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Evaluating the Potential Socio-Economic Impact of Personalized Medicine

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Rapport de projet
Project report

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Evaluating the Potential Socio-Economic Impact of Personalized Medicine

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Summary

Since 2000, Québec and Canada have made significant R&D investments in the area of genomics, with a particular focus on technological platform development and genetics.

To justify these and future major investments in genomic research, clear benefits of genomic technologies to society must be demonstrated.

The goals of the study are to provide methodology to evaluate potential socio-economic impact of personalized medicines, to demonstrate it on two applications of genomic technology and to summarize obstacles to realize the potential socio-economic benefits of genomic research.

The following report is the presentation of the project made at Genome Quebec.

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Evaluating the Potential Socio-Economic Impact of Personalized Medicine

Research Report
for Génome Québec
prepared by CIRANO

Goals of the study

Background

- Since 2000, Québec and Canada have made significant R&D investments in the area of genomics, with a particular focus on technological platform development and genetics.
- To justify these and future major investments in genomic research, clear benefits of genomic technologies to society must be demonstrated.

Goals of the study

- To provide methodology to evaluate potential socio-economic impact of personalized medicines
- To demonstrate the methodology on 2 applications of genomic technology
- To summarize obstacles to realize the potential socio-economic benefits of genomic research

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Report Outline

- Background
  - What is personalized medicine?
  - Current state of genomic research in Quebec
  - Commercialization of genomic research
- Economic evaluation in healthcare
  - What is economic evaluation in healthcare?
  - Methodology to evaluate the potential socio-economic impact of health technologies and health research
  - Socio-economic impact vs. other methodologies
- Two applications of personalized medicine
  - Case I: BD GeneOhm™ MRSA
  - Case II: Genetic testing for COX deficiency, French Canadian type
- Discussion
  - Obstacles to clinical practice penetration
  - Data availability
- Conclusion
- References

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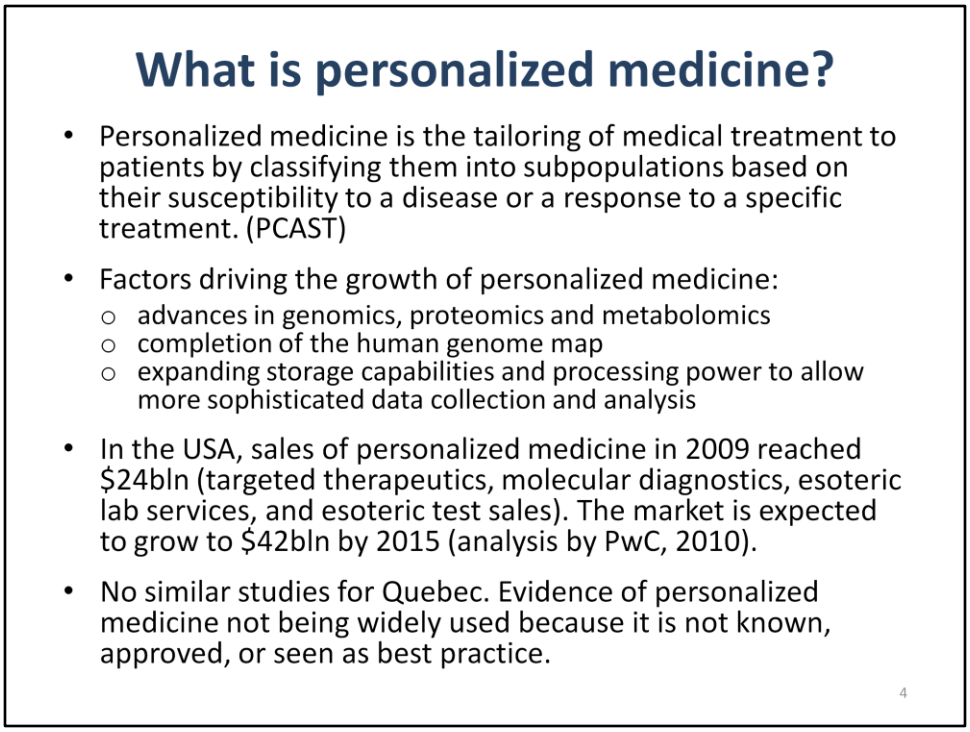
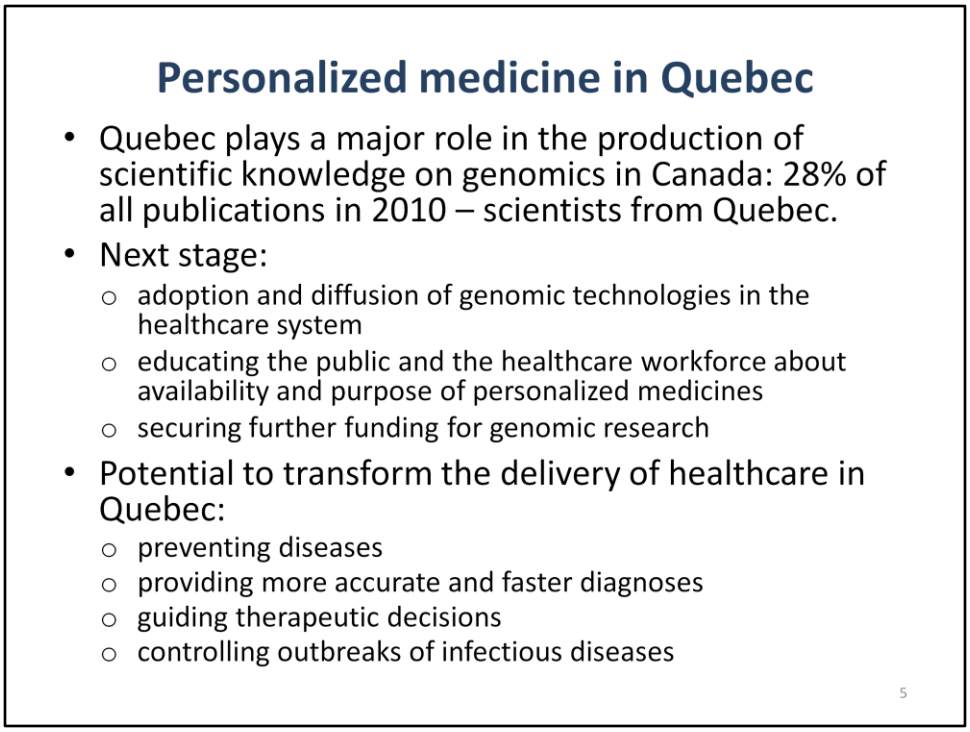
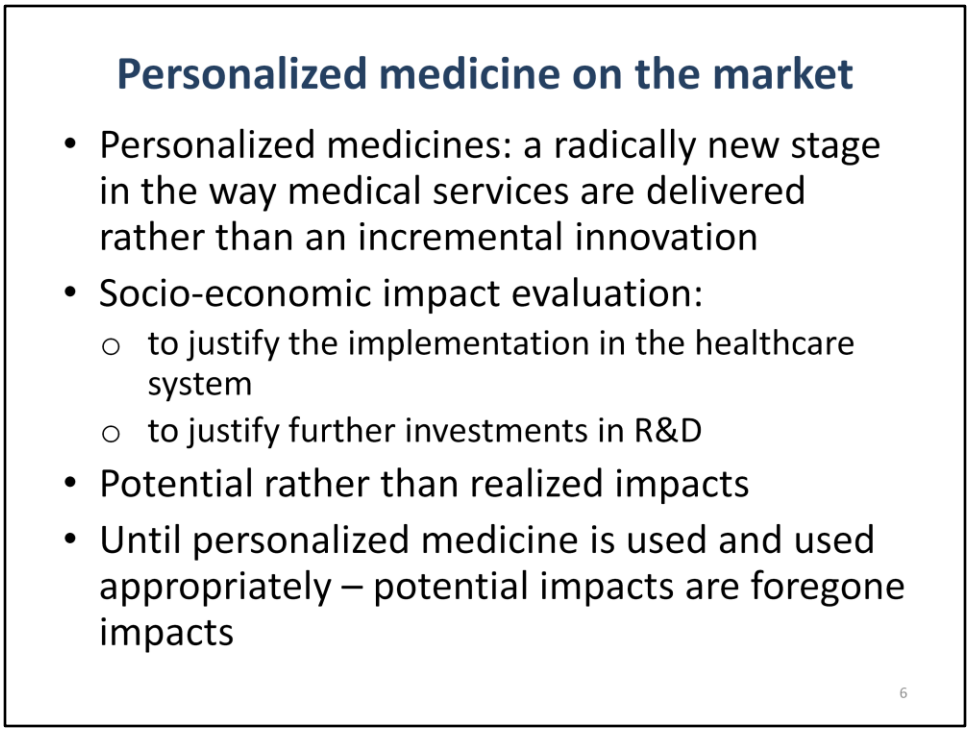


1. The definition of personalized medicines is borrowed and rephrased from the President's Council of Advisors on Science and Technology (PCAST), "Priorities for Personalized Medicine", September 2008.
2. "Today, several factors are accelerating the growth of personalized medicine, moving it beyond concept to enabling tailored approaches to prevention and care. Among them, advances in genomics, proteomics and metabolomics, completion of the human genome map, and development of targeted diagnostics and therapeutics are driving a more personalized approach to healthcare. Expanding storage capabilities and processing power are allowing for sophisticated data collection on individual patients, which, when de-identified and aggregated, can predict public health trends and other benefits." (McDougall, 2010).
3. "If viewed in its entirety, the field of personalized medicine reaches beyond a core of targeted therapeutics and diagnostics to encompass personal health record management, disease management, wellness and nutrition. PricewaterhouseCoopers estimates that the core market alone accounts for $24 billion in sales in 2009, and will grow 10% annually to $42 billion by 2015." (analysis by PricewaterhouseCoopers, 2010, cited in *Healthleaders Media Breakthroughs*).



1. By now, Quebec has established a solid position in genomic research in Canada: in 2009-2010, 28% of all scientific publications on genomics in Canada were done by researchers from Quebec (Report by SECOR, 2010). With its well-established pool of researchers, developed facilities, and secured research funding, Quebec has the potential to keep and increase its role in the global advancement of knowledge.
2. Next stage:
    - integrating new practice into established patient pathways by putting in place the systems and structures to facilitate adoption and diffusion of genomic technologies in the healthcare system
    - educating the public and the healthcare workforce about availability and purpose of personalized medicine
    - securing further funding for genomic research
3. Personalized medicine has the potential to transform the delivery of healthcare in Quebec by preventing diseases, providing more accurate and faster diagnoses, guiding therapeutic decisions, and controlling outbreaks of infectious diseases.



1. Personalized medicines are not an incremental innovation, it is a radically new stage in the way medical services are delivered and diseases/treatments are understood. In order to achieve the next stage goals, the complexity of this phenomenon must be comprehended and evaluated keeping in mind all stakeholders affected by the introduction of personalized medicines.
2. Why economic evaluation of genomic technologies? a) To justify more funding: Studies say that more research, and therefore, more funding is needed to continue the developments towards personalized medicine. However, their opponents claim that enough money has been invested already and the results are not yet there to be seen. Therefore, clear benefits to society must be shown to justify these major investments and attract future investments. b) To justify the implementation of the applications of genomic technologies: A considerable part of benefits from any health research comes from using innovations in health practice. Hence, discoveries must move from the innovation to the marketing stage before there can be any perceivable benefits for the general public. Their value to the healthcare system relative existing standards of care or alternative new interventions has also to be justified.
3. The proposition is to use the methodology of Socio-Economic Impact evaluation. In the context of personalized medicine, *potential* rather than *realized* impacts will be evaluated.

Why apply economic evaluation to healthcare?

- Allows moving from asking “Does it work?” to asking “Should it be done?”
- Social resources are scarce – economic evaluation allows choosing among multiple alternative uses of these resources.
- Alternative uses may include a new technology vs. a standard of care or several new technologies.
- The process involves identification, measurement, evaluation, and comparison of benefits and costs.

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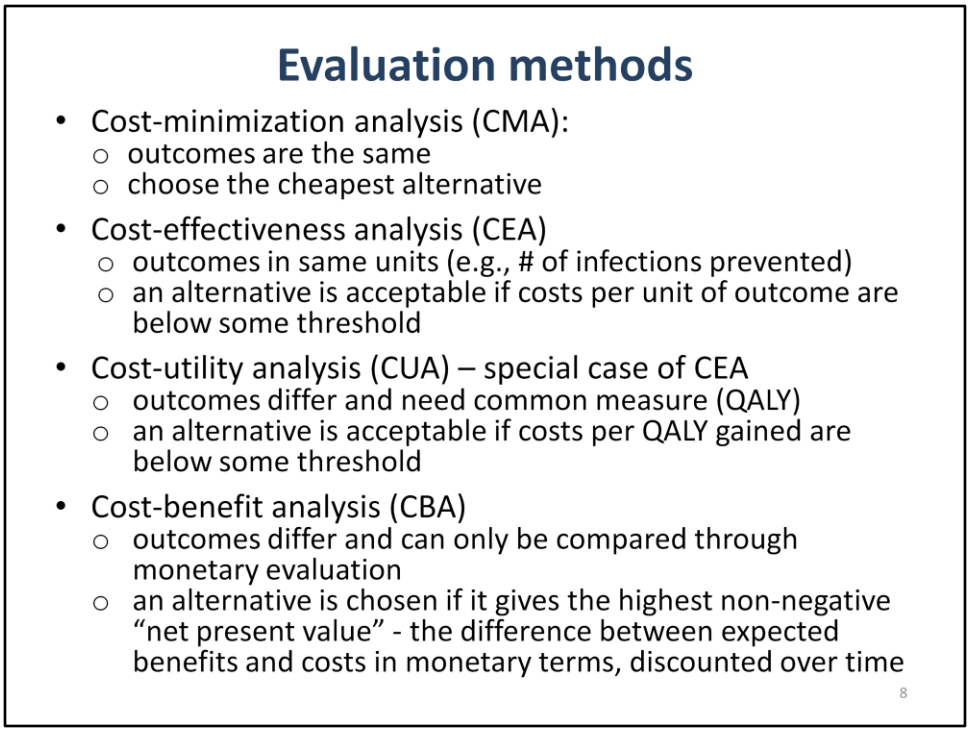
1. In healthcare, economic evaluation provides a framework within which a range of evidence can be assembled to move from the stage “Does it work?” to “Should it be done?”, that is, to move from the stage of discovery and development of health technologies to the stage of their implementation.
2. Scarcity of resources (funds, equipment, hospital beds, staff) makes one carefully consider how these resources are used to avoid their inefficient allocation. Economic evaluation provides the means to decide whether resources should or should not be spent in each particular case.
3. Economic evaluation may be defined as “the comparative analysis of alternative courses of action in terms of both their costs and consequences” (Drummond *et al.*, 2005). These alternative courses could be a new technology versus the standard of care, or two new technologies where no standard of care is established. The process involves identifying, measuring, valuing, and comparing the costs and benefits based on available information.



1. Economic evaluation in healthcare takes a number of forms, and most forms are defined in terms of the way in which benefits are measured. Economic evaluations techniques present a spectrum of options with cost-minimization and cost-benefit analyses at its extremes. The choice of the method is determined by the question to be answered and resources available to evaluate benefits (e.g., data constraints).
2. Other methods of economic evaluation include: cost minimization analysis (CMA), cost-effectiveness analysis (CEA), cost-utility analysis (CUA), and cost-benefit analysis (CBA). Examples when to use each method:

a) CMA: when comparing two alternatives that were proven to have exactly the same outcome
b) CEA: when outcomes are measured in the same units and these are natural units (e.g., number of kilograms lost)
c) CUA: when outcomes come in different units and require unification
d) CBA: when judgment of importance of very different initiatives is required, when monetary terms is the only way to compare outcomes.

3. The first three methods are also known as methods of financial evaluation. Economic literature criticizes the use of the CEA and CUA: CEA for the lack of theoretical grounds to answer the question it poses, CUA for the way it is implemented, although theoretically it has a potential to be used properly. Among the main problems with both methods is their reliance on the incremental cost-effectiveness ratio (ICER). The ICER, used by the CEA and CUA methods does not help to answer the question 'should it be purchased?' because it doesn't take into account where the resources come from, what the foregone benefits and the opportunity costs are. It is the CBA that considers foregone benefits and therefore opportunity costs. CEA and CUA are also often referred to as tools of managerial considerations rather than economic considerations. The latter is based on welfare economics rather than financial analysis and accounting.

Socio-Economic Impact Analysis

- Economic impact analysis examines the effect of a policy, program, or intervention.
- Comparison of situations “with” and “without” an intervention. Unrealized interventions have “potential” rather than “realized” impact.
- When applied to healthcare interventions, socio-economic impacts come from the utilization of an intervention in the healthcare system and commercial activities:
  - Direct net benefits
  - Indirect (social) benefits
  - Impacts due to commercial activities

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1. Economic impact analysis examines the effect of a policy, program, or intervention.
2. The impact is measured as the difference between what happened (or would happen) with the considered course of action and what would otherwise be expected if the course of action did not occur.
3. The economic impact of an intervention that has not taken place yet is “expected” or “potential impact”. The realization of a potential impact is conditional on the proper implementation of the intervention.

Socio-economic impact vs. other methods

- Evaluates interventions from a broader perspective: society rather than payer (provider) to influence social decision-making.
- Considering multiple stakeholders allows a more comprehensive consideration of benefits and costs. For example, some costs may be transferred from the healthcare system on an individual. Traditional financial methods do not account for this.
- Accounts for indirect impacts that come mostly from the social consequences of the intervention, unaccounted for by other methods.
- It is broader than CBA because it accounts for impacts due to commercial activities that affect other economic sectors.
- It does not rely on ICER, the rules for which are questionable.

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1. Economic impact analysis is taken from the societal perspective, rather than the payer's perspective. Consideration of only selected stakeholders rather than all of them would lead to an underestimation or omission of costs or gains incurred by stakeholders that are not taken into account. To see the effect of this case, consider for example, a new medical procedure that results in savings for a hospital due to shorter hospital stays. However, this procedure leaves a patient with large expenses on over-the-counter medications (e.g., painkillers). A similar situation would be if, as a result of this new procedure, a patient has to hire a nurse or helper (or engage a family member) to take care of him/her during the period of temporary disability or has to follow a special diet forcing him to spend more than usual on grocery bills. In this situation perceived gains or savings enjoyed by the hospital may be offset or even overshadowed by costs to other stakeholders unaccounted for by the method. Direct costs due to short-term absence from work are sometimes accounted for by cost-effectiveness studies but these studies rarely go beyond productivity losses. The main argument for economic evaluation is that it helps us see the whole picture.
2. Economic impact analysis is broader than the most comprehensive CBA: it counts effects on business activity outside healthcare through spending multiplier effects in the given area, whereas CBA ignores the effects of business activity shifts. Economic impact considers how advancements in healthcare affect other economic sectors, the benefits or costs to which are not considered by CMA, CEA, and CUA. For example, in order to implement a new procedure, medical equipment industry will have to produce a specialized machine or tool. As a result, the industry will maintain its employees or hire new employees and buy materials to build the required equipment. Employees will benefit from their earnings, and suppliers of materials will receive profits from their sales. A company producing the equipment will in turn also make profits from selling the equipment to a hospital. Many economic impacts would be considered only transfers in the social CBA methodology, because it would assume that monies gained in one sector would be simply transferred from another sector: e.g., revenues, taxes, personal income.
3. The outcome of the CEA and CUA methods is an amount of required expenditures per unit of outcome or QALY. The threshold between cost-effective and cost-ineffective alternatives is a subjective matter (why is it considered cost-effective under 50,000/QALY? Why not 100,000? Should it change with time? Should it vary across diseases?) The outcome of the economic impact analysis is easy to measure and easy to understand.

Direct Net Benefits

- Direct net benefits to the healthcare system are costs avoided due to the intervention minus the costs of the intervention. Avoided costs may include:
  - Savings due to reduced frequency and duration of hospital stays
  - Savings due to reduced outpatient and ER visits
  - Savings due to reduced utilization of medications and medical equipment
- Direct net benefits to patients and their families are similar, except the beneficiaries are individuals:
  - Reduced out-of-pocket expenditures on prescription medications
  - Reduced expenditures on over-the-counter medications
  - Reduced expenditures on care-takers
  - Savings due to reduced reliance on long-term care facilities
  - Reduced travel costs to and from the point of care

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1. Utilization of a new health technology results in direct savings to the healthcare system and to affected individuals and their families (i.e., direct benefits). Direct savings are costs avoided thanks to the utilization of new techniques that a) prevent a disease, b) reduce severity of a disease, c) speed up recovery, d) reduce toxicity of a treatment.
2. Calculation of these costs is straightforward and unambiguous. The required data include per unit costs (e.g., cost of a hospital admission) and frequencies (e.g., number of avoided hospital admissions). Possible data sources included relevant literature, hospital databases, and government databases.

Indirect benefits (social benefits)

- Utilization of a new health intervention will affect the patients by:
  - preventing diseases
  - providing cure for diseases
  - reducing morbidity of diseases
  - reducing morbidity of treatments
- In terms of population health, these improvements will impact:
  - improvement in quality of life (QoL)
  - increased longevity
  - reduced pre-mature mortality
- How to evaluate the social value of health improvements in patients?

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1. The effect of new health technology on population health results in more than just savings. Healthier individuals are more productive and more present at work, they enjoy greater quality of life during their free time, and their families benefit from healthy family-members. These benefits from health improvements are Social benefits, or Indirect benefits.
2. The prevailing approach in the healthcare outcomes literature is to count health improvements (e.g., number of lives saved) or to use specific weights to account for changes in the quality of life, specific to various diseases. Quality-adjusted life-years gained (QALY), Disability-adjusted life-years gained (DALY).
3. Economists have two methods to put a monetary value on gained time and its quality: human capital approach and willingness-to-pay approach.

Human capital approach

- Human capital approach: value of gained time and health=value of gained productivity at work
- Issues:
  - children, elderly, disabled and gravely ill – valued significantly less (if at all) than healthy individuals of working age
  - higher-paid individuals are valued higher (higher productivity is assumed)
  - the value of "non-market" time (time outside work) is ignored
  - may be incorrect if wages are not representative of productivity (market inefficiencies)
  - ignores the value of healthy individuals to their families
  - Ignores individuals' preferences
- The approach could still be used when comparing alternatives affecting similar socio-economic groups of individuals, or impacts directly on productivity (e.g., minor injuries or time saved on receiving care).
- Solution: willingness-to-pay approach

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1. Two methods exist to put a monetary value of reduced mortality and improved quality of life: human capital approach and willingness to pay approach.
2. In the human capital approach, an individual's "social" value is measured according to his potential future productivity, based on the present value of his expected working income. Gained life and health are measured through gained productivity (e.g., healthier individual can re-enter labour force, have fewer sick leaves, and be more efficient). This was the most frequently used method prior to the early 1990s in most industrialized countries, and is still used in Canada.
3. The approach undervalues individuals who do not work. For example, even though children do not work, improving their health or saving their lives will pay off in the future, when they become productive members of society. But this method would give a social value of 0 to saving a young cancer-patient, who may remain disabled even cancer is cleared or put under control, thus making cancer treatments a wasteful expense. Gravely ill patients, patients with disabilities, or senior citizens will not necessarily return to work after improvement in their health, so no productivity gains should be expected. The human capital approach ignores non-market time (time outside work). For example, a healthier old individual can be a more productive member of the household (e.g., an involved grandparent). Finally, it ignores the value of healthy individuals to their families.
4. In the case of market inefficiencies, wages are not representative of productivity. Therefore, the method would use a wrong measure for the value of gained time.
5. The method takes into account an individual's total expected income from working. Higher paid individuals may be perceived as more productive and therefore more valued by the method.

Willingness-to-pay approach

- Two economic models: Nordhaus (1999) and Murphy & Topel (2006).
- Accounts for value of market and non-market time and is based on individuals' preferences
- Empirical values come from 2 type of studies:
  - Studies of revealed preferences:
    - Labour market studies (risk-wage trade-offs)
    - Consumer purchase decisions (risk-price trade-offs)
  - Studies of stated preferences:
    - Contingent valuation studies
- The approach is widely used to evaluate public policies affecting life and well-being by government agencies in the USA: e.g., Environmental Protection Agency, Transportation Department, and Food and Drug Administration.
- The method is widely used to evaluate the cost of illness as well.

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1. Gains from reduced mortality are evaluated using a concept of the value of a statistical life (VSL): The VSL is the value placed on changes in the likelihood of death, not the value of life per se. This is very important to remember when assessing skepticism surrounding the concept.
2. Two models to evaluate the gains from reduced mortality: Nordhaus 1999 (Yale University) and Murphy and Topel, 2006 (University of Chicago). The model of Nordhaus only allows evaluating gains of reduced mortality, whereas Murphy and Topel (2006) account for both reduced mortality and improved quality of life.
3. Empirically, most studies determine the value of a life-year by assessing the value of a "fatality prevented'" with the "willingness to pay" (WTP) approach being the most generally accepted method of assessing this value. Studies of revealed preferences (actual behaviour) include labour market studies which look at the risk-wage tradeoff (e.g., knowing an accepted wage-premium for an incremental health risk allows calculating the value of a statistical life), and consumer purchase decisions, which look at the risk-price tradeoff (e.g. the amount people pay for a reduction in the risk of death/injury/disease: smoke alarms or airbags in cars, or the discount in rent demanded to live near chemical factories). Studies of stated preferences: contingent valuation studies.
4. Many government agencies in the US and abroad have adopted WTP approach. In Canada, the human capital approach is still used.

The value of statistical life

- Estimates for VSL differ. Moreau (2007) conducts a meta-analysis of 8 Canadian studies: $7.5mln per statistical life (2005 dollars). Range of estimates: $3.6mln – $9.9mln.
- From estimated VSL, a value per year can be obtained (VSL_{pa})
- To evaluate gained longevity: N_{years} * VSL_{pa}
- To evaluate gained QoL: QALY * VSL_{pa} (Cutler and Richardson, 1998).
- Debate: how ethical is it to put a $ on life?
- Answer:
  - value of a statistical life - value of gained time and its quality
  - determined from actions of people who in certain situation place a value on their life (e.g., insurance)
  - "ICER of ≤50,000/QALY" is also in a sense using WTP approach to value human life: ICER is a marginal cost of an intervention. The intervention is accepted if its marginal cost equals marginal benefit. Therefore, health authorities value an additional QALY at $50,000.

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1. Estimates for the VSL are presented in a variety of studies for many countries. For Canada, Moreau (2007) conducts a meta-analysis of 8 Canadian studies. He finds an average VSL of $7.5 mln (range: $3.6 mln -$9.9 mln).
2. Using a value for an average life, a value per life-year is calculated. In order to apply this seemingly large number to a specific case, one needs to ask – how many years of life were gained due to an intervention. This number is then multiplied by a VSL per year to obtain an estimate of the gain.
3. Such a calculation would imply a constant annual VSL regardless of age. Murphy and Topel (2006) suggest that annual VSL goes down with age. Other studies found no empirical evidence for VSL per life-year to be less for older people (e.g., Alberini *et al* 2002).
4. In the case when no life-years is gained but the quality of life has been improved (e.g., due to reduced morbidity), a VSL per year is weighed by QALY gained and then multiplied by the number of years that an individual gets and enjoys with a better quality of his/her life.
5. The ethical aspect of this approach is often questioned by non-economists. The answer to them is the following: economists agree that a human life is priceless. They just want to estimate the value of gained TIME and its QUALITY, rather than asking how much money would compensate a loss of someone. Moreover, the numbers used to value a statistical life come from real-life individuals' decisions to be compensated for additional risks or to pay to avoid them. For example, no-one questions the ethical aspect of life-insurance. Buying a life-insurance of $200,000 does not mean valuing one's life with this amount. The VSL concept is exactly the same thing. In addition, human capital approach is not considered un-ethical, even though it values a human similarly to a piece of machinery – based on his or her productivity.
6. The conclusion is that although both methods have issues, they are both widely used in welfare analysis and program evaluation. Which method to use depends on the nature of social benefits to be evaluated.

Impacts due to commercial activities

- Direct impacts on the producing sector:
  - creating employment (measured in jobs created and labour income)
  - generating output (business revenues)
  - increasing government tax revenues at all levels
- Indirect (induced) impacts on other economic sectors:
  - creating employment (measured in jobs created and labour income)
  - generating output (business revenues)
  - increasing government tax revenues at all levels
- The effect of activity in one economic sector on the rest of the economy is evaluated using the Input/Output model. For Quebec, the Input/Output model is developed at the *Institut de la statistique du Québec.*

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1. Commercial activities leading to the production of the proposed intervention produce impacts through creating employment, generating revenues, and taxes.
2. Moreover, since the economy consists of many sectors that are interrelated, economic activity in one sector begins to propagate throughout the economy and thus generates (or induces) economic activity in other sectors by affecting suppliers of machinery, tools, and raw materials used to produce the proposed intervention.
3. Economic impact studies produced by the *Institut de la statistique du Québec* (ISQ) present direct, indirect, and total effects on manpower, wages and salaries, value added and imports. They also provide an estimate of tax and quasi-tax revenues of expenditure projects.

Part II:
Applications
of Personalized Medicine

Suggested applications

Application	Purpose	Stage
BD methicillin-resistant Staphylococcus aureus - molecular diagnostic test	Screening newly admitted hospital patients for methicillin-resistant Staphylococcus aureus	Approved in 2004 but not widely adopted in QC
BD Group B Streptococcus assay	Screening pre-partum women for Group B Streptococcus	Approved but not widely adopted in QC
Genetic testing for cytochrome oxidase deficiency, French Canadian type	Screening potential parents with family history of COX deficiency	Approved and used in QC
Genetic screening for other types of rare diseases	Screening potential parents with family history	Approved and used in QC
BRCA1 -BRCA2 screening test for breast cancer	To identify women at risk of breast cancer	Development stage
Test for susceptibility to complications due diabetes melitus type 2	Screening patients with diabetes melitus type 2 for complications	Development stage
RET test for medullary thyroid cancer	Screening individuals with family history	Commercialized

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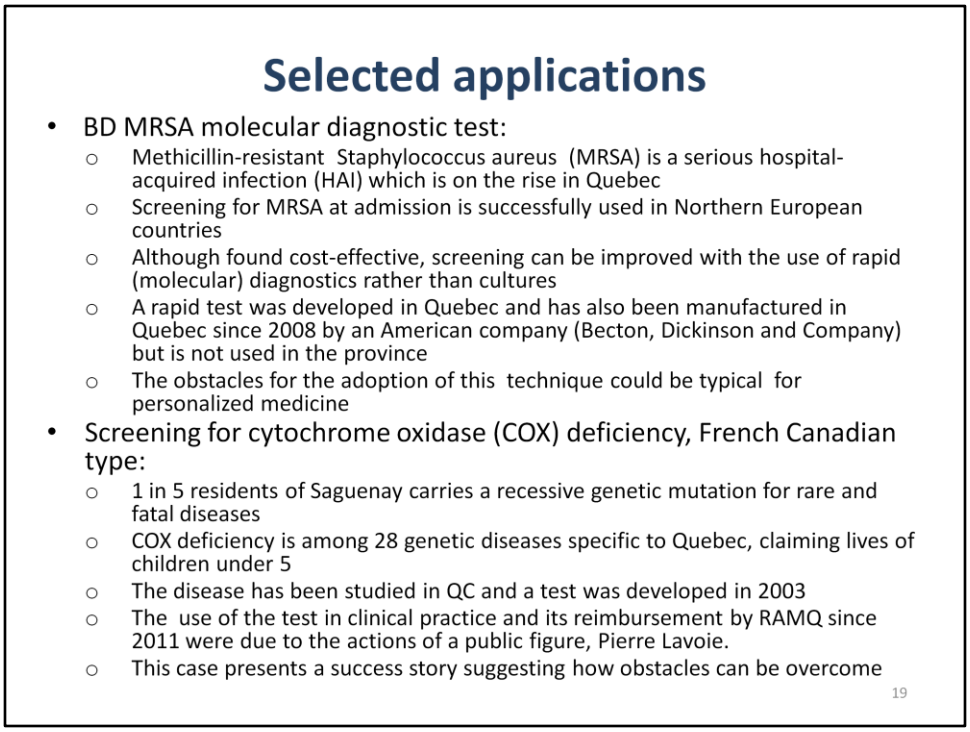
During our interviews of the members of scientific community, the following applications of personalized medicine were identified. They can be grouped as: molecular diagnostics for bacteria, genetic tests for rare inherited diseases, and tests for disease susceptibility.
Two of the proposed tests (BRCA 1 and 2 and test for complications due to diabetes melitus type 2) were still in development as reported by Dr. Simard and Dr. Hamet. Very little information was found regarding the RET test for medullary thyroid cancer. The four remaining technologies belonged to two groups: infections diseases and rare inherited diseases. We chose one example from each group; these cases and the reasons for their selection out of four technologies are explained on the next slide.



BD MRSA Assay was an attractive option for 3 main reasons:

1. it has a potential to substantially reduce MRSA in Quebec hospitals, which is a serious problem to the healthcare system and is currently on the rise.
2. The technology was developed in Quebec by Infectio Diagnostics and since 2008 has also been manufactured in Quebec by Becton, Dickinson and Company (BD), an American company that acquired Infectio Diagnostics.
3. The technology was approved by the health authorities as safe in 2004. However, there exist major barriers to its adoption by the healthcare system, which provides a good example for our last section on obstacles to the adoption of personalized medicine.

Screening for COX deficiency also has 3 major reasons to be selected:

1. The disease is specific to Quebec and presents an important health issue for its population, especially in certain regions.
2. Research to identify the gene responsible for the disease was started in Quebec, and later supported by scientists in Ontario and Massachusetts.
3. The test became available in 2003, and some people were tested. However, the procedure was not reimbursed and offered to larger number of individuals until 2011, when a famous Quebec athlete, Pierre Lavoie, who lost two children to the disease raised government awareness of the issue. This case presents a success story towards the adoption of personalized medicine and provides an example of how to speed up the adoption of personalized medicine in the healthcare system.

Case I : Screening for methicillin-resistant *Staphylococcus aureus*

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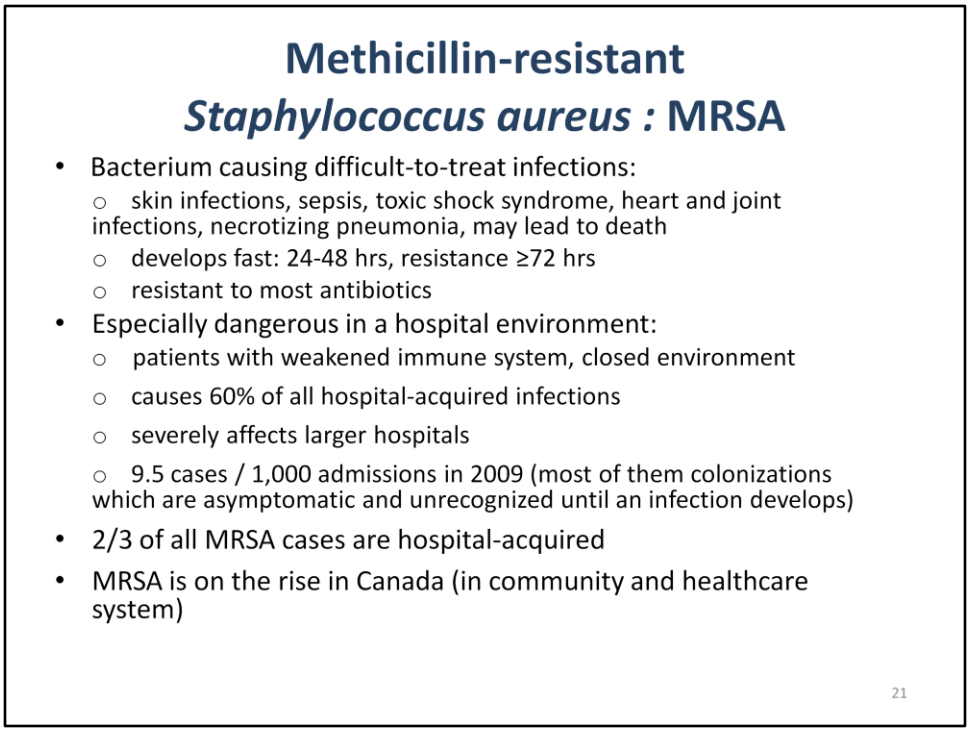

1. Hospital-acquired infections (HAIs) are infections that a patient contracts while in a hospital being treated for some other condition. HAIs have a significant impact on both patients and the province's health system. For patients, the impact of such infections can range from longer hospital stays to more serious conditions that may require surgery or result in negative long-term health effects. In severe cases, HAIs can cause death. For the health-care system, such infections increase treatment costs and result in longer wait times for a hospital bed for other patients. A 2003 Canadian study estimated that there are 220,000 cases of HAIs in Canadian hospitals each year, resulting in at least 8,000 deaths annually.
2. Colonization with *S. aureus* is a risk factor for eventual MRSA clinical infection, which is associated with high cost and poor clinical outcomes. MRSA acquisition is highly associated with subsequent infection (25% of newly detected MRSA carriers developed invasive disease within 18 months). The burden of health care–associated MRSA disease is high and may be increasing. The incidence of MRSA has approximately doubled between 1999 and 2006, according to data reported by the Canadian Nosocomial Infection Surveillance Program.

Burden of MRSA on the healthcare system in Canada

- In 2010:
  - $250mln in total healthcare costs
  - 36,000 new MRSA patients
  - 11,000 new MRSA infections
  - 2,200 MRSA-related deaths
- Costs of MRSA:
  - 95% - extra per-diem costs (nursing, laundry, housekeeping) due to longer hospital stays
  - 4% - cost of treatment
  - 1% - laboratory testing

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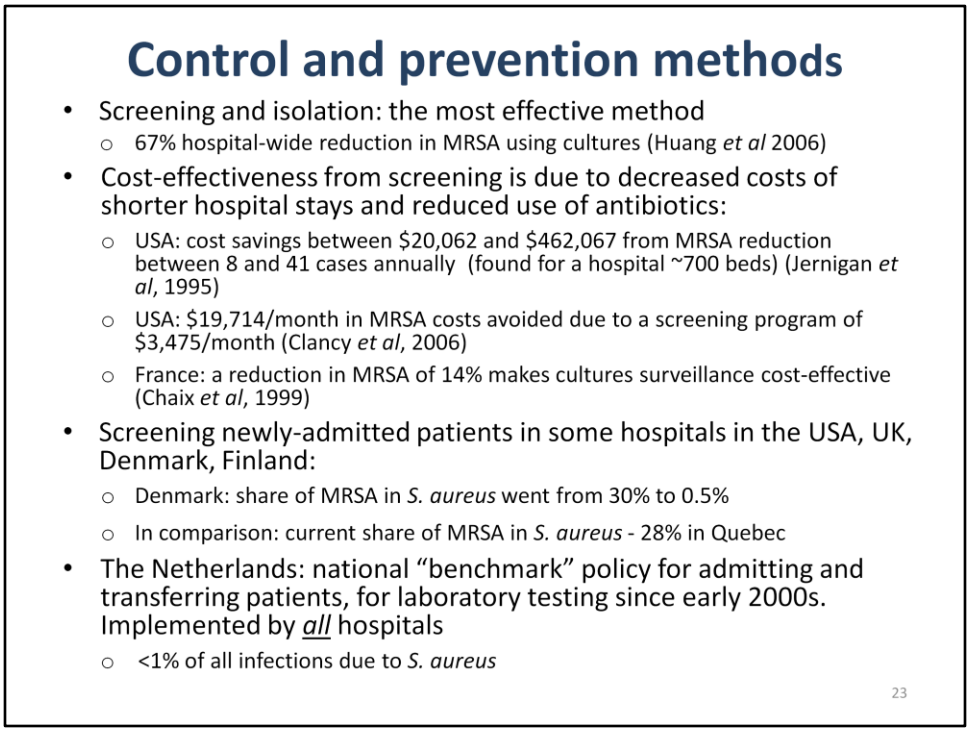
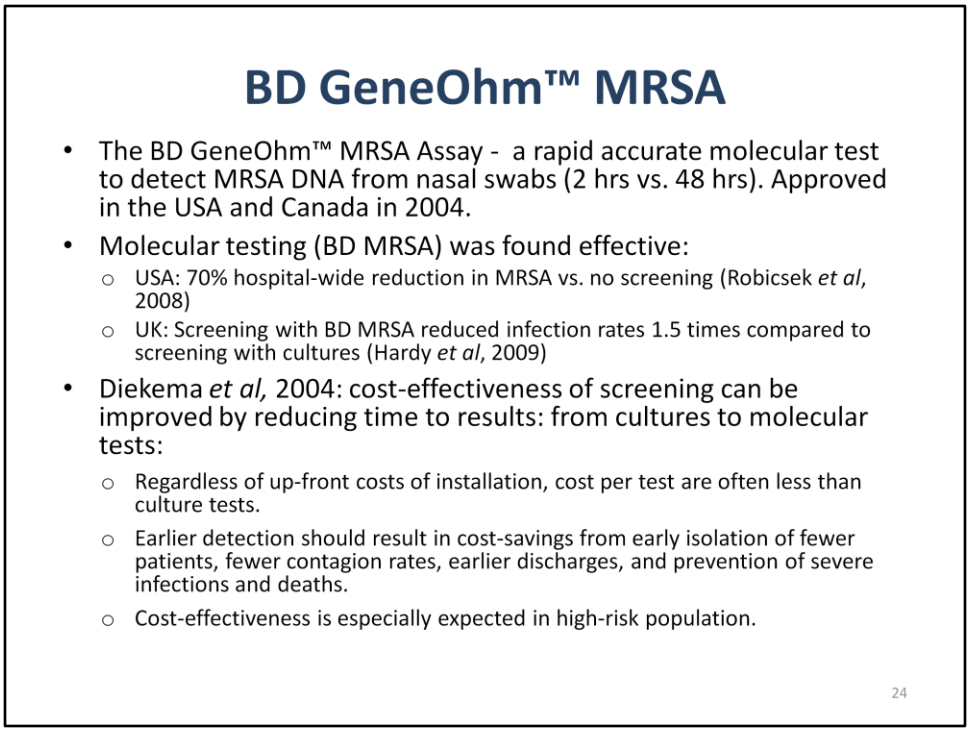
The burden of MRSA to Canadian hospitals: « Gram-Positives: Focus on MRSA From Bench to Bedside" a presentation by Andrew Simor: http://www.ammi.ca/annual_conference/presentations/0815-0900%20-%20Andrew%20Simor%20-%20Plenary%20(April%207).PPT



1. Routine surveillance for MRSA in intense-care units (ICUs) allowed earlier initiation of contact isolation precautions and was associated with large and statistically significant reductions in the incidence of MRSA in ICUs and hospital-wide. In their retrospective study of 9 years of various MRSA control programs, Huang et al (2006) reported a 67% hospital-wide reduction in the predicted rate of MRSA after the implementation of nasal surveillance in their ICU: 75% reduction in ICU patients and 40% reduction in non-ICU patients. In contrast, no similar decrease was attributable to other infection control interventions (e.g., maximal sterile barrier precautions during central venous catheter placement, the institution of alcohol-based hand rubs for hand disinfection, and the introduction of a hand hygiene campaign).
2. National search-and-destroy policy in the Netherlands allowed achieving a rate of MRSA of <1% among all *S. aureus* cases. In 2009, in Quebec MRSA accounted for 28.2% of new *S. aureus* cases (Prévention et Contrôle des Infection Nosocomiales, Plan d'action 2010-2015, Ministère de la Santé et des Services Sociaux).



Diekema *et al*, 2004:

1. "The screening techniques used at present require culture, which requires 48 to 72 h or more to perform. During the time that
it takes to return a result, patients must be placed in costly isolation (unnecessarily, if the result is negative) or may serve as reservoirs
for transmission if they are not isolated due to shortage of isolation rooms for so many patients and are found to be carriers of MRSA."
2. "Many of these obstacles could be overcome with the availability and implementation of rapid, sensitive, and inexpensive screening assays for detection of MRSA in clinical specimens. Tests that could be performed directly with patient samples (i.e., bacterial growth in culture would not be required) and in a matter of hours would greatly advance efforts to rapidly isolate MRSA carriers—or conversely, would decrease the unnecessary use of patient isolation by quickly excluding MRSA carriage."
3. "Although upfront costs and expertise are required to establish in-house molecular assays such as real-time polymerase chain reaction (PCR) tests, the cost of PCR per assay is often less than that of traditional culture techniques for vancomycin-resistant Enterococci (VRE) and MRSA detection"
4. "In addition, if earlier detection allows early isolation and prevents the spread of MRSA, the cost savings could be enormous,
as MRSA infections have been associated with higher rates of mortality and higher costs than infections with the susceptible forms of the organisms (and certainly compared to the rate of mortality and the cost from the outright prevention of infection)".

Socio-economic impacts

- Direct impact on the healthcare system:
  - Benefits: avoided costs of MRSA treatment thanks to a reduction in the number of infections
  - Costs: costs of equipment acquisition, costs of testing on admission, costs of isolation
  - Benefits>Costs => Net Benefits
- Direct impact on individuals:
  - For some patients with MRSA colonizations, small out-of-pocket expenditures may be required on post-hospitalization antimicrobial therapy
- Indirect impact on society:
  - Value of time gains due to shorter hospital stays to patients who avoided MRSA infections
  - Value of avoided morbidity due to a reduction in MRSA infections
  - Value of avoided mortality due to a reduction in MRSA infections
- Impact due to commercial activities:
  - Net benefit expected since the test is produced in Quebec

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Numerical example

- Since no data is available from a molecular screening pilot program for a particular hospital in QC, published data was used.
- The following assumptions were made to apply the data:
  - A hypothetical hospital has 1,100 beds admitting 16,800 patients annually for 8.5 days on average (Kim *et al*, 2001)
  - Baseline: no screening program in place
  - Average age of patients: 60 years old
  - Intervention: screening with BD MRSA (nasal swabs) on entry to a ward room, followed by a 5-day regimen of isolation and decolonization for all MRSA-positive patients (Robicsek *et al*, 2008)
  - Patients suspected of MRSA infection at admission are isolated immediately
  - All patients acquire MRSA at the same rate
  - Costs of treating complications of initial disease due to MRSA infections are not considered
  - MRSA colonization and infection rates in the hypothetical hospital are equal to average rates in Canada in 2009

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In order to work out a concrete numerical example, a set of the following assumptions has to be made. Since no data was available from a screening pilot program for a particular hospital, we had to rely on published data. In particular, the following data was used:

- The average prevalence of MRSA infections and colonizations in Canadian hospitals
- Empirical probabilities of MRSA transfer from colonized patients to unaffected patients, probabilities of acquiring MRSA infection conditional on being colonized, and probabilities of dying conditional on being infected.
- Extra hospital costs attributed to treating MRSA infection and isolating colonized patients
- Costs of screening with rapid molecular tests (BD MRSA)

Numerical example (cont.)

- Direct savings to the healthcare system: **$631,708/year**
  - Total costs of screening: **$520,420**:
    - Screening: 16,800 pts at $25/ea - **$420,000**
    - Isolation/decolonization: 121 pts (MRSA+) for 5 days at $830/patient-isolation: **$100,422**
    - Avoided MRSA infections: **56**
      - Avoided by MRSA+ patients at admission: 26
      - Avoided through lower transmission rates: 30
  - Avoided costs of treating 56 MRSA infections at $20,574/infection: **$1,152,130**

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Sources of model parameters:

1. Number of patients to screen: 16,800 – all admission to the hypothetical hospital in a year
2. Cost per 1 test: $25 – from the interview with Patrice Allibert (range $20-$30)
3. Number of patients testing positive: 121, given the average colonization rate 6.572/1,000 admissions and test sensitivity and its positive predictive value
4. Costs of isolation and decolonization policy for 5 days: $830, calculated using Kim *et al* (2001) and Consumer Price Index for healthcare services 2011 to 2001
5. Costs of treating 1 MRSA infection: $20,574 calculated using Kim *et al* (2001) and Consumer Price Index for healthcare services 2011 to 2001
6. Avoided MRSA infections by patients tested MRSA+ at admission: 26 (given the number of true positives and the infection rate given colonization of .25)
7. Avoided MRSA infections by patients who avoided contact with patients who tested MRSA+ at admission: transmission rates without isolation of 0.140/day, transmission rates with isolation of 0.009/day (Jernigan *et al*, 1998). Days in isolation – 5, average hospital stay 8.5 days.

Numerical example (cont.)

- Benefits to society from reduced mortality **$29,645,304**:
  - 13 avoided deaths due to MRSA
  - value of saved years of life for 13 patients at $2,280,408/pt: **$29,645,304**
- Conservative estimates: some value to society also exists due to reduced morbidity and reduced hospital stays (mean of 14 days per MRSA infection)
- Net benefits due to commercialization apply because the test is produced in Quebec

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Risks of mortality due to MRSA: .23 (BD MRSA). Alternative measure: .3 (Cosgrove *et al*, 2003)

Value of prevented mortality for 1 person at the age of 60: $2,280,408 (calculated from Murphy and Topel, 2006, using USD/CAD purchasing power parity and Consumer Price Index 2011 to 2006).

Challenges: MRSA

- Only screening during hospitalization (not on admission) is recommended by provincial guidelines (INSPQ, 2009).
- A protocol for screening and isolation at admission were adopted by 45% of hospitals (INSPQ, 2009).
- In 2009, the rates of isolation until discharge of MRSA-colonized patients in Quebec hospitals increased from 6% in 2004 to 31% in 2009. However, only 23% of hospitals used decolonization of MRSA-colonized patients, and this number fell by 8 percentage points since 2004.
- Patients colonized with MRSA or having MRSA infections other than bacteremia (bloodstream infection) are not recorded and/or reported.
- High costs of molecular tests : need to reorganize patient flows within hospitals, prepare isolation rooms, high initial costs ($1mln to acquire the platform, personnel training included in this price)

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The importance of controlling MRSA is not denied and province-wide policies are implemented. For example, $20mln were issued to hospitals in QC to control hospital-acquired infections, however, the main goal is to attack *C. difficile*.

The literature mentions high costs of molecular testing vs. mixed evidence on its efficacy when compared to cultures screening. Although some studies (Diekema *et al*, 2009) report that costs of molecular testing are lower than those of cultures screening, they may be referring to the cost of the test itself. What can be costly is acquiring the platform, and/or reorganizing laboratories or patient flows, or other parts of the screening program like isolation (room availability, etc.). For example, MRSA screening (regardless of the type of tests used for screening) requires isolation of patients who tested positive. Some hospitals may be constrained in the number of isolation rooms available. In the UK study by Hardy *et al* 2010, early notification of MRSA in the molecular arm resulted in a greater percentage of patients receiving decolonization treatment, whereas in the culture arm most patients were being discharged before the result was available and therefore receiving no decolonization treatment.

Challenges: MRSA (cont.)

- Perception that overall HAI prevention measures will be less efficient if a compulsory MRSA test is implemented because other HAI rates would go up (source: INESSS interview)
- Adoption by hospitals and/or laboratories in Quebec is challenged by hospital financing scheme and by doctor's payment system. Incentives to patient, value-added decision making are not present in actual financing scheme and doctor payment system (CMA, 2010).
- Mixed evidence on relative efficacy of rapid molecular tests at screening vs. culture tests (Tacconelli, 2009).
- In-house methods used with commercial alternatives (Robicsek *et al*, 2008).
- Some studies report low compliance with MRSA surveillance due to limited space for isolation.
- Cultures screening perceived as cheaper: patients are often discharged before the test results are available, no isolation, savings.

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Mixed evidence on relative efficacy of molecular testing vs. cultures testing is well described in Tacconelli, 2009. The meta-analysis of more than 10 studies reports that there is no clinical benefit of rapid testing. The main concern as presented in the study is low specificity of molecular tests (some report it as low as 80%), whereas the specificity of BD MRSA Assay is 94.6%. Although not mentioned in the study, it is possible that the reviewed studies used less modern molecular tests, tests from other producers, or even "in-house" tests. For example, Robicsek *et al,* 2008 report using BD MRSA and an "in-house" test. It is mentioned that the BD MRSA protocol was modified from what was prescribed by the manufacturer to "accommodate high volume testing". In addition, any MRSA screening program consists not only of testing but also of isolation and treatment. Low compliance with the last part of the program can significantly undermine the potential provided by the test to reduce or even eliminate the infection from hospitals.

Case II: Genetic screening for cytochrome oxidase deficiency, French Canadian type

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COX deficiency, French Canadian type

- Cytochrome oxidase (COX) deficiency, French Canadian type (FC): a very rare inherited metabolic disorder caused by deficiency of an enzyme that supplies energy to cells. Its onset is between ages of 3 months and 2 yrs old.
- COX FC causes developmental delay, poor muscle tone, crossed eyes, characteristic facial features, and a tendency toward life-threatening metabolic crisis and coma.
- Most prevalent in the Charlevoix and Saguenay—Lac-Saint-Jean regions of Quebec (carriers: 1 in 22), rare elsewhere.
- No cure or effective treatment. Life expectancy: 2-3 yrs after the onset of the disease.

Prevention

- Research began: 1987. Genetic mutation discovered and 5 tests available: 2003 (French Canadian Panel test).
- Dr. John Rioux: "We have heard so much about the power of genomics it is very gratifying to see it in an application that has immediate clinical implications."
- $60,000 granted by the *Régie régionale* to *Complexe hospitalier de la Sagamie (CHS*) for 2003-2005 to cover costs of testing
- When both parents carry the mutated gene:
  - 25% chance to have a child-non-carrier
  - 50% chance to have a child-carrier
  - 25% chance to have a child with COX FC
- Screening test for people with family history of COX deficiency (after consulting a genetic counselor)
- Options if both potential parents are carriers: adoption, donor insemination, assisted reproduction with pre-implantation genetic screening, prenatal tests of the fetus

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1. 2003: Andy Kennedy, Directeur de santé publique à la Régie régionale, ajoutant : «Il est maintenant possible d'offrir des tests de dépistage pour les cinq maladies récessives les plus fréquentes dans la région», soit l'acidose lactique métabolique, la tyrosinémie, la polyneuropathie sensori-motrice avec ou sans agénésie du corps calleux, l'ataxie récessive spastique de Charlevoix-Saguenay et la fibrose kystique. La Régie régionale a d'ailleurs récemment accordé un soutien financier de 60 000 $ au Complexe hospitalier de la Sagamie (CHS) pour les deux prochaines années, qui permettra de défrayer les coûts de ces tests de dépistage.»
2. «Le ministère de la Santé et des Services sociaux a accordé un financement de 75 000 $ annualisé à 150 000 $, qui s'appuyait précisément sur les développements d'un programme structurant de recherche en génétique communautaire dans la région, le projet ECOGENE-21»,

Socio-economic impact

- Direct impact on the healthcare system:
  - Benefits: avoided costs of treating COX deficiency (including episodes of lactic acidosis and other complications)
  - Costs: costs of testing potential parents, costs of genetic counseling pre- and post-testing, costs of assisted reproduction
  - If Benefits>Costs => Net Benefits
- Direct impact on individuals:
  - Benefits: avoided direct costs associated with caring for a child with COX deficiency
  - Costs: out-of-pocket expenditures on assisted reproduction and/or adoption
  - If Benefits>Costs => Net Benefits
- Indirect impact on society:
  - Reduced suffering due to having a child affected by COX deficiency
  - Benefits due to having healthy productive population
- Impact due to commercial activities:
  - Net costs if the test if imported from the USA
  - Net benefits if the test if produced in Quebec

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Part III:
Obstacles to Adoption of Personalized Medicine

Personalized medicine and decision-makers

- Personalized medicine includes a variety of tools:
  - Determination of disease susceptibility (e.g., cancers, rare diseases)
  - Treatment guidance (e.g., dose determination, targeted treatment typing, treatment selection)
  - Rapid molecular diagnostics (e.g., infections)
- Decisions to use personalized medicine are made by:
  - Administration of hospitals, laboratories, clinics
  - Doctors (general practitioners and specialists to diagnose and guide treatment)
  - Individuals (e.g., to learn inherited diseases, guide reproductive and healthcare behaviour, and to influence their physicians)
- The next few slides present adoption obstacles for each type of decision-maker

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Personalized medicine consists of a wide variety of tools and tests. The decision to utilize them or not is made at the micro level: depending on the type of the test it can be ordered by administrations of hospitals, laboratories, or clinics, by doctors, and sometimes directly by individuals/patients. Each decision-maker values the impact of their decision to use personalized medicine on their own budget and well-being, which may not necessarily be optimal for society as a whole.

For example, the decision to test infections using rapid molecular tests rather than cultures is taken at the level of a hospital or a laboratory. The degree of adoption of personalized medicine highly depends on whether hospitals' financing schemes to adopt more efficient technology and practices are properly designed.

The decision to use a molecular diagnostic test to guide treatment decisions or to diagnose a disease is taken by a doctor: a general practitioner or a specialist. Doctors make decisions based on their perceived benefit of testing to the patient and the doctor's future decision-making, and the perceived availability of tests and their costs.

Finally, individuals decide to order genetic tests (for example from companies like 23andme, Knome, deCODE) or to ask their physicians to order testing for them. Individuals' decisions to order tests or not depends on individuals' awareness of their options, their attitudes to risks and information, and their perceived gains from information.

The next few slides present evidence from the literature and interviews with the members of the scientific community on these decisions which sheds light on the slow adoption of personalized medicine and main obstacles on its path to patients.

Health-care system and adoption of personalized medicine

- Personalized medicine is a novel approach and its introduction is accompanied by high direct and indirect costs:
  - Costs of acquiring new equipment
  - Costs of training
  - Costs of reorganizing patient and information flows
  - Costs of IT (additional equipment, enhanced data security, training)
- These costs must be accompanied by sizeable benefits (e.g., savings) to hospitals in order for hospital administration to see the costs as worthwhile and have an incentive to adopt the change. However,
  - The evidence on benefits is questioned (e.g., real-life efficacy, adherence to proper use of tests and proper treatment guidelines).
  - A large portion of gains goes to society and does not affect the hospital

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Health-care system in QC

- Quebec's hospital financing mechanism is focused on cost control not value for the money
  - The system does not encourage the adoption of innovative treatment or prevention strategies that will improve value for the money to patients and to society (Thomson *et al*, 2012; Boulenger *et al,* 2012; CMA, 2010)
- This mismatch between costs and gains results in the lack of incentives to adopt personalized medicines:
  - The example with the adoption of molecular MRSA testing: the decision to replace traditional cultures testing with rapid molecular testing must be done by the director of a hospital laboratory. The laboratory needs to pay $1mln to acquire the equipment. Using rapid molecular testing would result in reduced hospital costs due to fewer MRSA infections. But these gains do not go directly to the lab. Now, the administration of the hospital can decide to adopt molecular testing, but then they would have to cut budgets in other departments of the hospital to finance the acquisition of equipment by the lab. This may cause conflicts and other issues. As a result, the administration of the hospital has no incentive to adopt the new screening technology.

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Health-care system and adoption of personalized medicine: Economics

- Economic theory suggests that misaligned incentives would result in socially inefficient decisions calling for government interventions.
- Similar examples in other areas:
  - Basic research is funded mostly from public sources because it is too costly for the profit-oriented private sector and it generates uncertain benefits in the remote future
  - Industrial pollution: producers are not interested in large costs of clean technologies (private cost) because they do not directly benefit from clean environment (social gain). Government intervenes by either increasing their costs of polluting (fines) or by reducing costs / redistributing benefits (subsidies on clean technologies)
- If decisions to adopt personalized medicine are left to hospitals and clinics, they will never make a socially-optimal decision, because it is not optimal for them given their perceived costs and benefits. Their financial mechanisms do not provide incentives to delivery better value for the money, only cost control.
- Government intervention is needed:
  - To lift the burden of deciding to adopt personalized medicine by hospitals and to introduce a nation-wide policy on personalized medicine adoption
  - To re-align hospitals' incentives by reducing their costs or increasing their benefits through the provision of assistance, funding, training, guidelines, reimbursements, or imposing requirements
  - To change the financial mechanisms to switch incentives from cost control to provision of better value for the money and efficiency

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Economic theory suggests that a decision that would be optimal to a hospital (i.e., not to adopt personalized medicine) is a "market failure" or an inefficiency from the social point of view (due to so-called negative externality). In this case, the government should intervene to fix this inefficiency by providing additional incentives and/or reducing adoption costs of personalized medicine.

This case is similar to government-financed basic research, which is expensive and brings benefits in remote future with some uncertainty. Thus, it will never be undertaken by the private sector to the extent that is optimal for society because businesses are profit-oriented and have a short-run planning horizon (shareholders' interest, etc.).

Another example is environmental protection: Producers will not carry large costs of installing clean technologies since they do not directly gain from cleaner environment (they care about their bottom-line). It is society that benefits from cleaner environment. In order to make producers invest in clean technologies, the government should intervene and change the incentives. For example, it can make polluting more expensive by imposing fines, so that investing in clean technologies is cheaper for producers than polluting. Alternatively, the government can redistribute social benefits from cleaner environment back to producers by subsidizing clean technologies.

Similarly, the introduction of new medicines in the healthcare system will never be undertaken if individual clinics and hospitals have to make the decision to adopt them. Their incentives are not properly aligned with those of society: the burden of the cost is carried by hospitals, whereas the majority of the benefits is enjoyed by society. The government, which receives a part of these social benefits through additional tax revenues may have to redistribute some of these gains back into the healthcare system by providing subsidies, clinical guidelines, training programs, recommendations, or imposing strict rules on how things should be done. Regardless of the type of intervention (helping vs. imposing), the government needs to intervene.

Adoption of personalized medicine and behaviour of doctors

- Doctors decide whether to order or not tests to diagnose and choose treatments: what determines their decisions to adopt/to resist?
- Rich literature exists on determinants of prescribing behaviour of doctors with regards to new medicines (in general): attitudes to risk, knowledge/understanding of benefits, attitudes to novelties, reaction to information from different sources (peers, academic literature, pharma reps, etc.).
- Determining factors: demographics, size and location of practice, education and experience determine doctors' degree of adoption of new medicines/techniques.
- Doctors' payment scheme per activity rather than patients' outcomes does not encourage the adoption of innovation that will improve health results
- Some of possible obstacles towards the adoption of personalized medicine – doctors' (un)awareness, potential, and incentives to adopt.

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Tests to diagnose diseases and guide treatment decisions are ordered by doctors. Their decisions to order/not order pharmacogenomic tests depend on perceived costs, risks, and benefits to doctors themselves and their patients. It is important to understand their motivation to adopt or resist personalized medicine.

Rich literature exists on the adoption of new medicines and medical practices by family physicians and specialists (not with regards to personalized medicine but medicine in general). Several main reasons were reported as obstacles towards adoption of new practices: lack of exposure to new information and practice and conservativeness of doctors. Lack of exposure affected practices in rural and remote locations (fewer visits of pharmaceutical representatives or lack of front-line doctors-leaders), size of practice (the more doctors in the clinic, the more the chance of having more progressive or more informed doctors influencing the practice and knowledge of others). Conservatism was a feature of old doctors who preferred to wait until reliable information about drug performance in real practice was well established (risk-aversion). Informed patients often were found to be an important factor in doctors' adoption of new technologies.

Some possible obstacles towards the adoption of personalized medicine – doctors' (un)awareness and potential to adopt. The next slide presents a study by Bonter *et al* (2011) who surveyed Canadian doctors towards their opinion and experience with personalized medicine.

Bonter *et al,* 2011: Canadian survey

- Survey of Canadian general practitioners, cardiologists, and oncologists on awareness, attitude, and practice of personalized medicine.
- Sample – 341 physicians:
  - General practitioners (GP) – 43%
  - Cardiologists – 30%
  - Oncologists – 27%
- Sample characteristics:
  - ON - 33%, QC – 20%, MB, SK, AB – 24%, BC – 9%, and Maritimes– 14%
  - 1/3 of respondents: 46-55 yrs-old
  - Mean work experience – 12 yrs (oncology), 18 yrs (cardio) and 22 yrs (GP)
  - Majority of specialists held academic appointments (73%-79%) and practiced in academic health sciences centres.
  - Family physicians practiced predominantly in offices and clinics.
- Respondents from QC: 50% cardiologists, ~35% GPs, and ~12% - oncologists.

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In 2011, Bonter, Desjardins and co-authors performed a pan-Canadian survey of family physicians, cardiologists, and oncologists to know their attitudes and views towards personalized medicine.

Thirty-three per cent of the respondents practiced in Ontario, 20% in Quebec, 24% in Manitoba, Saskatchewan and Alberta, 14% in the Atlantic provinces and 9% in British Columbia. Of the cardiologist and oncologist respondents, 73% and 79%, respectively, held academic appointments, compared to 41% of family physician respondents. One-third of survey respondents were in the 46 - 55 age range. The average time since completion of training was 12 years for participating oncologists, 18 years for cardiologists and 22 years for family physicians. Family physicians reported working predominantly in offices or clinics, cardiologists predominantly in academic health science centres, community hospitals and private offices/clinics, and oncologists predominantly in academic health sciences centres.

Awareness and attitudes

- Canadian physicians responding to the survey are optimistic about the promise of personalized medicine, and open to its use:
  - Agree on potential to improve outcomes (70%)
  - Agree that personalized medicine can influence treatment plans (83%)
  - Reported no formal training on personalized medicine (90%)
  - Attempted self-education (73%)
  - Would like to continue education (75%)

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The majority of respondents agreed that genetic testing as a component of personalized medicine can influence treatment plans (83%) and improve outcomes (70%).The results of the survey show that in general doctors agree that there could be benefits of using personalized medicine but not many currently use them for a variety of reasons, which differ by field of work and region. The results of Bonter *et al* (2011) are consistent with findings in other countries (EU, Australia).

Experience with personalized medicine

- Insufficient evidence on efficacy (mean – 49%, QC – 60%)
- Poor general information about personalized medicine (mean - 79%)
- Inability to interpret results (mean - 71%, QC – 80%)
- Tests ordering varies by field: oncologists (59%) vs. GP /cardiologists (22%)
- More use and knowledge in oncology than GP and cardio
- Test results influenced treatment decisions (mean - 54%, QC - 38%)
- “Current physician knowledge, real-world data and guidelines relating to personalized medicine have often been insufficient for appropriate adoption, even where testing is recommended or publicly funded.”

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Barriers to adoption of personalized medicine by clinicians

- Lack of clinical guidelines (mean - 60%)
- Limited provider knowledge (mean – 57%)
- Lack of evidence-based clinical information (mean – 53%)
- Prohibitive costs (mean – 48%)
- Medical informatics would be crucial for adoption of personalized medicine (mean – 62%)
- Specific to cardiology: no useful tests available
- Other:
  - lack of resources to educate patients
  - results take too long to affect treatment decisions
  - bureaucracy
  - lack of insurance coverage
  - insufficient regulatory framework
- The results of Bonter *et al*, 2011 are consistent with findings in other countries (EU, Australia)

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Patients' awareness and attitudes

- Patient engagement is an important factor in physicians' attitudes towards adopting new practices.
- Certain personalized medicine (e.g., disease susceptibility tests) are ordered directly by individuals.
- Factors affecting patients' decisions:
  - Awareness and attitudes towards personalized medicine
  - Knowledge and perception of their risks
  - Attitudes to risks (risk-aversion vs. risk-seeking)
  - Perception of benefits and losses (attitude to negative information, fear of discrimination)
- Awareness:
  - 37% of doctors reported that their patients were enquiring about genetic testing and other personalized medicine, mostly oncologists (Bonter *et al*, 2010)
- Perception of risks and outcomes:
  - 19% of QC residents perceived the risks of using personalized medicine in the health system as high/very high, 14% did not know the risks (de Marcellis-Warin & Peignier, 2012)
  - 34% of QC residents opposed the use of personalized medicine in healthcare, 20% had no opinion (de Marcellis-Warin & Peignier, 2012)
  - QC residents who had no opinion on risks, also had no opinion on utilization (de Marcellis-Warin & Peignier, 2012)
  - 40% of physicians reported that patients expressed fear of discrimination based on genetic testing (Bonter *et al*, 2011)
- More behavioural studies are warranted to understand this issue better

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Patient engagement has been identified as a possible factor in physicians' attitudes towards adopting new practices. Some types of personalized medicine can be ordered directly by individuals (e.g., genetic disease susceptibility).

Decisions to use personalized medicine at the level of patients would be affected by a patients' awareness of personalized medicines, their knowledge/perception of risks and their attitudes to risks, their perception of benefits, fear of negative information, and conservatism. Bonter *et al*, 2010 and de Marcellis-Warin & Peignier, 2012 give us first insights into population and patients' attitudes and knowledge of personalized medicine.

More behavioural studies are needed to understand individuals' behaviour with regards to personalized medicine to design proper mechanisms of its adoption in the system.

Difficulties with demonstrating socio-economic value of some types of personalized medicine

- Genetic tests with no immediate action - uncertain benefit to evaluate socio-economic impact:
  - Disease susceptibility (not yet a diagnosis)
  - Rare disease with no treatment
- These tests provide information:
  - What is the value of this information?
  - What is the value of negative information?
  - Possible negative effects on human capital acquisition (Huntington's)
  - Decrease in quality of life (fear, depression)
  - Moral hazard (overuse of healthcare system or negligence towards one's health)

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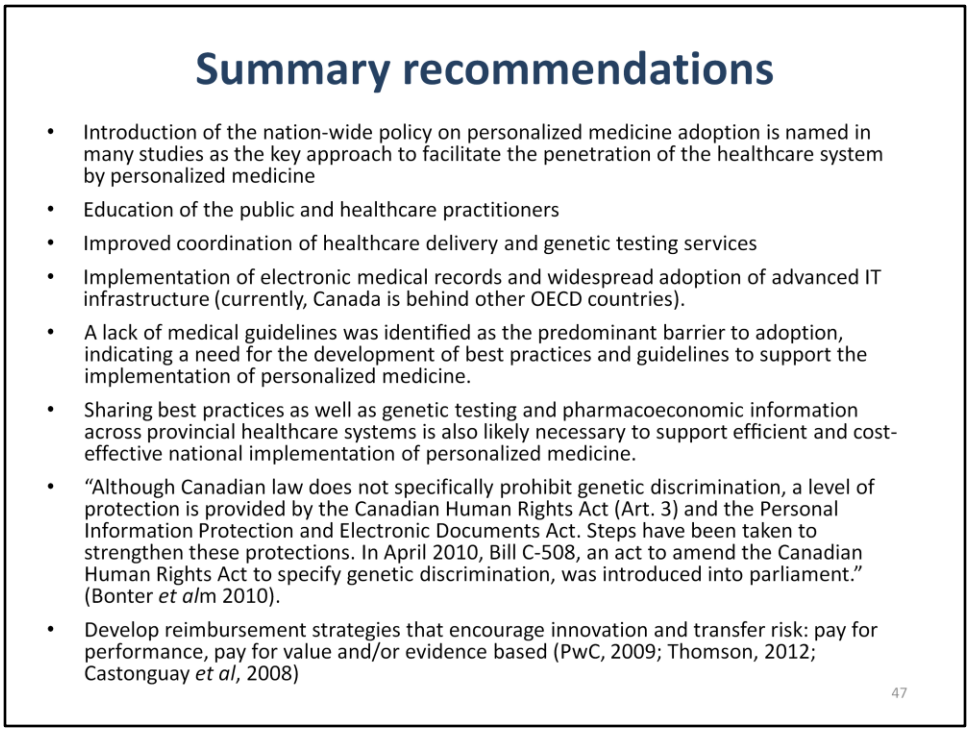

It has been suggested that decision-making related to predictive genetic testing is ad hoc and variable across Canada and that a coordinated national approach is needed. Work in this area is critical to ensuring equitable access and improving parity of healthcare across Canada.

Medical informatics will be critical to delivering personalized medicine. Indeed, vast amounts of data will be generated with widespread adoption, and an IT infrastructure for collection, storage, analysis, interpretation and reporting will be needed. Furthermore, decision support tools, including electronic medical records, will be needed to facilitate interpretation and point-of-care decision-making. This may pose a significant barrier in Canada where IT infrastructure and electronic medical record implementation is targeted for completion only in 2015, significantly later than in other OECD nations. (Bonter *et al*, 2011).

A lack of medical guidelines was identified by respondents (61%) as the predominant barrier to adoption, indicating a need for the development of best practices and guidelines to support the implementation of personalized medicine. Sharing best practices as well as genetic testing and pharmacoeconomic information across provincial healthcare systems is also likely necessary to support efficient and cost-effective national implementation of personalized medicine.

Data issues

Data to evaluate socio-economic impact

- Healthcare costs:
  - Time delays to obtain data from RAMQ and Med-Echo, limited number of cost elements available
  - Hospital data – difficult access
  - No direct costs available: special cost models and time-and-motion studies are required
  - Direct costs of personalized medicine: reimbursement vs. out-of-pocket, costs of introducing personalized medicine (e.g., hospital reorganization of patient flows)
  - Post-testing costs: costs of interpretation and decision-making, (ex: 1. MRSA: isolation and treatment, 2. COX FC: genetic consulting, reproductive techniques)
- Lack of data on real-life efficacy due to the lack of clinical practice (may substantially differ from efficacy based on clinical trial)
- Personal and social costs and gains:
  - Value of negative information (disease susceptibility, rare diseases) – decreased quality of life, reproductive decisions, decreased investment in human capital and savings, increased use of the healthcare system
  - Value of positive information (moral hazard) – decreased attention to health leading to overlooked issues
  - Behavioural studies are needed to evaluate these costs
  - Evaluation of treatment effects: sample selection for behavioural studies (impossibility of clinical trials, statistical methods to account for bias due to self-selection)

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