CIHR IRSC Canadian Institutes of Health Research / Instituts de recherche en santé du Canada

Discoveries for life / Découvertes pour la vie

What is the Drug Safety and Effectiveness Network (DSEN)?

A national resource that can help fill evidence gaps

Affordability
Are Canadians getting value from new and more expensive prescription drugs?

Appropriate use
Can more appropriate prescribing practices improve patient outcomes?

Accessibility
What can be done to improve timely access to new drugs and therapies that are safe and effective?

DSEN has the mandate, expertise and capacity to systematically conduct "real-world" drug safety and effectiveness research required by decision makers. Established in 2009 as a partnership between the Canadian Institutes of Health Research and Health Canada, this pan-Canadian network of more than 200 independent investigators responds directly to "queries" submitted by Health Canada, public drug plans and other relevant stakeholders (e.g., Canadian Agency for Drugs and Technologies in Health).

DSEN researchers use data mining and analysis and original research to determine:

- If marketed prescription drugs (biologics and pharmaceuticals) are safe for different patient populations
- How different groups respond to an approved drug ("effectiveness")
- Whether new drugs should be publicly insured (are they more effective than what is already available?)
- How specific drugs should be safely and optimally prescribed and used

What each DSEN research team does

Knowledge synthesis

MAGIC *(Methods and Applications Group for Indirect Comparisons)*

- Finds evidence through reviews of published and unpublished literature, regulatory documents, etc.
- Summarizes/synthesizes evidence from relevant and related studies to identify combined results and key messages from the data

Observational studies

CNODES *(Canadian Network for Observational Drug Effect Studies)*

- Examines the appropriate and inappropriate real-world use of drugs across and between provinces
- Assesses safety of prescription drugs
- Studies the comparative effectiveness of prescription drugs
- Has ready access to anonymized health care data on more than 100 million patients

Prospective observational studies

CAN-AIM *(Canadian Network for Advanced Interdisciplinary Methods for Comparative Effectiveness Research)*

- Analyzes historical data on patients (retrospective analyses)
- Uses observational studies of patients over time to assess real-world safety and effectiveness of drugs (prospective study)
- Integrates diverse data sources, including clinical cohorts
- Evaluates new data sources (e.g., use of social media to detect drug safety signals)

SEARCH & PREVENT *(Active Surveillance and Evaluation of Adverse Reactions in Canadian Healthcare Team and Pharmacogenomics of Adverse Events National Team)*

- Conduct studies with Canadian patients to identify clinical and genetic factors that put certain people at higher risk of adverse drug reactions (e.g., children, pregnant women)
- Access to 10 children's and 18 adult hospitals across Canada
- Access to biological samples (e.g., blood, saliva)

For more information, please contact the **DSEN Coordinating Office** at
DSEN-RIEM@cihr-irsc.gc.ca

MAGIC

MAGIC brings together top Canadian researchers in knowledge synthesis to form a critical mass of expertise in synthesizing key evidence from the literature to inform decision making related to the real-world safety and effectiveness of drugs.

Strengths

- Leading Canadian scientists supported by a large team of more than 50 research staff with extensive experience in knowledge synthesis
- Expertise in narrative, scoping, rapid and systematic reviews
- Expertise in synthesizing evidence focused on comparing pairs of therapies (meta-analysis) or many therapies (network meta-analysis)
- Expertise conducting reviews with studies of all designs
- Answers within 12 months or less (matching product to end-user needs)
- Expertise in knowledge translation strategies to maximize research impact

Examples of **queries**

- Comparative effectiveness and safety of cognitive enhancers for treating Alzheimer's disease (systematic review)
- Approaches to the appropriate use of medications (scoping review)
- Comparing efficacy and completion rates and harms of treatment for latent tuberculosis infection (rapid review)
- Comparing antithrombotic agents for the prevention of stroke and major bleeding in patients with atrial fibrillation (network meta-analysis)

Types of data used

- Published scientific studies
- Unpublished ("grey") literature
- Regulatory documents
- Alternative or novel forms of evidence (e.g., social media)

CNODES

CNODES provides high-quality evidence on real-world use of widely used drugs, and timely responses to drug safety and effectiveness queries.

Strengths

- A distributed network of over 100 scientists, including pharmacoepidemiologists, clinicians, statisticians, data analysts and other researchers
- Access to administrative health care data on millions of medication users across Canada and internationally
- Common protocols ensure multiple datasets are comparable across provinces
- Provincial nodes conduct independent and simultaneous studies of the same drugs
- Ability to analyze and integrate results (meta-analysis) from different provincial datasets to create a national picture of a drug's utilization, safety and benefits, with additional data from international sources (US and UK)
- Expertise in descriptive cohort studies, comparative control studies, and nested case-control studies

Examples of **queries**

- Studies of adverse effects (e.g., impact of using high- vs. low-potency statins on the risk of diabetes)
- Drug utilization (e.g., opioid usage and opioid-related death rates across Canada)
- Quality of care (e.g., trends in isotretinoin [Accutane] use in women during pregnancy and related adverse pregnancy outcomes)
- Comparative effectiveness (e.g., the reduction in the incidence of stroke associated with direct oral anticoagulants vs. warfarin for non-valvular atrial fibrillation)

Types of data used

Core
- Health insurance registries
- Prescription drug claims
- Physician service claims
- Hospital discharge abstracts
- Emergency department records
- Vital statistics

Supplementary
- Cancer registries
- Pregnancy registries
- Laboratory test results
- Health surveys
- CPRD: EMR-based risk factor data (e.g., smoking and alcohol use, BMI)

www.cnodes.ca

CAN-AIM

CAN-AIM uses prospective longitudinal cohorts and other data sources, and develops and validates cutting-edge statistical methods, to provide relevant real-world information on drug safety and effectiveness.

Strengths

- Pan-Canadian network of 35 investigators from 14 universities, located in six provinces
- Interdisciplinary expertise in clinical and methodological research
- Real-world drug safety and effectiveness analyses
- Data integrated from diverse sources, including clinical cohorts and administrative databases
- Development and validation of new methods to enhance the analysis of prospective studies of drug safety and effectiveness which:
  - Improved drug exposure modelling
  - Control for potential study biases
- Expertise in analyzing the cost-effectiveness of drugs

Examples of **queries**

- Evaluation of crowdsourcing and social media to increase awareness of drug safety
- Comparative effectiveness of antihypertensive drugs for the treatment of hypertension in non-diabetic patients
- Use of HIV antiretroviral drug (Darunavir) and risk of congenital abnormalities
- Safety and effectiveness of biosimilars vs. legacy drugs
- Comparative effectiveness of newer agents to treat rheumatoid arthritis

Types of data used

Clinical cohorts, e.g.

- Canadian Partnership for Tomorrow Project
- Canadian Longitudinal Study on Aging
- Canadian Multicentre Osteoporosis Study
- Quebec Pregnancy Cohort
- Canadian Early Arthritis Cohort
- Canadian Network on Hepatitis C

Claims and administrative databases, e.g.

- RAMQ
- PopDataBC
- PharmaNet BC
- Clalit (Israel)
- MarketScan (US: 230 million people)

SEARCH & PREVENT

SEARCH & PREVENT conducts studies with Canadian patients to identify the clinical and genetic factors that put certain patients, such as children and pregnant women, at higher risk of adverse drug reactions (ADRs).

Strengths

- Pan-Canadian network of over 15 Canadian scientists and more than 30 clinicians in six provinces, and more than 20 international collaborators
- Expertise in the clinical study of drugs (pharmacology) and the genetic factors that influence an individual's response to a particular drug (pharmacogenomics) to address drug safety concerns of children and adults
- Trained ADR surveillance clinicians: MDs, registered nurses, clinical pharmacists
- Ability to evaluate drug safety in broad patient populations, sub-populations (e.g., age, ethnicity, gender), and "orphan" populations (e.g., pregnant women, and children) excluded from clinical trials
- Expertise in developing genotype-based dosing guidelines to predict safety and avoid severe ADRs (genetic factors account for an estimated half of all ADRs)

Examples of **queries**

- Confirming or refuting safety and effectiveness signals found in Canadian observational trials through active surveillance
- Confirming or refuting safety and effectiveness signals found in other international jurisdictions
- Establishing genetic causality of ADRs (e.g., codeine and infant/toddler mortality)
- Establishing post-market safety and effectiveness of drug therapies
  (e.g., inhaled corticosteroids in children and during pregnancy)

Types of data used

Data sources

- Active surveillance in clinical settings
- Canadian Pharmacogenomics Network for Drug Safety clinical database
- Pharmacogenomics, pharmaco-kinetics and personalized data

Data types

- Detailed clinical data on ADRs
- Clinician assessment of ADR causality
- Medication doses and dates
- Concurrent medications
- Comorbid conditions
- Ancestry data
- DNA samples (blood/saliva)
- Patient charts/clinical data
- Genomic data

www.canaim.ca

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