Developing a National Newborn Screening Strategy for Canada

Kumanan Wilson, Shelley J. Kennedy, Beth K. Potter, Michael T. Geraghty, & Pranesh Chakraborty

Introduction

Newborn screening is a population-based program that aims to identify disorders in neonates that could lead to mental retardation or have life-threatening consequences and for which treatments are available. Heel prick blood samples are taken from newborns in the population during the first few days of life and analysed to identify those who are at high risk of particular diseases. Diseases that are targets of newborn screening are generally rare, with the most common disease being congenital hypothyroidism with an incidence of ~1/3000 births. As well, the diseases have in common a pre-clinical phase during which diagnosis may be established, and treatment instituted, before the onset of symptoms that would otherwise bring the baby to clinical attention. The vast majority of diseases targeted by such programs internationally are of genetic etiology. Increasingly, there is interest in additional targets, especially congenital infections such as Human Immunodeficiency Virus, Cytomegalovirus and Toxoplasmosis, where early treatment may be of benefit to the infant.

Clinical benefit to the affected infant has been the historical goal of pre-symptomatic diagnosis by newborn screening, in accordance with traditional criteria for disease screening.[1] However, other reasons for newborn screening are being increasingly legitimized. These include reproductive decision-making for parents (given the autosomal recessive heritability of most of the screened diseases), avoidance of lengthy work-ups for the non-specific symptoms that often herald rare diseases (diagnostic odyssey), and identification of cohorts for investigational therapies that will only be effective early in the course of a disease.[2]

An increasing number of jurisdictions are expanding the number of conditions for which they screen, at least partly in response to technological advances (such as the application of tandem mass spectrometry) that have made screening for additional diseases feasible and economical on a mass population basis. However, there is considerable variability across jurisdictions in the diseases for which screening is offered, and this variability is evident in provincial programs in Canada.[3] While there are a multitude of factors that influence the decision on whether or not to screen for a condition, including provincial scientific assessment and prevalence of a condition within a province, there have been calls to nationalize the approach to the various components of newborn screening.[4] In this article we examine the rationale for a national approach and different mechanisms by which the federal government could create a national newborn screening strategy.

The state of newborn screening in other countries

The practice of newborn screening is reported to occur in at least 64 countries worldwide.[5] At the international level, the disorders targeted by newborn screening vary greatly from country to country. In part, this is due to differential prioritization of disorders based on a variety of

factors which include, but are not limited to: prevalence of the target disorders in a given country, clinical practice, availability of treatment for the target disorders, and differential interpretation of both screening criteria and empirical evidence. In particular, the rarity of the screened conditions and the rapid advancement of testing technologies have meant that evidence supporting the clinical benefits of newborn screening has often not been fully available at the time the ability to incorporate additional diseases into screening panels emerged. This in turn has fueled policy debates about the appropriate criteria to justify the expansion of newborn screening programs and whether those criteria have been met for specific diseases or groups of diseases.[6]

Canadian provinces often have different decision-making processes and/or their medical and scientific communities may differ in their interpretations of the suitability of specific candidate disorders even when using similar criteria such as the classic principles.

Even within a given country, such as the United States, there has been considerable variation among states.[7] In response to the recommendations of a task force on newborn screening led by the American Academy of Pediatrics (2000), the American College of Medical Genetics (ACMG) was commissioned by the Health Services and Resources Administration (HRSA) to develop guidelines for newborn screening, with the aim of producing parity across states. The final recommendation was that 29 primary target conditions should form the core screening panel, and that an additional 25 secondary conditions should be reported when identified.[8] The 25 secondary conditions were not recommended as primary targets of the newborn screening process, in part because they were viewed as lacking evidence based treatment protocols or there was limited knowledge of their natural history, but they are often revealed in the newborn screening process for the 29 core target conditions.

The ACMG recommendations were endorsed by several groups, including the Secretary's Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children, the American Academy of Pediatrics, and the March of Dimes. However, some authors have been highly critical of the approach used to develop the recommendations, including the methods that were used to interpret and summarize the evidence demonstrating clinical benefits, and the consideration that was given to non-clinical benefits.[9] Indeed a systematic review of similar evidence carried out in the UK led to much more limited recommendations for the expansion of newborn screening.[10] Ultimately, the decision about whether to implement the ACMG recommendations resides with individual state health departments, although the vast majority of state programs have expanded to include universal screening for the core panel conditions.[11] A comparison of disorders screened in England, Australia and the Netherlands, compared to the ACMG recommended core panel in the United States, is listed in Table 1.

The state of newborn screening in Canada

Newborn screening practices and policies in Canada are quite varied from province to province.[12] This variation includes: differences in the number of diseases screened, reasons for screening, technologies used, legal framework and consent, governance and the use of advisory committees, treatment and follow-up practices, and funding/access to treatments for potential target diseases. Some of these differences are attributable to political culture and priorities and the economic capacity of the province. Other reasons for the variation have a scientific basis, such as the ethnic variation within a province and the prevalence of specific genetic isolates. As well, as in other countries, Canadian provinces often have different decision-making processes and/or their medical and scientific communities may differ in their interpretations of the suitability of specific candidate disorders even when using similar criteria such as the classic principles outlined in Wilson and Jungner's seminal report for the World Health Organization.[13] Table 2 describes the state of newborn screening across Canada. As can be seen, some conditions, such as phenylketonuria (PKU) and congenital hypothyroidism, are targeted in every province. There is more variability in screening for other conditions such as congenital adrenal hyperplasia and biotinidase deficiency.

Table 1: Comparison of the ACMG recommended screening panel and conditions screened for or recommended for screening in England, Australia and the Netherlands

Disorder	Recommended ACMG pane(2006)[a]	England (Pollitt, 2007)	Australia (Padilla and Therrell, 2007) [b]	Netherlands (Health Council of the Netherlands, 2005)
Congenital Hypothyroidism	+	+	+	+
Congenital Adrenal Hyperplasia	+		+	+
Hemoglobinopathies (S/S, S/C, S/β-thal)	+	+	+	+
Biotinidase Deficiency	+		+	+
Galactosemia	+		+	+
Cystic Fibrosis	+	+	+	+
Carnitine Uptake Deficiency	+		+	
Long Chain 3-hydroxyacyl-CoA dehydrogenase deficiency (LCHAD)	+		+	+
Medium chain Acyl-CoA dehydrogenase deficiency (MCAD)	+	+	+	+
Trifunctional protein deficiency	+			
Very Long Chain Acyl-CoA dehydrogenase deficiency (VLCAD)	+		+	+
Glutaryl-CoA dehydrogenase deficiency	+		+	+
3-Hydroxy-3-methylglutaryl CoA lyase deficiency	+		+	+
Isovaleric Acidemia	+		+	+
3-Methylcrotonyl-CoA carboxylase deficiency	+		+	+
Methylmalonic academia (Vitamin B12 disorders, Cbl-A, B)	+		+	
Beta-ketothiolase deficiency	+		+	
Methylmalonyl-CoA mutase (MUT)			+	
Proprionic Acidemia	+		+	
Multiple carboxylase deficiency	+		+	+
Argininosuccinic Aciduria	+		+	
Citrullinemia	+		+	
Homocystinuria	+		+	+
Maple Syrup Urine Disease	+		+	+
Phenylketonuria	+	+	+	+
Tyrosinemia Type I	+		+	+

ACMG – American College of Medical Genetics

[a] Although the core panel is recommended in the United States, variation exists amongst the US states in implementation.

[b] Note: Although the core panel is recommended in Australia, variation exists amongst the states.

Table 2: Conditions screened for in provincial programs (Hanley, 2005; Therrell and Adams, 2007)

Disorder	BC	AB	SK	MB	ON	QC	NB	NS	PE	NL
Congenital Hypothyroidism	+	+	+	+	+	+	+	+	+	+
Congenital Adrenal Hyperplasia	*	+	+	+	+					
Galactosemia	+		*	+	+					
Sickle Cell Disease	+				+					
Biotinidase Deficiency		+	*	+	+					
Cystic Fibrosis	+	+	*		+					
Phenylketonuria	+	+	+	+	+	+	+	+	+	+
Maple Syrup Disease	+	+	+		+		+	+	+	
Homocystinuria	+		+		+		+	+	+	
Tyrosinemia Type I	+		+		+	+				+
Citrullinemia	+	+	+		+	#				
Argininosuccinic Aciduria	+		+		+	#				
Very Long Chain Acyl-CoA deyhydrogenase deficiency (VLCAD)	+	+	+		+		+	+	+	
Long Chain 3-hydroxy-CoA dehydrogenase deficiency (LCHAD)	+	+	+		+		+	+	+	
Medium chain Acyl-CoA dehydrogenase deficiency	+	+	+		+		+	+	+	
Carnitine Uptake Deficiency		+	+		+		+	+	+	
Proprionic Acidemia	+	+	+		+					
Methylmalonic acidemia (Vitamin B12 disorders, Cbl-A, B)	+	+	+		+	#				
Methylmalonyl-CoA mutase deficiency (MUT)	+	+	+		+	#				
Isovaleric Acidemia	+	+	+		+	#	+	+	+	
Glutaryl-CoA dehydrogenase deficiency	+	+	+	+[a]	+	#	+	+	+	
Multiple carboxylase deficiency			+		+					
3-Hydroxy-3-methylglutaryl Co-A lyase deficiency		+	+		+	#				
Beta-ketothiolase deficiency			+		+					
3-Methylcrotonyl-CoA carboxylase deficiency			+		+	#				
Glutaric Aciduria Type II			¤		¤		+	+	+	
CPT1			¤		¤		+	+	+	
CPT2			¤		¤		+	+	+	
CACT			¤		¤		+	+	+	

Infants born in the federal territories are screened by provincial programs as follows: Yukon – British Columbia; NWT and Nunavut (Kitikmeot region) – Alberta; Nunavut (Kivalliq) - Manitoba,; Nunavut (Baffin) – Quebec.
a - Targeted screening of Oji-Cree newborns.
*=announced; ¤=disease not targeted but expected to be ascertained as its primary markers are the same as those for other diseases that are targeted; # =targeted by the Quebec urine newborn screening program.

The argument for a national newborn screening program

There is increasing interest in many countries in improving uniformity and standardization of their neonatal screening programs. At present the Canadian federal government has no role in newborn screening beyond the licensing of some tests and other medical devices and the regulation of foods, drugs and supplements for treatment of rare and orphan diseases. National structures may facilitate the development of better newborn screening practices in Canada in several ways. For example, newborn screening programs have been recognized as having 5 key components: screening (the test itself), follow-up (for initial positive results), diagnosis, treatment/management, and evaluation.[14] Thus, screening is a system of care that goes beyond the actual test itself. As such, there is a need for: the institution of processes to ensure the inclusion of up to date screening panels and practices; the clarification of the legal status of screening and consent requirements; the modernization of policies for education, treatment and follow-up; and the development of mechanisms for long term follow-up and program evaluation. A national approach to such processes would facilitate the transfer of relevant infrastructure/systems and policies developed in one jurisdiction to other jurisdictions. This could include, for example, common laboratory testing protocols, blood collection cards and requisitions, feedback information systems, educational materials, and diagnostic and other follow-up recommendations. With respect to program evaluation in particular, the current gaps in evidence and lack of consensus regarding the clinical benefits of screening for many of the screened diseases have led to the suggestion that expanded newborn screening should be implemented in a "research paradigm" that incorporates rigorous evaluation of outcomes.[15] Given the rarity of the diseases, such research will require collaboration across jurisdictions, including agreement on case definitions and on protocols for follow-up and treatment services. A national structure would facilitate this collaborative work.

A national approach would also help to improve equal access to newborn screening tests and treatments across Canada. The goal of providing equal access to newborn screening services across jurisdictions was a motivator for the national policy processes in the US[16] and the UK.[17] A desire for uniform access across Canada has also been expressed.[18]

However, importantly, a national strategy must allow for the recognition of regional variation. National standards would need to establish criteria to be used in considering the appropriateness of targeting a disease, provide minimum standards for consent for screening and secondary uses of residual blood spots, and perhaps assist in the removal of financial barriers to the effective implementation of comprehensive provincial/territorial programs. The latter is particularly important given that rates for many of the potentially screened for conditions significantly vary from province to province, and the adoption of expensive high-throughput technologies would be more difficult to justify for provinces with smaller populations and/or lower incidence rates.

Strategies for the development of a national newborn screening program

Legislation

To determine what options a federal government agency would have in developing a harmonized national program for newborn screening, it is important to first determine the extent to which the federal government would have constitutional jurisdiction over the area. The degree of constitutional authority will define the limits within which the federal government could impose its vision within provincial borders. If, for example, the federal government had clear constitutional authority it could use legislation to achieve its policy objectives. Unclear but potential authority may make a legislative approach unpalatable but would perhaps justify the use of potentially coercive strategies to encourage provincial compliance with federal/national goals. The clear absence of constitutional authority would suggest that the federal government would have to achieve its objective with a minimum degree of coercion or perhaps simply act as an equal partner and facilitate consensus amongst all provincial/territorial partners.[19]

Newborn screening lies at the intersection of the health care system and the public health system. The administration of the program may be at the level of the health care institution or public health facilities that are clearly within provincial jurisdiction. Administration of health care services is constitutionally a provincial/territorial jurisdiction, with the exception of health care services for first nations and military personnel and marine hospitals.[20] Therefore, from the perspective of newborn screening as a health care service, the federal

government could not pass legislation that would require action in this area at the provincial level. However, newborn screening as a population wide program could arguably be considered a public health intervention. Public health is not referred to in the Constitution but is considered a shared jurisdiction based on previous decisions.[21] Federal authority to pass regulations has primarily been based on federal criminal powers. The *Food and Drugs Act* and the *Canadian Environmental Protection Act, 1999*, are two examples of legislation that provide the federal government with the authority to regulate over matters pertaining to public health.[22] However, this authority is based on addressing risks that have the potential to cross borders. Unlike unsafe food or unclean water, it is difficult to argue that failures in newborn screening within one province have the potential to adversely impact the health of citizens in another province, although the federal government could use the *Food and Drugs Act* to regulate diagnostic tests and treatments for conditions which are screened for. The other potential constitutional authority the federal government has in public health is also likely not applicable. Federal quarantine powers are not relevant to this area and, in general, the courts have been reluctant to justify expansion of federal authority based on the "peace order and good government" residual power.[23]

In the absence of explicit constitutional authority to legislate a harmonized newborn screening program, the federal government could instead involve itself through the use of the federal spending power.

Spending power

In the absence of explicit constitutional authority to legislate a harmonized newborn screening program, the federal government could instead involve itself through the use of the federal spending power. This could justify the use of conditional funding to encourage provincial governments to structure newborn screening programs based on federal standards. Such an approach would be constitutionally permitted and would have the advantage of providing assistance to provinces to financially support expansion of their existing programs. Such a program would be analogous to the *Canada Health Act* and Canada Health Transfer, where funds are provided to the provinces/territories with the condition that the programs the funds are intended for meet specific federal standards.[24] However, the provinces/territories could perceive this to be an overreach of federal authority and an unnecessary invasion of their jurisdiction. In the case of universal hospital insurance the impetus for the federal program was provincial pressure; in the case of medical insurance, it was public pressure.[25] Neither of these exists in sufficient measure to justify a new federal conditional funding program specifically aimed at newborn screening. The federal government could make an argument based on the principle of justice, that regardless of where in the country a child is born he or she should have similar access to interventions that could improve his or her health. However, current trends in federalism would make it highly unlikely that the federal government would utilize such an option.

Non-conditional federal funding could also be utilized, and would be viewed by provincial/territorial officials as a less invasive option. An example would be the creation of a newborn screening trust. Such an approach was utilized in the development of the National Immunization Strategy.[26] A trust involves the federal government directing a portion of money to an independent fund. Once funds are transferred to a trust the provinces/territories become the beneficial holders of the funds. The trust can be structured in such a way that the provinces/territories can access the funds as needed, over a given fiscal time period. This would permit provinces to gradually expand their programs to meet federal standards and access money to help them do so. Importantly, while the funds would be transferred to the trust for an explicit purpose, expansion of newborn screening, the provinces are not obliged to use the money for this purpose. However, a provincial/territorial government whose screening programs do not meet national standards would feel political and public pressure to use the dedicated funds to enhance their programs to meet these standards.

National Guidelines

A standard approach the federal government has used in public health is the development of national guidelines. These can be issued by federal agencies or be agreed

upon through federal/provincial/territorial consensus. The National Advisory Committee on Immunization is an example of a federal body that develops national guidelines on a public health issue. In contrast, the Canada Wide Standards on Particulate Matter and Ground Level Ozone is an example of a set of standards agreed upon by all federal/provincial/territorial partners.[27] Guidelines, in and of themselves, have no enforcement capabilities. However, they can be an effective mechanism by which to pressure provinces and territories. The influence of guidelines may be more effective for higher profile areas, and health services provided to newborn children would fall under this category. A set of national guidelines on minimum standards for a newborn screening program and harmonization of mechanisms by which newborn screening decisions are made would logically be a necessity for the development of any national program.

Intergovernmental agreements

Memoranda of Understanding or intergovernmental agreements can be effective in formalizing the link between guidelines and funding if such were to exist. Memoranda of Understanding would not be as coercive as legislation given that they would require provinces to voluntarily approve the agreement. And the effective ability of the federal government to enforce a Memorandum of Understanding is limited. Nevertheless, they would add further legitimacy to national guidelines and clarify rules by which funding could be provided to provinces/territories.

Suggested strategy for the development of National Newborn Screening Initiative

To summarize, newborn screening is an issue which is of relevance to every newborn infant in Canada. It is potentially a high profile issue within a province. In fact, public attention to a lack of screening for some conditions within Ontario created pressure that likely contributed to the expansion of that province's program.[28] So far, the failures of one province have had little effect on another. It is a highly technical area in which comparatively few people across the country have expertise. It is an area in which the federal government has questionable, if any, constitutional authority to directly legislate.

It remains uncertain as to whether the federal government would want to assume a leadership role in an area where it has no clear constitutional authority and for which national spillovers do not exist. Interprovincial disparities and differences in newborn screening between countries could provide a compelling argument for federal involvement. Furthermore, the introduction of such a program could be viewed as comparatively non-contentious and good optics for a federal government that wants to show leadership in child health issues. If the federal government were to financially assist the development of a national program, the investment would be small in comparison to other federal programs.

The need for funding to "buy" provincial cooperation could lead to the use of a non-conditional newborn screening trust and guidelines approach, analogous to the National Immunization Strategy.

If the momentum existed for the development of a national program, and the federal government chose to show leadership in facilitating the institution of such a program, the most effective strategy would be a minimally intrusive one. Federal legislation would constitutionally not be an option. In the current political environment a conditional funding option is also likely not viable. Guidelines would be the most palatable option, but may have uncertain effectiveness. The need for funding to "buy" provincial cooperation could lead to the use of a non-conditional newborn screening trust and guidelines approach, analogous to the National Immunization Strategy. The National Immunization Strategy has been effective in achieving harmonization of the pediatric vaccines offered throughout the country, and in many ways is a policy area similar to newborn screening. However, the National Immunization Strategy had been in the works for many years; it required the SARS outbreak to place it sufficiently high on the policy agenda.

How then should a national newborn screening program be structured? Newborn screening experts, including representatives from all federal/provincial/territorial

partners would develop a mechanism by which diseases for inclusion in provincial programs would be determined. This could occur within the context of a federal agency – Health Canada or the Public Health Agency of Canada, for example – a federal/provincial/territorial organization, or perhaps a separate arms' length body of experts. The federal government could establish a trust fund to assist provinces in upgrading their programs to meet national minimal standards. Funds would be allocated to all provinces, even those that have already met federal standards. These provinces could choose to use these funds to further improve their existing screening program, allowing for provincial innovation. The nature of the relationship between the federal/provincial/territorial partners could be formalized through a Memorandum of Understanding. The program would need a mechanism to ensure ongoing review and a level of continued contribution of the federal government to the provincial programs after they have been deemed to meet national guidelines.

Conclusion

A strong argument on the basis of the right to equity of access and the facilitation of collaboration with respect to infrastructure and evaluation can be made for the development of a national newborn screening strategy for Canada. Such a strategy would be based on the establishment of guidelines/standards for the various components of newborn screening – in particular, the criteria to determine for what conditions children should be screened. We suggest that the most effective mechanism for the federal government to facilitate the development of such a strategy, given their lack of explicit constitutional authority in the area, is to model the National Immunization Strategy. A mechanism for establishing national minimum standards that is inclusive of the provinces can be created, and then the federal government could facilitate the "up-grading" of provincial programs to meet these standards by flowing monies through a newborn screening trust. The creation of a national strategy using such a mechanism offers many potential advantages, including equity of access, economies of scale, and interprovincial learning and rigorous evaluation facilitation. All of these would go a long way to improving the health of vulnerable children with rare genetic conditions.

Kumanan Wilson, Department of Medicine, Ottawa Health Research Institute, University of Ottawa; Institute of Intergovernmental Relations, Queen's University, Kingston, Ontario; Department of Epidemiology & Community Medicine, University of Ottawa.

Shelley J. Kennedy, Ontario Newborn Screening Program, Children's Hospital of Eastern Ontario; Department of Genetics, Children's Hospital of Eastern Ontario.

Beth K. Potter, Department of Epidemiology & Community Medicine, University of Ottawa.

Michael T. Geraghty, Department of Genetics, Children's Hospital of Eastern Ontario; Department of Pediatrics, University of Ottawa.

Pranesh Chakraborty, Ontario Newborn Screening Program, Children's Hospital of Eastern Ontario, Department of Pediatrics, University of Ottawa

Dr. Kumanan Wilson is supported by the Canada Research Chair in public health policy.

Correspondence: Dr. Kumanan Wilson, The Ottawa Hospital, Civic Campus, 1053 Carling Avenue, Administrative Services Building, Room 1009, Box 684, Ottawa, ON K1Y 4E9

Endnotes

1 J.M. Wilson & Y.G. Jungner, "Principles and Practice of Mass Screening for Disease" (1968) 65:4 Boletin de la Oficina Sanitaria Panamericana 281.

2 Michael S. Watson *et al.*, "Newborn Screening: Toward a Uniform Screening Panel and System" (2006) 8:5 Genetics in Medicine 1S; Duane Alexander & Peter C. van Dyck, "A Vision of the Future of Newborn Screening" (2006) 117 Pediatrics S350.

3 Bradford L. Therrell & John Adams, "Newborn screening in North America" (2007) 30 Journal of Inherited Metabolic Disease 447.

4 Denise Avard *et al.*, "Newborn Screening by Tandem Mass Spectrometry: Ethical and Social Issues" (2007) 98 Canadian Journal of Public Health 284; William B. Hanley, "Newborn Screening in Canada – Are We Out of Step?" (2005) 10 Journal of Paediatrics and Child Health 203.

5 O.A. Bodamer, G.F. Hoffman & M. Lindner, "Expanded newborn screening in Europe 2007" (2007) 30 Journal of Inherited Metabolic Disease

439; G.J.C. Borrajo, "Newborn screening in Latin America at the beginning of the 21st century" (2007) 30 Journal of Inherited Metabolic Disease 466; Carmencita D. Padilla & Bradford L. Therrell, "Newborn screening in the Asia Pacific region" (2007) 30 Journal of Inherited Metabolic Disease 490; A.A. Saadallah & M.S. Rashed, "Newborn screening: Experiences in the Middle East and North Africa" (2007) 30 Journal of Inherited Metabolic Disease 482; *supra* note 3.

6 Watson *et al.*, *supra* note 2; Alexander & van Dyck, *supra* note 2; Jeffrey R. Botkin *et al.*, "Newborn Screening Technology: Proceed With Caution" (2006) 117 Pediatrics 1793; Scott D. Grosse *et al.*, "From Public Health Emergency to Public Health Service: The Implications of Evolving Criteria for Newborn Screening Panels" (2006) 117 Pediatrics 923; R. Rodney Howell, "We Need Expanded Newborn Screening" (2006) 117 Pediatrics 1800; Virginia A. Moyer *et al.*, "Expanding Newborn Screening: Process, Policy and Priorities" (2008) 38:3 Hastings Center Report 32.

7 *Supra* note 3.

8 Watson *et al.*, *supra* note 2.

9 Botkin *et al.*, *supra* note 6; Moyer *et al.*, *supra* note 6.

10 A. Pandor *et al.*, *Clinical effectiveness and cost-effectiveness of neonatal screening for inborn errors of metabolism using tandem mass spectrometry: a systematic review* (Tunbridge Wells: Gray Publishing, 2004).

11 *Supra* note 3.

12 Hanley, *supra* note 4.

13 *Supra* note 1.

14 Kenneth A. Pass *et al.*, "U.S. Newborn Screening System Guidelines II: Follow-Up of Children, Diagnosis, Management, and Evaluation Statement of the Council of Regional Networks for Genetic Services (CORN)" (2000) 137 Journal of Pediatrics S1.

15 Botkin, *supra* note 6.

16 AAP Newborn Screening Task Force, "Serving the Family From Birth to the Medical Home Newborn Screening: A Blueprint fo the Future A Call for a National Agenda on State Newborn Screening Programs" (2000) 106 Pediatrics 389; Watson *et al.*, *supra* note 2.

17 UK Newborn Screening Programme Centre, *Newborn blood spot screening in the UK: Policies and standards* (London: UK Newborn Screening Programme Centre, 2005).

18 Hanley, *supra* note 4; *supra* note 3.

19 Kumanan Wilson & Harvey Lazar, *Creative Federalism and Public Health* (Kingston: Institute of Intergovernmental Relations School of Policy Studies, Queen's University, 2008).

20 Andre Braen, *Discussion Paper No. 2: Health and the Distribution of Powers in Canada* (Ottawa: Commission on the Future of Health Care in Canada, 2002); Martha Jackman, "The Constitutional Basis for Federal Regulation of Health" (1996) 5:2 Health Law Review 3.

21 Jackman, *ibid.*;, Kumanan Wilson, "The Complexities of Multi-Level Governance in Public Health" (2004) 95 Canadian Journal of Public Health 409.

22 R.S.C. 1985, c. F-27; S.C. 1992, c. 37. See Amir Attaran, "Hazardous Waste? The criminal law power, federal environmental jurisdiction, and Ottawa's policy since *R. v. Hydro-Quebec*" (2000) 49 U.N.B.L.J. 97; Kumanan Wilson & Christopher MacLennan, "Federalism and public health law: opportunities and unanswered questions" (2005) 14:2 Health Law Review 3.

23 Amir Attaran & Kumanan Wilson, "A Legal and Epidemiological Justification for Federal Authority in Public Health Emergencies" (2007) 52 McGill L.J. 381.

24 R.S.C. 1985, c. C-6. See Kumanan Wilson, "Health care, federalism and the new Social Union" (2000) 162 Canadian Medical Association Journa1 1171.

25 Malcolm G. Taylor, *Health Insurance and Canadian Public Policy: The Seven Decisions that Created the Canadian Health Insurance System* (Montreal: McGill-Queen's University Press, 1978).

26 Jennifer Keelan, Harvey Lazar & Kumanan Wilson, "The national immunization strategy: a model for resolving jurisdictional disputes in public health" (2008) 99 Canadian Journal of Public Health 376.

27 Karen Thomas, *Canada-Wide Standards for Particulate Matter and Ground-Level Ozone: A Shared Approach to Managing Air Quality in Canada* (Kingston: Institute of Intergovernmental Relations School of Policy Studies, Queen's University Press, 2008).

28 Andre Marin, *The Right To Be Impatient: Whether the Ministry of Health and Long-Term Care has failed to properly administer Newborn Screening in Ontario* (Toronto: Ombudsman Ontario, 2005).