THE LANDSCAPE OF PERSONALIZED MEDICINE IN CANADA

Best Practices in Personalized Medicine – B2PM
Vancouver, March 8, 2011

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Centre of Excellence in Personalized Medicine

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OVERVIEW

Cepmed and its Initiatives

Canadian Landscape of Personalized Medicine (PM)

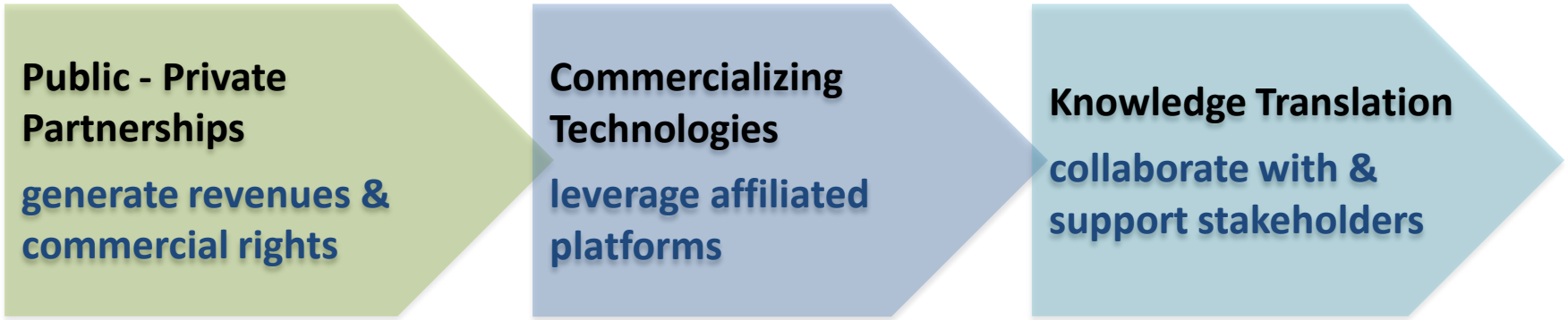
- Investment in ‘omics infrastructure
- Regulation and oversight of medical testing
- Commercialization of and access to testing
- Genetic non-discrimination

ABOUT CEPMED

A federally funded Centre of Excellence in Research & Commercialization (CECR)

Founded in 2008 by the Montreal Heart Institute (MHI) & Genome Quebec with industry support

Promoting the science & practice of personalized medicine in Canada through



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MONTREAL HEART INSTITUTE

NCE RCE
Networks of Centres of Excellence of Canada | Réseaux de centres d'excellence du Canada

AstraZeneca NOVARTIS MERCK

Public - Private Partnerships, PGx Studies

ID biomarkers for personalizing treatment of CVD, a study carried-out in parallel with a Phase III clinical trial of Dalcetrapib

ID biomarkers for predicting the efficacy and safety of Ivabradine, as part of large-scale phase III SIGNIFY clinical trial

ID biomarkers with potential as a companion diagnostic Torceptrapib – as part of a Phase III Torceptrapib trial (currently halted)

ID genomic biomarkers of statin toxicity, ID patients at risk of side-effects

Monitoring PTT variation and optimizing dose in warfarin therapy

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Commercialization of Technology Platforms

Montreal Health Innovations Coordinating Center (MHICC)

- Non-profit CRO (Phase II - IV trials)
- 130 employees (US and Canada)
- Gateway to pharmaceutical companies

Montreal Heart Institute Biobank

- one of the largest CVD biobanks in the world
- 11,000 high-quality samples with extensive phenotype info and consent

Pharmacogenomics Centre

- Expertise in custom SNP panel development, GWAS, deep sequencing

Impact of Cepmed initiatives

- Leveraged 3 platforms in public-private partnerships
- Added 5,000 samples to the MHI biobank
- Positioned MHICC as leader in clinical trials coupled with PGx studies
- Negotiated 5 licenses, supported filing and prosecution 15+ patent applications
- Jobs created/maintained: 15/180+

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Canadian Physician Survey in Personalized Medicine

Design and objectives

Access physicians' perceptions and experiences in genetic testing and PM

Openness to adoption, state of practice, benefits/impacts and barriers to adoption

Compare across specialties and provinces

Some of the findings….

Majority of respondents:

Have positive perception of PM and report positive impact in practice

Do not feel sufficiently informed or confident practicing in this area

Cite a lack of guidelines and clinical evidence and limited provider knowledge as key barriers

Report that genetic tests useful in their practice are not readily available

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Knowledge Translation: Expert Physician Panels

Objectives

- Describe optimal use and adoption of PM based on best available evidence
- Provide strategy for continuing medical education
- Promote efficient use of resources

Status

- Terms of reference & 2-yr contracts signed by 22 members
- Two meetings held for each panel
- Scope of mandate established
- Outreach to enabling stakeholders in progress

CARDIOLOGY PANEL

Chair: Dr. Jean-Claude Tardif

Members:
Dr. Andrew Krahn,
Dr. Bob Roberts
Dr. Paul Khairy
Dr. Candace Lee
Dr. Gregor Andelfinger
Dr. Milan Gupta

ONCOLOGY PANEL

Chair: Dr. Charles Butts

Members:
Dr. Gerry Batist
Dr. Malcolm Moore
Dr. Charles Blanke
Dr. Suzanne Kamel-Reid
Dr. Michael Sawyer

STRATEGIC PANEL

Chair: Dr. Simon Sutcliffe

Members:
Dr. Sean Blaine
Dr. David Keast
Dr. Mark Elwood
Dr. Jeffery Hoch
Ms. Jill Davies
Dr. Serge Dulude

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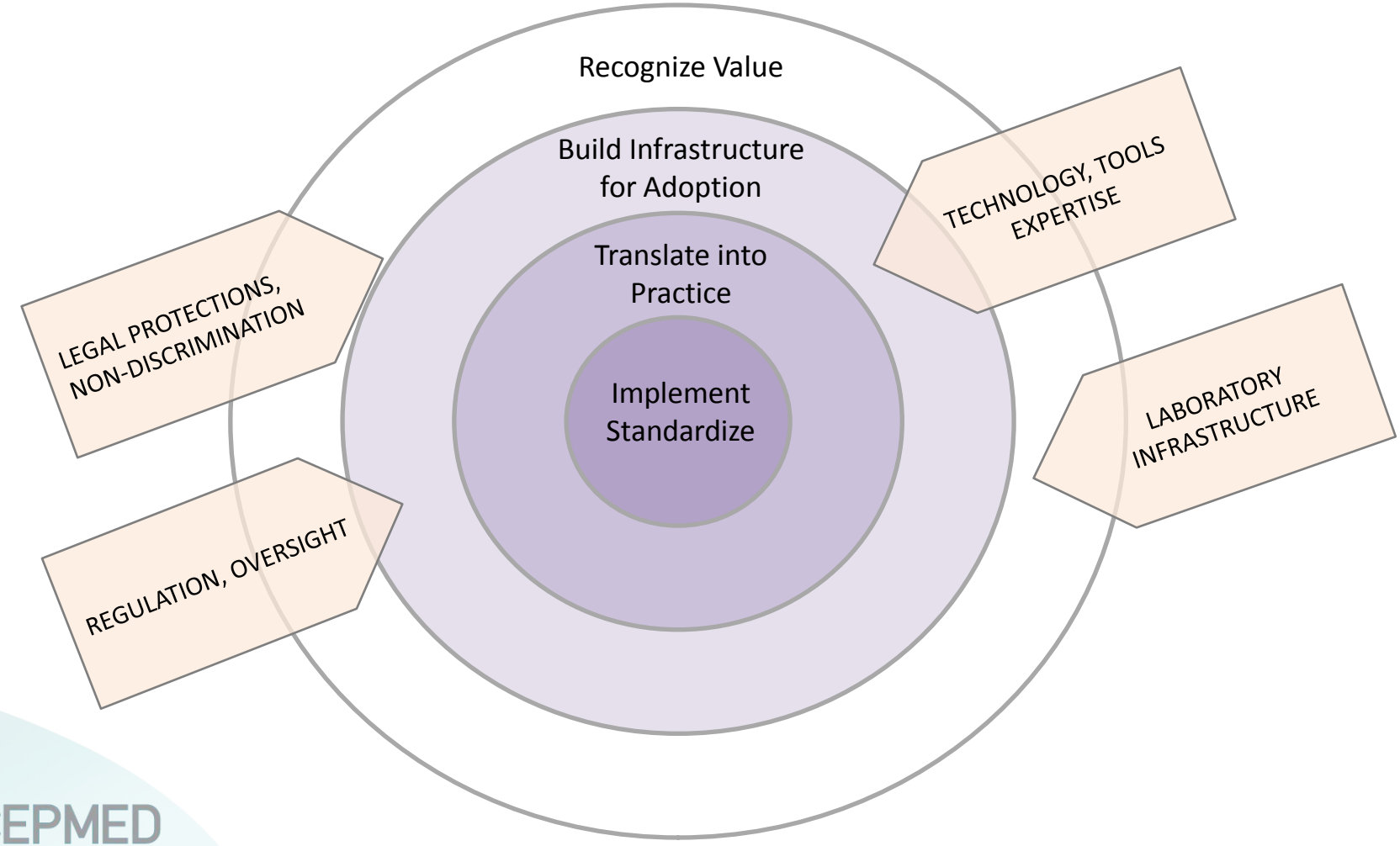
Canadian Personalized Medicine Landscape



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Adapted from Case for Personalized Medicine, 2009, "Convergence of Forces", Personalized Medicine Coalition

Canadian Investment in 'Omics

Genome Canada Investments (2001-10)

$277 M build, operate provincial genome centres

$63 M develop new technologies and applications

$33 M legal, ethical & socio-economic research (GE^3LS)

Health Research Funded

$700 M fundamental research

$24 M target ID and drug discovery

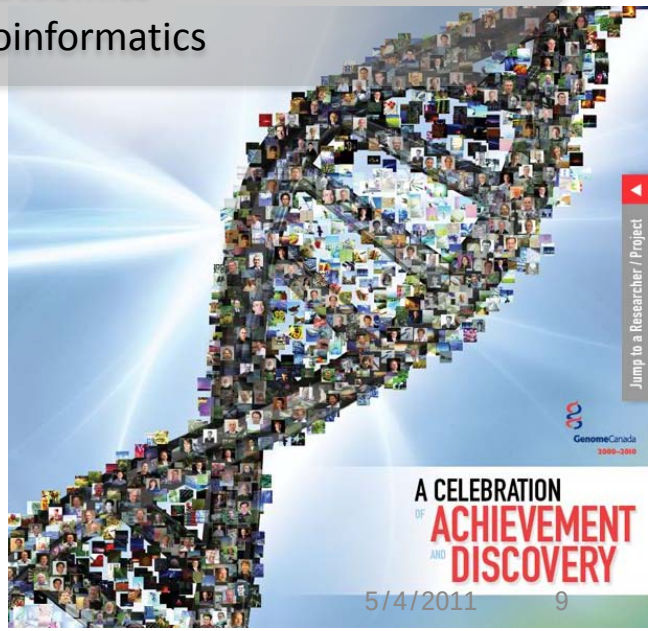
$210 M biomarker ID

$46 M biomarker validation, diagnostic development

$30 M clinical stage pharmacogenomics

An enabling infrastructure is in place

- DNA sequencing
- Microarray and gene-chip expression analysis
- Proteomics
- Bioinformatics



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Regulation & Oversight of Medical Testing in Canada

Laboratory developed tests (LDT) are most often used for PM

- Subject only to provincial regulation and oversight (no national standard)
- Regulation is variable across provinces - even lacking in some or differentially enforced
- Absence of regulation to ensure clinical validity
- Funding decisions are not coordinated nationally or often even provincially

As a result, delivery, access, QC vary across the provinces and even within provinces

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Regulated Practices by Province

Issue	NF	NS[b]	NB	PE	QC	ON	MB[c]	SK	AB	BC[c]	CCMG
Laboratory practice											
Definition					*	*	*		*	*	*
Certification/accreditation			*		*	*	*	*	*	*	*
Personnel standards					*	*	*	*	*	*	*
Quality assurance					*	*	*	*	*	*	*
Quality control					*	*	*	*	*	*	*
External quality assessment					*	*		*	*	*	*
Clinical validity											*
Analytic validation					*	*		*	*	*	*
Record retention					*	*	*	*	*	*	*
Report requirements					*	*		*	*	*	*
Follow-up testing					*	*		*	*	*	*
Total issues addressed	0	0	1	0	10	10	6	9	10	10	11
Patient management											
Informed consent[a]	*	*	*	*	*	*	*	*	*	*	*
Genetic counselling					*			*	*	*	*
Use of residual samples					*				*	*	*
Privacy/confidentiality[a]	*	*	*	*	*	*	*	*	*	*	*
Access to services[a]	*	*	*	*	*	*	*	*	*	*	*
Educational component					*	*		*	*	*	*
Total issues addressed	3	3	3	3	6	4	3	5	6	6	6

Source: Quality Issues in Clinical Genetic Services, Kristoffersson et al, 2010

Standardization of genetic tests needed

Published at www.cmaj.ca on Sept. 14

Evolving knowledge of the genetic indicators of disease is rapidly changing medical care, and overwhelming the ability of regulatory agencies to ensure the quality and accuracy of such tests.

"We're doing [genetic testing] for lung cancer, for colon cancer, for breast cancer, for melanoma, myeloma," says Dr. Suzanne Kamel-Reid, head of laboratory genetics and director of molecular diagnostics at the University Health Network in Toronto, Ontario, and head of the Molecular Oncology Task Force which is sponsored by Cancer Care Ontario. "It's used much, much more frequently than it used to be." According to the task force, referrals for cancer-related genetic testing rose 61% in 22 clinics surveyed between 2002 and 2008.

The increased use is also evident in the United States, so much so that the US Food and Drug Administration (FDA) says about 10% of pharmaceuticals are now labelled as being especially useful — or not so useful — for patients with specific genetic conditions.

But a lack of standardization in

Commercialization in Oncology: CA vs. US

Biomarker Test	Drug	CA Drug Label	US Drug Label	Test Types Available	Dx Device approval	Dx commerc. in US	Test commerc. in CA	blocking IP
HER2/neu expr.	Herceptin	M	M	LDT, D	FDA	many	yes	no
HER2/neu amp	Herceptin	M	M	LDT, D	HC, FDA	Dako, Invitrogen	yes	no
Bcr-Abl mut.	Gleevec	M	M	LDT	no	Genzyme	no	no
c-KIT+ mut.	Gleevec	M	M	D	FDA	Dako, Ventana	no	no
EGFR amp	Iressa ; Tarceva	M	M	LDT	HC, FDA	many	yes	no
EGFR amp	Erbitux; Vectibix	M	M	LDT	HC, FDA	many	yes	no
KRAS mut scan	Erbitux; Vectibix	M	M	LDT, D	HC, FDA	many	Yes	no
TPMT expr.	6-mercatopurine	C	R	LDT	no	many	yes	yes
UGT1A1 var	Camptostar	C	R	LDT	FDA	many	no	Mayo
Amplichip CYP	Tamoxifen	C	no	D	FDA	Roche	no	Roche
KRAS mut scan	Iressa ; Tarceva	no	no	LDT, D	HC, FDA	many	yes	no
BRCA1, BRCA2	na	na	na	LDT	no	Myriad	Yes	Myriad
ALK mutation	Tarceva	no	no	LDT	no	Genzyme	no	yes
EGFR mut scan	Iressa ; Tarceva	no	no	LDT, D	FDA	yes	no	?
OncotypeDX	na	na	na	LDT	no	Genomic Health	no	yes
MamaPrint	na	na	na	LDT	FDA	Agendia	no	Agendia

M-testing mandatory; R-testing recommended; C-testing mentioned
LDT-laboratory developed test; D-diagnostic device

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Observations – Potential Impacts in Canada?

Pharmacogenomic info. on drug labeling is similar (US v. CA)

- Consideration, incorporation of pharmacogenomics by regulatory agencies is similar in Oncology

More commercialization approved devices in the US (9 US, 5 CA)

- Standardized tests available as companions to approved drugs - commercialization of clinical validated tests
- Facilitates development of standardized practices
- Support commercial activity - recognizes value of 'diagnostic' technologies
- Foster competition between companies selling similar products – expertise, innovation

Tests are increasingly available only through exclusive foreign providers (i.e. Oncotype DX, Amplichip®, BRAC*Analysis*®)

- Exclusive provider strategy maybe necessary for ROI
- Difficulties in enforcing IP impact commercialization strategies
- Test interpretation requires proprietary database, proprietary algorithms
- Potential negative impact on Canadian HC system, expertise, commercial activity….

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Access to PM through Private Companies in Canada

Routes of Access

- Testing & PM services via physicians, geneticists and genetic councilors at private clinics
- Tests carried out by licensed private CA labs (not publically funded) with physician req.
- Foreign testing services via private lab or clinic
- Direct-to-consumer genetic testing companies (usually foreign testing services)

Related Developments

- Private CA clinics and labs are expanding genetic testing-PM services
- CA insurance companies are being lobbied to increase coverage of diagnostic testing
- Private CA health care payors are aware and interested (CHLIA statement on genetic testing)

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WARNEX

Medisys

MEDCAN since 1987 CLINIC

Canadian Life and Health Insurance Association Inc.

Gamma-Dynacare Medical Laboratories

LifeLabs Medical Laboratory Services

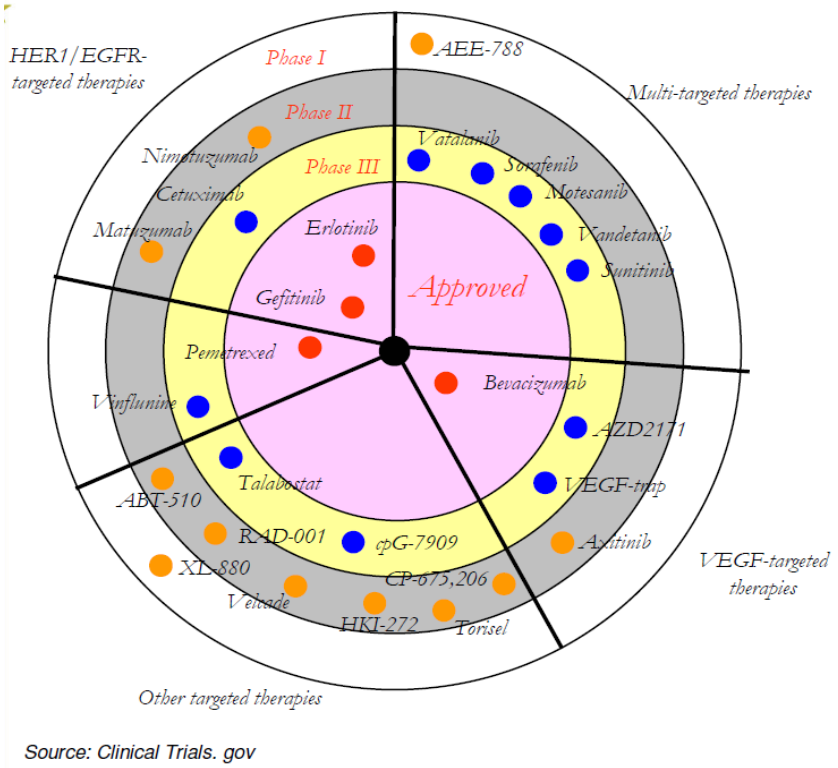
THIS IS ONLY THE BEGINNING

25% of FDA approved drugs have PGx information on the label*

- 10%+ specify genetic based sub-populations

26+ drugs in development have an associated companion diagnostic

Many widely prescribed drugs are efficacious only in 40-60% of patients



Source: Clinical Trials. gov

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*Frueh F. et al., Pharmacotherapy 28(8) 2008.

Genetic Non-Discrimination – Canadian Landscape

Current Protections

Canadian Human Rights Act (Art. 3) prohibits discrimination based on disability (including real or perceived ailment)

Personal Information Protection and Electronic Documents Act (PIPEDA 2000) has provisions relating to consent, privacy, limited use, reasonable use

Public Awareness

90% of Canadians feel that insurance companies and employers should not have access to their genetic information[1]

40% of physicians surveyed report that their patients are concerned about genetic discrimination[2]

Many not aware of the potential implications of consent given to employers as part of benefits/employment agreements

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1. *Government of Canada. Pollara Research, Earnscliffe Research and Communications. 2003. Ottawa.*
2. *Cepmed Data*

Recent Developments - Genetic Non-Discrimination

Canadian Developments

Private members bill C-508, introduced Apr.2010, proposes to amend the Human Rights Act to specify genetic characteristics as a prohibited ground of discrimination

Little pressure otherwise to adopt legislation in Canada for this purpose

Foreign Developments

US Genetic Non-Discrimination Act (GINA) enacted in 2008 prohibits genetic discrimination by healthcare insurance providers (Title I) and employers (Title II)

In addition, 45 states have genetic non-discrimination statutes

Massachusetts Genetic Bill of Rights, introduced in Jan. 2011, aims to address gaps in GINA with respect to property rights, sale, transfer or use of personal genetic information

Council of Europe's Convention on Human Rights and Biomedicine explicitly prohibits genetic discrimination

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**Government of Canada. Pollara Research, Earnscliffe Research and Communications. 2003. Ottawa*

THANK YOU

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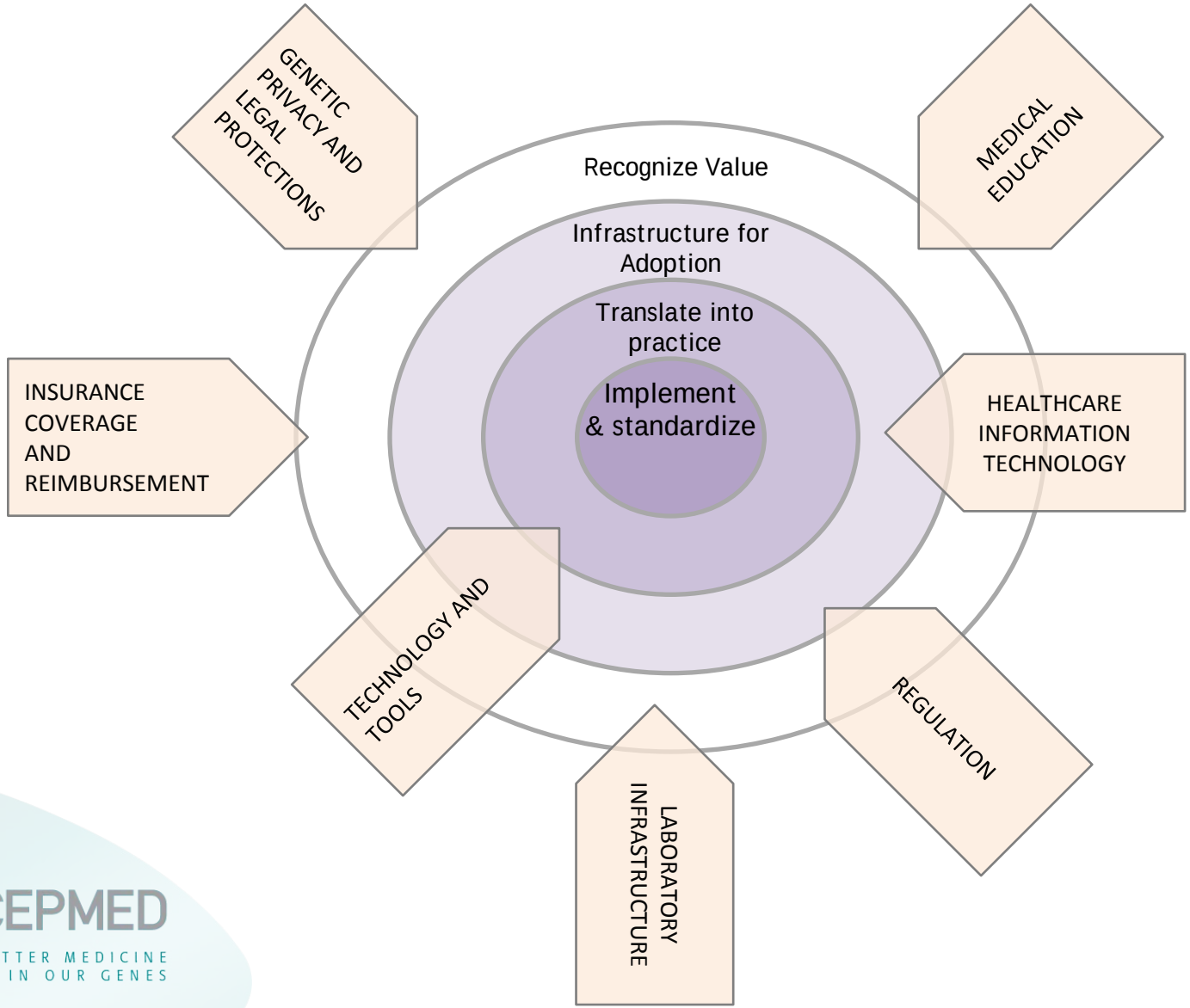
CANADIAN LANDSCAPE OF PM



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"PERSONALIZED MEDICINE IS A TECHNOLOGY ENABLER WHICH IS TRANSFORMING MEDICINE FROM INTUITIVE, TO EMPIRICAL, TO PRECISION MEDICINE"*

- Healthcare costs represent almost 50% of many provincial budgets and rising
- This is an issue being faced by all industrialized countries
- Demographic changes and technological advances are inevitable
- Trend to control cost has often been to ration care rather than rationalizing treatment based on evidence
- Medical advances and new technologies can be adopted to improve healthcare; increase efficacy and safety (reducing cost), enable prevention (reducing cost)

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*Christenden Clayton M, The Innovator's Prescription (2009)

Examples of high impact health research funded

A Haplotype Map of the Human Genome

- International research network (CA CN JP NG UK US)
- massive data set generated had major commercial impact
- successful use of open innovation
- Canadian efforts led by Dr. Thomas Hudson (McGill)

Genotype-Specific Approaches to Therapy in Childhood

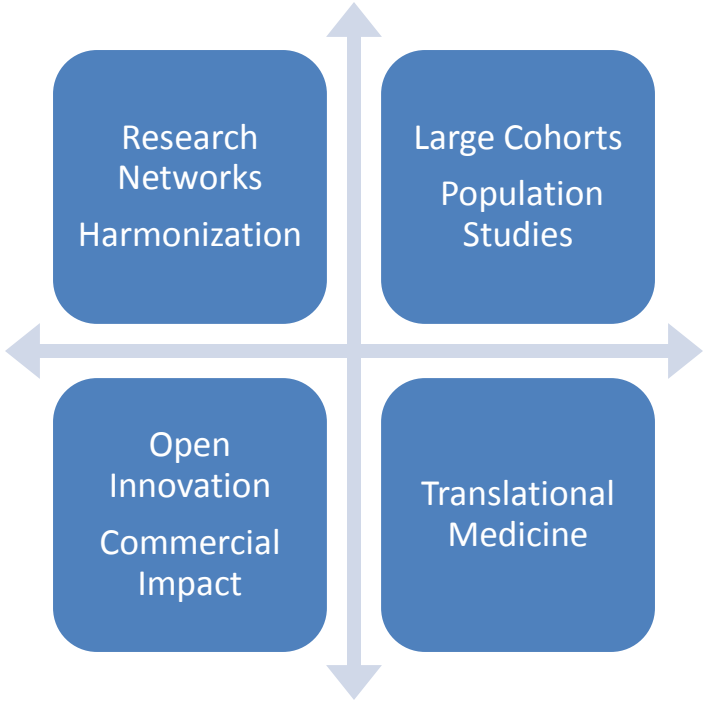
- large cohort multi-site study in translational medicine
- network of 2,300 pediatricians and 10 Canadian hospitals

PI: Dr. Bruce Carlton (UBC)

Public Population Project in Genomics - P3G Observatory

- International harmonization of project designs, biobanks to enable large cohorts for population genomics studies

PI : Dr. Bartha Maria Knoppers (McGill)



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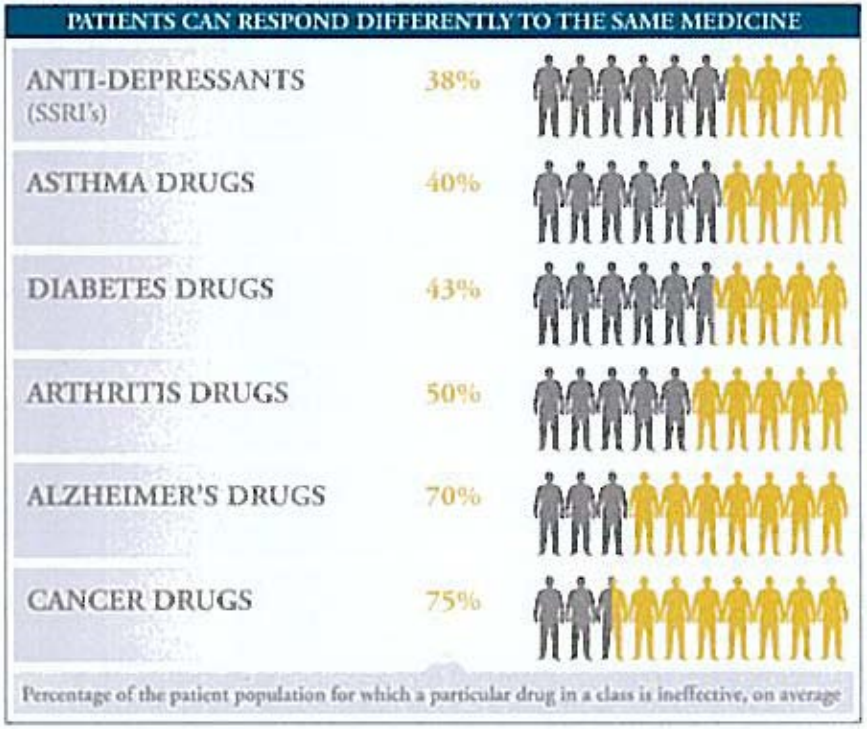
ONE SIZE DOES NOT FIT ALL

Figure 1 shows the % of the patient population for which the drug class indicated is ineffective

Genetic differences are a key element to understanding and identifying an individual's response to a drug

Figure 1: One Size Does Not Fit All



Source of data: Brian B. Spear, Margo Heath-Chiozzi, Jeffrey Huff. "Clinical Trends in Molecular Medicine, Volume 7, Issue 5, 1 May 2001, Pages 201-204.

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A COMMERCIALIZATION STORY

Macula-Risk®, developed by ArticDX (Toronto): a genetic prognostic test for Age-related Macular Degeneration (ADM)

- 1of 5 patients with AMD will progress to severe vision loss (affects 1/10 over age 60 and 1/4 over 75)
- Patients with AMD or with a high risk of vision loss can be ID using Macula Risk®
- Treatment with Lucentis® (anti-VEGF antibody) which prevents or arrests the development in 95% of patients (early stage, vision mostly intact)
- Preventative vitamin therapy and other interventions (ie. smoking cessation, blood pressure control) can delay vision loss
- Macula-Risk® is currently reimbursed in the US at $450 but not commercialized in Canada

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MULTI-DISCIPLINARY STAKEHOLDER GROUPS

Health Canada established PM working group in 2010

- includes representatives from: Health Canada, Public Health Agency of Canada, CIHR, Patented Medicines Prices Review Board
- Mandate: to develop a harmonised 'Health Portfolio' response to personalised medicine
  - facilitate collaborative interactions amongst Portfolio members on initiatives related to personalised medicine

Centre for Advancement of Health Innovation

- coalition of public and private Stakeholders
- Mandate: to publish in-depth analysis innovation and commercialization in Canada's health-care system
  - engage stakeholders and leaders in policy discussions
  - identify best practices in health

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