FISCAL COST-BENEFIT ANALYSIS OF ANTIRETROVIVAL THERAPY(ART)FOR THE MANAGEMENT AND THE PREVENTION OF HUMAN IMMUNODEFFIECIENCY VIRUS (HIV) IN CANADA 1987-2021

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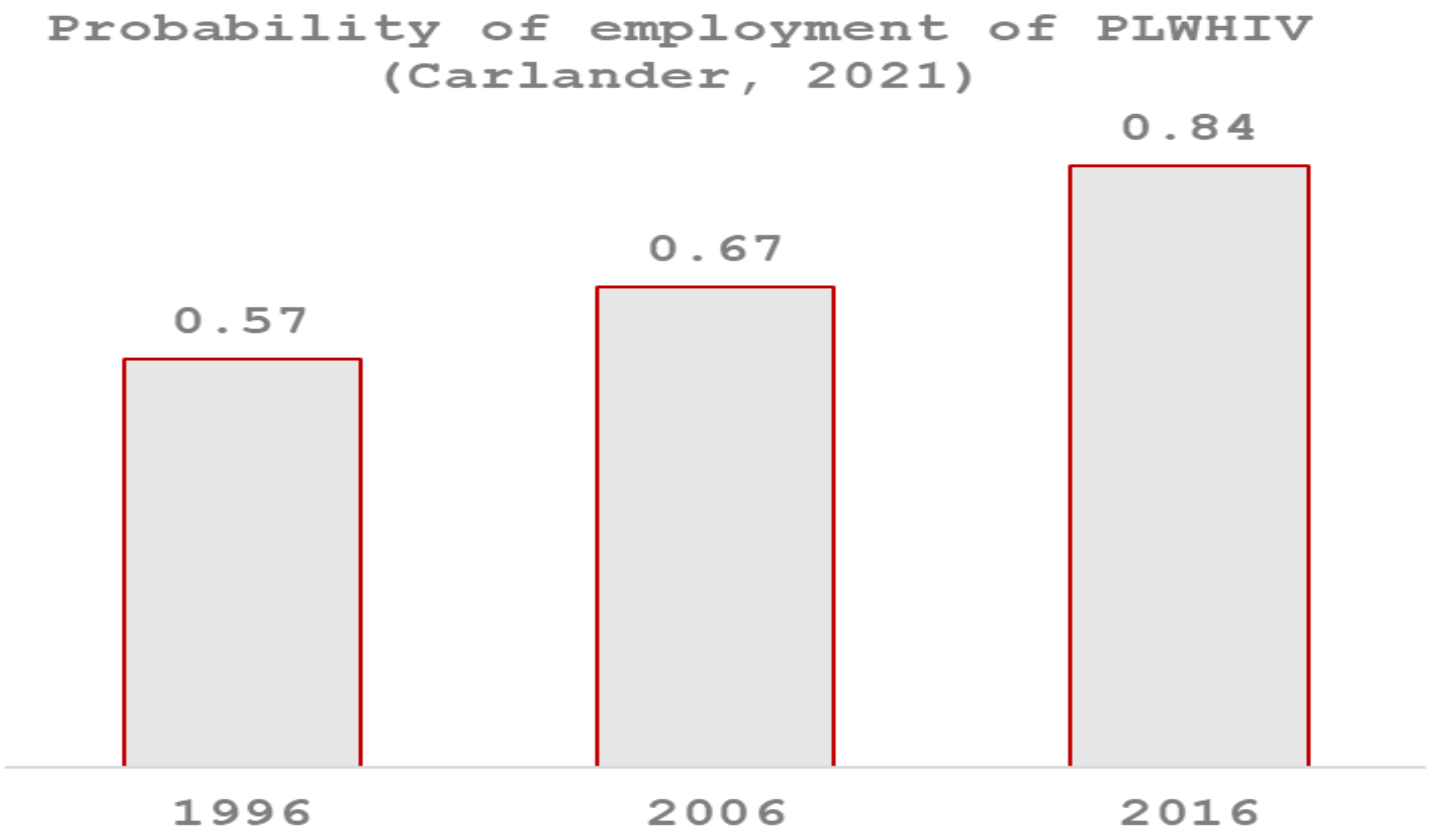
4. Gilead, Canada

Disclosure: The work described here was funded by Gilead

Background

- *Since the introduction of antiretroviral therapy (ART) in 1987, governments and health services have been investing to improve the lives of people living with HIV (PLWHIIV) & reduce disease transmission*
- *Several studies have demonstrated that testing positive and living HIV has disruptive effects on labor force participation and wages*
- *Reduced labour force participation rates may result in public economic losses for government*

Employment among PLWHIV

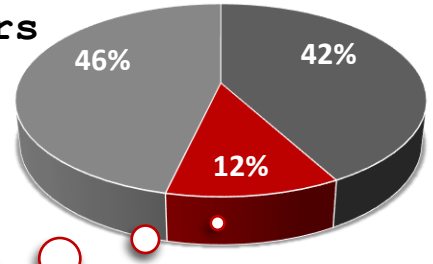


Annual impact of working-aged adults' ill-health on government accounts (2007, £ billions)

Workless benefits	£29
Healthcare costs	£5 – 11
Foregone taxes	£28 – 36
Total impact	£62 – 76

Governmental fiscal costs i.e., transfers to citizens

Revenue fiscal loss i.e., reduced transfers from citizens



Focal point of economic evaluation

- Workless benefits
- Healthcare costs
- Foregone taxes

Burden of Disease(BoD)from the perspective of the government: Health has cross-sectorial economic consequences and public economic impact which is not captured by conventional healthcare economic analyses(e.g., healthcare perspective economic evaluations (Black, 2008)

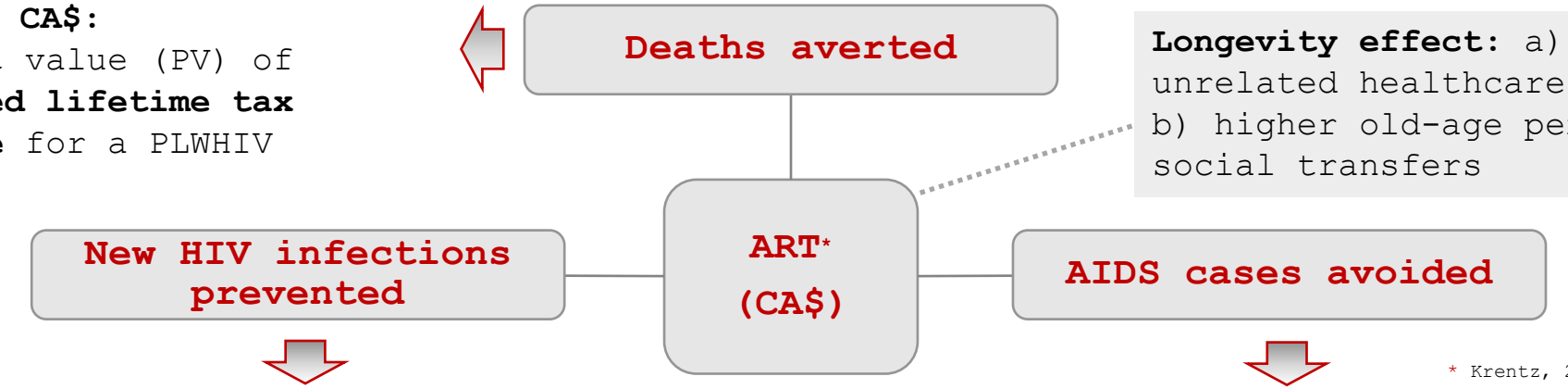
Methods

- *Ex-post cost-benefit analysis (CBA) from the perspective of the Canadian government for the period 1987-2021*
- *Comparison of historical data on HIV deaths, AIDS cases and HIV incidence with…*
  - *Hypothetical scenario in which ART was not available for either treatment or preventing mother-to-child transmission (excludes PrEP)*
- *Each year the model estimated the number of averted deaths, AIDS cases and new HIV infections*
  - *Epidemiological outcomes were monetized to reflect fiscal outcomes*
  - *Historical fiscal outcomes converted to 2021 CA$ prices*
  - *Future (2021+) fiscal flows for PLWHIV discounted at 4%*

Cost-benefit analysis method

Benefit in CA$:

1. Present value (PV) of **expected lifetime tax revenue** for a PLWHIV



* Krentz, 2004; Krentz 2018; Krentz, 2020

Avoidable burden in CA$:

1. **Tax revenue loss** from PLWHIV that compared to the general population (GP) generate lower PV of expected lifetime tax revenue due to
   a) lower employment rates by **16%** (Carlander, 2021)
   b) lower life expectancy (varying)
2. **HIV-related healthcare costs** (varying)*
3. **Disability costs** increased by **8%** (Legarth, 2014) & employment insurance costs by **42%** (Joy, 2008) compared to GP

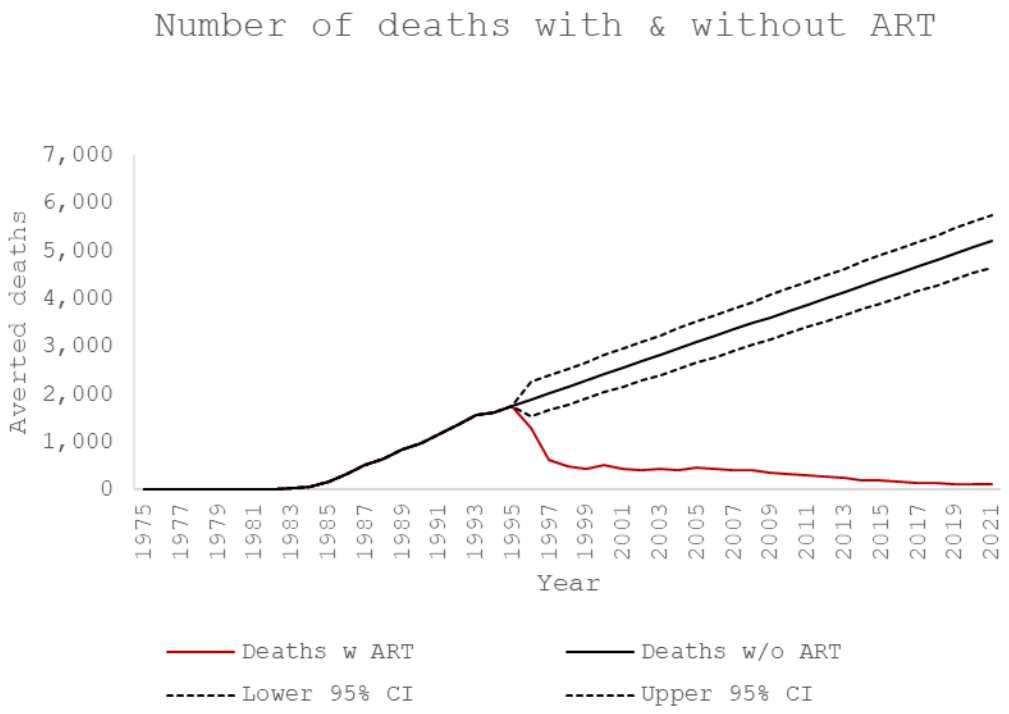
Avoidable burden in CA$:

1. **Tax revenue loss**
   a) lower employment rates by **57%** (Garcia. 2012)
   b) lower life expectancy (varying)
2. **HIV-related healthcare costs** (varying)*
3. **Disability costs higher** by **58%** (Annequin, 2015) & employment insurance costs by **82%** (Ibrahim, 2008) compared to GP

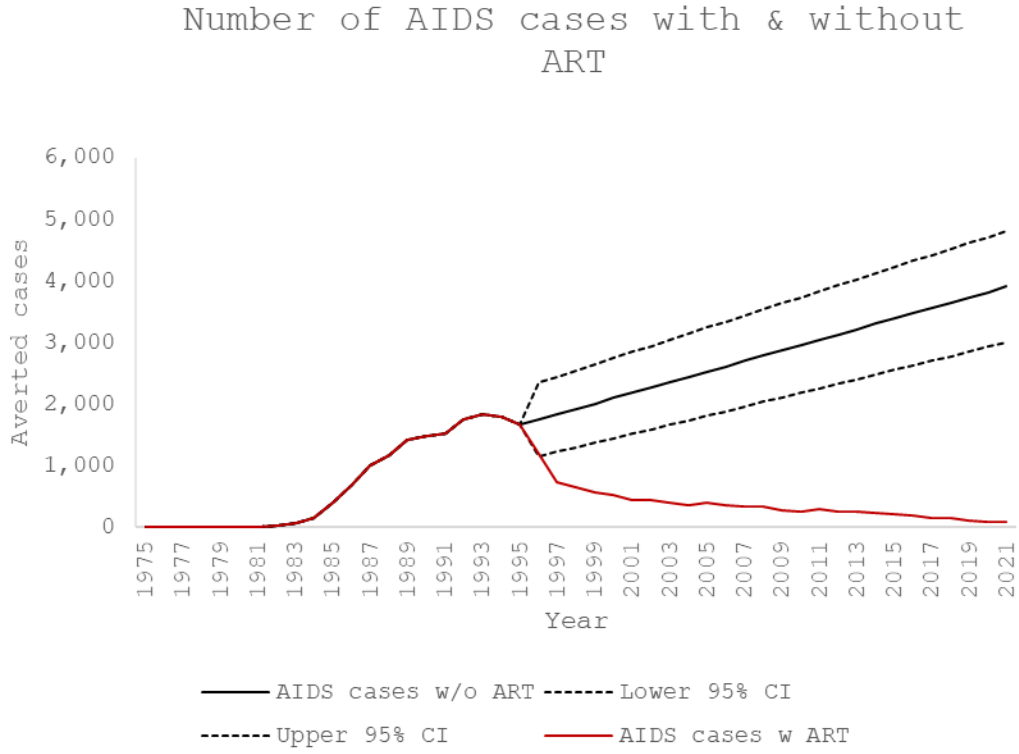
Analyses conducted estimated annual costs ART for the period 1987 – 2022 & expected benefits for the lifetime of PLWHIV

Results: Estimation of averted deaths & AIDS cases

Averted number of deaths



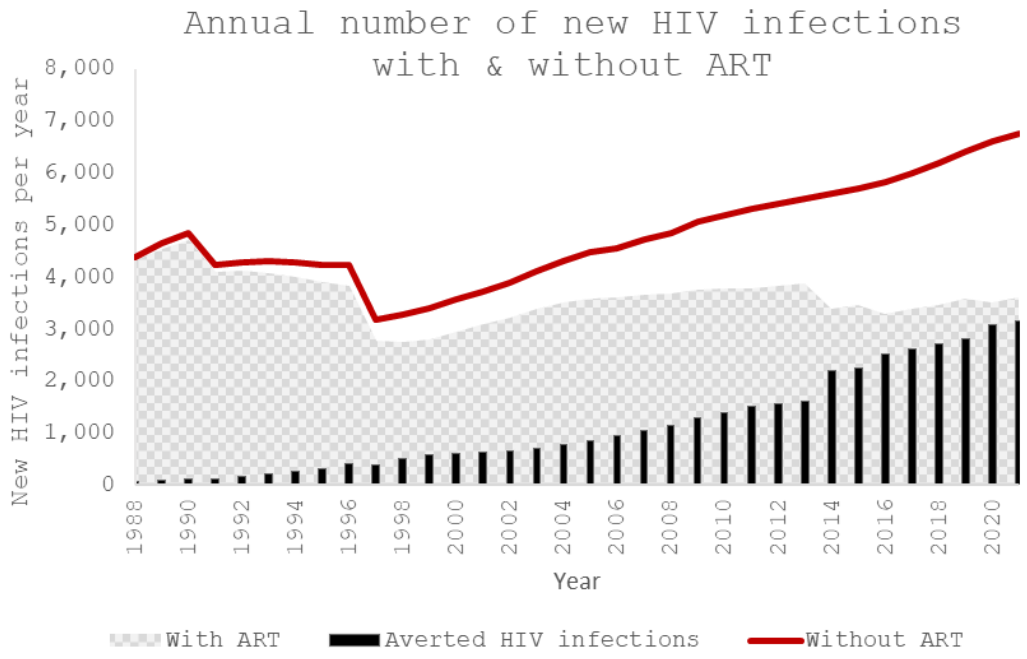
Averted AIDS cases



Forecasting of deaths & AIDS cases without ART based on time series analysis methods (Holt & Winters)

Results: Estimation of averted new infections

Annual number of new HIV infections with and without ART & averted new HIV infections



New transmission estimation method

$$N_{new\ infections} = \beta_0 \times N_{no\ ART}^{infections} + RR_{ART} \times N_{ART}^{infections} \div N_{total\ population}$$

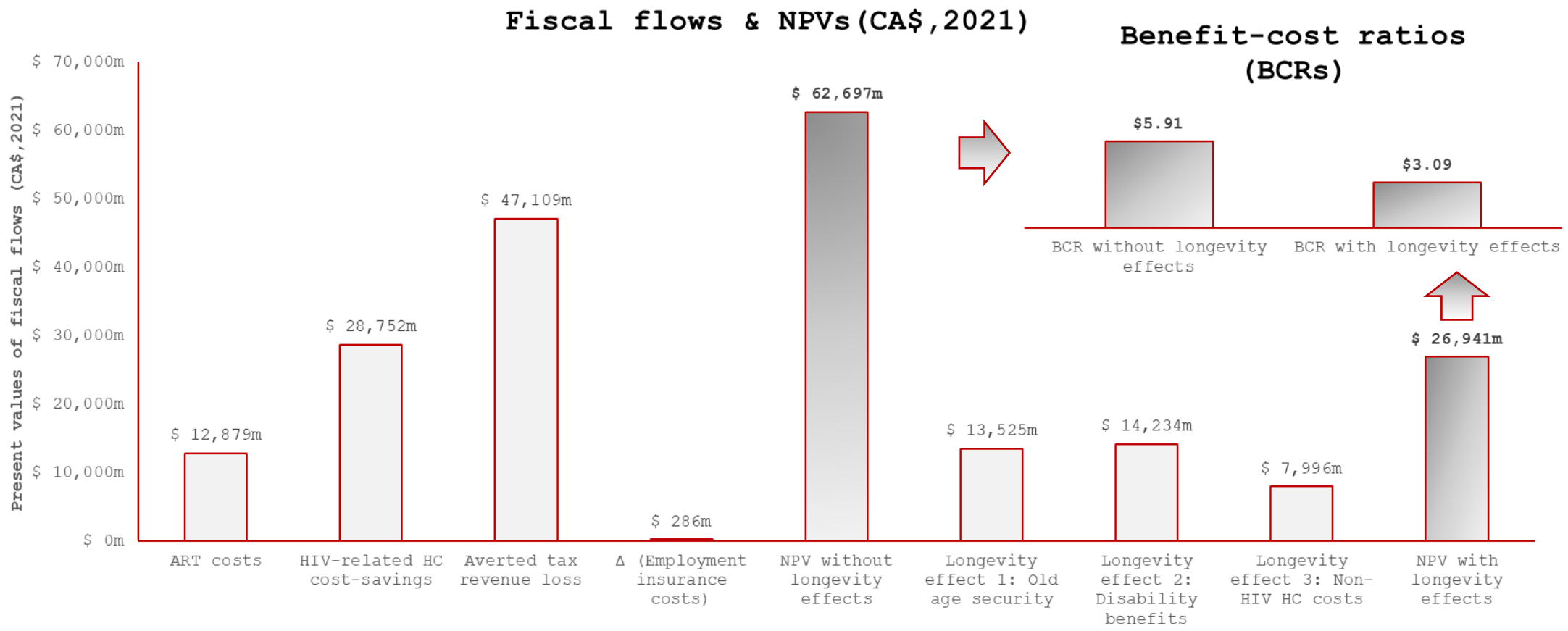
N is the number of people in a given group i.e., ART/no ART

$N_{no\ ART}^{infections}$ is infected not on treatment, and unsuppressed ART patients

$N_{ART}^{infections}$ is infected on treatment and suppressed

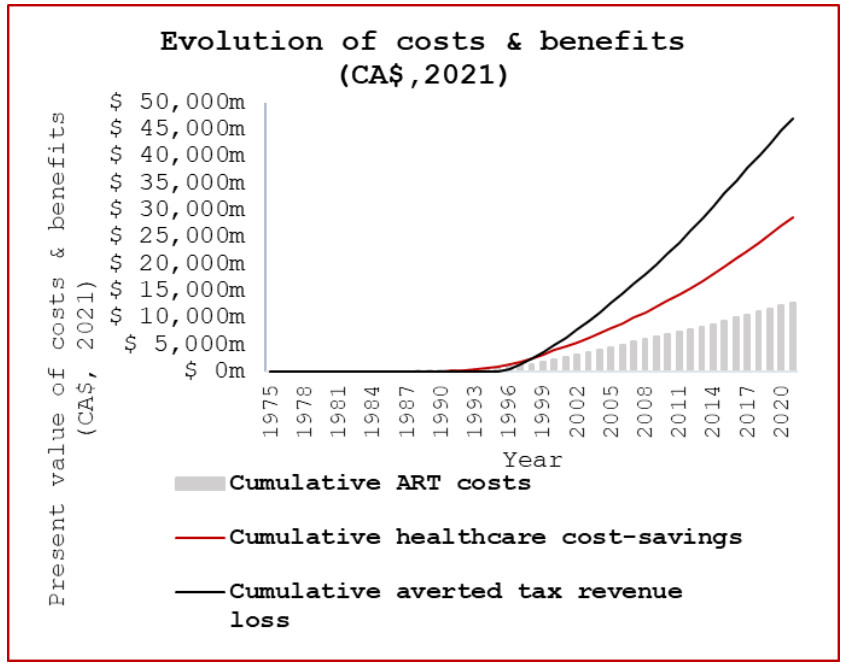
RR_{ART} is the relative infectiousness of persons on ART and suppressed vs. other persons.

Results: Fiscal cost-benefit analysis

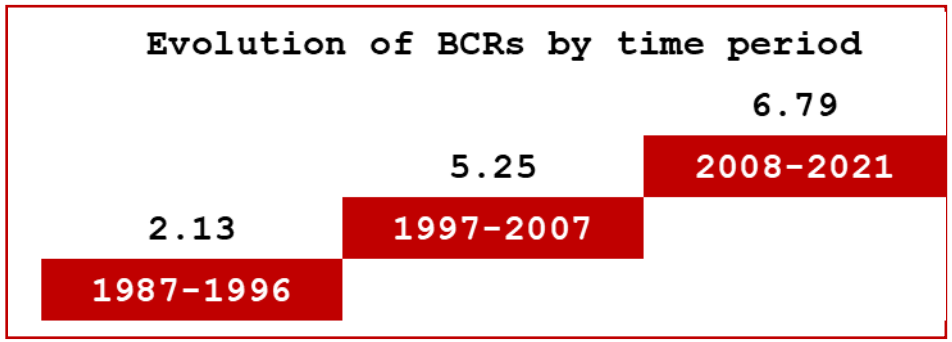


Since introduction of ART significant fiscal returns generated from investments

Evolution of ARTs, costs & benefits



Cabenuva; Cabotegravir, 2021
Fostemsavir, 2020
Dovato, 2019
Biktarvy; Cimduo; Delstrigo; Doravirine; Ibalizumab; Symfi; Symtuza; Temixys, 2018
Juluca, 2017
Descovy; Odefsey, 2016
Evotaz; Genvoya; Prezcobix, 2015
Cobicistat; Elvitegravir; Triumeq, 2014
Dolutegravir, 2013
Stribild, 2012
Complera; Nevirapine XR; Rilpivirine, 2011
Etravirine, 2008
Maraviroc; Raltegravir, 2007
Atripla; Darunavir, 2006
Tripanavir, 2005
Epzicom; Truvada, 2004
Atazanavir; Emricitabine; Enfuvirtide; Fosamprenavir, 2003
Tenofovir DF, 2001
Didanosine EC; Kaletra; Trizivir, 2000
Amprenavir, 1999
Abacavir; Efavirenz, 1996
Combivir; Delavirdine; Nelfinavir, 1997
Indinavir; Nevirapine; Ritonavir, 1996
Lamivudine; Saquinavir, 1995
Stavudine, 1994
Zalcitabine, 1992
Didanosine, 1991
Zidovudine, 1987



Probabilistic & deterministic sensitivity analysis

Probabilistic SA results

	Mean	SD	Lower 95% CI	Upper 95% CI
NPV without longevity effects	$61,879m	$10,721m	$61,214m	$62,543m
BCR without longevity effects	5.90	0.75	5.85	5.95
NPV with longevity effects	$27,682m	$ 8,168m	$27,175m	$28,188m
BCR with longevity effects	3.15	0.70	3.11	3.20

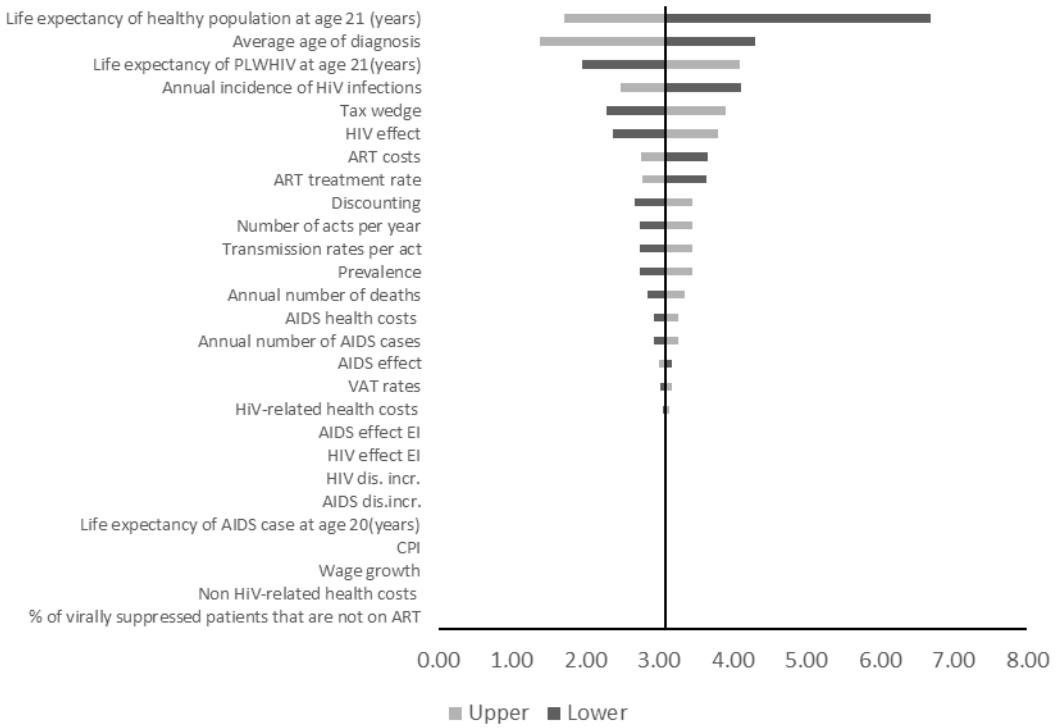
NPV: Net present value; BCR: Benefit cost ratio; SD: Standard deviation

CI: Confidence interval;

Longevity effects: Inclusion of non-related healthcare costs & social transfers e.g., old-age pensions

SA: Sensitivity analysis

Deterministic SA (±25%) for the BCR with longevity



Favorable BCRs persisted when the parameters of the model were probabilistically and deterministically varied

Summary of results

- *Investing in ART yielded*
  - ***$28.7** billion in avoided healthcare costs*
  - ***$47.1** billion in averted tax revenue loss*
  - *Spending on employment insurance for PLWHIV increased by **$0.28** billion*
- *Without the fiscal effect of longevity, the estimated benefit-cost ratio (BCR) was **5.91***
- *The BCR remained favorable **(3.09)** when the fiscal effects of longevity were considered*
  - *Increased fiscal expenditure, by **$13.5** billion in old-age benefits, **$14.2** billion in disability benefits and **$7.9** billion in non-HIV related healthcare costs*

The Canadian government has generated significant fiscal returns from investing in ART

Contact information

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References

Annequin, M., F. Lert, B. Spire, R. Dray-Spira, and Vespa Study Group. 2015. 'Has the employment status of people living with HIV changed since the early 2000s?', AIDS, 29: 1537-47.

Black, Carol. Dame Carol Black's review of the health of Britain's working age population: Working for a healthier tomorrow. Stationery Office, 2008. https://www.gov.uk/government/publications/improving-health-and-work-changing-lives

Carlander, C., P. Wagner, A. Yilmaz, P. Sparen, and V. Svedhem. 2021. 'Employment by HIV status, mode of HIV transmission and migrant status: a nation-wide population-based study', AIDS, 35: 115-23.

García-Gómez, Pilar, José Labeaga, and Juan Oliva-Moreno. 2012. 'Employment and wages of people living with HIV/AIDS', Journal of Biotechnology - J BIOTECHNOL.

Ibrahim, F., J. Anderson, C. Bukutu, and J. Elford. 2008. 'Social and economic hardship among people living with HIV in London', HIV Med, 9: 616-24.

Joy, R., E. F. Druyts, E. K. Brandson, V. D. Lima, C. A. Rustad, W. Zhang, E. Wood, J. S. Montaner, and R. S. Hogg. 2008. 'Impact of neighborhood-level socioeconomic status on HIV disease progression in a universal health care setting', J Acquir Immune Defic Syndr, 47: 500-5.

Krentz, H. B., M. C. Auld, and M. J. Gill. 2004. 'The high cost of medical care for patients who present late (CD4 <200 cells/microL) with HIV infection', HIV Med, 5: 93-8.

Krentz, H. B., and M. John Gill. 2018. 'Long-term HIV/AIDS survivors: Patients living with HIV infection retained in care for over 20 years. What have we learned?', Int J STD AIDS, 29: 1098-105.

Krentz, H. B., Q. Vu, and M. J. Gill. 2020. 'Updated direct costs of medical care for HIV-infected patients within a regional population from 2006 to 2017', HIV Medicine, 21: 289-98.

Legarth, R., L. H. Omland, G. Kronborg, C. S. Larsen, C. Pedersen, G. Pedersen, U. B. Dragsted, J. Gerstoft, and N. Obel. 2014. 'Employment status in persons with and without HIV infection in Denmark: 1996-2011', AIDS, 28: 1489-98.

Comparing approaches to determine the costs of treating burn victims in Quebec

Chouinard N[1,2,3], Beaudoin Cloutier C[2,3,4], Chang SL[2,4], Laberge M[1,5], Poder TG[6], Lachapelle P[4], Guertin JR[1, 2, 3]

[1] Département de médecine sociale et préventive, Faculté de médecine, Université Laval, Québec, Canada. [2] Axe santé des populations et pratiques optimales en santé, Centre de recherche du CHU de Québec-Université Laval, Québec, Canada. [3] Centre de Recherche en Organogénèse Expérimentale de l'Université Laval/LOEX, Québec, Canada. [4] CHU de Québec – Université Laval, Québec, Canada. [5] Vitam, Centre de recherche en santé durable - Université Laval. [6] École de santé publique - Département de gestion, d'évaluation et de politique de santé, Université de Montréal.

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Why focus on burn injuries?

1. Clinical aspects

Why focus on burn injuries?

Burn injuries are rare!

1. Clinical aspects

Why focus on burn injuries?

Burn injuries are rare!

The prevalence of partial deep dermal and full thickness burns is of between 0.01% – 0.05% according to the portal for rare diseases and orphan drugs.

1. Clinical aspects

The portal for rare diseases and orphan drugs. *Partial deep dermal and full thickness burns*.

Why focus on burn injuries?

The mortality rate of major burn victims has significantly decreased

1. Clinical aspects

Mason SA, Nathens AB, Byrne JP, Gonzalez A, Fowler R, Karanicolas PJ, et al. Trends in the epidemiology of major burn injury among hospitalized patients: A population-based analysis. J Trauma Acute Care Surg. 2017;83(5):867-74.

Why focus on burn injuries?

The mortality rate of major burn victims has significantly decreased

30-day mortality rate went from **47%** between 2003-2006 to **31%** between 2010-2013 in burn centers

1. Clinical aspects

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Why focus on burn injuries?

Baux score

Death risk in adults with burns after trauma

1. Clinical Aspects

Osler T, Glance LG, Hosmer DW. Simplified estimates of the probability of death after burn injuries: extending and updating the baux score. J Trauma. 2010;68(3):690-7.

Why focus on burn injuries?

Baux score

Death risk in adults with burns after trauma= **age + % total body surface area (TBSA)**

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Baux score

Death risk in adults with burns after trauma= **age + % total body surface area (TBSA)**

Revised version: +17 points if inhalation burns

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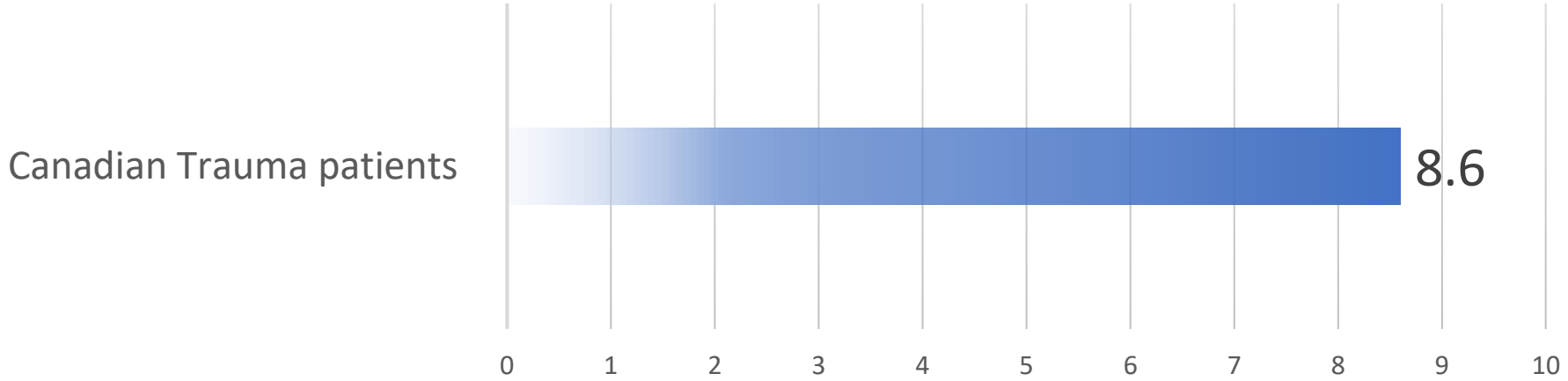
Why focus on burn injuries?

AVERAGE DURATION OF HOSPITAL STAY



1. Clinical aspects

Moore, L., Stelfox, H. T., Turgeon, A. F., Nathens, A., Bourgeois, G., Lapointe, J., Gagné, M., & Lavoie, A. (2014). Hospital length of stay after admission for traumatic injury in Canada: a multicenter cohort study. Annals of surgery, 260(1), 179–187. https://doi.org/10.1097/SLA.0000000000000624

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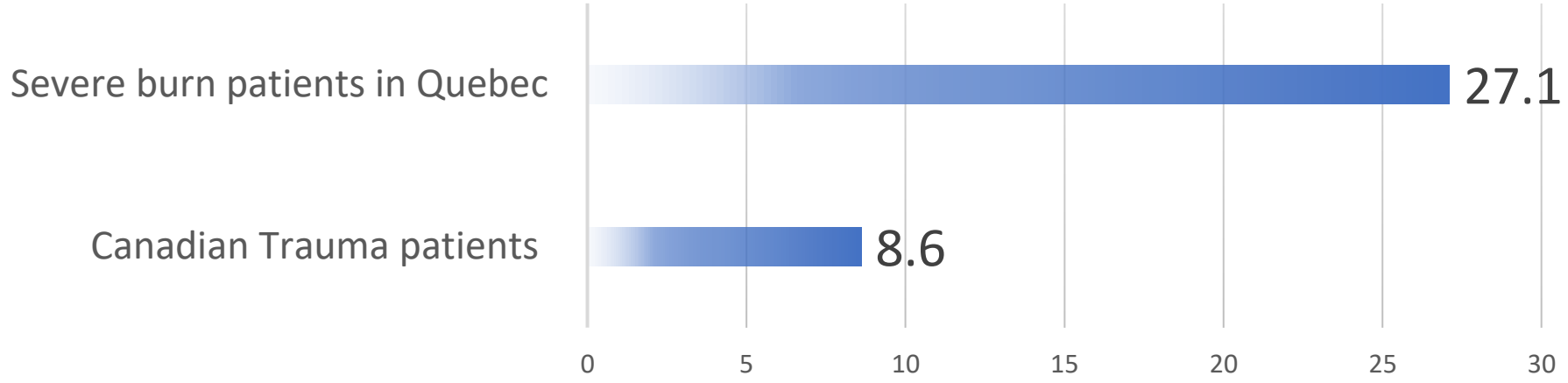

1. Clinical aspects

Institut national d'excellence en santé et en services sociaux (INESSS). Portrait du réseau québécois de traumatologie adulte : 2013 à 2016. 2019.

Why focus on burn injuries?

Severely burned patients have the **longest hospital stay duration among adult traumas** in Quebec

1. Clinical aspects

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Why focus on burn injuries?

The length of hospital can be influenced by:

- %TBSA (total body surface area)
- Sex
- Number of surgeries
- Inhalation burns

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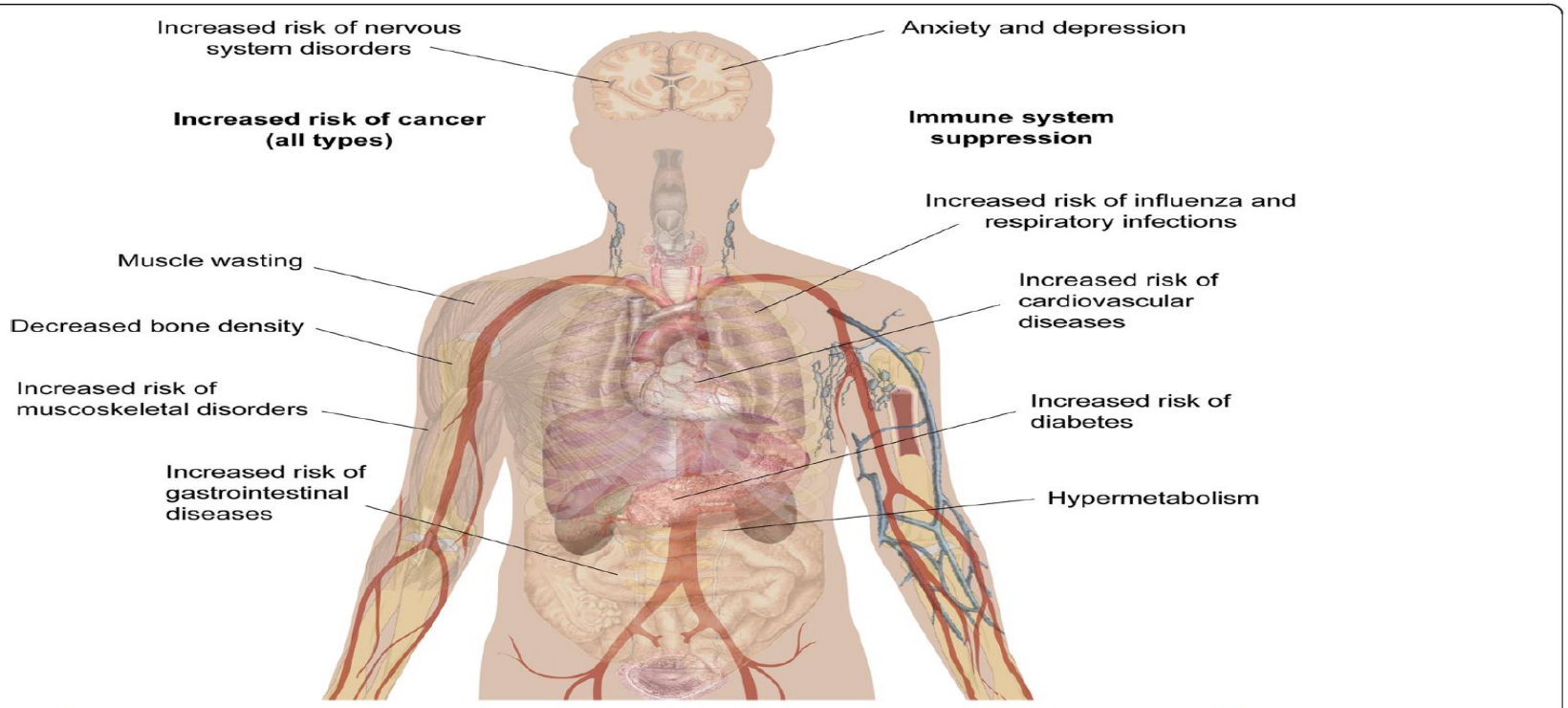


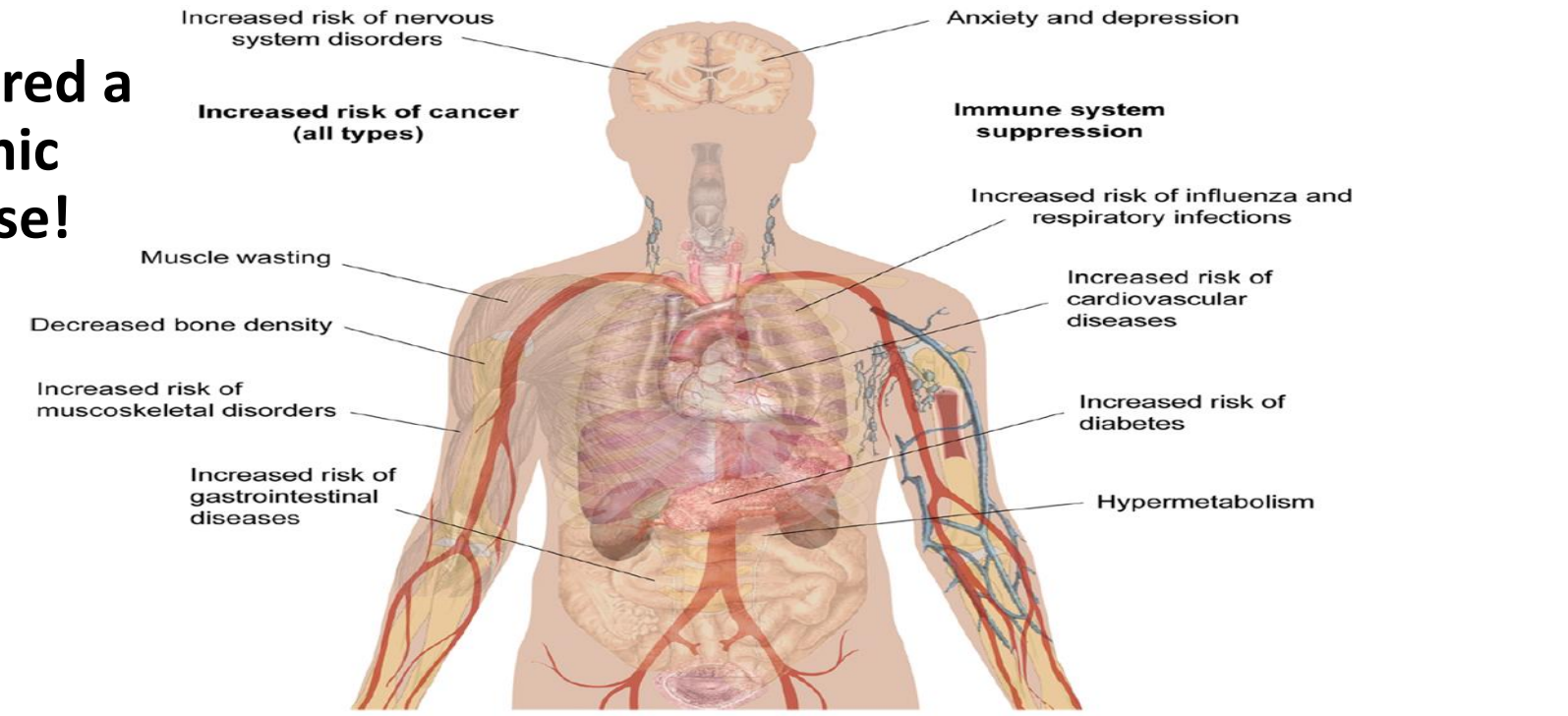
Fig. 1 Long-term pathological effects of burn injury. Burn injury is associated with an increased risk of numerous secondary pathologies. The human body schematic is a copyright free image obtained from google images

1. Clinical aspects

Barrett, L. W., Fear, V. S., Waithman, J. C., Wood, F. M., & Fear, M. W. (2019). Understanding acute burn injury as a chronic disease. Burns & trauma, 7, 23. https://doi.org/10.1186/s41038-019-0163-2

Why focus on burn injuries?

Considered a chronic disease!



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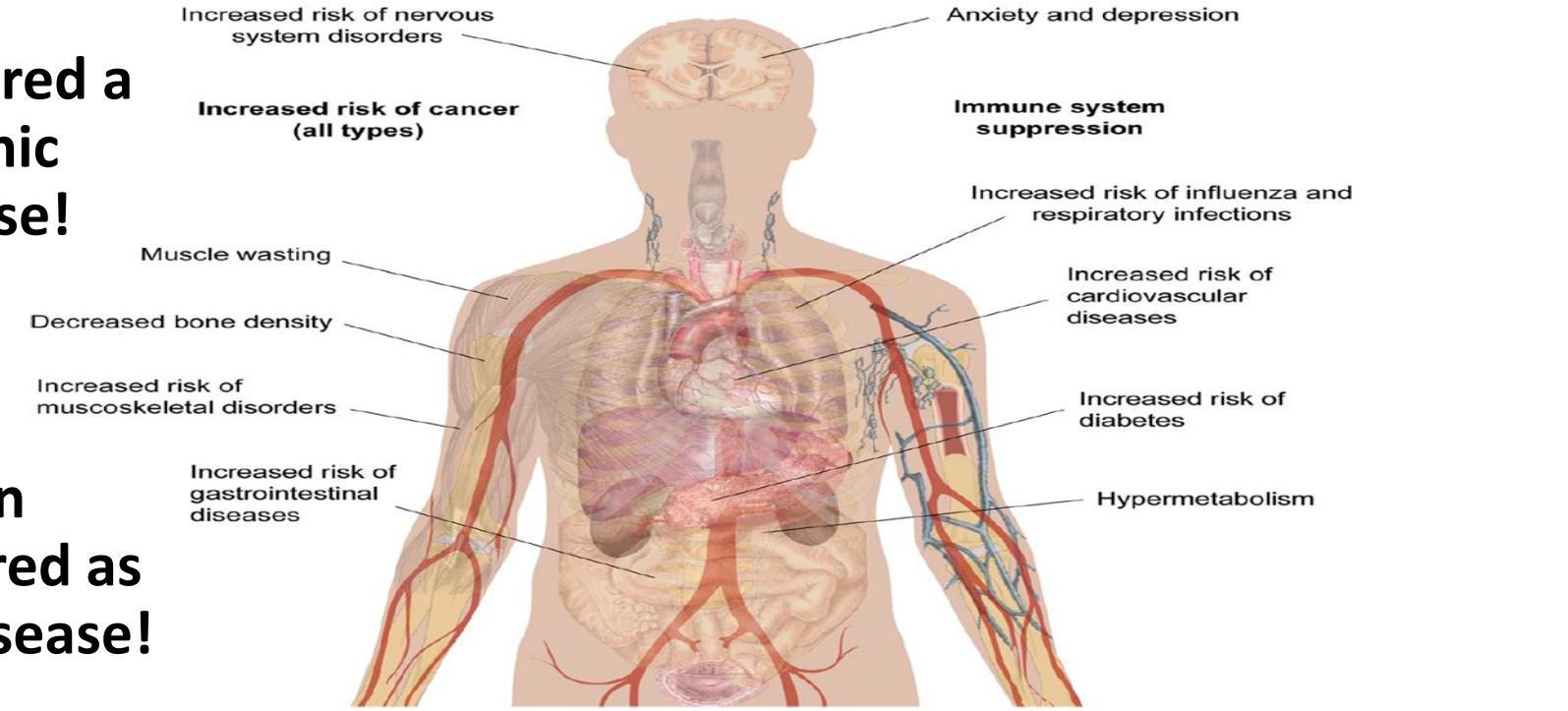
Why focus on burn injuries?

Considered a chronic disease!

Even considered as a rare disease!



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Why focus on burn injuries?

2. Economic aspects

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Currently unknown in Quebec

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Nickel KJ, Omeis T, Papp A. Demographics and clinical outcomes of adult burn patients admitted to a single provincial burn centre: A 40-year review. Burns. 2020;46(8):1958-67.

Why focus on burn injuries?

Currently unknown in Quebec

Average daily cost of $1,903 in 2021 CAD

Only for minor burns in Vancouver

2. Economic aspects

Nickel KJ, Omeis T, Papp A. Demographics and clinical outcomes of adult burn patients admitted to a single provincial burn centre: A 40-year review. Burns. 2020;46(8):1958-67.

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cost
s

2. Economic aspects

Hussain A, Dunn KW. Predicting length of stay in thermal burns: a systematic review of prognostic factors. Burns. 2013;39(7):1331-40.

How hospital costs are estimated in Quebec

3. Databases

Ministère de la Santé et des Services sociaux (MSSS). Banque de données dérivée : APR-DRG (J57) version 24.0. In: ressources. Sdlad, editor. 2017. p. 215.

How hospital costs are estimated in Quebec

Approach 1

Funding based on recurring historical budget

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How hospital costs are estimated in Quebec

Approach 1

Funding based on recurring historical budget

- ✓ **MedEcho:** Quebec hospitalization database
- ✓ **Indicator of resource use NIRRU (Quebec equivalent of the RIW)**

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NIRRU conversion to obtain costs (approach 1)

Example of a patient hospitalized in 2022-2023

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Patient has a NIRRU of 2: Patient used 2x resources of the average patient

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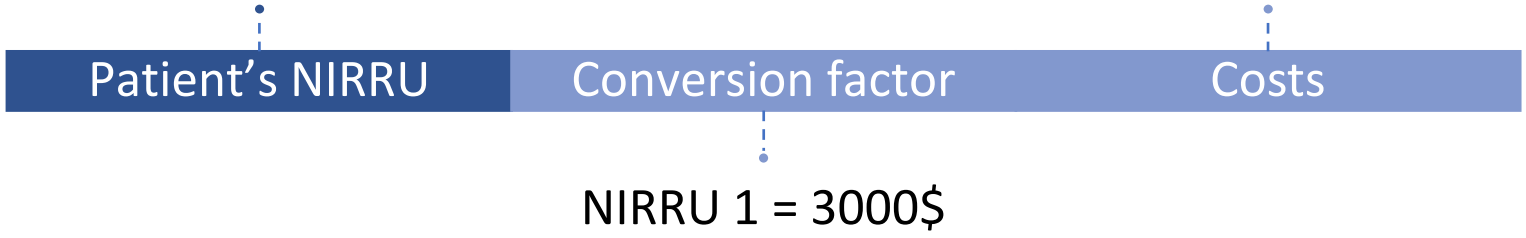

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NIRRU conversion to obtain costs (approach 1)

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Cost of patient:

2 x 3000$ = 6000$

NIRRU 1 = 3000$

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Approach 2

Activity based funding : Function of the volume of care provided

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How hospital costs are estimated in Quebec

Approach 1

Funding based on recurring historical budget

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Approach 2

Activity based funding : Function of the volume of care provided

New database: *Coût par parcours de soins et services* (**CPSS)**

- ✓ **Tends towards a micro-costing approach**

3. Databases

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Hypothesis and objective

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Hypothesis: We assume that the measurement of treatment costs for burn victims will vary depending on the method.

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Objective: Assess and compare the costs of the care provided to adult patients admitted to the major burn unit of the CHU de Québec-Université Laval according to these two approaches.

Methods

- A retrospective cohort study was undertaken using in-hospital economic data matched to hospital chart data

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- Patients admitted to the burn unit of the Hôpital de l'Enfant-Jésus between April 1st 2017 and March 31st 2021 for their **index hospitalization**

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- The costs will be obtained using **i) The NIRRU and ii) The CPSS**

Methods

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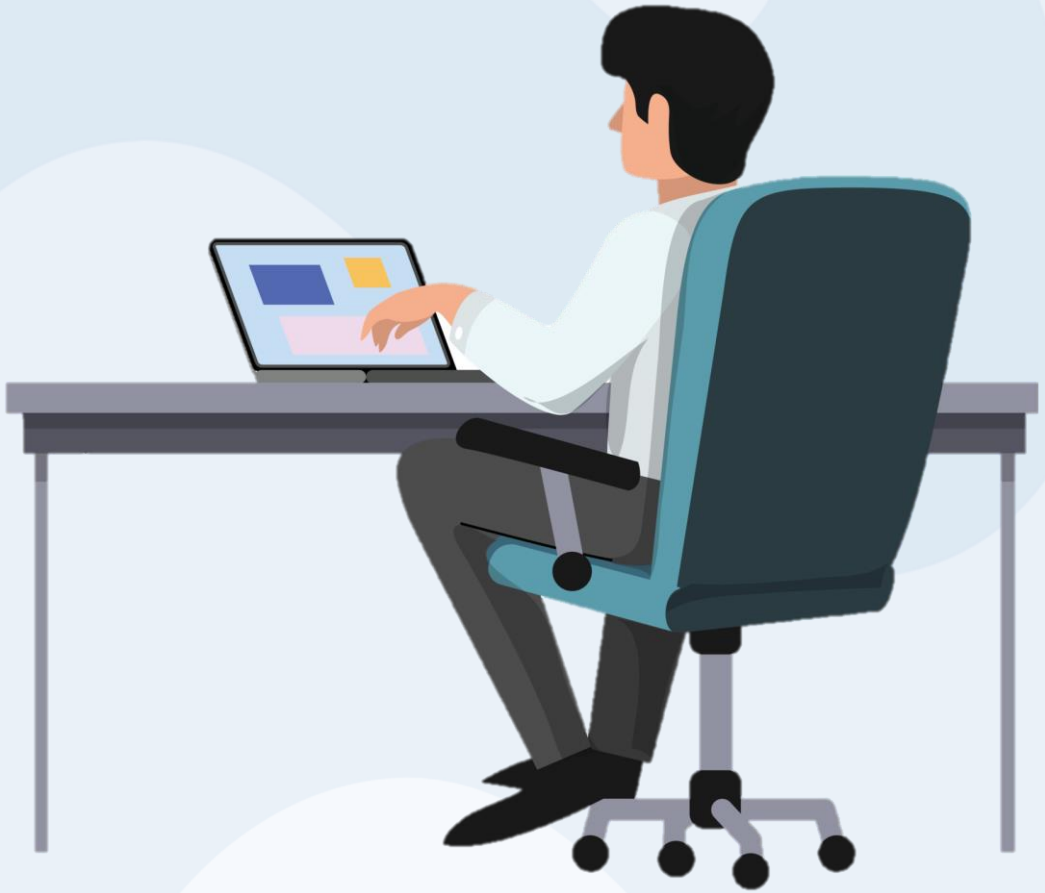
- Patients admitted to the burn unit of the Hôpital de l'Enfant-Jésus between April 1st 2017 and March 31st 2021 for their **index hospitalization**
- The costs will be obtained using **i) The NIRRU and ii) The CPSS**
- Comparison with the paired t-test



Results

Patient characteristics

Percentage of total body surface area (TBSA)	Average age*	Masculine sex+	Resides in an urban area+	Average percentage of TBSA*	Presence of inhalation burns+	Revised Baux Score *
<20% N=297	49 (19.0)	228 (76.8%)	190 (64.0%)	6.3% (4.8%)	22 (7.4%)	57% (19.3%)
≥20% N=65	54 (17.9)	49 (75.4%)	37 (57.0%)	31.2% (13.0%)	20 (30.8%)	90% (28.3%)
Total N=362	50 (18.9)	277 (76.5%)	227 (62.7%)	10.7% (11.8%)	42 (11.6%)	63% (24.7%)

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Average directs costs of the index hospitalization based on the NIRRU and CPSS approaches according to total body surface area (TBSA)

	N (%)	Average directs costs NIRRU*	Average directs costs CPSS*	Ratio of CPSS/NIRRU costs
% TBSA <20%	297 (82.0)	10,309 (9,051 – 11,568)	18,459 (16,324 – 20,595)	1.79
% TBSA ≥20%	65 (18.0)	37,774 (28,901 – 46,646)	62,554 (47,317 – 77,791)	1.67
Average cost	**362 (100)**	**15,241 (13,077 – 17,405)**	**26,377 (22,731 – 30,023)**	**1.73**

All P-values of the paired t-tests <0,001. All costs are in 2021 CAD$

*average (standard deviation)

Discussion

- Average cost of a hospitalization in Quebec between 2020-2021: 7,871$ (in Canada, 7,619$)

Your Health System. Ottawa, ON: Canadian Institute for Health Information (CIHI); 2019.

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Your Health System. Ottawa, ON: Canadian Institute for Health Information (CIHI); 2019.

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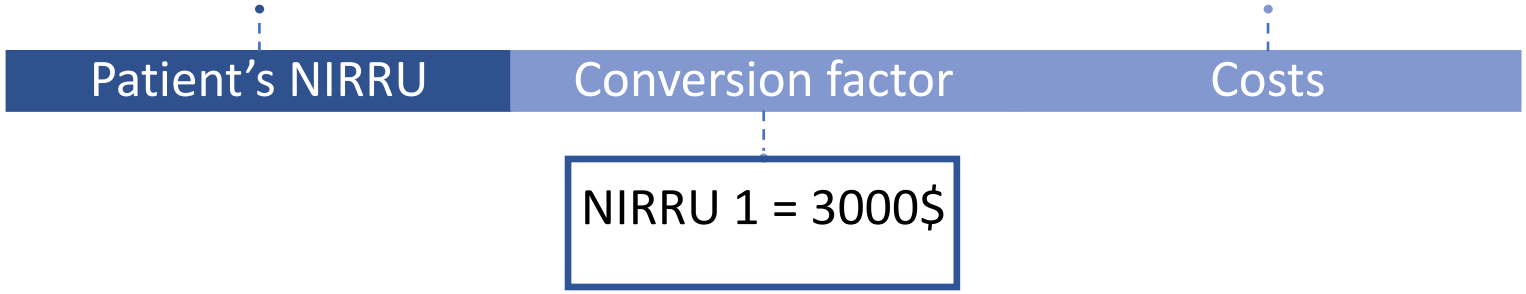
NIRRU conversion to obtain costs (approach 1)

Example of a patient hospitalized in 2022-2023

Patient has a NIRRU of 2: Patient used 2x resources of the average patient

Cost of patient:

2 x 3000$ = 6000$



Ministère de la Santé et des Services sociaux (MSSS). Banque de données dérivée : APR-DRG (J57) version 24.0. In: ressources. Sdlad, editor. 2017. p. 215.

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Information bias on the cost variable in the two approaches!

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Information bias on the cost variable in the two approaches!

Unable to determine which method is closest to the real cost

Strengths

- Contributions

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  - First comparison between these two approaches
  - Quantification of the cost of burn injuries

Key points

The use of NIRRU or CPSS to calculate the costs of treatment for burn patients in Quebec shows a **difference of $4 million for only 362 patients**

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It is **impossible to determine which method is valid** as no standardized method exists

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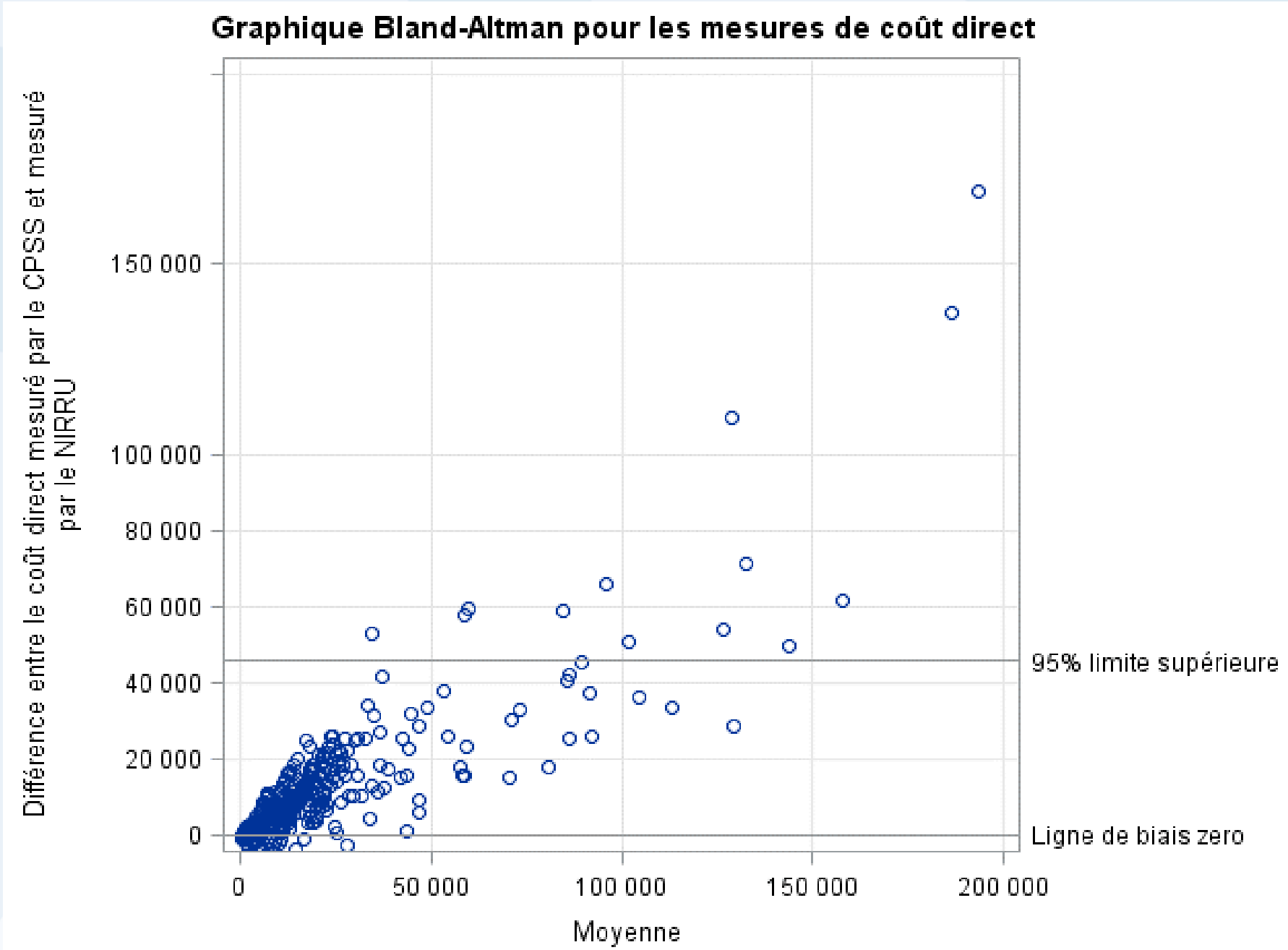
Questions?


Graphique Bland-Altman pour les mesures de coût direct
Différence entre le coût direct mesuré par le CPSS et mesuré par le NIRRU
150 000
100 000
80 000
60 000
40 000
20 000
0
95% limite supérieure
Ligne de biais zero
0
50 000
100 000
150 000
200 000
Moyenne

Extended-release prescription opioids and HCV infection in people who inject drugs: Findings from the HEPCO cohort in Montreal

Stine B Høj[1], Julie Bruneau[1,2], Geng L Zang[1], Autumn Neville[3], **Marina G Birck[3]***, Cristiano S Moura[3], Sasha Bernatsky[3]

1 Centre de recherche du Centre hospitalier de l'Université de Montréal (CRCHUM)
2 Department of Family Medicine and Emergency Medicine, Université de Montréal
3 Centre for Outcomes Research and Evaluation, The Research Institute of the McGill University Health Centre, Montreal, Canada

CAN-AIM

The **CAnadian Network for Advanced Interdisciplinary Methods for comparative effectiveness research** (CAN-AIM) is a team funded to do high-priority research projects for Health Canada and other stakeholders.

Our **mission** is to enhance Canadian research of real-world drug effectiveness and safety.

CAN-AIM was developed and funded through the Drug Safety and Effectiveness Network (DSEN), a partnership between CIHR and Health Canada. Now, we are network collaborator of CADTH's CoLab Network (PMDE – Post Market Drug Evaluation).

https://canaim.ca

CAN-AIM

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

CoLab

RISK OF HCV AMONG PWID USING OPIOIDS

- Injection of prescription opioids is associated with health-related harms among people who inject drugs (PWID), including hepatitis C virus (HCV) infection
  - HCV infection is rising
  - Injection drug use is a leading factor
- Whether risk of contracting HCV may be mediated by opioid formulation (immediate vs. extended-release) remains unclear.
- Controlled-release hydromorphone a coating which resists crushing; the resulting slurry leaves residual drug in injection equipment, which if reused/shared, allows multiple opportunities for contamination across PWID.

Meyer M et al. *J Viral Hepat*. 2020;27(8):774-780. | Silverman M et al. *Lancet Infect Dis*. 2020;20(4):487-497. | Kasper KJ et al. *PLoS ONE*. 2019;14(8). | Roy É et al. *Subst Use Misuse*. 2011;46(9):1142-1150. | Weir MA et al. CMAJ. 2019;191(4) E93-E99.

OBJECTIVE

Objective: To compare HCV incidence among PWID injecting different types of opioids in Montreal.

- Increasing prevalence of pharmaceutical opioids in the unregulated drug supply
- This study was a response to a request by Health Canada's Marketed Health Products Directorate.
- Policymakers requested real-world data to better understand the risks of different formulations of opioids for PWID.

METHODS

THE COHORT

COHORTE H·E·P·C·O
Recherche · Personnes utilisant des substances · Santé

CRCHUM
CENTRE DE RECHERCHE

HEPCO Cohort (PWID)

Epidemiological and biological data on HCV and HIV infections

Recruitment includes street-level strategies, and referrals from community services

At baseline and Q3M visits, participants complete an interviewer-administered questionnaire on socio-demographic characteristics, drug use and related behaviours, treatment and health services use. At each visit, blood samples are performed.

Our study criteria

- Adults (18+ years) who reported injecting drugs during the past 6 months (baseline or follow-up) over 2011-2020, were HCV RNA-negative at that time, and had at least 1 follow-up.

ANALYSIS

Exposure: self-reported past-month opioid injection

- Hydromorphone controlled release (CR) injection
- Other prescription opioids (except controlled-release formulations)
- Heroin
- Other drug injection (e.g. cocaine)

Outcome: testing HCV antibodies using enzyme immunoassay

Statistics

Incidence rate

HCV seroconversion, per 100 person-years

Follow-up starts from our study cohort entry definition (first injection of the drug of interest)

Risk of HCV

Multivariate time-dependent Cox regression estimated adjusted hazard ratios (aHR) for time to HCV infection

RESULTS AND DISCUSSION

COHORT CHARACTERISTICS

- 809 people contributed to 5,465 visits (710 with 1+ visits)
- 82% males (sex at birth), with a median age of 40.6y (IQR 32-48)
- 90% identified as White.

Characteristic	Baseline visit (Individual) Overall (n=809) n (%)	All visits (Visit-level analysis) No PO[2] (n=6,173) n (%)	HCR[3] (n=95) n (%)	Other PO[4] (n=1981) n (%)
History of substance use (years), median (IQR)				
Age at first injection drug use	**22 (18 – 30)**	24 (19 – 32)	21 (18 – 26)	21 (18 – 27)
Overdose history	50 (6.2)	156 (2.5)	12 (12.6)	128 (6.5)
Injection drug use				
Opioids	**400 (49.4)**	1,034 (16.8)	95 (100)	1981 (100)
Other substances	**426 (52.7)**	2,405 (39.0)	**58 (61.1)**	1,004 (51)
Syringe borrowing	**94 (11.6)**	270 (4.4)	10 (10.5)	175 (8.8)
Use of condoms with regular partners	*n=243*	*n=1593*	*n=23*	*n=478*
Always	48 (19.8)	385 (24.2)	**10 (43.5)**	110 (23.0)
Use of condoms with casual partners	*n=162*	*n=699*	*n=9*	*n=294*
Always	**75 (46.3)**	344 (49.2)	3 (33.3)	149 (50.7)

HCV INCIDENCE

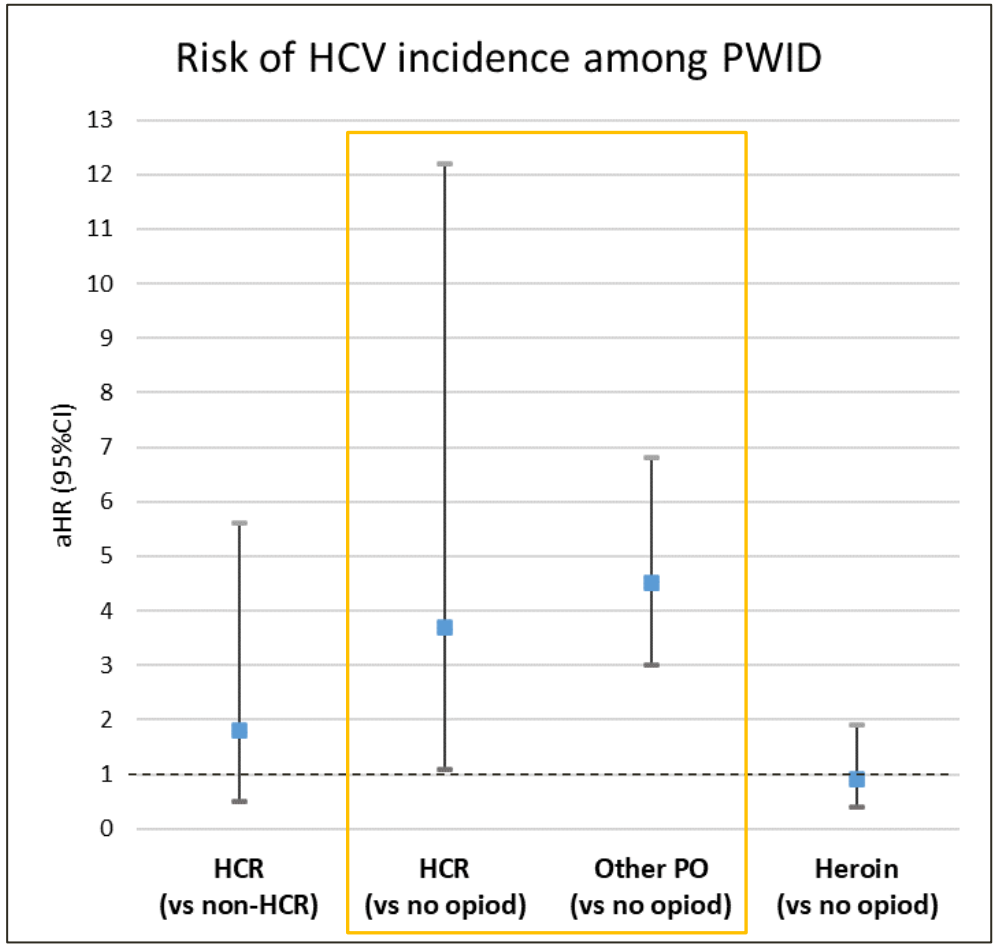
HCV incidence was **higher** with hydromorphone CR and other prescription opioid injection

The small number of hydromorphone CR users precluded precise estimations

HCV (N=580)				
Characteristic	**Mean follow-up**	**N new cases**	**Incidence per 100 person-years (95% CI)**	**HR (95%CI) unadjusted**
Type of injection				
HCR	18.4	3	**16.3 (4.1 – 44.3)**	**3.5 (1.1 – 11.2)**
Other PO	373.5	79	**21.1 (16.9 – 26.2)**	**5.1 (3.5 – 7.4)**
Heroin	268.6	9	3.3 (1.6 – 6.1)	0.9 (0.5 – 1.9)
No opioid	1200.4	43	3.6 (2.6 – 4.8)	1(ref)
Age (years)				
< 30	216.4	41	**18.9 (13.8 – 25.4)**	**2.6 (1.8 – 3.8)**
≥ 30	1644.8	93	5.6 (4.6 – 6.9)	1 (ref)
Sex at birth				
Male	1561.9	108	6.9 (5.7 – 8.3)	0.8 (0.5 – 1.3)
Female	299.3	26	8.7 (5.8 – 12.5)	1 (ref)
Calendar period				
2011-2015	999.1	90	9.0 (7.3 – 11.0)	1.0 (0.7 – 1.5)
After 2016	862.1	44	5.1 (3.8 – 6.8)	1 (ref)

HCR: Injected any controlled-release prescription opioids in the past month. **No opioid**: injected only non-opioid substances (e.g., cocaine, prevalent in Montreal) or did not inject in the past month.

RISK OF HCV INFECTION AMONG PWID



Compared with no opioid injection, risk of **HCV** infection was **elevated** among people injecting **hydromorphone CR** or **other PO** but not heroin

A precise estimation might have been precluded by the relatively small number of hydromorphone CR users and HCV infection

HCR: Injected any controlled-release prescription opioids in the past month.
No opioid: injected only non-opioid substances (e.g., cocaine, prevalent in Montreal) or did not inject in the past month.
Adjusted for: sex, age, race, calendar year, and other factors (addiction treatment access, syringe sharing, overdose, incarceration history, sex trade involvement, use of condoms)

STUDY STRENGTHS AND LIMITATIONS

Strength

- HCV identified by lab. tests, not just by billing codes or medical services
- Availability of detailed clinical and demographic, and risk factor data
- Reported drug injection is more reliable than using a proxy of drug dispensation from admin data
- Relatively frequent follow-up visits (~3m) – less likely to miss HCV cases

Limitations

- Potential self-report error
- Low frequency of HCR use and HCV infection limited precise estimation and comparison
- Loss of follow-up / censoring: frequent (vulnerable population)
- Potential residual confounders

KEY CONCLUSION

Among PWID in Montreal, **HCV risk is elevated when injecting opioids**

Opioid injection is prevalent and strongly associated with HCV infection, so it remains a **target for prevention** strategies

A trend for higher infection exists for controlled-release formulations, though we were unable to produce precise estimates in adjusted analyses

- Research efforts like this are needed to help **decision-makers minimize harm** by proposing/adjusting **strategies for PWID**.
- Continued monitoring and research is needed to understand the reasons of choosing certain types of opioid (e.g. driven by availability or preference), education regarding potential risk reduction practices, etc.

Q&A

Thank you!
Merci!
Obrigada!

Our research was conducted in Montreal, located on unceded Indigenous lands. The Kanien'kehá:ka Nation is recognized as the custodians of the lands and waters. Tiohtiá:ke/Montreal has long served as a site of meeting and exchange amongst Indigenous peoples, including the Haudenosaunee and Anishinaabeg nations. We acknowledge and thank the diverse Indigenous peoples whose presence marks this territory on which peoples of the world now gather.

This work was funded by the Drug Safety and Effectiveness Network, a collaboration between Health Canada and the Canadian Institutes of Health Research.

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UNIVERSITY OF TORONTO
LESLIE DAN FACULTY OF PHARMACY

Changes in Diclectin Utilization Trends in Ontario Following Media Attention: A Time-Series Analysis

Canadian Association for Population Therapeutics (CAPT) 2023

Shenthuraan Tharmarajah

Monday, October 23rd, 2023

What is Diclectin?

- Diclectin (doxylamine and pyridoxine combination)
- Antiemetic used to treat nausea and vomiting of pregnancy (NVP), or morning sickness
- Currently only prescription drug authorized by Health Canada

But is it actually effective?

- Clinical trial in 2009 found Diclectin users reported 0.7 reduction in NVP symptoms on 13-point scale
  - Fell short of company's threshold for proving efficacy (3)
  - Company kept findings confidential for several years

- Widely used as only prescription drug option authorized by HC
  - Prescription filled in 1 of every 2 live births in Canada

Jan 2018 media attention - bad news!

Popular morning sickness drug is not effective, new analysis finds

TORONTO STAR

> "I don't think it should be prescribed, I don't think patients should take it."

— Dr. Navindra Persaud, family doctor and researcher at St. Michael's Hospital, Toronto

Objective

To assess impact of media coverage in January 2018 on Diclectin utilization trends in Ontario and across Canada

Research Questions

- Did Diclectin utilization trends shift following negative press?
- Were there differences in Diclectin dispensation based on prescriber specialty?

Methods

- Study Design
  - Repeated cross-sectional analysis of monthly dispensing data for Diclectin between July 2016 and March 2022

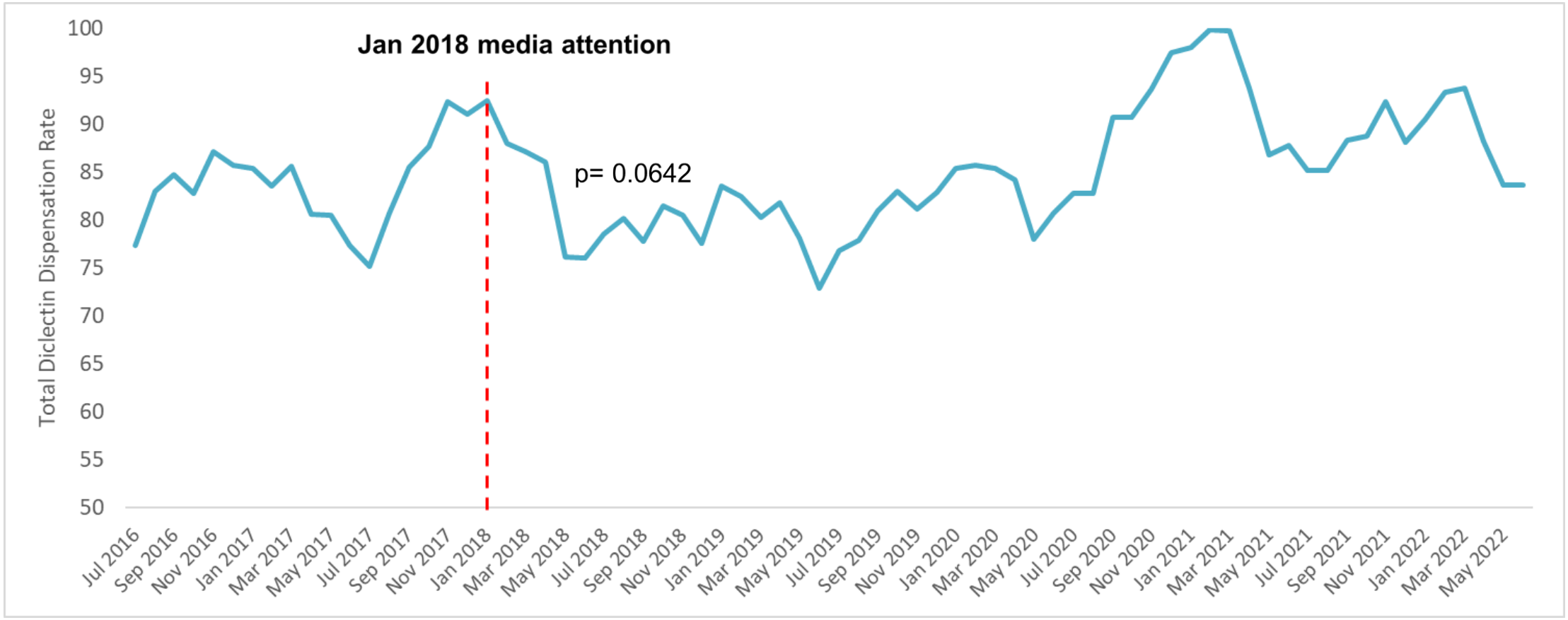
- Data Source
  - IQVIA, CompuScript data
    - Estimates prescriptions dispensed in Canadian retail pharmacies (excludes hospitals; includes new and refills)

Analysis

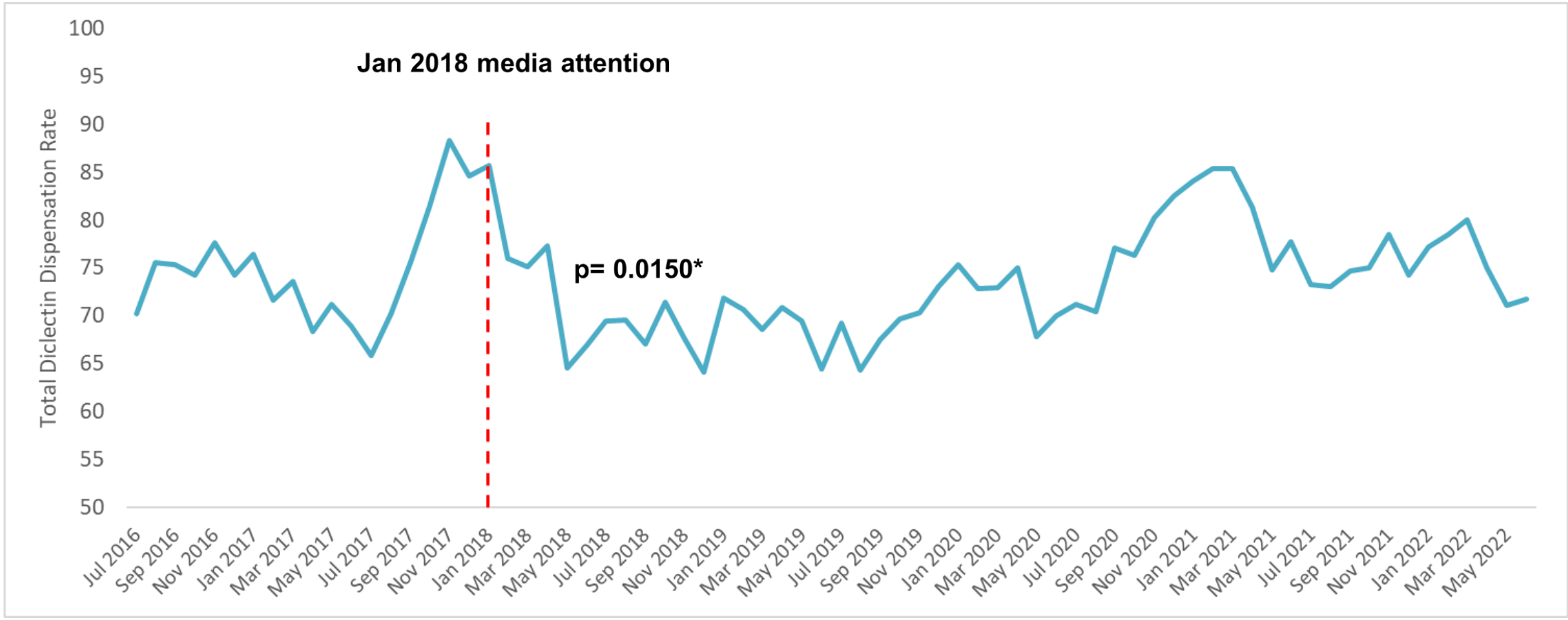
- Data Analysis
  - Trends in total volume of Diclectin dispensed by retail pharmacists in Ontario and across Canada adjusted by pregnancy rates from StatCan birth data
  - Reported:
    - Overall
    - Province
    - By prescriber specialty (family medicine and obstetrician-gynecologists)

- Statistical Analysis
  - Autoregressive integrated moving average (ARIMA) model with step functions to assess impact of January 2018 media coverage on Diclectin utilization

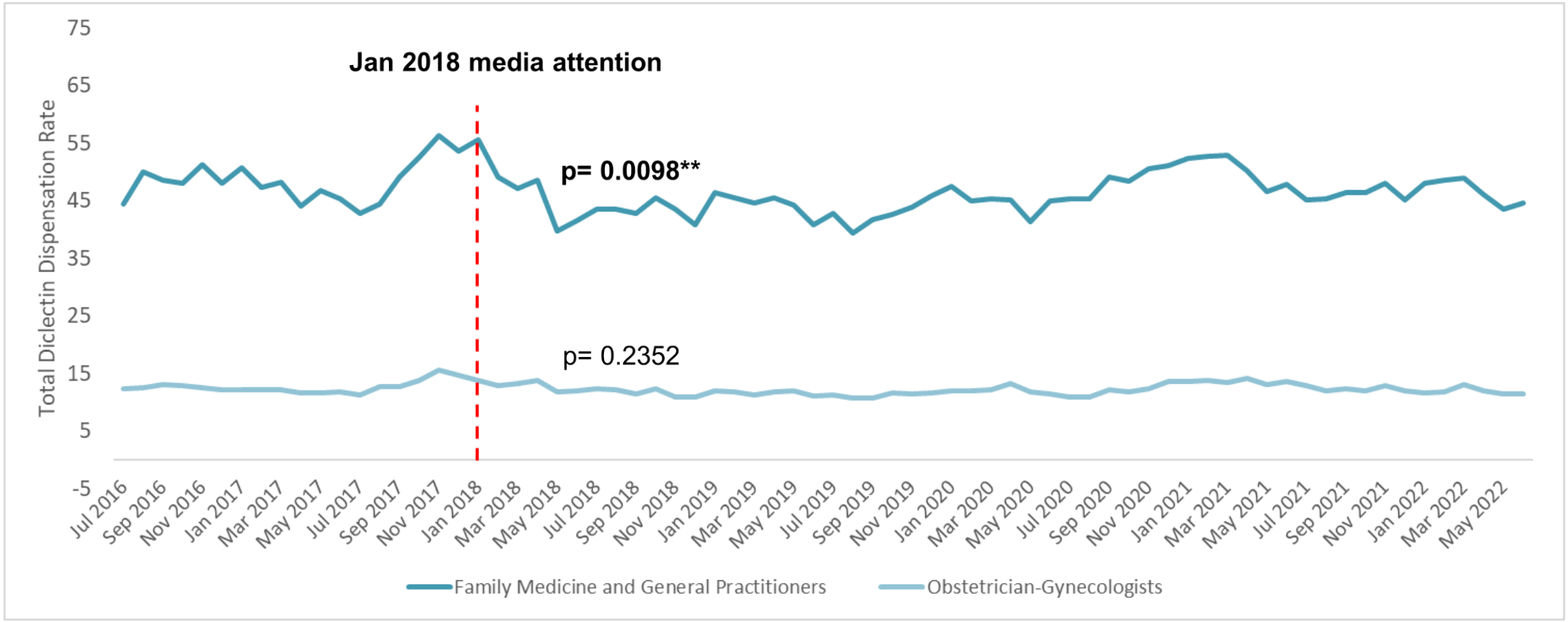
Despite media attention, no shift overall in Diclectin dispensation rates in Canada



Shift in Diclectin dispensation rates in Ontario following media attention



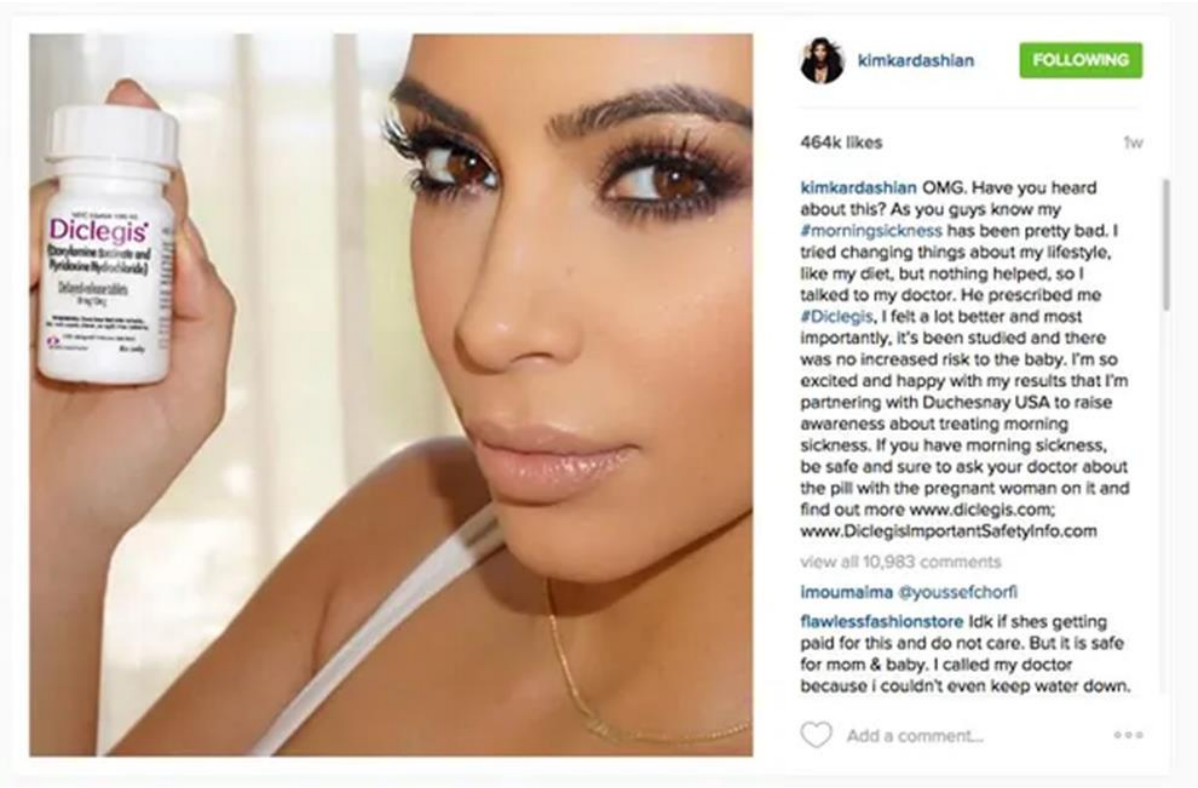
Diclectin dispensation rates in Ontario by prescriber specialty



Takeaways

- Despite national media attention, Diclectin utilization trends significantly impacted only in ON
- Within Ontario, Diclectin dispensation significantly declined among FM+GP but not among OB-GYN
- Lack of alternatives for pregnant individuals suffering from NVP

The most important takeaway…



Acknowledgments

Setayesh Yazdani

Cherry Chu

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Contact

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