment mechanisms. Prior to that year, CVS use declined from 152 in 1991/92 to 118 tests in 1994/95.

This downward trend represents in part emerging efficacy data suggesting an unfavourable harm to benefit ratio, even though CVS provides definitive diagnostic information on chromosomal abnormalities earlier in pregnancy than amniocentesis. CVS is more expensive per procedure than amniocentesis, amounting to \$957.95 which includes the cost of the procedure itself (fee code #00794), ultrasonic guidance (#08657), cytogenetic analysis (# 933025) and an OB consultation (# 04010).

Ultrasound

1) Trends

The volume and cost of prenatal ultrasound at less than 14 weeks has been reasonably stable over the time period examined: 28,476 test at a cost of \$1,820,924 in 1991/92; 28,966 tests at a cost of \$1,960,014 in 1994/95 and 26,990 tests at a cost of \$1,844,963 in 1996/97. The fee-for-service price of prenatal ultrasound before 14 weeks is \$68.00.

The volume and cost of prenatal ultrasounds at 14 weeks' gestation and over has also been reasonably stable over time. The fee-for-service price of prenatal ultrasound before 14 weeks is \$90.63.

Regional distribution of prenatal testing

The use of prenatal tests has steadily increased over the time period in most regions (**Figure 11** identifies Health Regions of the province). The highest use of TMS testing occurred in Vancouver, South Fraser Valley, North Shore, Simon Fraser and Capital health regions as indicated by both medical services commission and GEM data. The GEM program provided data on the regional distribution of physicians who have ever ordered or received the results of a triple-marker screening test (**Table 13**). The pattern of amniocentesis use also follows this pattern.

Tables 14 - 17 present total services and payment data from the BC Medical Services Commission administrative database on alpha fetoprotein serum testing, cytogenetic analysis of amniotic fluid, transabdominal amniocentesis and ultrasonic guidance of amniocentesis for fiscal years 1991/92, 1994/95 and 1996/97. These time periods were chosen to illustrate general trends.

Figure 11: British Columbia Health Regions

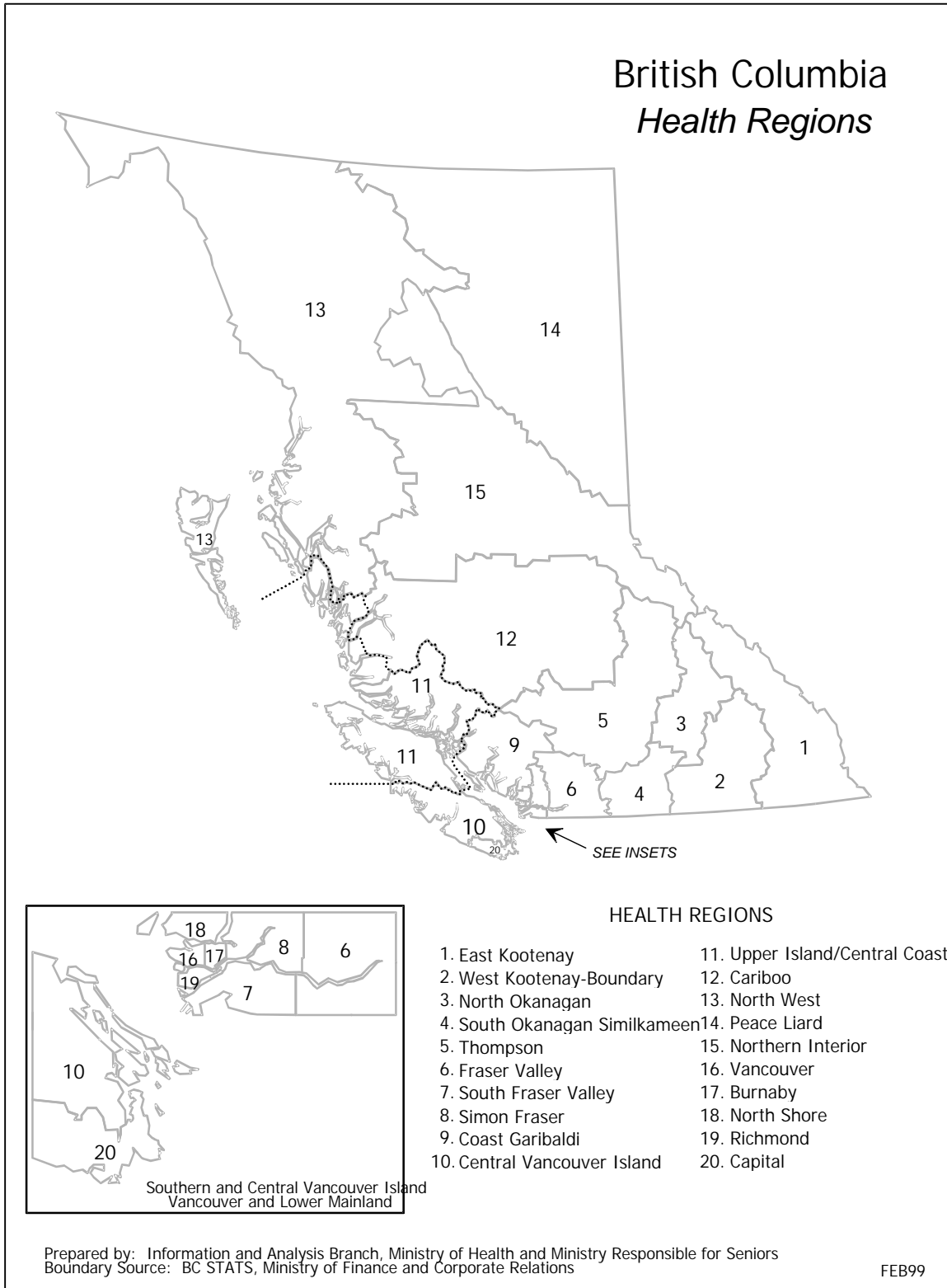


Table 13: Number by Health Region of physicians ordering or receiving TMS screening test results.

	BC Health Region	Number of ordering physicians
1	East Kootenay	48
2	West Kootenay - Boundary	68
3	North Okanagan	101
4	South Okanagan - Similkameen	180
5	Thompson	118
6	Fraser Valley	169
7	South Fraser Valley	441
8	Simon Fraser	723
9	Coast Garibaldi	187
10	Central Vancouver Island	218
11	Upper Island/Central Coast	131
12	Cariboo	60
13	North West	105
14	Peace Liard	54
15	Northern Interior	116
16	Vancouver	884
17	Burnaby	170
18	North Shore	185
19	Richmond	125
20	Capital	291

Source: GEM program data

Table 14: Total Services and Payments for Cytogenetic Analysis of Amniotic Fluid for Fiscal Years 1991/92, 1994/95 and 1996/97

Fee code #09542 & 93030		1991/92		1994/95		1996/97	
	BC Health Region	Services	Payments	Services	Payments	Services	Payments
1	East Kootenay	2	823	1	426	0	0
2	West Kootenay - Boundary	16	6,580	20	8,638	25	10,806
3	North Okanagan	23	9,259	22	9,491	30	12,967
4	South Okanagan - Similkameen	71	29,152	64	27,555	78	33,713
5	Thompson	23	9,409	37	15,962	29	12,534
6	Fraser Valley	36	14,728	37	15,950	63	27,230
7	South Fraser Valley	190	78,156	290	124,980	304	131,395
8	Simon Fraser	151	61,634	342	147,354	237	102,436
9	Coast Garibaldi	26	10,503	29	12,511	47	20,314
10	Central Vancouver Island	46	18,800	64	27,602	113	48,841
11	Upper Island/ Central Coast	10	4,081	19	8,206	28	12,102
12	Cariboo	9	3,702	10	4,298	3	1,297
13	North West	17	7,053	20	8,626	15	6,483
14	Peace Liard	2	794	0	0	0	0
15	Northern Interior	18	7,462	11	4,742	31	13,399
16	Vancouver	1,624	664,149	1,624	700,009	1,899	820,786
17	Burnaby	85	34,839	118	50,883	178	76,935
18	North Shore	136	55,776	200	86,169	264	114,106
19	Richmond	75	30,781	127	54,790	174	75,206
20	Capital	254	104,821	332	143,187	346	149,548
	Other	12	4,936	66	28,401	7	3,026
TOTAL		2,826	1,157,438	3,433	1,479,782	3,871	1,673,124

Table 15: Total Services and Payments (\$) for Transabdominal Amniocentesis for Fiscal Years 1991/92, 1994/95 and 1996/97

Fee code # 00787		1991/92		1994/95		1996/97	
BC Health Region		Services	Payments	Services	Payments	Services	Payments
1	East Kootenay	0	0	1	32	0	0
2	West Kootenay - Boundary	3	67	6	191	2	64
3	North Okanagan	18	532	6	191	8	255
4	South Okanagan - Similkameen	25	750	17	541	11	350
5	Thompson	4	122	7	223	6	191
6	Fraser Valley	19	572	10	318	13	414
7	South Fraser Valley	29	854	26	826	121	3,836
8	Simon Fraser	16	480	23	731	19	605
9	Coast Garibaldi	5	149	6	191	0	0
10	Central Vancouver Island	36	1,068	47	1,489	45	1,432
11	Upper Island/Central Coast	8	241	11	350	19	605
12	Cariboo	2	62	8	255	6	191
13	North West	17	466	36	1,130	35	1,114
14	Peace Liard	10	302	6	191	15	477
15	Northern Interior	9	268	17	542	34	1,082
16	Vancouver	388	11,532	737	23,399	843	26,705
17	Burnaby	7	214	10	318	5	159
18	North Shore	5	153	11	350	6	191
19	Richmond	5	153	7	223	1	32
20	Capital	306	9,216	329	10,454	350	11,109
	Other	7	207	5	159	4	127
TOTAL		919	27,407	1,326	42,104	1,543	48,939

Table 16: Total Services and Payments (\$) for Ultrasonic Guidance of Amniocentesis for Fiscal Years 1991/92, 1994/95 and 1996/97

Fee code # 08657		1991/92		1994/95		1996/97	
BC Health Region		Services	Payments	Services	Payments	Services	Payments
1	East Kootenay	2	168	1	91	0	0
2	West Kootenay - Boundary	10	850	7	636	8	732
3	North Okanagan	21	1,790	14	1,272	13	1,189
4	South Okanagan - Similkameen	46	3,867	25	2,268	19	1,741
5	Thompson	15	1,287	17	1,542	9	824
6	Fraser Valley	32	2,652	12	1,090	14	1,283
7	South Fraser Valley	79	6,760	74	6,716	150	13,744
8	Simon Fraser	76	6,482	94	8,531	48	4,398
9	Coast Garibaldi	12	1,021	9	817	14	1,283
10	Central Vancouver Island	40	3,078	45	4,085	56	5,134
11	Upper Island/ Central Coast	9	787	9	818	11	1,007
12	Cariboo	6	504	7	636	5	458
13	North West	8	698	21	1,907	23	2,106
14	Peace Liard	9	773	15	1,182	15	1,374
15	Northern Interior	17	1,448	11	999	37	3,391
16	Vancouver	690	57,953	464	41,934	377	34,534
17	Burnaby	39	3,364	43	3,814	45	4,125
18	North Shore	65	5,577	46	4,173	58	5,315
19	Richmond	25	2,130	41	3,725	26	2,383
20	Capital	63	5,545	375	34,049	410	37,565
	Other	5	421	33	2,907	8	733
TOTAL		1,269	107,154	1,363	123,192	1,346	123,317

Table 17: Total Services and Payments (\$) for Alpha Fetoprotein Serum Testing for fiscal years 1991/92, 1994/95 and 1996/97

Fee code # 09480 & 91095		1991/92		1994/95		1996/97	
BC Health Region		Services	Payments	Services	Payments	Services	Payments
1	East Kootenay	0	0	18	617	13	446
2	West Kootenay - Boundary	7	230	45	1,544	102	3,503
3	North Okanagan	4	135	94	3,228	119	4,086
4	South Okanagan - Similkameen	48	1,570	112	3,843	424	14,560
5	Thompson	6	195	42	1,441	97	3,331
6	Fraser Valley	31	1,015	98	3,364	233	8,001
7	South Fraser Valley	49	1,615	379	13,005	1,215	41,723
8	Simon Fraser	31	1,005	232	7,961	732	25,137
9	Coast Garibaldi	10	327	25	859	120	4,121
10	Central Vancouver Island	12	395	74	2,540	231	7,933
11	Upper Island/ Central Coast	6	200	53	1,820	228	7,830
12	Cariboo	9	300	15	515	32	1,099
13	North West	52	1,747	114	3,912	269	9,237
14	Peace Liard	0	0	8	274	35	1,202
15	Northern Interior	12	390	38	1,304	95	3,262
16	Vancouver	1,389	45,296	3,797	130,301	4,867	167,133
17	Burnaby	61	2,001	227	7,790	583	20,020
18	North Shore	15	488	217	7,448	774	26,579
19	Richmond	19	601	150	5,148	356	12,225
20	Capital	109	3,556	522	17,896	674	23,145
	Other	2	68	53	1,818	102	3,503
TOTAL		1,872	61,132	6,313	216,631	11,301	388,076

APPENDIX F: TMS AND DOWN SYNDROME IN A VANCOUVER SOUTH ASIAN COMMUNITY

This appendix chapter considers the experiences of mothers caring for their children with Down syndrome who are also part of a distinct ethnic group, in this case the Vancouver South Asian community. In-depth interviews were carried out with members of the community regarding all aspects of their individual and family lives and is reported elsewhere.¹⁶⁵ Opinions and attitudes relevant to TMS are presented here.

The perspective of the South Asian community of Vancouver is included not to characterize this ethnic group, but rather to raise general issues related to ethnicity and genetics. In fact, the perspectives of the women interviewed from Vancouver South Asian community are remarkably similar to the views expressed by women who are members of the dominant ethnic group descended from Western Europe. They differ only in how they relate their perspectives to their respective ethnic communities.

The Vancouver South Asian community

The South Asian community in Vancouver is a difficult community to define. Similar to other ethnic groups, it includes younger members who were born in Canada and older members who immigrated to Canada from various countries around the world. For the purposes of this project, the use of the term ‘South Asian community’ is intended to describe a sector of the population that includes Sikhs, Hindus, and Muslims. Of the seven women interviewed, four are Sikhs, two are Hindus, and one is Muslim.

While the use of the term ‘South Asian community’ is convenient, the goal of this work is not to classify the community as a monolith of static, cultural beliefs. Instead, the Vancouver community holds in continual flux certain beliefs and values, rigidly honoured by some members and virtually ignored by others. The voices of these seven women represent a small group of people who happen to be both members of a visible minority while simultaneously raising a disabled child. The common ground for these women is in the stories they share.

As addressed in earlier chapters, this review does not seek to ignore the opinions or views of South Asian fathers who are also raising children with Down syndrome. However, it needs to be borne in mind that the subject of reproductive technology or prenatal screening is one that has a major impact specifically on the lives of women. Within South Asian families as in the general population, the job of child-rearing tends to be more in the hands of mothers.

The present chapter continues with a brief literature review focussing on issues such as prenatal screening and its relationship to ethnicity. This is followed by a closer examination of some key issues relevant to a study of TMS among the South Asian Down syndrome community. This includes recipient experiences with TMS, women’s concerns and attitudes towards TMS, and finally a review by some members of the South Asian community of the four TMS options.

The problem of reproductive technology stereotypes

For South Asian women, the notion of ‘choice’ and ‘freedom’ in relation to reproduction is worth exploring in more detail.

Thobani critically examines¹⁶⁶ the way that the South Asian community in Vancouver has been targeted by advertisements promoting the use of ultrasound for sex selection, which, according to the advertised claims, can determine the sex of the fetus as early as twelve weeks’ gestation. The results derived from this test are acknowledged as being used to abort female fetuses.

“As you know, every ill that befalls us [South Asians] has been blamed on our ‘culture’ in one way or another. As women of colour living in the West, we have been told that our society is a backward, traditional society and that is the main reason why women in our communities are oppressed. Since colonial times, we have been told that patriarchal attitudes and oppressions are inherent in our culture, and that machismo is very much a Third World phenomenon. Of course, I would not deny that our culture is patriarchal, but this singling out of cultures of people of colour as inherently backward and oppressive is what is racist.”¹⁶⁶ (p170.)

Since the South Asian community is stereotyped as a community interested in sex selection technology, it seems appropriate to relate this to a discussion about disability selection through TMS. Women were asked to express their opinions about a possible connection between the two. One of the women interviewed felt that they were separate issues.

“Those who go forward to see what the sex of their baby is ... I really feel sorry for those people. With most of the people I know, primarily you have a child because you want to have a child. You’re not doing it because you want to have a boy. You have what God will choose to give you. I don’t believe in this sort of playing around with developing boys or developing girls. I’m not against it, but that’s something that I would never do. I look at both of those things [disability selection and sex selection] as being completely different ... Why do we need to know what we’re having? It’s only for information purposes. It doesn’t really help in any true way.”

On the other hand, some other women interviewed saw a connection between the two issues. In their minds, sex selection was no different from disability selection because both interfere with nature’s course.

“Why do we have to have these types of tests? Sex selection and disability selection both provide us with information about our unborn child. But what we make of this information is the key. Knowledge is good ... But when you start playing around with these types of technology you are ultimately dealing with serious dilemmas. Fetuses are aborted because of their sex and because of various disabilities. I believe as a society, we need to question how far we are willing to go with this. It’s a dangerous area ... I question the benefits of using either sex selection technology or disability detection technology if it is only going to force us to ‘get rid of our problem’ by simply having an abortion. If this is the case, then society is in serious trouble.”

Within current literature on prenatal screening relevant to ethnicity there is a discussion about the actual ‘choices’ women have regarding their own reproduction. Rowland examines¹⁶⁷ the relationship between women’s demand for choice in reproduction and sexuality and male control of conception and reproduction. She suggests that the notions of ‘choice’ and ‘freedom’ in regard to prenatal screening technology are ideological constructs which may “entrap women further and limit their choice to say ‘no’ to increased male control of the reproductive process.”¹⁶⁷

Key issues among the South Asian Down syndrome community

In an effort to provide more insight into the cultural specific perceptions of TMS, this group of South Asian women were asked to speak about their personal experiences of pregnancy. This included a discussion of their impressions, if any, in receiving TMS, the emotional impact of test results on them and their families, and their own and their families’ attitudes towards disability in general.

Experiences with pregnancy and TMS

All the women included in this study were under the age of thirty-five when they had their child with Down syndrome. Of the seven women interviewed, only two had direct experience with TMS. They had the test only after their first child was born with Down syndrome, and both of these women were over the age of thirty-five when expecting their second child. Although the risk of their having another child with Down syndrome was low, both women opted for the testing, primarily to provide some sort of reassurance.

“At some subconscious level, I knew that the chance of me having another child with Down syndrome was very low. However, when you’ve been through the wringer the first time – I was 31 when my first son with Down syndrome was born, you just can’t shake the feeling that something else could go wrong. It happened once before, and who’s to say it couldn’t happen again? I just didn’t want to take that chance. In my mind, it was worth getting the testing done so that I could at least have some peace of mind.”

While both women chose to accept the offer of TMS prior to the birth of their second child, it is important to point out how unexpectedly having a child with Down syndrome can also change one’s view towards future pregnancies. By looking beyond the impact of maternal serum screening on one’s pregnancy experience, it is evident that women who have their first child with Down syndrome are suddenly confronted with a new set of issues surrounding the birth of a second child that challenges their beliefs about disability.

“I wasn’t over 35, I wasn’t a smoker or a drinker, or had been near a nuclear reaction or anything that could have caused any type of an anomaly. It just happened...that is why we went through all of the necessary testing. Even though I had the appropriate tests, you tend to worry about other things that may go wrong. What if it’s really bad labour or something happens and he ends up getting [cerebral palsy]? What if they didn’t pick up on the fact that he may have spina bifida? You worry about all of the things that are out there all of a sudden that you never worry about when you’re pregnant the first time around because you haven’t confronted any of them.”

Women's concerns with TMS

During our interviews with the South Asian women, a number of important concerns and attitudes surfaced towards the procedure itself. This section provides a brief synopsis of what some of these women raising a child with Down syndrome have to say about this type of prenatal diagnosis.

One concern related to the availability of information about TMS to members of a visible minority group. All the women interviewed said that information about TMS, or other prenatal screening techniques was not readily available to them. Some of the women attributed this obstacle both to language barriers, and to a general ignorance on this subject among fellow community members.

If a woman's command of the English language is poor and she is unable to communicate effectively with her physician, she may miss specific information. Some women also suggested that ignorance toward the issue of disability continues because nobody wants to speculate about the possibility of having a child with special needs until they are confronted with the reality.

“All of this scientific jargon about alpha-fetoprotein, etc ... is still complicated for me to grasp even though I am a fluent English speaker. So imagine how difficult it would be for a South Asian woman who has a weak understanding of the [English] language to understand all of this stuff? How would you even begin to explain the notion of ‘false-positives’ or ‘false-negatives’? Perhaps one way of increasing a South Asian woman's knowledge about TMS would be to provide literature ... pamphlets, brochures ... that would be written in either Hindi, Punjabi, Gujarati, or some other South Asian language to these women ... Maybe that would be the key to making the community more aware of these issues.”

One of the most common issues to emerge was the need for prenatal screening to resolve the ‘fear of the unknown’.¹⁶⁸ Within the South Asian community, the notion of the ‘fear of the unknown’ seemed to prevail among stories articulated by women who had undergone some form of prenatal testing, whether TMS or amniocentesis.

“It was important for me and [my husband] to have some confirmation that everything was going to be okay this time. It was great to have that test done—the amniocentesis ... to say everything is going okay. This satisfied me. You know you never get over it. All pregnant women feel the same way—not just me. You always worry to the very end. But the fact that you're sort of 95% certain that everything is going to be okay gives you a lot of reassurance.”

Most of the women interviewed claimed that ‘fear of the unknown’ is a universal phenomenon; one that extends across cultural boundaries. The South Asian community is not exceptional in having fears about the future.

“You always want to know what lies ahead. That is a part of human nature. If we weren't so afraid of what lies ahead of us, we wouldn't be so anxious to try and create new ways of prenatal screening. In some sense, screening provides us with a way of dealing with our fears of the unknown by making us more aware about what we should expect. I'd say, in general, the South Asian community is by no means distinct when it comes to this belief.”

Another issue that emerged in discussions was the pressure of giving birth to a ‘perfect baby’. Some of the women admitted that prior to the birth of their child with Down syndrome, they had not imagined their child could be born with some form of a disability. Once presented with a child with special needs, however, one woman describes going through different phases, confronting her own fears, and learning to view her child as the ‘perfect baby’ in her eyes.

“I believe that all parents, regardless of their ethnicity, wish for a ‘perfect child’. But I think that the important issue here is trying to define what is a ‘perfect child’? In my mind, my child [with Down syndrome] is perfect. She is healthy and happy ... as a parent I couldn’t possibly ask for anything more ... When [my daughter] was born, I was worried and scared that she was going to have a terrible life because of her condition. But I think that initial view was based entirely on my ignorance. Now when I think about it, I wouldn’t change her for the world.”

When asked about the existence of pressures placed on women to participate in some form of prenatal screening, differing opinions arose. Some felt that there are no pressures in society forcing women to take these tests, and suggested that they have the right to make their own decisions about reproduction without being controlled. Others, recalling their own experiences, felt pressure can exist from both outside forces such as doctors, and inside forces, including other family members.

“Pressure can be a dangerous thing ... After having my first child with Down syndrome, I felt apprehensive about future births. Although there was never any direct discussions about the benefits of future screening, when I was pregnant with my second child ... both my husband and I decided to wait until we had the results from an amniocentesis before announcing our pregnancy to the rest of the family. Once we knew that the baby was okay, we decided to tell everyone. And as I went through the pregnancy, I noticed that more questions about my health and my future baby’s health were coming from different members of our family, like our parents, siblings, etc. For some reason, I seemed to get more attention, and more pressure from other family members this time around to deliver a child that was ‘normal’ ... If for some reason something was not right with this child, I know that I would have received pressure to terminate this pregnancy from both my husband and our parents.”

Another issue that emerged during discussions about TMS was the idea that society in general, and the medical community in particular are biased against people with disabilities. Women mentioned that when they are in public, they get curious stares from other people. They noted that this extra attention initially bothered them, but they have adjusted to these situations. One woman stated that she had a tendency to hug her son when she felt that others were watching him.

“Society is biased against people with disabilities ... People tend to fear what is different...what they don’t understand. These attitudes have to be changed. But it is very hard. Where are we supposed to begin? South Asian families are usually classified as being ‘inward-looking’ people who have a difficult time discussing important issues such as disability, etc ... If there is no dialogue within our community, how can we hope to change things? We go to the [Sikh] temples and that is where we usually make our contacts with other people from our community.

But we never talk about any of these issues. Yes, we do get support from other families who know us and see us there, but there never is any discussion about how we can improve the views of society. Instead there seems to be this overwhelming tendency to pity us for having a special needs child—a child who is different.”

Other women articulated how they felt about the treatment that they received from their family doctors after their child with Down syndrome was born. Some women said they were informed about the condition of their child by doctors who acted as though it ‘was the end of the world.’

“When I was first told about [my son’s] condition, I remember how our doctor came into our room and told us. The look on his face was one of complete gloom. Before he could say any of the words I knew that something was wrong. When he finally told us that our child had Down syndrome, within the next breath he started talking about other options such as giving up our child for adoption. He really had nothing positive to say about having a child with Down syndrome. After hearing the news, both my husband and myself went to the nursery to see our child. It was at that moment in time that we decided he was perfect just the way that he was ... there was no way that we could ever give him up. While I didn’t notice it at first, when I think back now, I realize that this doctor definitely had some sort of bias against children with disabilities.”

Review of TMS Options

Option 1. Support for continuing current funding for *ad hoc* use of TMS by women of all ages, was favoured as reflecting the demand for screening better than the other options, and as the most cost-effective way to provide some sort of a screening option to women.

Option 2. Funding a TMS program for women over age 35 and older, was preferred by women who felt that it is important to provide as much information to as possible to potential mothers in order to enable them to make decisions which are right for themselves.

Option 3. The option of no public funding of TMS was strongly favoured by those women are against abortions. They felt that any allocation of scarce health-care dollars into a screening program which takes direct aim at children with disabilities would be a waste of money and an insult to their children.

“I think that genetic screening interferes too much with nature’s course. What is so important about knowing what is wrong with our child in advance? I think that the major problem for us is to accept, as members of society, beauty in different forms ... The problem lies with us. For some reason we find it very difficult to accept the unpleasant things in life ... This is what we need to change.”

Option 4. A full TMS program be funded for pregnant women of all ages was favoured by one of the women interviewed as a beneficial program allowing women of all ages to learn more about their pregnancies and to prepare for the forthcoming birth of their child.

Summary

Responses and opinions surrounding TMS among the South Asian community varied greatly, along with the extent of knowledge concerning this technology.

All the women interviewed saw TMS as having strengths and weaknesses. The strengths lay in the fact that TMS provides a chance for them to become more knowledgeable about their pregnancy. In addition, it could provide women with a sense of reassurance about the health of their unborn child. It also allowed potential parents to know what to expect prior to the birth of their child and to prepare for the birth, whether or not Down syndrome is present.

The weaknesses associated with offering TMS to women centred on issues surrounding eugenics, and the notion of creating the 'perfect child'. Some of the women interviewed described how any technology used to identify certain fetuses as being at a higher risk for a certain abnormality, can lead to a dangerous form of 'societal cleansing'. Many see a thin line between any form of prenatal screening and eugenics, mainly because of the way that results are interpreted.

While there is no clear consensus among the individuals interviewed on which of the four TMS options would be the most beneficial, there seems to be an emerging voice within the community questioning the very existence and potential benefits of any TMS program.

APPENDIX G: TMS MODEL ASSUMPTIONS AND DATA SOURCES

Model to assess population impact and cost

A simulation-planning model was used to estimate the population impact of various TMS program options. The model was developed in two stages:

The first step was to estimate the number of pregnant women for each year of age in British Columbia¹ and estimating the number of fetuses with Down syndrome in each age group.² The number of fetuses with Down syndrome was estimated for the 2nd trimester, the time of TMS testing, as opposed to live births. The spontaneous abortion rate for fetuses with Down syndrome between the 2nd trimester and term is taken as 23%.¹⁶⁹

The second stage was to estimate the effect of applying TMS to the modelled 2nd trimester population. TMS test characteristics are known to vary according to maternal age, that is the sensitivity (detection rate) of the test increases as the prevalence increases with advancing maternal age. Because data from BC regarding TMS test characteristics³ have been reported, for the purposes of this analysis women are divided into two groups, those over and those under 35 years of age. The model allows for estimates of the detection rate, the false-positive rate, and the false-negative rate, for each sub-population and for the total population.

The actual population impact of TMS depends on several key variables:

1. TMS utilization at various ages. As shown by GEM data (**Table 13**), TMS utilization, at least in this initial phase, is strongly identified with women over age 30 and close to age 35, the established eligible age for amniocentesis without prior TMS. GEM data of utilization rates for each age group were factored into the model. Also in keeping with GEM experience, the model is based on the assumption that 50% of women age 35 and older would continue to select amniocentesis first, rather than TMS.
2. Population impact is very sensitive to the decisions of having amniocentesis after a TMS-positive result, and of having an abortion if Down syndrome is confirmed by cytogenetics. Amniocentesis rates are known to depend on access to services, which in BC favours women in Vancouver and Victoria.⁵² Amniocentesis utilization also varies with age, with the highest utilization in the younger age groups. GEM data were used to estimate the rate of amniocentesis utilization by year of age.
3. Population impact is also dependent on how many women age 35 and older continue to select amniocentesis first, rather than TMS. For the population 35 years and older, we assume at least half the women who would have chosen amniocentesis in the past will continue to choose amniocentesis, despite the availability of TMS.

Table 18: Triple-marker screening statistics (January 1, 1998 - December 31, 1998) *

AGE GROUP (years)	TOTAL WOMEN	NEGATIVE SCREENS	POSITIVE SCREENS				SCREEN POSITIVE RATE %				POST-SCREEN AMNIOCENTESIS				UPTAKE %				TRUE - POSITIVE SCREENS †		FALSE- POSITIVE SCREENS †
			T21	T18	SB	ALL	T21	T18	SB	ALL	T21	T18	SB	ALL	T21	T18	SB	ALL	T21	T18	TOTAL
<20	173	168	1	0	4	5	0.6	0	2.3	2.9	0	0	3	3	0	0	75	60			1
20-24	951	917	22	2	10	34	2.3	0.2	1.1	3.6	14	1	5	20	63.6	50	50	59	1	1	9
25-29	2519	2407	77	10	25	112	3.1	0.4	1.0	4.4	47	1	11	59	61	10	44	53	1	2	29
30-34	3945	3657	254	13	21	288	6.4	0.3	0.5	7.3	195	5	10	210	76.8	38	48	73	2		115
35-39	1763	1436	302	6	19	327	17.1	0.3	1.1	18.5	187	3	6	196	61.9	50	32	60	3		102
40-44	247	172	68	4	3	75	27.5	1.6	1.2	30.4	28	2	0	30	41.2	50	0	40	2		12
≥45	8	3	4	1	0	5	50.0	12.5	0	62.5	2	0	0	2	50	0	0	40			
ALL	9608	8760	728	36	82	846	7.6	0.4	0.9	8.8	473	12	35	520	65	33	43	61	9	3	268

T21 = trisomy 21
T18 = trisomy 18
SB = spina bifida

† Outcomes from known amniocenteses (193 unknown)
2 negative screens were false-negative
1 positive screen was a true-positive, but patient refused amniocentesis
3 positive screens had other anomalies found from karyotyping studies

* Source: Genes, Elements, Metabolism (GEM) Program, Children's & Women's Health Centre of British Columbia

Cost estimates

Cost estimates were limited to those found in the Medical Services Plan billing records and GEM budget. Although incomplete, because the costs do not contain operating budgets, overheads, shared resources, capital, buildings or land, the estimates seemed valid for the purpose of comparing the TMS Options in this review. The primary items and costs are:

- TMS (including genetic counselling) \$112
- amniocentesis \$635.10
- induced miscarriage follow-up care \$210.42

Table 19 provides further details of the components included in each item.

Table 19: Cost estimates for TMS, amniocentesis, follow-up care of amniocentesis- induced abortions and therapeutic abortions

TRIPLE-MARKER SCREEN*		AMNIOCENTESIS**		FOLLOW-UP CARE OF AMNIOCENTESIS INDUCED ABORTIONS**		2 nd TRIMESTER THERAPEUTIC ABORTION**	
Serum screening	\$90.00	Transabdominal #04680	\$87.17	Cervix dilatation and curettage #04500	\$76.70	By D&E or amniocentesis - 18 weeks and over # 04027)	\$149.95
Genetic counselling	\$22.00	Ultrasound guidance #04680	\$57.53	Anaes. Level 1 X 30 min.	\$45.52	Anaes. Level 2 X 45 min.	\$72.12
		Cytogenetic analysis #93030	\$402.20	OB Consult # 04010	\$88.20	OB Consult #04010	\$88.20
		OB Consult # 04010	\$88.20				
TOTAL	\$112.00		\$635.10		\$210.42		\$310.27

Sources: * Genes, Elements, Metabolism (GEM) Program estimates of their cost per TMS test

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Population at risk

In 1981, Baird and Sadovnik reported that the rate of birth of babies with Down syndrome in British Columbia was 1.46/1000.¹⁶ They were able to report this figure because at the time of their study, BC maintained a register of world-wide repute on congenital birth defects. Following loss of funding, however, this data resource is not sufficiently reliable for current purposes.

The 1981 data, although from BC, are of limited use because they do not take into account changes in the age distribution of women giving birth in the province between 1979 and 1999. In particular, they do not provide age-specific risk estimates which could be applied to the current age distribution of women giving birth. Therefore, alternative age-specific risk of Down syndrome profiles were sought.

The updated Hecht and Hook '96 model of maternal age specific risks for a Down syndrome birth was used because these authors based their meta-analysis on cohorts of women in which ascertainment of outcome was most likely to be complete. It is therefore more appropriate for contemporary estimates.² The incidence rates³ from the GEM pilot project (**Table 20**) provide an indication of local data, although since they are not population-based these data cannot be considered as representing the true incidence in BC.

Table 20: Incidence of chromosomal abnormalities from the GEM TMS pilot study

AGE GROUP	TRISOMY 21 (Down syndrome)	TRISOMY 21 (Down syndrome) or TRISOMY 18 (open neural tube defects including anencephaly and spina bifida)
Overall:	29 of 8333 1:287 3.5 per 1000 0.35%	32 of 8333 1:260 3.8 per 1000 0.38%
Age 35+:	13 of 2116 1:162 6.1 per 1000 0.61%	14 of 2116 1:151 6.6 per 1000 0.66%
<Age 35:	16 of 6217 1:389 2.6 per 1000 0.26%	18 of 6217 1:345 2.9 per 1000 0.29%

Utilization rates

Prenatal diagnostic tests: Current TMS testing rates were obtained directly from the GEM program (**Figure 3**). The rate of uptake of amniocentesis following positive TMS screen was taken from the GEM 1998 data.³ Amniocentesis rates for advanced maternal age in 1996/1997 were obtained from the Amniocentesis Business Plan for 1998,⁵² which included regional data.

Amniocentesis rates were not obtained from the Medical Services Plan administrative database because it does not distinguish between amniocentesis for prenatal testing and other indications. Utilization rates for cytogenetic testing for 1996/1997 were taken from an original analysis of the Medical Services Commission administrative database (see **Appendix E**).

Abortion: The rate of abortion following positive amniocentesis is unknown for BC; estimates were accordingly taken from the literature.^{170,171} The rate of induced abortion as an adverse effect following amniocentesis was also taken from the literature.⁴¹

TMS test parameters

TMS test characteristics, such as sensitivity and specificity, used in the population impact model were taken from a meta-analysis by Conde-Agudelo et al '98.¹⁵⁰ This meta-analysis was chosen for the rigor of its methodology in systematically reviewing and analysing the available studies of TMS screening in populations of women under and over age 35. The GEM TMS pilot project study data follow (**Table 21**).³ Test parameters correspond fairly closely with those obtained in other jurisdictions.

Table 21: Summary of test parameters from GEM TMS pilot study 1995 to 1997

AGE GROUP	BOTH TRISOMY 21 AND 18
Overall	Sensitivity: 72% Specificity: 91% False-negative rate: 28% False-positive rate: 87% Positive Predictive Value: 3.1% Negative Predictive Value: 99.9%
>35	Sensitivity: 79% Specificity: 79% False-negative rate: 21% False-positive rate: 21% Positive Predictive Value: 2.5% Negative Predictive Value: 99.8%
<35	Sensitivity: 67% Specificity: 95% False-negative rate: 33% False-positive rate: 5% Positive Predictive Value: 4.0% Negative Predictive Value: 99.9%

APPENDIX H: QUESTIONNAIRES AND INTERVIEW PROTOCOLS

I. GENETIC COUNSELLOR QUESTIONNAIRE

Distributed to all genetic counsellors within the Department of Medical Genetics at Children's and Women's Health Centre of BC:

1. Why do you think women/couples have the maternal serum triple screen?
2. What is the most important thing that you believe women/couples contemplating screening should consider?
3. What are some of the 'other' things that they should consider?
4. How long would you say that it takes to adequately explain the triple screen to a patient?
5. Is there any particular aspect of the triple screen that you feel is frequently misunderstood? If so, how would you attempt to explain it best?
6. What do you think individuals considering screening need to know about Down syndrome and Spina Bifida before deciding whether or not to test?
7. Do you think that knowing their child has Down syndrome or Spina Bifida prior to birth can help 'prepare' the family/couple for having a child with special needs? How?
8. Do you think that genetic counsellors and geneticists/pediatrician can educate families about the benefits of raising a child with Down syndrome or Spina Bifida and still remain non-directive? How?
9. If a couple asks for information on Down syndrome or Spina Bifida what sort of materials do you provide? What resources do you find most useful?
10. How would you describe children/individuals with Down syndrome to a patient that is unfamiliar with the condition?
11. How would you describe children/individuals with Spina Bifida to a patient that is unfamiliar with the condition?
12. What type of information do you think SHOULD BE included in a pamphlet on the triple screen?
13. What type of information do you think should NOT be included in a pamphlet on the triple screen?
14. Do you think that information regarding ultrasound markers and amniocentesis should be included in such a pamphlet? Why or why not?
15. Do you think that information about Down syndrome, Trisomy 18 and neural tube defects should be presented in the pamphlet? If so, what type of information?
16. Do you think it may be useful to include statements made by different couples regarding how they choose to have or not to have screening? Why or why not?
17. Do you feel that the pamphlet should state clearly that there are no cures for the conditions being screened for and that the screen provides information for couples that may help them 'prepare' for having a child with special needs or 'stop' the pregnancy? Why or why not?
18. What approach(es) do you use to help patients understand the difference between a screen and a diagnostic test?
19. Do you think that a 'visual aid' along with an interpretation guide might be useful in a pamphlet to help couples understand false/true positives and false/true negatives ?
20. If you could change any aspect(s) of the implementation of triple screening (as it currently stands) would you? What change(s) would you make and why?
21. Do you think that the triple-marker screen should be part of a provincially funded program? Why or why not? Any restriction criteria?
22. *Optional hypothetical question:*
If you were 28-32 years old and pregnant for the first time, do you think you would have the triple screen? Why or why not? What things would you need to consider? What about if you were 38 years old and this were your first pregnancy?

II. DOWN SYNDROME RESEARCH FOUNDATION FOCUS GROUP QUESTIONS

1. Why do you think women undergo testing?
2. Do you think that learning your baby has Down syndrome after testing (20+ weeks) could help 'prepare' the family for having a child with Down syndrome? How?
3. If you believe that one of the reasons women undergo testing for Down syndrome is out of fear of the unknown, do you think that is a relatively new phenomenon?
4. Why do you think that many prospective parents doubt their ability to raise a child with Down syndrome?
5. If you believe that women are pressured to have testing, who do you think does most of the pressuring? Why do you think they do that?
6. How do you think we can best educate people about the positive aspects of raising a child with Down syndrome? Do you think genetic counsellors can present such information and remain 'non-directional'? How?
7. Do you think women that decline having screening for Down syndrome might become 'blamed' by society for having a child with special needs?
8. Do you think that having screening alters the pregnancy experience: How and why?
9. What are some of the issues surrounding 'wrongful life' suits. Thoughts? Feelings?
10. What is the most important thing that you would want women contemplating having the triple screen to consider?

III. INTERVIEW QUESTIONS FOR BC PROVIDERS

1. What is your connection to or involvement with TMS?
2. Under which circumstances do you suggest TMS?
3. What do you like about it?
4. What are your concerns about TMS?
5. Do you have concerns about the rate of false positives?
6. False negatives?
7. Do you have concerns about the way in which TMS results are being reported to physicians and to women?
8. Are the results difficult to understand?
9. How could these difficulties be overcome?
10. What is the most important thing that you would want women thinking about having TMS to consider?
11. Does TMS present particular ethical concerns?
12. How TMS fits in other tests? (ultrasound, amniocentesis)
13. Impact on laboratory services and costs?
14. There are a number of different policy/program recommendations that might be made to the Ministry about TMS. I'd like to go through them (4) with you ask for your comments.
15. Option 1: Current situation with *ad hoc* funding for TMS
16. Option 2: No public funding for TMS; amniocentesis and CVS for women over 35
17. Option 3: Funding to offer TMS routinely only to women 35 and older
18. Option 4: Offering TMS to all pregnant women?
19. Is there an option other than these four which you would support?
20. What do you see as the important payment issues around TMS?
21. What are the barriers to developing an effective TMS program?

APPENDIX J

Table 22: Cost * summaries at various utilization levels

TMS TEST LEVEL	OPTION 1	OPTION 2	OPTION 3	OPTION 4
12,000	\$1,344,000	\$336,000	\$0	\$1,718,100
16,000	\$1,792,000	\$448,000	\$0	\$2,166,100
20,000	\$2,240,000	\$560,000	\$0	\$2,614,100
25,000	\$2,800,000	\$700,000	\$0	\$3,174,100
30,000	\$3,360,000	\$840,000	\$0	\$3,734,100

* Total costs of serum testing, genetic counselling and co-ordination (Option 4 only) excluding amniocentesis and follow-up care of amniocentesis induced abortions.

BIBLIOGRAPHY

- Al-Mufti R, McCarthy A, Fisk NM. Survey of obstetricians' personal preference and discretionary practice. *Eur J Obstet Gynecol Reprod Biol* 1997 May;73(1):1-4.
- Asch A. Prenatal diagnosis and selective abortion: a challenge to practice and policy. *Am J Public Health* 1999;89(11):1649-57.
- Assessing guidelines: prenatal ultrasound. *Protocols & Guidelines Update* 1999;2(1):2.
- Ayme S. Value of registries in decision making in public health: the example of trisomy 21. *Rev Epidemiol Sante Publique* 1996;44 Suppl 1:S82-9.
- Baillie C, Hewison J, Dormandy E, Fitzgerald T. Antenatal screening [letter]. *BMJ* 1999; 318: 805.
- Bajos N, Leridon H, Warszawski J, Bouyer J. The legalization of abortion: a major public health issue. *Am J Public Health* 1999;89(11):1763.
- Barker JC. Cultural diversity: changing the context of medical practice. *West J Med* 1992 Sep;157(3):248-54.
- Beazoglou T, Heffley D, Kyriopoulos J, Vintzileos A, Benn P. Economic evaluation of prenatal screening for Down syndrome in the USA. *Prenat Diagn* 1998;18(12):1241-52.
- Becker MH, Kaback MM, Rosenstock IM, Ruth MV. Some influences on public participation in a genetic screening program. *J Community Health* 1975 Fall;1(1):3-14.
- Bishop JC, Dunstan FD, Nix BJ, Reynolds TM, Swift A. All MoMs are not equal: some statistical properties associated with reporting results in the form of multiples of the median. *Am J Hum Genet* 1993 Feb;52(2):425-30.
- Botkin JR, Mehlman MJ. Wrongful birth: medical, legal, and philosophical issues. *J Law Med Ethics* 1994;22(1):21-8.
- Botto LD, Moore CA, Khoury MJ, Erickson JD. Neural-tube defects. *N Engl J Med* 1999;341(20):1509-19.
- Bouchard L, Renaud M. Female and male physicians' attitudes toward prenatal diagnosis: a pan-Canadian survey. *Soc Sci Med* 1997;44(3):381-92.
- Bouchard L, Renaud M, Kremp O, Dallaire L. Selective abortion: a new moral order? Consensus and debate in the medical community. *Int J Health Serv* 1995;25(1):65-84.
- Boyd PA, Chamberlain P, Hicks NR. 6-year experience of prenatal diagnosis in an unselected population in Oxford, UK. *Lancet* 1998;352:1577-81.
- Bray I, Wright DE, Davies C, Hook EB. Joint estimation of Down syndrome risk and ascertainment rates: a meta-analysis of nine published data sets. *Prenat Diagn* 1998 Jan;18(1):9-20.
- Bray IC, Wright DE. Estimating the spontaneous loss of Down-syndrome fetuses between the times of chorionic villus sampling, amniocentesis and livebirth. *Prenat Diagn* 1998 Oct;18(10):1045-54.

- British Columbia. Ministry of Health and Ministry Responsible for Seniors. British Columbia health regions. [cited October 14, 1999] Available from URL: <http://www.hlth.gov.bc.ca/cpa/regional/hrmap.html>.
- British Columbia. Vital Statistics Agency. Birth by age of mother and live births by birth order, British Columbia, 1997. [cited Sept 30, 1999] Available from URL: <http://www.hlth.gov.bc.ca/vs.stats/ammual/1997/tab07.html>.
- The California expanded alpha-fetoprotein screening program: prenatal care provider handbook. Berkeley, CA: The Branch; 1994.
- The Canadian Early and Mid-Trimester Amniocentesis Trial (CEMAT) Group. Randomised trial to assess safety and fetal outcome of early and mid-trimester amniocentesis. *Lancet* 1998;351:242-7.
- Canick JA, Saller DN. Maternal serum screening for aneuploidy and open fetal defects. In: Blakemore KJ, editor. *Prenatal diagnosis: present and future perspectives*. Toronto: WB Saunders Company; 1993. p443-63. (Obstetrics and gynecology clinics of North America; v.20, no.3).
- Carothers AD, Boyd E, Lowther G, Ellis PM, Couzin DA, Faed MJW, Robb A. Trends in prenatal diagnosis of Down syndrome and other autosomal trisomies in Scotland 1990 to 1994, with associated cytogenetic and epidemiological findings. *Genetic Epidemiol* 1999;16(2):179-190.
- Carroll JC. Maternal serum screening. *Can Fam Phys* 1994 Oct;40:1756-64.
- Carroll JC, Reid AJ, Woodward CA, Permaul-Woods JA, Domb S, Ryan G, et al. Ontario Maternal Serum Screening Program: practices, knowledge and opinions of health care providers. *CMAJ* 1997 Mar;156(6):775-84.
- Chambers K, Milner R. Maternal triple marker screening. *BCMJ* 1999 May;41(5):211-13.
- Chapple J. Screening issues: the public health aspect. In: Abramsky L, Chapple J, editors. *Prenatal diagnosis: the human side*. New York: Chapman & Hall; 1994. p55-69.
- Cheng EY, Luthy DA, Zebelman AM, Williams MA, Lieppman RE, Hickok DE. A prospective evaluation of a second-trimester screening test for fetal Down syndrome using maternal serum alpha-fetoprotein, hCG, and unconjugated estriol. *Obstet Gynecol* 1993 Jan;81(1):72-7.
- Children's and Women's Health Centre of British Columbia. Maternal serum screening study in British Columbia, January 1995 to March 1997: outcome information for physicians, midwives and patients. Vancouver (BC): Children's and Women's Health Centre of British Columbia; 1998.
- Chitty L. Prenatal screening for chromosome abnormalities. *Br Med Bull* 1998;54(4):839-56.
- Clarke A, Parsons E. *Culture, kinship and genes: toward cross-cultural genetics*. London, England: Macmillan Press Ltd; 1997.
- Clarke A. Genetics, ethics, and audit. *Lancet* 1990 May 12;335(8698):1145-7.
- Clayton EW. What should be the role of public health in newborn screening and prenatal diagnosis? *Am J Preve Med* 1999;16(2):111-5.
- Conde-Agudelo A, Kafury-Goeta AC. Triple-marker test as screening for Down syndrome: a meta-analysis. *Obstet Gynecol Surv* 1998 Jun;53(6):369-76.

- Coughlin SS. The intersection of genetics, public health, and preventive medicine. *Am J Prev Med* 1999;16(2):89-90.
- Cragan JD, Roberts HE, Edmonds LD, Khoury MJ, Kirby RS, Shaw GM et al. Surveillance for anencephaly and spina bifida and the impact of prenatal diagnosis--United States, 1985-1994. *MMWR* 1995 Aug 25;44(4):1-13.
- Crandall BF, Robinson L, Grau P. Risks associated with an elevated maternal serum alpha-fetoprotein level. *Am J Obstet Gynecol* 1991 Sep;165(3):581-6.
- Cuckle H. Improved parameters for risk estimation in Down's syndrome screening. *Prenat Diagn* 1995 Nov;15(11):1057-65.
- Cuckle H. Maternal serum screening policy for Down's syndrome. *Lancet* 1992;340:799.
- Cuckle HS. Effect of maternal age curve on the predicted detection rate in maternal serum screening for down-syndrome. *Prenat Diagn* 1998 Nov;18(11):1127-30.
- Cuckle HS, Wald NJ, Thompson SG. Estimating a woman's risk of having a pregnancy associated with Down's syndrome using her age and serum alpha-fetoprotein level. *Br J Ob Gyn* 1987;94:387-402.
- Cuckle HS, Wald NJ, Barkai G, Fuhrmann W, Altland K, Brambati B, et al. First-trimester biochemical screening for Down syndrome. *Lancet* 1988 Oct 8;2(8615):851-2.
- Cuckle HS, Wald NJ, Nanchahal K, Densem J. Repeat maternal serum alpha-fetoprotein testing in antenatal screening programmes for Down's syndrome. *Br J Obstet Gynaecol* 1989 Jan;96(1):52-60.
- Danzeisen DP, Reitler EG. Tort law: wrongful birth and wrongful life actions. *Harvard J Law Public Pol* 1988;11(3):859-65.
- Davidov B, Goldman B, Akstein E, Barkai G, Legum C, Dar H et al. Prenatal testing for Down syndrome in the Jewish and non-Jewish populations in Israel. *Israel J Med Sci* 1994 Aug;30(8):629-33.
- De Wals P, Trochet C, Pinsonneault L. Prevalence of neural tube defects in the province of Quebec, 1992. *Can J Public Health* 1999; 90(4):237-9.
- Dick PT. Periodic health examination, 1996 update: 1: Prenatal screening for and diagnosis of Down syndrome: Canadian Task Force on the Periodic Health Examination. *CMAJ* 1996 Feb 15;154(4):465-79.
- Down syndrome screening: ACOG Committee Opinion: Committee on Obstetric Practice. *Int J Gynaecol Obstet* 1994 Nov;47(2):186-90.
- Dumaret AC, Devigan C, Julianreynier C, Goujard J, Rosset D, Ayme S. Adoption and fostering of babies with Down-syndrome: a cohort of 593 cases. *Prenat Diagn* 1998 May;18(5):437-445.
- Dunstan FD, Nix AB. The impact of maternal age on the cost effectiveness of Down's syndrome screening. *Br J Obstet Gynaecol* 1997 Feb;104(2):269-70.
- Durand-Zaleski I, Chaix C. Modelling of decision analysis and costs. *Eur Radiol* 1998;8(3):491-3.

- Ennever FK, Lave LB. Parent preferences and prenatal testing for neural tube defects. *Epidemiology* 1995 Jan;6(1):8-16.
- EUCROMIC Workshop. Proceedings (1996: Paris). Prenatal diagnosis in Europe : proceedings of an EUCROMIC Workshop, Paris, May 23-24, 1996. New York: S. Karger, 1997. *Eur J Hum Genet* 1997 Mar;5(suppl 1):1-90.
- Extermann P, Bischof P, Marguerat P, Mermillod B. Second-trimester maternal serum screening for Down's syndrome: free beta-human chorionic gonadotrophin (HCG) and alpha-fetoprotein, with or without unconjugated oestriol, compared with total HCG, alpha- fetoprotein and unconjugated oestriol. *Hum Reprod* 1998 Jan;13(1):220-3.
- Fairgrieve S, Magnay D, White I, Burn J. Maternal serum screening for Down's syndrome: a survey of midwives' views. *Public Health* 1997 Nov;111(6):383-5.
- Farag TI, Al Awadi SA. Community genetics and counseling in the Arab countries. In: Ball S, editor. *Strategies in genetics counseling: the challenge of the future, volume 1*. New York: Human Sciences Press; 1988. p241-2.
- Fletcher J, Hicks NR, Kay JD, Boyd PA. Using decision analysis to compare policies for antenatal screening for Down's syndrome. *BMJ* 1995 Aug 5;311(7001):351-6.
- Ford C, Moore AJ, Jordan PA, Bartlett WA, Wylde MP, Jones AF, MacKenzie WE. The value of screening for Down's syndrome in a socioeconomically deprived area with a high ethnic population. *Br J Obstet Gynaecol* 1998 Aug;105(8):855-9.
- Forrester MB, Merz RD, Yoon PW. Impact of prenatal diagnosis and elective termination on the prevalence of selected birth defects in Hawaii. *Am J Epidemiol* 1998 Dec 15;148(12):1206-11.
- Frame PS, Berg AO, Woolf S. U.S. Preventive Services Task Force: highlight of the 1996 report. *Am Fam Phys* 1997 Feb 1;55(2):567-76, 581-2.
- Fuhrmann W, Wendt P, Weitzel HK. Maternal serum-AFP as screening test for Down syndrome. *Lancet* 1984 Aug 18;2(8399):413.
- Fuhrmann W, Weitzel HK. Maternal serum alpha-fetoprotein screening for neural tube defects. *Hum Genet* 1985;69:47-61.
- Gabarron J, Ramos C. Prenatal diagnosis in Spain. *Eur J Hum Genet* 1997;5 Suppl 1:64-9.
- Ganiats TG, Cantor SB. Cost-effectiveness and Down syndrome. *Am J Public Health* 1999 Jan;89(1):110-12.
- Garver KL, Garver B. Eugenics: past, present, and the future. *Am J Hum Genet* 1991 Nov;49(5):1109-18.
- Gekas J, Gondry J, Mazur S, Cesbron P, Thepot F. Informed consent to serum screening for Down syndrome: are women given adequate information? *Prenat Diagn* 1999 Jan;19(1):1-7.
- Georges E, Mitchell L. Baby talk: the rhetorical production of maternal and fetal selves. In: Longino H, Kohlstedt S, editors. *Writing and speaking the body: rhetorical and feminist studies of reproductive technologies*. Madison (WI): University of Wisconsin Press; 1999. In press.
- Glazier R, Goel V, Holzapfel S, Summers A, Pugh P, Yeung M. Written patient information about triple-marker screening: a randomized, controlled trial. *Obstet Gynecol* 1997 Nov;90(5):769-74.

- Glover NM, Glover SJ. Ethical and legal issues regarding selective abortion of fetuses with Down syndrome. *Ment Retard* 1996 Aug;34(4):207-14.
- Goel V, Glazier R, Summers A, Holzapfel S. Psychological outcomes following maternal serum screening: a cohort study. *CMAJ* 1998 Sep;159(6):651-6.
- Goodman MJ, Goodman LE. The overselling of genetic anxiety. *Hastings Cent Rep* 1982 Oct;12(5):20-7.
- Grebner EE. Basic concepts in biochemical antenatal diagnosis. In: Blakemore KJ, editor. *Prenatal diagnosis: present and future perspectives*. Toronto: W.B. Saunders Company; 1993. p421-31. (*Obstetrics and gynecology clinics of North America*; v.20, no.3).
- Green J, Statham H, Snowdon C. Screening for fetal abnormalities: attitudes and experiences. In: Chard T, Richards MPM, editors. *Obstetrics in the 1990s: current controversies*. London: Mac Keith Press; 1992. p65-89. (*Clinics in developmental medicine*; nos. 123/124).
- Green JM. Calming or harming?: a critical review of psychological effects of fetal diagnosis on pregnant women. Galton Institute, *Occasional Papers, Second Series* ; no. 2. Northfields, London: The Galton Institute; 1990.
- Green JM, Snowdon C, Statham H. Pregnant women's attitudes to abortion and prenatal screening. *J Reprod Infant Psychol* 1993;11(1):31-9.
- Green JM. Serum screening for Down's syndrome: experiences of obstetricians in England and Wales. *BMJ* 1994 Sep 24;309(6957):769-72.
- Green JM. Women's experiences of prenatal screening and diagnosis. In: Abramsky L, Chapple L, editors. *Prenatal diagnosis: the human side*. New York: Chapman & Halls; 1994. p. 36-53.
- Green JM, Statham H, Snowdon C. Women's knowledge of prenatal screening tests. 1: relationships with hospital screening policy and demographic factors. *J Reprod Infant Psychol* 1993;11(1):11-20.
- Gressens P, Collin P, Lebarbier P, Husson I, Pennecot G, Blot P, et al. Prenatal diagnosis and outcome of patients with spina bifida. *Arch Pediatr* 1998 Sep;5(9):1004-8.
- Grevengood C, Shulman LP, Dungan JS, Martens P, Phillips OP, Emerson DS, et al. Severity of abnormality influences decision to terminate pregnancies affected with fetal neural tube defects. *Fetal Diagn Ther* 1994 Jul-Aug;9(4):273-7.
- Haddow JE, Palomaki GE, Knight GJ, Williams J, Pulkkinen A, Canick JA, et al. Prenatal screening for Down's syndrome with use of maternal serum markers. *N Engl J Med* 1992 Aug 27;327(9):588-93.
- Haddow JE, Palomaki GE, Knight GJ, Cunningham GC, Lustig LS, Boyd PA. Reducing the need for amniocentesis in women 35 years of age or older with serum markers for screening. *N Engl J Med* 1994 Apr;330(16):1114-8.
- Haddow JE, Palomaki GE, Knight GJ, Williams J, Miller WA, Johnson A. Screening of maternal serum for fetal Down's-syndrome in the first trimester. *N Engl J Med* 1998 Apr 2;338(14):955-61.
- Haddow JE, Palomaki GE. Similarities in women's decision-making in the US and UK during prenatal screening for Down's syndrome. *Prenat Diagn* 1996 Dec;16(12):1161-2.

- Halliday J, Lumley J, Bankier A. Karyotype abnormalities in fetuses diagnosed as abnormal on ultrasound before 20 weeks' gestational age. *Prenat Diagn* 1994 Aug;14(8):689-97.
- Hatcher Roberts J. Coalition building and public opinion: new reproductive technologies and Canadian Civil Society. *Int J Technol Assess Health Care* 1999;15(1):15-21.
- Hausler MC, Berghold A, Zierler H, Behmel A, Pertl B. The triple test scenario for Styria: With data of the Styria Abnormalities Register. *Gynakol Geburtshilfliche Rundsch* 1996;36(3):169-77.
- Health Council of the Netherlands. Committee Genetic Screening. Genetic screening: report of a committee of the Health Council of the Netherlands. The Hague: Health Council; 1994.
- Health status registry: a unique and valuable health planning tool. Victoria (BC): Division of Vital Statistics, BC Ministry of Health and Ministry Responsible for Seniors; 1994.
- Health status registry: congenital anomalies, genetic defects, selected disabilities, British Columbia to 1994. Victoria (BC): Division of Vital Statistics, BC Ministry of Health and Ministry Responsible for Seniors; 1996.
- Hecht CA, Hook EB. Rates of Down syndrome at livebirth by one-year maternal age intervals in studies with apparent close to complete ascertainment in populations of European origin: a proposed revised rate schedule for use in genetic and prenatal screening. *Am J Med Genet* 1996 Apr 24;62(4):376-85.
- Helm DT, Miranda S, Chedd NA. Prenatal diagnosis of Down-syndrome: mothers reflections on supports needed from diagnosis to birth. *Ment Retard* 1998 Feb;36(1):55-61.
- Henderson B, Azar SR, Oosthuizen S. Is it cost effective to prevent Down syndrome in the Free State Province - South Africa? *Teratology* 1998;57(1):43.
- Herrmann J. Triple-marker screening of serum for Down's syndrome. *N Engl J Med* 1994 Sep;331(10):681-2.
- Holtzman NA, Faden RR, Leonard CO, Chase GA, Ulrich SR. The effect of education on physician's knowledge of a laboratory test: the case of maternal serum alpha-fetoprotein screening. *J Clin Ethics* 1991;2(4):243-7.
- Hook EB, Waller DK. Prenatal screening for neural tube defects and chromosome abnormalities: the complexities of program evaluation. *Epidemiology* 1995 Jan;6(1):1-4.
- Hook EB. Rates of chromosome abnormalities at different maternal ages. *Obstet Gynecol* 1981;58:282-5.
- Howe DT, Gornall R, Wellesley D, Boyle T, Barber J. Six year survey of screening for Down's syndrome by maternal age and mid-trimester ultrasound scans. *BMJ* 2000;320:606-10.
- Hsu JJ, Hsieh TT, Hsieh FJ. Down syndrome screening in an Asian population using alpha-fetoprotein and free beta-hCG: a report of the Taiwan Down Syndrome Screening Group. *Obstet Gynecol* 1996 Jun;87(6):943-7.
- Hubbard R, Henifin MS. Genetic screening of prospective parents and of workers: some scientific and social issues. *Int J Health Serv* 1985;15(2):231-51.
- Isada NB, Blakemore KJ. Basic concepts in molecular (DNA) diagnosis. In: Blakemore KJ, editor. *Prenatal diagnosis: present and future perspectives*. Toronto: W.B. Saunders Company; 1993. p413-19.

Johnson AM, Palomak GE, Haddow JE. Maternal serum a-fetoprotein levels in pregnancies among black and white women with fetal open spina bifida: a United States Collaborative Study. *Am J Obstet Gynecol* 1990;162:328-31.

Johnson J-A, Summers A, SOGC Genetics Committee. Prenatal genetic screening for Down syndrome and open neural tube defects using maternal serum marker screening. *J Soc Obstet Gynaecol Can* 1999;21(9):887-91.

Johnson JP, Streets K, Fitzgerald J, Priest J, Vanisko M, Haag M. Influence of triple-marker screen risk versus a priori risk in decision for amniocentesis in women of advanced maternal age. *Prenat Diagn* 1998 Sep;18(9):979-80.

Kenen RH. The at-risk health status and technology: a diagnostic invitation and the 'gift' of knowing. *Soc Sci Med* 1996 Jun;42(11):1545-53.

Kimlova I, Prochazkova. Screening for Down's syndrome--results of a 3-year study. *Ceska Gynecol* 1996 Apr;61(2):75-8.

Knight GJ, Palomaki GE, Haddow JE. Use of maternal serum alpha-fetoprotein measurements to screen for Down's syndrome. *Clin Obstet Gynecol* 1988 Jun;31(2):306-27.

Knoppers BM, Le Bris S. Reproductive genetics: Canadian and European perspectives. *Fetal Diagn Ther* 1993;8(suppl 1):189-201.

Kolker A, Burke BM. *Prenatal testing: a sociological perspective*. Westport, CT: Bergin & Garvey; 1994.

Kornman LH, Beekhuis JR, Mantingh A, Morssink LP. Serum screening for fetal Down syndrome in pregnant women with an indication for prenatal diagnosis because of age: fewer amniocenteses. *Nederlands Tijdschrift voor Geneeskunde* 1995 Sep;139(36):1840-4.

Kramer RL, Jarve RK, Yaron Y, Johnson MP, Lampinen J, Kasperski SB, Evans MI. Determinants of parental decisions after the prenatal diagnosis of Down-syndrome. *Am J Med Genetics* 1998 Sep;79(3):172-74.

Kraut AM. *Silent travelers: germs, genes, and the 'immigrant menace'*. New York: BasicBooks; 1994.

Kupperman M, Goldberg JD, Nease RF, Washington AE. Who should be offered prenatal diagnosis?: the 35-year-old question. *Am J Public Health* 1999;89(2):160-3.

Kuppermann M, Gates E, Washington AE. Racial-ethnic differences in prenatal diagnostic test use and outcomes: preferences, socioeconomics, or patient knowledge? *Obstet Gynecol* 1996 May;87(5 Pt 1):675-82.

Larsen SO, Christiansen M, Norgaard-Pedersen B. Inclusion of serum marker measurements from a previous pregnancy improves Down syndrome screening performance. *Prenat Diagn* 1998 Jul;18(7):706-12.

Lenke R, Nadel A. Cost-effectiveness of strategies used in the evaluation of pregnancies complicated by elevated maternal serum alpha-fetoprotein levels. *Obstet Gynecol* 1997;90(2):317-18.

Lippman A. Embodied knowledge and making sense of prenatal diagnosis. [Forthcoming].

Lippman A. Led (astray) by genetic maps: the cartography of the human genome and health care. *Soc Sci Med* 1992 Dec;35(12):1469-76.

Lippman A. Prenatal genetic testing and geneticization: mother matters for all. *Fetal Diagn Ther* 1993;8(supl 1):175-88.

Lockitch G, Halstead C. Maternal serum screening study in British Columbia, January 1995 to march 1997: outcome information for physicians, midwives and patients. Vancouver (BC): Children's & Women's Health Centre of British Columbia; 1998.

Lockitch G. A provincial regionalised program of second trimester pregnancy screening by Maternal Serum Triple Marker and Fetal Ultrasound. Vancouver (BC): Children's & Women's Health Centre of British Columbia; 1998.

Lockitch G, Langlois S, Wilson RD. Summary of proposal for a provincial regionalised maternal triple marker serum screening program. Vancouver (BC): Children's & Women's Health Centre of British Columbia; 1998.

Lofsky S. Maternal serum screening. *CMAJ* 1999 Apr;160(8):1125-6.

Lumsden CJ, Wilson EO. Genes, mind, and culture: the coevolutionary process. Cambridge, Mass: Harvard University Press; 1981.

Macintosh M, Ellis A, Cuckle H, Seth J. Variation in biochemical screening for Down's syndrome in the United Kingdom. *Br J Obstet Gynaecol* 1998 Apr;105(4):465-7.

Macintosh MC. The impact of maternal age on the cost effectiveness of Down's syndrome screening. *Br J Obstet Gynaecol* 1996 Nov;103(11):1175-7.

Macintosh MCM. The perceived risks of Down's syndrome screening. *Contemp Rev Obstet Gynaecol* 1996;8(1):15-19.

Macri JN, Spencer K, Anderson R. Dual analyte immunoassay - a new approach to neural tube defect. *Ann Clin Biochem* 1992;29:390-6.

Macri JN, Kasturi RV, Krantz DA, Cook EJ. Sensitivity and specificity of screening for Down syndrome with alpha-fetoprotein, hCG, unconjugated estriol, and maternal age. *Obstet Gynecol* 1991 Jun;77(6):963-5.

Madlon-Kay DJ, Reif C, Mersy DJ, Luxenberg MG. Maternal serum alpha-fetoprotein testing: physician experience and attitudes and their influence on patient acceptance. *J Fam Pract* 1992 Oct;35(4):395-400.

Mancini G, Perona M, Dall'Amico CD, Bollati C, Fulvia A, Carbonara AO. hCG, AFP, and uE3 patterns in the 14-20th weeks of Down's syndrome pregnancies. *Prenat Diagn* 1992 Jul;12(7):619-24.

Markens S, Browner CH, Press N. Because of the risks: how US pregnant women account for refusing prenatal screening. *Soc Sci Med* 1999;49(3):359-69.

Marks J. Historiography of eugenics. *Am J Hum Genet* 1993;52:650-52.

Marteau TM, Cook R, Kidd J, Michie S, Johnston M, Slack J, Shaw RW. The psychological effects of false-positive results in prenatal screening for fetal abnormality: a prospective study. *Prenat Diagn* 1992;12:205-14.

- Match making scheme solves Tay-Sachs problem. *JAMA* 1987 Nov 20;258(19):2636-9.
- McQueen DV. Social aspects of genetic screening for Tay-Sachs disease: the pilot community screening program in Baltimore and Washington. *Soc Biol* 1975;22(2):125-33.
- Meschino WS. Effect of genetic information on care. *CMAJ* 1996 Sep;155(5):509,512.
- Miller-Catchpole R. Maternal serum alpha-fetoprotein testing and Down's Syndrome. *Diagnostic and Therapeutic Technology Assessment (DATTA)* ; May 12, 1988. Chicago, IL: American Medical Association; 1988.
- Milunsky A, Alpert E. Results and benefits of a maternal serum a-fetoprotein screening program. *JAMA* 1984 Sep;252(11):1438-42.
- Mittman I. A model perinatal genetics program. In: Paul N, Kavanagh L, editor. *Genetics for underserved populations. Proceedings of the National Symposium on Genetic Services for Underserved Populations*; 1989 May; Arlington VA. Washington (DC): National Center for Education in Maternal and Child Health; 1990 p. 93-100.
- Montgomery J. Legal issues in prenatal diagnosis. In: Abramsky L, Chapple J, editors. *Prenatal diagnosis: the human side*. New York: Chapman & Hall; 1994. p. 23-36.
- Murray D, Tennison B. Decision analysis and screening for Down's syndrome: estimate of uptake of amniocentesis is overoptimistic. *BMJ* 1995 Nov 18;311(7016):1371-3.
- Murray J, Cuckle H, Taylor G, Littlewood J, Hewison J, National Coordinating Centre for Health Technology Assessment (UK). *Screening for cystic fibrosis. Health technology assessment (NCCHTA)* ; 3(8) Southam, SO, UK: National Coordinating Centre for Health Technology Assessment; 1999.
- Murray RF Jr, Chamberlain N, Fletcher J, Hopkins E, Jackson R, King PA, Powledge TM. Special considerations for minority participation in prenatal diagnosis. *JAMA* 1980 Mar 28;243(12):1254-6.
- Mutton D, Ide RG, Alberman E. Trends in prenatal screening for and diagnosis of Down's syndrome: England and Wales, 1989-97. *BMJ* 1998 Oct 3;317(7163):922-3.
- Nadel AS, Norton ME, Wilkins-Haug L. Cost-effectiveness of strategies used in the evaluation of pregnancies complicated by elevated maternal serum alpha-fetoprotein levels. *Obstet Gynecol* 1997;89(5 I):660-65.
- Nelson KB, Ellenberg JH. Childhood neurological disorders in twins. *Paediatr Perinat Epidemiol* 1995 Apr;9(2):135-45.
- Norup M. Attitudes towards abortion among physicians working at obstetrical and paediatric departments in Denmark. *Prenat Diagn* 1998 Mar;18(3):273-80.
- Nsiah-Jefferson L, Hall EJ. Reproductive technology: perspectives and implications for low-income women and women of color. In: Ratcliff KS, Ferree MM, Mellow GO, Wright BD, Price GD, Yanoshik K, Freston MS, editors. *Healing technologies: feminist perspectives*. Ann Arbor (MI): University of Michigan Press; 1989. p. 93-117.
- O'Connor B. More collaboration is needed about benefits of new genetic screening tests. *BMJ* 1998 Aug;317:471.
- Oakley GP Jr. Prevention of neural-tube defects. *N Engl J Med* 1999;341(20):1546.

- Odibo A, Wald NJ, George L, Wallace EM, Hackshaw A. Serum screening for Down's syndrome between 8 and 14 weeks of pregnancy. *Br J Obstet Gynaecol* 1996;103(11):1173-75.
- Olsen CL, Cross PK. Trends in the use of prenatal diagnosis in New York State and the impact of biochemical screening on the detection of Down syndrome: 1984- 1993. *Prenat Diagn* 1997 Dec;17(12):1113-24.
- Osborne NG, Feit MD. The use of race in medical research. *JAMA* 1992 Jun 17;267(2):275-9.
- Palomaki GE, Haddow JE, Beauregard LJ. Prenatal screening for Down's syndrome in Maine, 1980 to 1993. *N Engl J Med* 1996 May;334(21):1409-10.
- Palomaki GE, Knight GJ, McCarthy JE, Haddow JE, Donhowe JM. Maternal serum screening for Down syndrome in the United States: a 1995 survey. *Am J Obstet Gynecol* 1997;176:1046-51.
- Palomaki GE, Neveux LM, Haddow JE. Can reliable Down's syndrome detection rates be determined from prenatal screening intervention trials? *J Med Screen* 1996;3(1):12-7.
- Palomaki GE, Panizza DS, Canick JA. Screening for Down syndrome using AFP, uE3, hCG: Effect of maternal weight. *Am J Human Genet* 1990;47:282.
- Paul A. Drawing new legal road map: wrongful-birth lawsuit devoid of hard, fast rules. *Winnipeg Free Press* 1994 Sep 6:B2.
- Paul A. MD sued over birth. *Winnipeg Free Press* 1994 Sep 6:A1.
- Pearson V. Antenatal genetic screening. Bristol, England: Health Care Evaluation Unit, University of Bristol; 1995.
- Permaul-Woods JA, Carroll JC, Reid AJ, Woodward CA, Ryan G, Domb S, Arbitman S, Fallis B, Kiltz J. Going the distance: the influence of practice location on the Ontario maternal serum screening program. *CMAJ* 1999;161(4):381-5.
- Phillips DP, Kanter EJ, Bednarczyk B, Tastad PL. Importance of the lay press in the transmission of medical knowledge to the scientific community. *N Engl J Med* 1991 Oct 17;325(16):1180-3.
- Phillips OP, Elias S, Shulman LP, Andersen RN, Morgan CD, Simpson JL. Maternal serum screening for fetal Down syndrome in women less than 35 years of age using alpha-fetoprotein, hCG, and unconjugated estriol: a prospective 2-year study. *Obstet Gynecol* 1992 Sep;80(3 Pt 1):353-8.
- Platt LD, Feuchtbaum L, Filly R, Lustig L, Simon M, Cunningham GC. The California maternal serum a-fetoprotein screening program: the role of ultrasonography in the detection of spina bifida. *Am J Obstet Gynecol* 1992;166:1328-9.
- Pregnancy after 35: what's the real risk? *Patient Care* 1996 Mar;7(3):81-91.
- Prenatal screening for fetal trisomy and neural tube defects. Vancouver (BC): BC Children's and Women's Hospital.
- Press N, Browner CH. Why women say yes to prenatal diagnosis. *Soc Sci Med* 1997;45(7):979-89.
- Press N, Browner CH. Why women say yes to prenatal diagnosis. *Soc Sci Med* 1997 Oct;45(7):979-89.

Press NA, Browner CH. 'Collective fictions': similarities in reasons for accepting maternal serum alpha-fetoprotein screening among women of diverse ethnic and social class backgrounds. *Fetal Diagn Ther* 1993 Apr;8 Suppl 1:97-106.

Practice guidelines for health care providers involved in prenatal screening and diagnosis. Society of Obstetricians and Gynecologists of Canada. *J Soc Obstet Gynaecol Can.* Aug 1998;Vol 75.

Prevention program for reducing risk for neural tube defects: South Carolina, 1992-1994. *MMWR* 1995 Mar;44(8):141-2.

Protocol Steering Committee. Protocols & Guidelines Update. Assessing guidelines: prenatal ultrasound. BC Ministry of Health & Ministry Responsible for Seniors. 1999;2(1):2

Provincial Amniocentesis Steering Committee. The Provincial Amniocentesis Program business plan. Vancouver, (BC): BC Women's Hospital & Health Centre; 1998.

Pueschel SM. Maternal alpha-fetoprotein screening for Down's syndrome. *N Engl J Med* 1987 Aug 6;317(6):376-8.

Quéniart A. Risky business: medical definitions of pregnancy. In: Currie D, Raoul V, editors. *The anatomy of gender.* Ottawa: Carleton University Press; 1992. p161-74.

Raeburn S. Evidence based screening for Down's syndrome: we should be prepared to re-examine entrenched practices. *BMJ* 2000;320:592-3.

Reid M. The diffusion of four prenatal screening tests across Europe. Diffusion of medical technology in Europe. London, England: King's Fund Centre; 1991.

Richards S. Prenatal diagnosis: amniocentesis or chorion villus sampling. Briefing paper ; no. 6. Bristol, England: R & D Directorate, South and West Regional Health Authority; 1995.

Riley MM, Halliday JL, Lumley JM. Congenital malformations in Victoria, Australia, 1983-95: an overview of infant characteristics. *J Paediatr Child Health* 1998 Jun;34(3):233-40.

Roberts T, Mugford M, Piercy J. Choosing options for ultrasound screening in pregnancy and comparing cost effectiveness: a decision analysis approach. *Br J Obstet Gynaecol* 1998 Sep;105(9):960-70.

Roelofsen EEC, Kamerbeek LI, Tymstra TJ, Beekhuis JR, Mantingh A. Women's opinions on the offer and use of maternal serum screening. *Prenat Diagn* 1993;13:741-7.

Sadovnick AD, Baird PA. A cost-benefit analysis of a population screening programme for neural tube defects. *Prenat Diagn* 1983 Apr-Jun;3(2):117-26.

Sadovnick AD, Baird PA. A cost-benefit analysis of prenatal detection of down syndrome and neural tube defects in older mothers. *Am J Med Genet* 1981;10(4):367-78.

Salonen R, Kurki L, Lappalainen M. Experiences of mothers participating in maternal serum screening for Down's syndrome. *Eur J Hum Genet* 1996;4(2):113-9.

Sanders RC. Legal problems related to obstetrical ultrasound. *Ann N Y Acad Sci* 1998 Jun;847:220-7.

- Sanders RC. Ultrasonic clues to the detection of chromosomal anomalies. In: Blakemore KJ, editor. *Prenatal diagnosis: present and future perspectives*. Toronto: WB Saunders Company; 1993. p455-83.
- Santalahti P, Aro AR, Hemminki E, Helenius H, Ryyanen M. On what grounds do women participate in prenatal screening. *Prenat Diagn* 1998 Feb;18(2):153-165.
- Santalahti P. *Prenatal screening in Finland: availability and women's decision-making and experiences*. Helsinki, Finland: National Research and Development, Centre for Welfare and Health, STAKES; 1994.
- Santalahti P, Hemminki E, Latikka AM, Ryyanen MU. Women's decision making in prenatal screening. *Soc Sci Med* 1998 Apr;46(8):1067-76.
- Saridogan E, Djahanbakhch O, Naftalin AA. Screening for Down's syndrome: experience in an inner city health district. *Br J Obstet Gynaecol* 1996 Dec;103(12):1205-11.
- Screening for Down Syndrome. In: *Guide to clinical preventive services: report of the U.S. Preventive Services Task Force*. 2nd ed. Philadelphia (PA): Williams & Wilkins; 1996. p449-65.
- Seror V, Costet N. Down-syndrome serum marker screening: decision criteria and implicit values. *Health Policy* 1998 Jan;43(1):83-96.
- Serra-Prat M, Gallo P, Jovell AJ, Aymerich M, Estrada MD. Trade-offs in prenatal detection of Down syndrome. *Am J Public Health* 1998 Apr;88(4):551-7.
- Shackley P, Cairns J. Evaluating the benefits of antenatal screening: an alternative approach. *Health Policy* 1996;36(2):103-115.
- Sheldon TA, Simpson J. Appraisal of a new scheme for prenatal screening for Down's syndrome. *BMJ* 1991;302:1133-36.
- Sheldon TA, Parker H. Race and ethnicity in health research. *J Public Health Med* 1992 Jun;14(2):104-10.
- Simpson JL. Noninvasive screening for prenatal genetic diagnosis. *Bull WHO* 1995;73(6):799-804.
- Smith DK, Shaw RW, Marteau TM. Informed consent to undergo serum screening for Down's syndrome: the gap between policy and practice. *BMJ* 1994 Sep;309:776.
- Social impacts of technological diffusion: prenatal diagnosis and induced abortion in Brazil. Novaes HMD.
- Society of Obstetricians and Gynaecologists of Canada. *The use of ultrasound in conjunction with maternal serum screening for aneuploidy. Committee opinion; no. 17*. Ottawa (ON): Society of Obstetricians and Gynaecologists of Canada, 1997.
- Society of Obstetricians and Gynaecologists of Canada. *Guidelines for the performance of ultrasound examination in obstetrics and gynaecology. Policy Statement No 24*. Ottawa (ON) October 1993.
- Society of Obstetricians and Gynaecologists of Canada. *Practice guidelines for health care providers involved in prenatal screening and diagnosis*. *J Soc Obstet Gynaecol Can*. Aug 1998;Vol 75.

Society of Obstetricians and Gynaecologists of Canada. Prenatal genetic screening for Down syndrome and open neural tube defects using maternal serum marker screening: SOGC Committee Opinion: Policy & Practice Guideline Committee. *J Soc Obstet Gynaecol Can* 1999 Aug;21(9):887-91.

Somerville MA. Genetics, reproductive technologies, euthanasia and the search for a new societal paradigm. *Soc Sci Med* 1996 Jun;42(12):ix-xii.

Steering Committee of the Maternal Serum Screening Pilot Program. Report on the Ontario Maternal Serum Screening Pilot Program: the two year pilot program on maternal serum screening July 1, 1993 to June 30, 1995. North York (ON): Institutional Services Branch, Ministry of Health; 1995.

Steinhorn RH. Prenatal ultrasonography: first do no harm? *Lancet* 1998;352:1568-9.

Stetten G. Prenatal cytogenetic analysis of the fetus. In: Blakemore KJ, editor. *Prenatal diagnosis: present and future perspectives*. Toronto: WB Saunders Company; 1993. p. 433-41.

Stranc LC, Evans JA, Hamerton JL. Prenatal diagnosis in Canada, 1990: a review. *Prenat Diagn* 1994;14:1253-65.

Tarkki J. The debate over prenatal genetic screening in Finland. *Policy Options* 1996 Mar; 17(2): 34-7.

ten Have H. Letters to Dr Frankenstein? Ethics and the new reproductive technologies. *Soc Sci Med* 1995 Jan;40(2):141-6.

Thix J. Prenatal serum screening of aneuploidy and of neural tube defects in the second trimester of pregnancy among the population of Luxembourg [French]. *Bull Soc Sci Med* 1997;25(1):25-9.

Thornton JG, Lilford RJ. Decision analysis for medical managers. *BMJ* 1995 Mar;310(6982):791-4.

Torgerson DJ. The impact of maternal age on the cost effectiveness of Down's syndrome screening. *Br J Obstet Gynaecol* 1996 Jun;103(6):581-3.

Torgerson DJ, Spencer A. Marginal costs and benefits. *BMJ* 1996 Jan;312(7022):35-6.

Torgerson DJ, Spencer A. Methods used in economic evaluations of prenatal screening are disputed. *BMJ* 1996 Aug;313(7052):303.

Toth T, Findlay I, Papp C, Toth-Pal E, Marton T, Nagy B, Quirke P, Papp Z. Prenatal detection of trisomy 21 and 18 from amniotic fluid by quantitative fluorescent polymerase chain reaction. *J Med Genet* 1998 Feb;35(2):126-9.

Trimble BK, Baird PA. Congenital anomalies of the central nervous system incidence in British Columbia 1952-72. *Teratology* 1978;17:43-50.

Trimble BK, Baird PA. Maternal age and Down syndrome: age-specific incidence rates by single-year intervals. *Am J Med Genet* 1978;2:1-5.

Tymstra T. Prenatal diagnosis, prenatal screening, and the rise of the tentative pregnancy. *Int J Technol Assess Health Care* 1991;7(4):509-16.

- Valerio D, Aiello R, Altieri V, Fagnoni P. Maternal serum screening of fetal chromosomal abnormalities by AFP, UE3, hCG and free-beta hCG: prospective and retrospective results. *Minerva Ginecologica* 1996 May;48(5):169-73.
- van der Veen WJ, Beekhuis JR, Cornel MC, Mantingh A, de Walle HE, de Wolf BT. A demographic approach to the assessment of Down syndrome screening performance. *Prenat Diagn* 1997 Aug;17(8):717-24.
- Vintzileos AM, Guzman ER, Smulian JC, McLean DA, Ananth CV. Choice of second-trimester genetic sonogram for detection of trisomy 21. *Obstet Gynecol* 1997 Aug;90(2):187-90.
- Vintzileos AM, Ananth CV, Fisher AJ, Smulian JC, Day-Salvatore D, Beazoglou T. An economic evaluation of first-trimester genetic sonography for prenatal detection of Down syndrome. *Obstet Gynecol* 1998 Apr;91(4):535-9.
- Vintzileos AM, Ananth CV, Fisher AJ, Smulian JC, Day-Salvatore D, Beazoglou T, Knuppel RA. An economic evaluation of prenatal strategies for detection of trisomy 18. *Am J Obstet Gynecol* 1998 Nov;179(5):1220-24.
- Vintzileos AM, Ananth CV, Fisher AJ, Smulian JC, Day-Salvatore D, Beazoglou T, Knuppel RA. An economic evaluation of second-trimester genetic ultrasonography for prenatal detection of down syndrome. *Am J Obstet Gynecol* 1998 Nov;179(5):1214-9.
- Wald NJ, editor. Antenatal and neonatal screening. New York: Oxford University Press; 1984.
- Wald N, Cuckle H, Densem J. Maternal serum specific beta 1-glycoprotein in pregnancies associated with Down's syndrome. *Lancet* 1989 Aug 19;2(8660):450.
- Wald NJ, Densem JW, George L, Muttukrishna S, Knight PG. Prenatal screening for Down's syndrome using inhibin-A as a serum marker. *Prenat Diagn* 1996;16(2):143-53.
- Wald NJ, Hackshaw AK, Huttly W, Kennard A. Empirical validation of risk screening for Down's syndrome. *J Med Screen* 1996;3:185-7.
- Wald NJ, Kennard A, Densem JW, Cuckle HS, Chard T, Butler L. Antenatal maternal serum screening for Down's syndrome: results of a demonstration project. *Br Med J* 1992 Aug 15;305(6850):391-4.
- Wald NJ, Kennard A, Hackshaw AK. First trimester serum screening for Down's syndrome. *Prenat Diagn* 1995 Dec;15(13):1227-40.
- Wald NJ, Kennard A, Hackshaw A, McGuire A. Antenatal screening for Down's syndrome. *Health Technol Assess* 1998;2(1):i-iv, 1-112.
- Wald NJ, Kennard A, Hackshaw A, McGuire A. Antenatal screening for Down's syndrome. *J Med Screen* 1997;4(4):181-246.
- Wald N, Watt H. When marginal costs and benefits should be used in screening. *BMJ* 1996 Apr;312(7037):1041-2.
- Wald NJ, Watt HC, Hackshaw AK. Integrated screening for Down's syndrome based on tests performed during the first and second trimesters. *NEJM* 1999;341:461-7.
- Watt HC, Wald NJ, Smith D, Kennard A, Densem J. Effect of allowing for ethnic group in prenatal screening for Down's syndrome. *Prenat Diagn* 1996 Aug;16(8):691-8.

- Weindling P. The survival of eugenics in 20th-century Germany. *Am J Hum Genet* 1993 Mar;52(3):643-9.
- Wenstrom KD, Desai R, Owen J, DuBard MB, Boots L. Comparison of multiple-marker screening with amniocentesis for the detection of fetal aneuploidy in women ≥ 35 years old. *Am J Obstet Gynecol* 1995 Oct;173(4):1287-92.
- Wertz DC, Fletcher JC. Ethical decision making in medical genetics: women as patients and practitioners in eighteen nations. 1989. In: Ratcliffe K, editor. *Healing technology: feminist perspectives*. Ann Arbor (MI): University of Michigan Press; 1989. p221
- Wertz DC, Gregg R. Optimizing genetics services: a social, ethical, and policy context: suggestions from consumers and providers in the New England Regional Genetics Group (NERGG). *Genetic Resource* 1996;10(2):1-106.
- Wheeler DM, Sinosich MJ. Prenatal screening in the first trimester of pregnancy. *Prenat Diagn* 1998 Jun;18(6):537-43.
- WHO Working Group. Fetal diagnosis of hereditary diseases. *Bull WHO* 1984;62(3):345-55.
- Wilkins-Haug L, Horton JA, Cruess DF, Frigoletto FD. Antepartum screening in the office-based practice: findings from the collaborative Ambulatory Research Network. *Obstet Gynecol* 1996 Oct;88(4 Pt 1):483-9.
- Wilson RD, Langlois S, Halstead C. Maternal triple marker screening: another view. *BC Med J* 1999 May;41(5):212-14.
- Wise J. Another option for Down's syndrome screening available. *BMJ* 2000;320:733.
- Wooldridge EQ, Murray RF Jr. The Health Orientation Scale: a measure of feelings about sickle cell trait. *Soc Biol* 1988 Spr-Sum;35(1-2):123-36.
- Yankowitz J, Howser DM, Ely JW. Differences in practice patterns between obstetricians and family physicians: use of serum screening. *Am J Obstet Gynecol* 1996 Apr;174(4):1361-5.
- Yankowitz J, Fulton A, Williamson R, Grant SS, Budelier WT. Prospective evaluation of prenatal maternal serum screening for trisomy 18. *Am J Obstet Gynecol* 1998 Mar;178(3):446-50.
- Zlotogora J, Reshef N. Prenatal testing for genetic disorders among Arabs. *Prenat Diagn* 1998 Mar;18(3):219-24.

REFERENCES

- ¹ British Columbia. Vital Statistics Agency. Birth by age of mother and live births by birth order, British Columbia, 1997. [cited Sept 30, 1999] Available from URL: <http://www.hlth.gov.bc.ca/vs.stats/annual/1997/tab07.html>.
- ² Hecht CA, Hook EB. Rates of Down syndrome at live birth by one-year maternal age intervals in studies with apparent close to complete ascertainment in populations of European origin: a proposed revised rate schedule for use in genetic and prenatal screening. *Am J Med Genet* 1996 Apr;62(4):376-85.
- ³ Children's and Women's Health Centre of British Columbia. Maternal serum screening study in British Columbia, January 1995 to March 1997: outcome information for physicians, midwives and patients. Vancouver (BC): Children's and Women's Health Centre; [1998].
- ⁴ Chodirker BN, Evans JA. Maternal serum AFP screening programs: the Manitoba experience. In: *Current practice of prenatal diagnosis in Canada: vol. 13*. Ottawa: Royal Commission on New Reproductive Technologies; 1993. p. 536-610.
- ⁵ Carroll JC, Reid AJ, Woodward CA, Permaul-Woods JA, Domb S, Ryan G, et al. Ontario Maternal Serum Screening program: practices, knowledge and opinion of health care providers. *CMAJ* 1997;156(6):775-84.
- ⁶ Permaul-Woods JA, Carroll JC, Reid AJ, Woodward CA, Ryan G, Domb S, et al. Going the distance: the influence of practice location on the Ontario maternal serum screening program. *CMAJ* 1999;161(4):381-5.
- ⁷ Dick PT. Periodic health examination, 1996 update: 1: Prenatal screening for and diagnosis of Down syndrome: Canadian Task Force on the Periodic Health Examination. *CMAJ* 1996 Feb;154(4):465-79.
- ⁸ Royal Commission on New Reproductive Technologies. Prenatal Diagnosis for Congenital Anomalies and Genetic Disease. In: *Proceed with care: final report of the Royal Commission on New Reproductive Technologies. Vol 2*. Ottawa (ON): The Commission; 1993. p. 777.
- ⁹ Marteau TM. Towards informed decisions about prenatal testing: a review. *Prenat Diagn* 1995;15:1215-26.
- ¹⁰ Lippman A. Embodied knowledge and making sense of prenatal diagnosis. [In press].
- ¹¹ Rothman. *The tentative pregnancy: prenatal diagnosis and the future of motherhood*. Virginia: Viking Press; 1986.
- ¹² Rapp R. Accounting for amniocentesis. In: Lindenbaum S, Lock M, editors. *Knowledge, power, and practice: the anthropology of everyday life*. Berkeley (CA): University of California Press; 1993. p. 55-78.
- ¹³ Green JM. Women's experiences of prenatal screening and diagnosis. In: Abramsky L, Chapple J, editors. *Prenatal diagnosis: the human side*. New York: Chapman and Halls; 1994. p. 37-53.
- ¹⁴ Carroll JC, Brown JB, Reid AJ, Pugh P. Women's experience of maternal serum screening. *Can Fam Physician* 2000;46:614-20.
- ¹⁵ Sadovnick AD, Baird PA. A cost-benefit analysis of a population screening programme for

-
- neural tube defects. *Prenat Diagn* 1983 Apr-Jun;3(2):117-26.
- ¹⁶ Sadovnick AD, Baird PA. A cost-benefit analysis of prenatal detection of Down's Syndrome and neural tube defects in older mothers. *Am J of Med Gen* 1981;10:367-78.
- ¹⁷ Gill M, Murday V, Slack J. An economic appraisal of screening for Down Syndrome in pregnancy using maternal age and serum alpha fetoprotein concentration. *Soc Sci Med* 1987;24:725-31.
- ¹⁸ Sheldon TA, Simpson J. Appraisal of a new scheme for prenatal screening for Down's syndrome. *BMJ* 1991;302:1133-6.
- ¹⁹ Merz B. Matchmaking scheme solves Tay-Sacks problem. *JAMA* 1987;258:2636-9.
- ²⁰ Royal Commission on New Reproductive Technologies. Prenatal diagnosis for congenital anomalies and genetic disease. In: *Proceed with care: final report of the Royal Commission on New Reproductive Technologies. Vol 2.* Ottawa (ON): The Commission; 1993. p. 804.
- ²¹ Palomaki GE, Knight GJ, McCarthy JE, Haddow JE, Donhove JM. Maternal serum screening for Down syndrome in the United States: a 1995 survey. *Am J Obstet Gynecol* 1997;176:1046-51.
- ²² Wald NJ, Kennard A, Hackshaw A, McGuire A. Antenatal screening for Down's syndrome. *Health Technol Assess* 1998;2(1):i-iv, 1-112.
- ²³ EUCROMIC Workshop. Proceedings (1996 : Paris) Prenatal diagnosis in Europe: proceedings of an EUCROMIC Workshop, Paris, May 23-24, 1996. *Eur J Human Gen* 1997 Mar;5(suppl 1):1-90.
- ²⁴ Santalahti P. Literature review: prenatal screening in Finland: availability and women's decision-making and experiences. Helsinki: Stakes National Research and Development Centre for Welfare and Health; 1994. p. 13.
- ²⁵ Reid M. The diffusion of four prenatal screening tests across Europe. London: King's Fund Centre; 1991.
- ²⁶ Steering Committee of the Maternal Serum Screening Pilot Program. Report on the Ontario Maternal Serum Screening Pilot Program : the two year pilot program on maternal serum screening July 1, 1993 to June 30, 1995. [Toronto (ON)]: Steering Committee of the Maternal Serum Screening Pilot Program; [1996].
- ²⁷ Tudiver S. Manitoba voices: a qualitative study of women's experiences with technology in pregnancy. Prenatal diagnosis: background and impact on individuals. Ottawa (ON): Royal Commission on New Reproductive Technologies; 1993: p. 347-460.
- ²⁸ BC Office of Health Technology Assessment. Personal interview with BC Ministry of Health official. Vancouver (BC): BCOHTA; 1996.
- ²⁹ Medical Genetics Department, University of British Columbia. AFP Screening Proposal submitted by the Medical Genetics Department, UBC, to the Ministry of Health. Vancouver (BC): Medical Genetics Department; 1989.
- ³⁰ Hook EB. Rates of chromosome abnormalities at different maternal ages. *Obstet Gynecol* 1981;58:282-5.
- ³¹ Trimble BK, Baird PA. Congenital anomalies of the central nervous system incidence in

-
- British Columbia 1952-72. *Teratology* 1978;17:43-50.
- ³² Royal Commission on New Reproductive Technologies. Prenatal diagnosis for congenital anomalies and genetic disease. In: *Proceed with care: final report of the Royal Commission on New Reproductive Technologies*. Ottawa (ON): The Commission; 1993. p. 749.
- ³³ Watt HC, Wald NJ, Smith D, Kennard A, Densem J. Effect of allowing for ethnic group in prenatal screening for Down's syndrome. *Prenat Diagn* 1996 Aug;16(8):691-8.
- ³⁴ Baumgarten, A. Racial differences and biological significance of maternal serum AFP. *Lancet* 1986;2:573-80.
- ³⁵ Burton BK, Nieb B. Effect of maternal race and weight on hCG and uE3 levels in the mid-trimester. *Am J Human Genetics* 1991;49:212-18.
- ³⁶ Crandall BF, Lebherz TB, Schroth PC, Matsumoto M. Alpha fetoprotein concentrations in maternal serum: relation to race and body weight. *Clin Chem* 1983;29:531-3.
- ³⁷ Bradby H. Genetics and racism. In: Marteau T, Richards M, editors. *The troubled helix: social and psychological implications of the new human genetics*. London: Cambridge University Press; 1993. p. 295-316.
- ³⁸ Duster T. *Backdoor to eugenics*. London: Routledge; 1990.
- ³⁹ Serjeant GR. *Sickle cell disease*. Oxford: Oxford University Press; 1985.
- ⁴⁰ Wald NJ, Kennard A, Hackshaw A, McGuire A. Antenatal screening for Down's syndrome. *Health Technol Assess* 1998;2(1):i-iv:63-7.
- ⁴¹ Tabor A, Madsen M, Obel EB. Randomized controlled trial of genetic amniocentesis in 4606 low-risk women. *Lancet* 1986;I:1287-92.
- ⁴² Drugan A, Johnson MP, Evans MI. Amniocentesis. In Eden RD, Boehm FH, editors, *Assessment and Care of the Fetus. Physiological, Clinical, and Medicolegal Principles*. Norwalk: Appleton and Lange; 1990. p. 284.
- ⁴³ Kupperman M, Goldberg JD, Nease RF, Washington AE. Who should be offered prenatal diagnosis?: the 35-year-old question. *Am J Public Health* 1999;89(2):160-3.
- ⁴⁴ BC Ministry of Health & Ministry Responsible for Seniors. Protocol Steering Committee. *Assessing guidelines: prenatal ultrasound. Protocols & Guidelines Update* 1999;2(1):2.
- ⁴⁵ Green CJ, Hadorn D, Bassett K, Kazanjian A. *Routine ultrasound imaging in pregnancy: how evidence-based are the guidelines?* Vancouver (BC): BC Office of Health Technology Assessment; 1996.
- ⁴⁶ Wald NJ, Kennard A, Hackshaw A, McGuire A. Antenatal screening for Down's syndrome. *Health Technol Assess* 1998;2(1):16.
- ⁴⁷ Children's and Women's Health Centre of British Columbia. *Maternal serum screening study in British Columbia, January 1995 to March 1997: outcome information for physicians, midwives and patients*. Vancouver (BC): Children's and Women's Health Centre; [1998].
- ⁴⁸ Triple Screen Proposal presented to the Pregnancy Screening Meeting, Ministry of Health, Victoria (BC): BCOHTA; 1993. [Unpublished].
- ⁴⁹ Society of Obstetricians and Gynaecologists of Canada. *Guidelines for the performance of*

-
- ultrasound examination in obstetrics and gynaecology. Policy Statement No 24. Ottawa (ON): Society of Obstetricians and Gynecologists of Canada; 1993.
- ⁵⁰ Rapp, R. Accounting for Amniocentesis. In: Lindenbaum S, Lock M, editors. Knowledge, power and practice: the anthropology of medicine and everyday life. Berkeley: University of California Press; 1993. p. 55-76.
- ⁵¹ Medical Genetics Department, University of British Columbia. Triple marker screening proposal. Vancouver (BC): Medical Genetics Department; 1993.
- ⁵² O'Sullivan P. The Provincial Amniocentesis Program business plan. Provincial Amniocentesis Steering Committee. Vancouver (BC); BC Children's & Women's Hospital; 1998.
- ⁵³ Second trimester Abortion access in BC: a summary of information. Background on access to abortion and unintended pregnancy prevention in British Columbia: a report to the Abortion Services Working Group. Victoria (BC): BC Ministry of Health & Ministry responsible for Seniors; 1998.
- ⁵⁴ US Preventive Services Task Force. Screening for Down Syndrome. In: Guide to clinical preventive service. 2nd ed. Baltimore: William and Wilkins; 1996.
- ⁵⁵ Hakim-Elahi E, Tovell HMM, Burnhill MS. Complications of first trimester abortion: a report of 170,000 cases. *Obstet Gynecol* 1990;76:129-135.
- ⁵⁶ Wald NJ, Kennard A, Hackshaw A, McGuire A. Antenatal screening for Down's syndrome. *Health Technol Assess* 1998;2(1):37.
- ⁵⁷ Johnson AM, Palomaki GE, Haddow JE. Maternal serum a-fetoprotein levels in pregnancies among black and white women with fetal open spina bifida: a United States collaborative study. *Am J Obstet Gynecol* 1990;162:328-31.
- ⁵⁸ Haddow JE, Palomaki GE. Similarities in women's decision-making in the US and UK during prenatal screening for Down's syndrome. *Prenat Diagn* 1996 Dec;16(12):1161-2.
- ⁵⁹ Press N, Browner C. Collective fictions: similarities in reasons for accepting maternal serum alpha-fetoprotein screening among women of diverse ethnic and social class backgrounds. *Fetal Diagn Ther* 1993;8(suppl 1):97-106.
- ⁶⁰ Press N, Browner C. Characteristics of women who refuse an offer of prenatal diagnosis: data from the California maternal serum alpha fetoprotein blood test experience. *Am J Med Genet* 1998;78:433-45.
- ⁶¹ Rapp R. Sociocultural differences in the impact of amniocentesis: an anthropological research report. *Fetal Diagn Ther* 1993;8(suppl 1):90-6.
- ⁶² Mitchell LM. The routinization of the other: ultrasound, women and the fetus. In: Basen G, Eichler M, Lippman S, editors. *Misconceptions: the social construction of choice and the new reproductive and genetic technologies*. Hull (QC): Voyageur Press; 1994. p. 146-60.
- ⁶³ Lee PM, Sroka H. The missing voices in the BC experience of maternal serum screening: a report. Vancouver (BC): The BC Centre of Excellence for Women's Health. [In press 1999].
- ⁶⁴ Stephenson P, Mitchell L. Social and cultural determinants of parental experiences with

-
- ultrasound detected foetal anomalies. Vancouver (BC): British Columbia Medical Services Foundation; 1998.
- ⁶⁵ Lee PM. From the anthropologist's point of view: towards a critical health technology assessment to explore the cultural context of maternal serum screening in British Columbia. *Health and cultures/Sante et cultures. Focus on Women's Health* 1995;11(5/6):6-12.
- ⁶⁶ Evans J, MacDonald K, Hamerton J. The characteristics of a population of Canadian women offered maternal serum alpha-fetoprotein screening during pregnancy. *Can J Public Health* 1986;77(Suppl 1):150-5.
- ⁶⁷ Rothman B. *The tentative pregnancy: prenatal diagnosis and the future of motherhood*. Virginia: Viking Press; 1986.
- ⁶⁸ Quéniart A. Risky business: medical definitions of pregnancy. In: Currie D, Raoul V, editors. *The anatomy of gender*. Ottawa (ON): Carleton University Press; 1992. p. 161-74.
- ⁶⁹ Searle J. Fearing the worst : why do pregnant women feel 'at risk'? *Aust N Z J Obstet Gynaecol* 1996;36(3):279-86.
- ⁷⁰ Green JM. Serum screening for Down's syndrome: experiences of obstetricians in England and Wales. *BMJ* 1994 Sep;309(6957):769-72.
- ⁷¹ Goel V, Glazier R, Summers A, Holzapfel S. Psychological outcomes following maternal serum screening: a cohort study. *CMAJ* 1998;159(6):651-6.
- ⁷² Huet M-H. *Monstrous imagination*. Cambridge (MA): Harvard University Press; 1993.
- ⁷³ Press N, Browner C. Why women say yes to prenatal diagnosis. *Soc Sci Med* 1997;45(5):979-89.
- ⁷⁴ Georges E, Mitchell L. Baby talk: the rhetorical production of maternal and fetal selves. In: Longino H, Kohlstedt S. *Writing and speaking the body: rhetorical and feminist studies of reproductive technologies*. Madison (WI): University of Wisconsin Press; 1999. [In press].
- ⁷⁵ Markens S, Browner CH, Press N. Because of the risks: how US pregnant women account for refusing prenatal screening. *Soc Sci Med* 1999;49(3):359-69.
- ⁷⁶ Saridogan E, Djahanbakhch O, Naftalin AA. Screening for Down's syndrome: experience in an inner city health district. *Br J Obstet Gynaecol* 1996 Dec;103(12):1205-11.
- ⁷⁷ Green JM, Statham H, Snowdon C. *Pregnancy: a testing time, report of the Cambridge Prenatal Screening Study*. Cambridge: Centre for Family Research, University of Cambridge; 1994.
- ⁷⁸ Evers-Kiebooms G, Swerts A, van den Berghe H. Psychological aspects of amniocentesis: anxiety feelings in three different risk groups. *Clin Genet* 1988;33:196-206.
- ⁷⁹ Roelofsen EE, Kamerbeek LI, Tymstra, et al. Women's opinions on the offer and use of maternal serum screening. *Prenat Diagn* 1993;13:741-7.
- ⁸⁰ Abuelo DN, Hoppmann MR, Barsel-Bowers G, Goldstein A. Anxiety in women with low maternal serum alpha-fetoprotein screening results. *Prenat Diagn* 1991;11:381-5.
- ⁸¹ Burton BK, Dillar RG, Clark EN. The psychological impact of false-positive elevations of maternal serum alpha-fetoprotein. *Am J Obstet Gynecol* 1985;151(1):77-82.

-
- ⁸² Salonen R, Kurki L, Lappalainen M. Experiences of mothers participating in maternal serum screening for Down's syndrome. *Eur J Hum Genet* 1996;4(2):113-9.
- ⁸³ Marteau TM, Johnston M, Plenicar M, Shaw RW, Slack J. Development of a self-administered questionnaire to measure women's knowledge of prenatal screening and diagnostic tests. *J Psychosomatic Res* 1988;32(4-5):403-8.
- ⁸⁴ Marteau TM. The psychological effects of false-positive results in prenatal screening for fetal abnormality: a prospective study. *Prenat Diagn* 1992;12:205-14.
- ⁸⁵ Rose H. Victorian values in the test-tube: the politics of reproductive science and reproductive technologies. In: Stanworth M, editor. *Gender, motherhood, and medicine*. Minneapolis (MI): University of Minnesota Press; 1987. p. 151-73.
- ⁸⁶ Green JM. *Calming or harming: a critical review of psychological effects of fetal diagnosis on pregnant women*. London: Galton Institute; 1990.
- ⁸⁷ American Society of Human Genetics Ad Hoc Committee on Genetic Counseling. Genetic counseling. *Am J Hum Genet* 1975;27:240-2.
- ⁸⁸ Baker DL, Schuette JL, Uhlmann WRA. *Guide to genetic counseling*. New York: Wiley-Liss; 1998.
- ⁸⁹ Sroka H. Data from Department of Medical Genetics, Children's & Women's Health Centre of BC (personal communication). [1999]
- ⁹⁰ Steele P, Wilson RD. Patient assessment of pretest information received from referring health care providers. Unpublished.
- ⁹¹ Glazier R, Goel V, Holzapfel S, Summers A, Pugh P, Yeung M. Written patient information about triple-marker screening: a randomized, controlled trial. *Obstet Gynecol* 1997 Nov;90(5):769-74.
- ⁹² Peters Y. *New reproductive technologies: a threat or a benefit to equality: four discussion papers on reproductive technologies*. S.I.: Canadian Disability Rights Council and Disabled Womens Network Canada; 1991. p. 6-20.
- ⁹³ Santalahti P, Hemminki E, Latikka AM, Ryynanen MU. Women's decision making in prenatal screening. *Soc Sci Med* 1998 Apr;46(8):1067-76.
- ⁹⁴ Dumaret AC, Devigan C, Julian-Reynier C, Goujard J, Rosset D, Aymé S. Adoption and fostering of babies with Down-syndrome: a cohort of 593 cases. *Prenat Diagn* 1998 May;18(5):437-45.
- ⁹⁵ Brookes MA, Alberman E. Early mortality and morbidity in children with Down syndrome diagnosed in two regional health authorities in 1989. *J Med Screening* 1996;3:7-11.
- ⁹⁶ Ben-Neria Z, Nissani R, Chemke J. Down's syndrome: denial of infant rights and the chance to live. *Harefuah* 1986;111:67-8.
- ⁹⁷ Julian C, Huard P, Gouvernet J, Mattei JF, Aymé S. Physicians' acceptability of termination of pregnancy after prenatal diagnosis in southern France. *Prenat Diagn* 1989;9:77-89.
- ⁹⁸ Grevengood C, Shulman LP, Dungan JS, Martens P, Phillips OP, Emerson DS, et al. Severity of abnormality influences decision to terminate pregnancies affected with fetal neural tube defects. *Fetal Diagn Ther* 1994 Jul-Aug;9(4):273-7.

-
- ⁹⁹ Saxton M. Prenatal screening and discriminatory attitudes about disability. In: D'Amedeo, editor. Embryos, ethics and women's rights. S.I.: Harrington Park Press; 1998.
- ¹⁰⁰ Botkin JR, Mehlman MJ. Wrongful birth: medical, legal, and philosophical Issues. *J Law Med Ethics* 1994;22(1):21-8.
- ¹⁰¹ Paul A. Drawing new legal road map: wrongful-birth lawsuit devoid of hard, fast rules. *Winnipeg Free Press* 1994 Sep 6;Sect. B:2
- ¹⁰² McLellan W. Suit claims 'wrongful birth'. *The Province, Final Edition* 1999 Feb 19;Sect. A:4.
- ¹⁰³ Field MJ, Lohr KN, Committee on Clinical Practice Guidelines. Guidelines for clinical practice: from development to use. Washington (DC): National Academy Press; 1992.
- ¹⁰⁴ Havighurst CC. Practice guidelines for medical care: the policy rationale. *Saint Louis University Law J* 1990;34(4):777-819.
- ¹⁰⁵ Society of Obstetricians and Gynaecologists of Canada. Practice guidelines for health care providers involved in prenatal screening and diagnosis: policy statement no. 75. Ottawa (ON): Society of Obstetricians and Gynaecologists of Canada; 1998.
- ¹⁰⁶ Society of Obstetricians and Gynaecologists of Canada. Prenatal Genetic Screening for Down syndrome and open neural tube defects using maternal serum marker screening: SOGC Committee Opinion: Policy & Practice Guideline Committee. *J Soc Obstet Gynaecol Can* 1999 Aug;21(9):887-91.
- ¹⁰⁷ McLellan W. Suit claims 'wrongful birth'. *The Province, Final Edition* 1999 Feb 19;Sect. A:4.
- ¹⁰⁸ Kinney ED, Wilder MM. Medical standard setting in the current malpractice environment: problems and possibilities. *Davis Law Rev* 1989;22:421-50.
- ¹⁰⁹ Domb SB, Yanover DF, Carrol JC, Wooward CA, Reid AJ, Permaul-Woods JA, et al. Medico-legal risk in maternal serum screening: perspective of Ontario health care providers. *J of the Society of Obstet Gyn of Canada* 1999;21(1):59-66.
- ¹¹⁰ College of Physicians and Surgeons of BC. *College Quarterly* 1998 Win;23.
- ¹¹¹ Canadian Medical Protective Association. Correspondence on file. [1999]
- ¹¹² Gekas J, Gondry J, Mazur S, Cesbron P, Thepot F. Informed consent to serum screening for Down syndrome: are women given adequate information? *Prenat Diagn* 1999 Jan;19(1):1-7.
- ¹¹³ Bernhardt L. Prenatal genetic testing: content of discussions between obstetric providers and pregnant women. *Obstet Gynecol* 1998;91(5):648-55.
- ¹¹⁴ Sadler M. Serum screening for Down's syndrome: how much do health professionals know? *Br J Obstet Gynaecol* 1997;104:176-9.
- ¹¹⁵ Walker AP. *The practice of genetic counselling: a guide to genetic counseling*. New York: Wiley-Liss; 1998.
- ¹¹⁶ Tymstra T. Prenatal diagnosis, prenatal screening, and the rise of the tentative pregnancy. *Int J Technol Assess Health Care* 1991;(4):509-16.
- ¹¹⁷ Daar A, Mattei J-F. *Mexical genetics and biotechnology: implications for public health*. S.I.:

-
- World Health Organization; 1999.
- ¹¹⁸ Scott A. Equal citizenship for Canadians with disabilities: Federal Government Task Force on Disability Issues. Ottawa (ON): Minister of Public Works and Government Services Canada; 1996.
- ¹¹⁹ The International Sub-Committee of BCODP. The New Genetics and Disabled People [cited July 10, 2000] Available from URL: <http://www/bcodp.org.uk/general/genetics.html>.
- ¹²⁰ Finger A. A lot to learn. *The Disability Rag* 1991;Mar/Apr:28.
- ¹²¹ Goundry, S. The new reproductive technology: triumph or modern science for some, threat to equality goals of many. In: Four discussion papers on new reproductive technologies. S.I.: Canadian Disability Rights Council and DisAbled Women's Network Canada; 1991. p. 40-60.
- ¹²² Meister J. Ethical guidelines for research with Pacific DAWN: S.I.: Pacific DisAbled Women's Network; 1999. Unpublished.
- ¹²³ Working Group on Women's Health and the New Genetics. Women's health and the new genetics community consultation: final report of community consultation, Winnipeg, Manitoba February 12-13th, 1999:3.
- ¹²⁴ Hook EB, Waller K. Prenatal screening for neural tube defects and chromosome abnormalities: the complexities of program evaluation. *Epidemiology* 1994;6:1-4.
- ¹²⁵ Baillie C, Hewison J. Antenatal screening: obtaining selective consent to scanning, rather than screening, is possible (letter). *BMJ* 1999;318:805.
- ¹²⁶ Smith DK, Shaw RW, Marteau TM. Informed consent to undergo serum screening for Down's syndrome: the gap between policy and practice. *BMJ* 1994;309:776.
- ¹²⁷ Wald NJ, Watt HC, Hackshaw AK. Integrated screening for Down's syndrome based on tests performed during the first and second trimesters. *N Engl J Med* 1999;341:461-7.
- ¹²⁸ Howe DT, Gornall R, Wellesley D, Boyle T, Barber J. Six year survey of screening for Down's syndrome by maternal age and mid-trimester ultrasound scans. *BMJ* 2000;320:606-10.
- ¹²⁹ Asch A. Prenatal diagnosis and selective abortion: a challenge to practice and policy. *Am J Public Health* 1999;89:1649-57.
- ¹³⁰ UK Collaborative Study on alpha-fetoprotein in relation to neural tube defects: maternal serum alpha-fetoprotein measurement in antenatal tests for anencephaly and spina bifida in early pregnancy. *Lancet* 1977;I:133-24.
- ¹³¹ Cuckle HS, Wald NJ, Lindenbaum RH. Maternal serum alpha-fetoprotein measurement: A screening test for Down syndrome. *Lancet* 1984;(I):926-929.
- ¹³² Bogart MH, Pandian MR, Jones OW. Abnormal maternal serum chorionic gonadotropin levels in pregnancies with fetal chromosome abnormalities. *Prenat Diagn* 1987;7:623-630.
- ¹³³ Canick JA, Knight GJ, Palomaki GE, Haddow JE, Cuckle HS, Wald NJ. Low second trimester maternal serum unconjugated estriol in pregnancies with Down syndrome. *Br J Obstet Gynaecol* 1988;95:330-33.
- ¹³⁴ AFP Expert V5.00. Benetech Medical Systems: interpretation of results. Toronto (ON): Benetech; [1999]. p. 4.

-
- ¹³⁵ Wald NJ, Cuckle HS, Densem JW, Nanchahal K, Royston P, Chard T, et al. Maternal serum screening for Down's syndrome in early pregnancy. *BMJ* 1988;297:883-7.
- ¹³⁶ Wald NJ, Hackshaw AK, Huttly W, Kennard A. Empirical validation of risk screening for Down's syndrome. *J Med Screen* 1996;3:185-7.
- ¹³⁷ Hook EB, Cross PK, Schreinmachers DM. Chromosomal abnormality rates at amniocentesis and in live-born infants. *JAMA* 1983;249:2034.
- ¹³⁸ Wald NJ, Cuckle HS, Densem JW, Kennard A, Smith D. Maternal serum screening for Down syndrome: the effect of routine ultrasound scan determination of gestational age and adjustment for maternal weight. *Br J Obstet Gynaecol* 1992;99:144-9.
- ¹³⁹ Palomaki GE, Panizza DS, Canick JA. Screening for Down syndrome using AFP, uE3, hCG: Effect of maternal weight. *Am J Human Genet* 1990;47:282.
- ¹⁴⁰ Johnson AM. Racial differences in maternal serum alpha-fetoprotein screening. In: Mizejewski GJ, Porter IH, editors. *Alpha-fetoprotein and congenital disorder*. New York: Academic Press; 1985. p. 183-96.
- ¹⁴¹ Wald NJ, Cuckle HS, Boreham J, Turnbull AC. Maternal serum alpha-feto protein and diabetes mellitus. *Br J Obstet Gynecol* 1979;86:101.
- ¹⁴² Wald NJ, Kennard A, Hackshaw A, McGuire A. Antenatal screening for Down's syndrome. *Health Technol Assess* 1998;2(1):7.
- ¹⁴³ Wald NJ, Kennard A, Hackshaw A, McGuire A. Antenatal screening for Down's syndrome. *Health Technol Assess* 1998;2(1):15.
- ¹⁴⁴ Wald NJ, Kennard A, Hackshaw A, McGuire A. Antenatal screening for Down's syndrome. *Health Technol Assess* 1998;2(1):15.
- ¹⁴⁵ The NICHD National Registry for Amniocentesis Study Group. Mid-trimester amniocentesis for prenatal diagnosis: safety and accuracy. *JAMA* 1976;236(13):1471-6.
- ¹⁴⁶ Simpson N, Dallaire L, Miller JR. Prenatal diagnosis of genetic disease in Canada: report of a collaborative study. *CMAJ* 1976;115:739-48.
- ¹⁴⁷ Wald NJ, Kennard A, Hackshaw A, McGuire A. Antenatal screening for Down's syndrome. *Health Technol Assess* 1998;2(1):5-8.
- ¹⁴⁸ Cuckle HS, Wald NJ, Thompson SG. Estimating a woman's risk of having a pregnancy associated with Down's syndrome using her age and serum alpha-fetoprotein level. *Br J Ob Gyn* 1987;94:387-402.
- ¹⁴⁹ Dick PT. Periodic health examination, 1996 update: 1: Prenatal screening for and diagnosis of Down syndrome: Canadian Task Force on the Periodic Health Examination. *CMAJ* 1996 Feb;154(4):465-79.
- ¹⁵⁰ Conde-Agudelo A, Kafury-Goeta AC. Triple-marker test as screening for Down syndrome: a meta-analysis. *Obstet Gynecol Surv* 1998 Jun;53(6):369-76.
- ¹⁵¹ Haddow JE, Palomaki GE, Knight GJ, Williams J, Pulkkinen A, Canick JA, et al. Prenatal screening for Down's syndrome with use of maternal serum markers. *N Engl J Med* 1992 Aug 27;327(9):588-93.

-
- 152 Phillips OP, Elias S, Shulman LP, Andersen RN, Morgan CD, Simpson JL. Maternal serum screening for fetal Down syndrome in women less than 35 years of age using alpha-fetoprotein, hCG, and unconjugated estriol: a prospective 2-year study. *Obstet Gynecol* 1992 Sep;80(3 Pt 1):353-8.
- 153 Wald NJ, Kennard A, Densem JW, Cuckle HS, Chard T, Butler L. Antenatal maternal serum screening for Down's syndrome: results of a demonstration project. *Br Med J* 1992 Aug 15;305(6850):391-4.
- 154 Cheng EY, Luthy DA, Zebelman AM, Williams MA, Lieppman RE, Hickok DE. A prospective evaluation of a second-trimester screening test for fetal Down syndrome using maternal serum alpha-fetoprotein, hCG, and unconjugated estriol. *Obstet Gynecol* 1993 Jan;81(1):72-7.
- 155 Piggot M, Wilkinson P, Bennet J. Implementation of an antenatal screening programme for Down's syndrome in two districts (Brighton and Eastbourne) *J Med Screen* 1994;1:45-9.
- 156 Goodburn SF, Yates JRW, Raggatt PR. Second trimester maternal serum screening using alpha-fetoprotein, human chorionic gonadotrophin and unconjugated oestriol: experience of a regional programme. *Prenat Diagn* 1994;14:391-402.
- 157 Mancini G, Perona M, Dall'Amico D. Maternal serum markers. Estimation of the risk of Down's syndrome: a prospective study. *Int J Clin Lab Res* 1994;14:49-53.
- 158 Kellner LH, Weiss RR, Weiner Z. The advantages of using triple-marker screening for chromosomal abnormalities. *Am J Obstet Gynecol* 1995;172:831-6.
- 159 Burton BK, Prins GS, Verp MS. A prospective trial of prenatal screening for Down syndrome by means of maternal serum alpha-fetoprotein, human chorionic gonadotropin and unconjugated estriol. *Am J Obstet Gynecol* 1993;169:526-30.
- 160 Prescia G, Dao Mh, Wekhs D. Le triple depistage de la trisomie 21: resultats prospectifs de 7039 evaluations. *Rev Med Suisse Romande* 1993;113:277-80.
- 161 Wald NJ, Kennard A, Hackshaw A, McGuire A. Antenatal screening for Down's syndrome. *Health Technol Assess* 1998;2(1):38.
- 162 Cuckle H. Maternal serum screening policy for Down's syndrome. *Lancet* 1992;340:799.
- 163 Torgerson DJ. The impact of maternal age on the cost effectiveness of Down's syndrome screening. *Br J Obstet Gynaecol* 1996 Jun;103(6):581-3.
- 164 Hamerton JL, Evans JA, Stanc L. Prenatal Diagnosis in Canada, 1990: A Review of Genetics Centres. In *Research Volumes of the Royal Commission New Reproductive Technologies. Proceed with Care. Final Report of the Royal Commission on New Reproductive Technologies. Research Volumes. Ottawa (ON): The Commission; 1993.*
- 165 Lal R. Prenatal genetic screening and Down syndrome: the impact on Indo-Canadian women and their families. Vancouver (BC): Department of Anthropology, University of British Columbia; 1998.
- 166 Thobani S. Fighting sex selection technology. In: Mukherjee A, editor. *Sharing our experience. Ottawa (ON): Mutual Press; 1993. p. 168-74.*

-
- ¹⁶⁷ Rowland R. Motherhood, patriarchal power, alienation and the issue of 'choice' in sex preselection. In: Corea G, editors. *Man-made women: how new reproductive technologies affect women*. Indianapolis (IN): Indiana University Press; 1987. p. 74-87.
- ¹⁶⁸ Farber D. Discrimination Issues and Genetic Screening. In: Bartels DM, LeRoy BS, Caplan AL, editors. *Prescribing Our Futures Ethical Challenges in Genetic Counseling*; Hawthorne, NY: Aldine De Gruyter; 1993. p. 65-78.
- ¹⁶⁹ Bray IC, Wright DE. Estimating the spontaneous loss of Down-syndrome fetuses between the times of chorionic villus sampling, amniocentesis and livebirth. *Prenat Diagn* 1998 Oct;18(10):1045-54.
- ¹⁷⁰ Wald NJ, Kennard A, Hackshaw A, McGuire A. Antenatal screening for Down's syndrome. *Health Technol Assess* 1998;2(1):37.
- ¹⁷¹ Haddow JE, Palomaki GE. Similarities in women's decision-making in the US and UK during prenatal screening for Down's syndrome. *Prenat Diagn* 1996 Dec;16(12):1161-2.
- ¹⁷² Cuckle HS, Wald NJ. Principles of screening. In: Wald NJ, editor. *Antenatal and neonatal screening*. New York: Oxford University Press; 1984. p. 1.