Health Canada Santé Canada

Canada

EMA Workshop on measuring the impact of pharmacovigilance activities

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Session 2

Health Canada's Approach to Measuring Impact of Pharmacovigilance and Regulatory Decisions

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YOUR HEALTH AND SAFETY... OUR PRIORITY.

Outline

- Health Canada context-measuring impact of Pharmacovigilance
- Logic Model for MHPD
- Direct outcome indicators
- Measuring impact at different levels of outcomes

Measuring Impact of Pharmacovigilance

- In Canada, all federal government programs are required to demonstrate that they meet their intended objectives and outcomes and deliver results for Canadians.

- Current approach to measure impact of pharmacovigilance is disparate and retroactive rather than systematic and prospectively designed.

- Future access to integrated national data on adverse events could help inform a more systematic approach to measurement of impact of our risk minimization efforts.

- In developing measurement matrix and defining what constitutes “success” of risk minimization measures, we will need to consider contextual factors such as:
  - role and impact of social media
  - competing messages
  - free will of the user, etc.

MHPD Program Logic Model - adopting a results driven approach

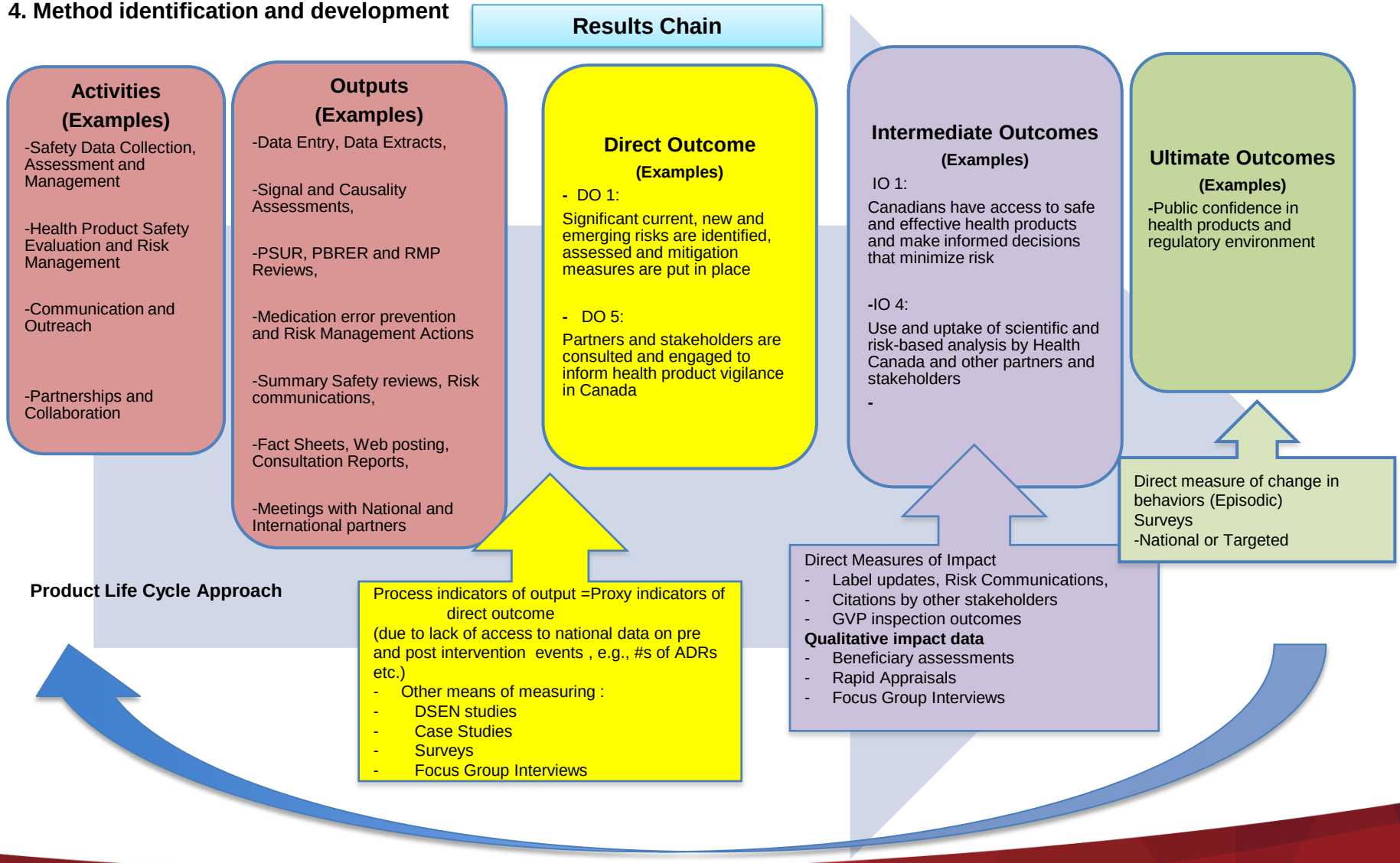
Health Canada Strategic Outcome 2: Canadians are Informed of and protected from health risks associated with food, products, substances and environments, and are informed of the benefits of healthy eating

Ultimate Outcomes	**International convergence in the regulatory environment**	**Public confidence in health products and regulatory environment**	**Sustainable, integrated, responsive and science-based national regulatory system**	**Safe and effective health products**
Intermediate Outcomes	**IO 1: Canadians have access to safe and effective health products and make informed decisions that minimize risk**	**IO 2: MHPD is recognized as a trusted source of scientific information nationally and internationally regarding health product vigilance**	**IO 3: Industry complies with policy frameworks and regulations and manage health product vigilance with due diligence**	**IO 4: Use and uptake of scientific and risk-based analysis by Health Canada and other partners and stakeholders**
Direct Outcomes	**DO 1: Significant current, new and emerging risks are identified, assessed and mitigation measures are put in place**	**DO 2: An appropriate mix of policy, regulations and voluntary instruments to support health product vigilance**	**DO 3: Regulated parties and others have access to timely, useful and relevant health product information**	**DO 4: Canadians and other parties are aware and informed of the risks, benefits, harm and uncertainties associated with health products**	**DO 5: Partners and stakeholders are consulted and engaged to inform health product vigilance in Canada**	**DO 6: Mechanisms are in place to support a harmonized and coordinated approach to program delivery**
Reach/ Audience	Canadian public, Consumer associations, F/P/T Governments, health care professionals, Industry, professional associations, media, researchers, Health Canada Regulators, Market Authorization Holders, International governments and/ or organizations, clinical community					
Activities and Outputs	**Policies, Frameworks and Regulations** **Framework, Policy and regulatory updates and revisions, Position Papers, Guidance material, Consultation Reports, Briefing materials**	**Safety Data Collection, Assessment and Management** **Data Entry, Quality Assessment; online CV database, RADAR reports, Statistics, Data Extracts, Search Requests, Uploads into WHO Database, scientific literature searches, environmental scanning and medical devices incidents database**	**Health Product Safety Evaluation and Risk Management** **Safety and Ad-Hoc Review Reports, Signal and Causality Assessments, PSUR, PBRER and RMP Reviews, Medication error prevention and Risk Management Actions**	**Communication and Outreach** **Summary Safety reviews, Risk communications, Fact Sheets, Infowatch, Web posting, Consultation Reports, Online Database for CV, Compliance promotion, Education , List of signals and SSRs**	**Partnerships and Collaboration** **National and International Engagements, Networks, Meetings, Joint Activities**	
Enablers	**People, Business and Financial Management, Planning and Reporting, Acts, Regulations, Policies, Science and Technology**					

Indicators for Measuring Direct Outcomes - attributable to MHPD's activities

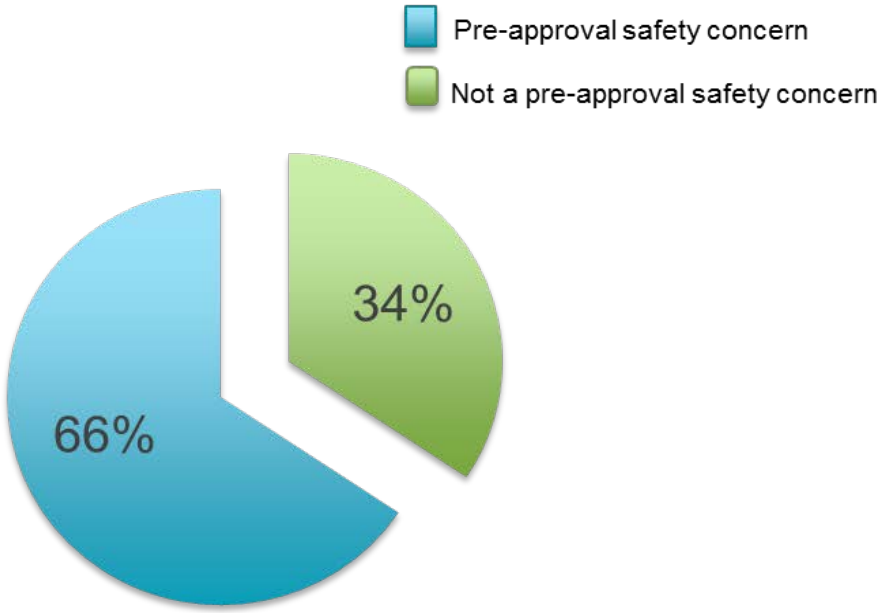
Direct Outcome	Significant current, new and emerging risks are identified, assessed and mitigation measures are put in place	# of signal assessments resulting in action by Health Canada
		Partner and stakeholder feedback on risk management and related instruments (i.e. comprehensive, responsive, usefulness etc.)
	An appropriate mix of policy, regulations and voluntary instruments to support health product vigilance	# of new policies, standards put in place to improve the regulation of HPs, e.g. Plain Language Labeling
		Partner and stakeholder feedback on regulatory environment and related instruments (i.e. comprehensive, responsive, use etc.)
	Regulated parties and others have access to timely, useful and relevant health product information	# of signal assessments completed and posted within published standard and summaries of signal assessments
		Stakeholder assessment of quality of Health Canada information/communications, in terms of: timeliness, accessibility, ease of understanding, usefulness
	Canadians and other parties are aware and informed of the risks, benefits, harm and uncertainties associated with health products	Stakeholder awareness and understanding of risks related to HPs
		# and nature of post-market safety reviews published
		Reach and nature of Health Canada consultations with external stakeholders regarding risks and benefits of human drugs
	Mechanisms are in place to support a harmonized and coordinated approach to program delivery	# and nature and type of standardized mechanisms in place to: track signal activities and evidence of responses to the recommended actions; and address policy and program issues (from May 2014 Evaluation recommendations) (i.e. multi-level working groups, joint planning activities etc.)
		# and nature of activities related to a) alignment of responsibilities for post-market surveillance with partners (i.e. Health Canada, Public Health Agency of Canada Provinces and Territories); and, b) agreements related to sharing of surveillance information across jurisdictions (to enable integrated surveillance system)

1. **Effectiveness of risk minimisation actions;**
2. **Effectiveness of specific pharmacovigilance processes;**
3. **Enablers of effective pharmacovigilance including stakeholder trust and engagement.;**
4. **Method identification and development**



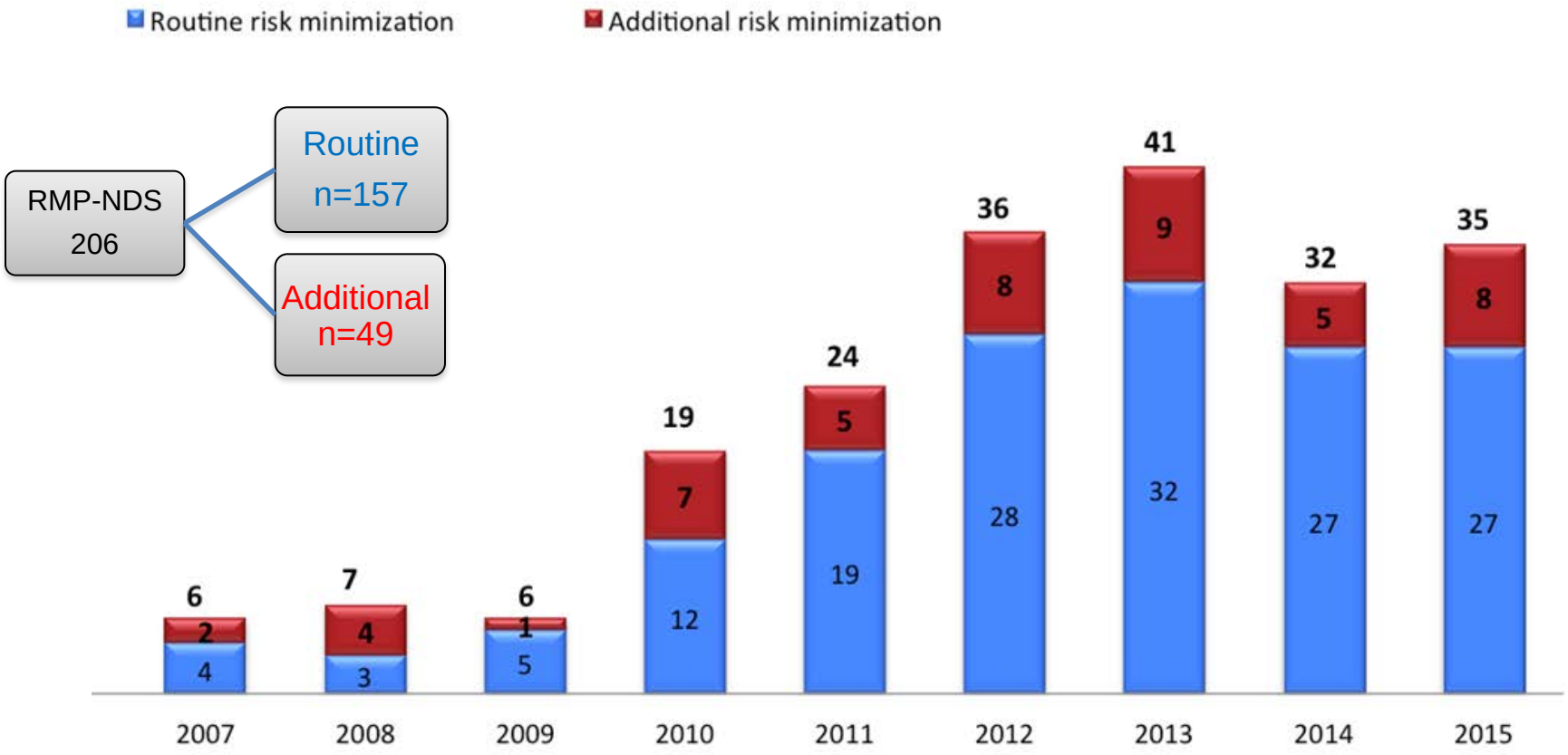
Effectiveness of pharmacovigilance processes - measured impact of RMPs in anticipating post market safety signals

- Period covered 2007-2015
- Risk communication as a marker of post-market safety events*.
- Examples of safety concerns anticipated:
  - QTc prolongation, liver injury, renal impairment, misuse and abuse, bleeding.
- Examples of safety concerns NOT anticipated:
  - Neoplasms, serotonin syndrome, pancreatitis, serious skin reactions (DRESS, TEN).
  - First in class, long-term studies/large exposure needed to detect the ADR.

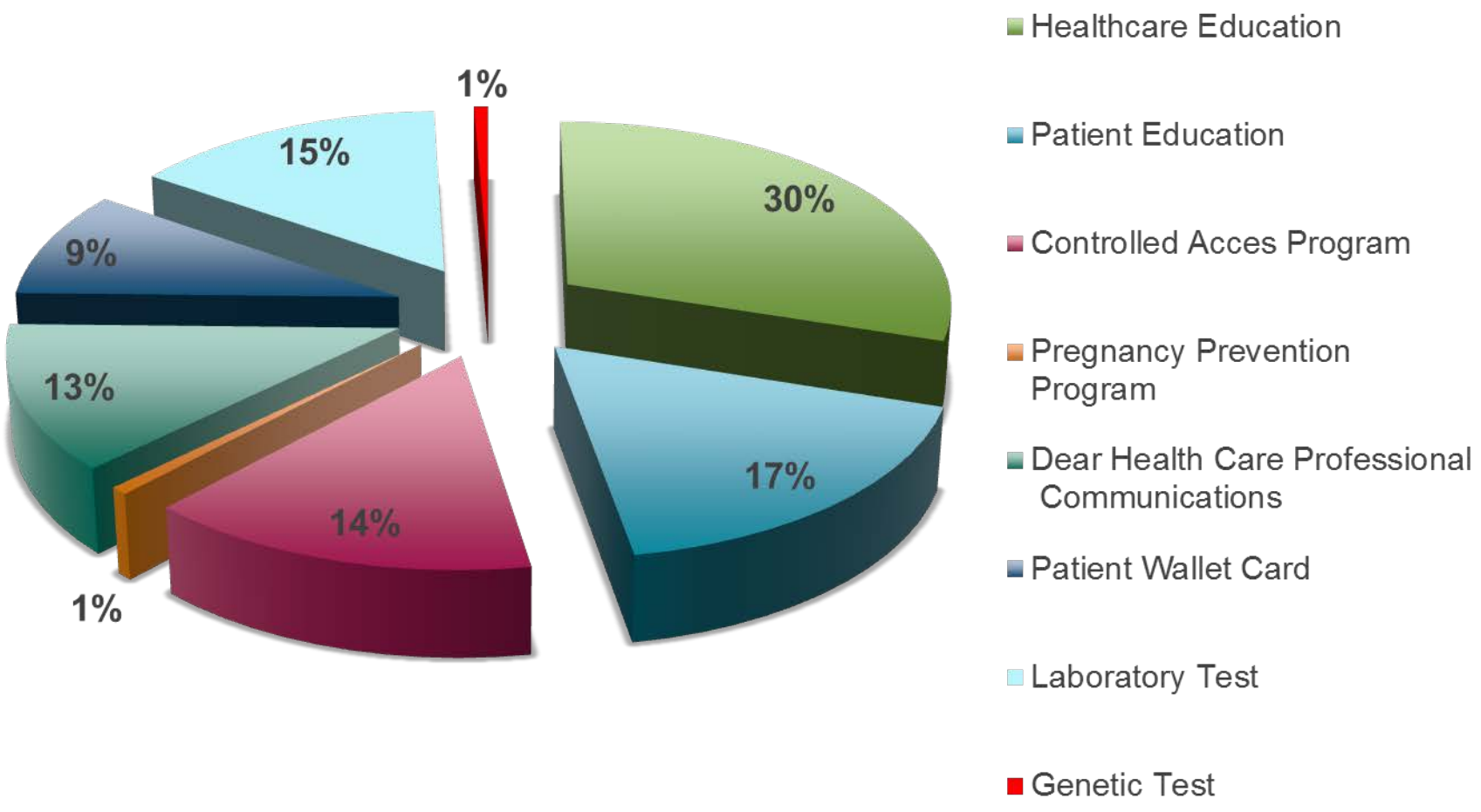


* *Carpenter D et al., N Engl J Med 2008; 358: 1354-1361.*

Effectiveness of pharmacovigilance processes - how often has Health Canada requested additional risk minimization activities?



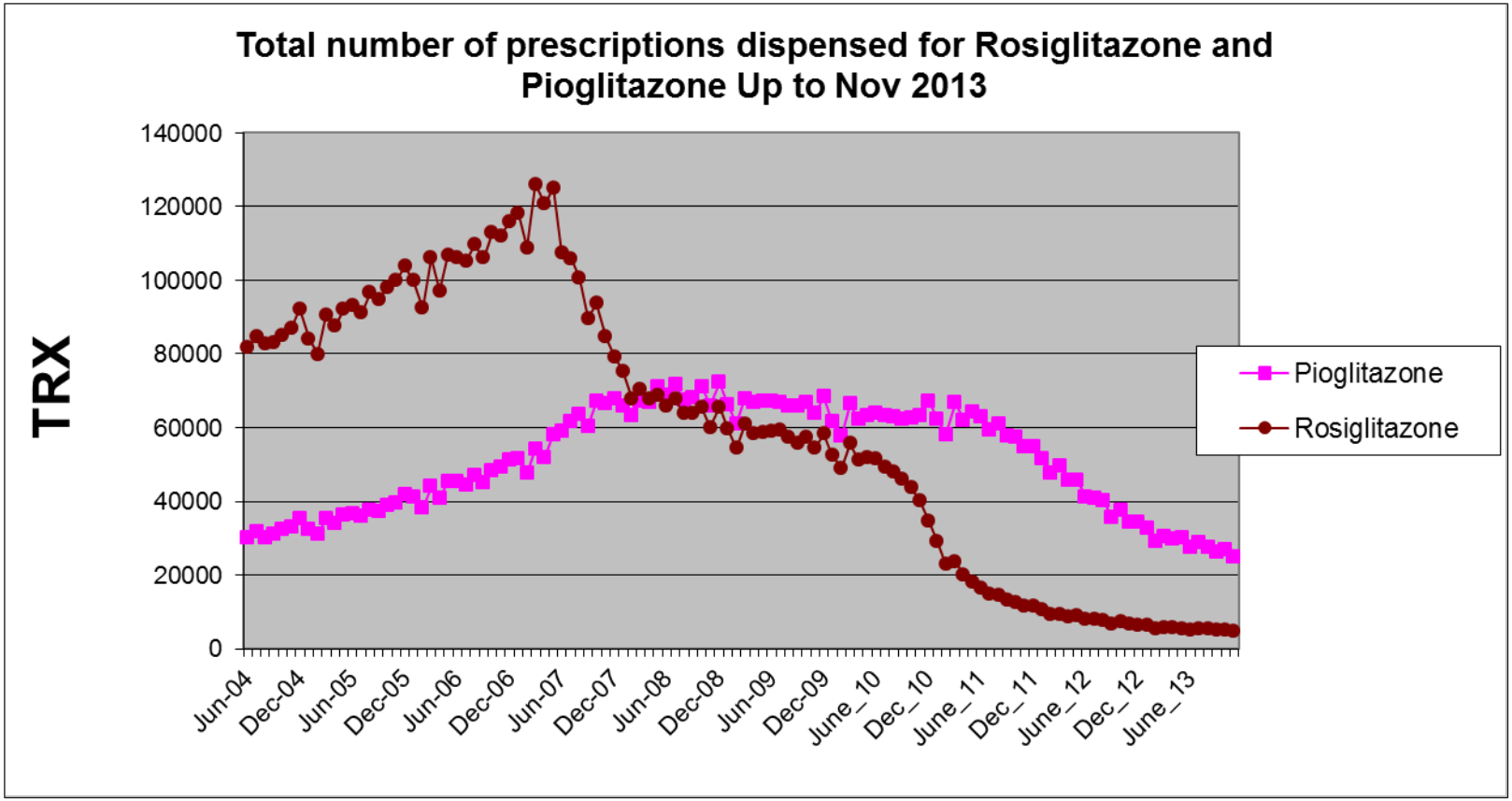
Effectiveness of pharmacovigilance processes - overview of additional risk minimization measures



- Effectiveness of product-specific risk minimisation (using drug utilization studies- Rosiglitazone)
- Effectiveness of product specific risk characterization (using PASS – Pioglitazone)

Drug	Targeted Risk	Approach	Impact
Pioglitazone	Assess risk of bladder cancer	PASS study/Update the label, risk communication	Decline in prescribing
Thalidomide	Fetal malformation	Restricted distribution	No fetal exposure
Rosiglitazone	Myocardial infarction	Update the label, risk communication, consent form	Decline in prescribing
Vismodegib	Fetal malformation	Restricted distribution	No fetal exposure
Isotretinoin	Fetal Malformation	Retrospective cohort study conducted by the Drug Safety and Effectiveness Network (DSEN) in 4 provinces, covering the period 1996-2011.*	Pregnancies occur in spite of the Pregnancy Prevention Program (PPP);

Impact of Effective Risk Minimization



Based on Canadian data

Case study: Impact of Effective Risk Minimization

CMAJ April 8, 2008 vol. 178 no. 8 doi: 10.1503/cmaj.071265

Research

Effect of regulatory warnings on antidepressant prescription rates, use of health services and outcomes among children, adolescents and young adults

Laurence Y. Katz MD, Anita L. Kozyrskyj PhD, Heather J. Prior MSc, Murray W. Enns MD, Brian J. Cox PhD, Jitender Sareen MD

- HC and other regulators further warned in 2004 about the use of all newer antidepressants (selective serotonin reuptake inhibitors and selective norepinephrine reuptake inhibitors) in children and adolescents.
- Study examined rates of antidepressant prescription to determine whether warnings issued by HC were associated with a decrease in the use of medications.
- Rate of antidepressant prescriptions decreased among children and adolescents (relative risk [RR] 0.86, 95% confidence interval [CI] 0.81–0.91)

- Enablers of effective pharmacovigilance including stakeholder trust and engagement.
  Acetaminophen: A collaborative education effort for increasing risk awareness

- In 2014, Health Canada completed a signal assessment on liver injury and acetaminophen use and noted that there was an increase in the rate of hospitalizations related to liver injury and acetaminophen overuse.

- Technical discussions on risk minimisation options received input from a diverse group of stakeholders and resulted in a strategy that was based on a better understanding of potential unintended consequences and resulted in a plan that was better informed.

- Health Canada worked with stakeholders on a collaborative education approach to increase consumer awareness of the risks associated with acetaminophen overuse.

- Stakeholders helped to amplify the messages by pushing out the information via Twitter; other online resources included pamphlets, web banners and a factsheet.

Efforts at a National level

- **2006 - General Public Opinion Survey on Key Issues Pertaining to Post-Market Surveillance of Marketed Health Products in Canada:**
  - In the spring of 2003, Decima Research conducted a benchmark study among Canadians and health professionals to understand the effectiveness of the current methods used to communicate new health information. As a result of this research, new communications tools were developed to better inform the public and health professionals about health product safety information.
  - In 2006, Health Canada commissioned Decima Research to conduct a follow-up to the 2003 study among the Canadian public. The overall objective of this study was to measure the effectiveness of new communications tactics that were created as a result of findings from the 2003 study.

- **2014 - Health Canada submitted a proposal to the Council of Canadian Academies (CCA), an independent body, to study how the effectiveness of risk communications can be measured and evaluated.**
  - (*Health Product Risk Communication: Is the Message Getting Through?* *http://scienceadvice.ca/en/assessments/completed/risk-comm.aspx*
- **2013 - Evaluating the Health Literacy Burden of Canada's Public Advisories: A Comparative Effectiveness Study on Clarity and Readability**
  - This study examined the health literacy burden of Public Advisories(PAs) before and after implementation of a new template.
  - Improvements made to Health Canada's PA template had a measurable, positive effect on reducing the health literacy burden, based on the Suitability assessment of materials (SAM) results.
  - The SAM test emerged as a robust, reliable, and informative health literacy tool to assess risk messages and identify further improvement efforts
  - (*Drug Safety December 2013, Volume 36, Issue 12, pp 1179–1187)*

Considerations:

- Access to e health records and national data will significantly enhance the capacity to be more proactive in measuring impact pre and post intervention
- Develop better measures
- Use real world data
- Internationally aligned / harmonized approach
- Systematic approach rather than a retroactive exercise

Next Steps:

- Develop an evaluation strategy based on the indicators established and taking into consideration:
  - Identifying clear goals and objectives of measuring impact
  - Identifying and selecting impact measures that are SMART – least costly but most informative
  - Selecting frequency of measurement- Episodic for longer term outcomes
  - Selecting study methods and sources of data