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EVALUATION OF THE LONG-TERM COST-EFFECTIVENESS OF THE DEXCOM G6 CONTINUOUS GLUCOSE MONITOR VERSUS SELF MONITORING OF BLOOD GLUCOSE IN PEOPLE WITH TYPE 1 DIABETES IN CANADA

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27/10/2020

Introduction

Maintaining optimal glycemic control in people with type 1 diabetes requires intensive insulin therapy and frequent glucose monitoring

Continuous glucose monitoring (CGM) systems have advanced to real-time systems that provide multiple daily readings to smart devices with alerts and alarms when glucose is out of range

RT-CGM is associated with improved glycemic control and reduced incidence of hypoglycemic events and reduced fear of hypoglycemia (FoH) relative to self-monitoring of blood glucose (SMBG), but at higher cost

A health economic analysis was performed to determine the long-term cost-effectiveness of the Dexcom G6 system versus SMBG in adults with type 1 diabetes (T1D) in Canada

Clinical Benefits

The DIAMOND trial was utilized for the baseline cohort:

Patient Characteristics	Baseline Value
Mean (SD) age, years	47.6 (12.7)
Mean (SD) duration of diabetes, years	20.3 (13.6)
Male, %	56
Mean (SD) HbA1c, %	8.6 (0.65)
Mean (SD) HbA1c, mmol/mol	70 (7)
Mean (SD) BMI, kg/m^2	27.5 (5.5)

Treatment effects:

- A reduction in A1c of 1.0% (10 mmol/mol) was applied to the G6 arm.
- A reduction of 0.4% (4 mmol/mol) was applied to the SMBG arm.

Severe hypoglycemic events (SHE):

- 4.2 per 100 person-years in the G6 arm.
- 12.2 per 100 person-years in the SMBG arm.

Beck RW, Riddlesworth T, Ruedy K, et al.; DIAMOND Study Group. Effect of continuous glucose monitoring on glycemic control in adults with type 1 diabetes using insulin injections: the DIAMOND randomized clinical trial. JAMA 2017; 317:371–378

Quality of Life Benefit

In the DIAMOND trial fear of Hypoglycemia (FoH) was measured using the worry subscale of the Hypoglycemia Fear Survey.

- The mean difference in FoH score between the treatment arms was 3.17 units, favoring G6
- This was converted to a utility benefit of 0.02536 based on a previously published mapping of changes in the FoH to the EQ-5D by Currie et al. (2006)

Similarly, a fingerstick avoidance benefit was applied to G6 based on the findings of a study by Matza et al. (2017) comparing flash glucose monitoring with SMBG

- This was converted to a utility benefit of 0.03

Both reduction in FoH and fingerstick use resulted in a total utility benefit of 0.05536 for G6 arm in DIAMOND (0.03 + 0.02536)

Polonsky WH, Hessler D, Ruedy KJ, Beck RW; DIAMOND Study Group. The impact of continuous glucose monitoring on markers of quality of life in adults with type 1 diabetes: further findings from the DIAMOND randomized clinical trial. Diabetes Care 2017;40:736–741

Currie CJ, Morgan CL, Poole CD, Sharplin P, Lammert M, McEwan P. Multivariate models of health-related utility and the fear of hypoglycaemia in people with diabetes. Curr Med Res Opin. 2006 Aug;22(8):1523-34

Matza LS, Stewart KD, Davies EW, Hellmund R, Polonsky WH, Kerr D. Health State Utilities Associated with Glucose Monitoring Devices. Value Health. 2017 Mar;20(3):507-51

Intervention Costs

The annual cost associated with the Dexcom G6 system was CAD 3,588, which included a total of 36 sensors per year (based on a sensor lifetime of 10 days each) and four transmitters per year

Annual costs in the SMBG arm were CAD 1,226, which assumed a mean of 4.6 SMBG tests per day, based on findings from the DIAMOND trial

Direct costs associated with the treatment and management of diabetes-related complications were sourced from the literature, and where necessary inflated to 2019 CAD

Canadian Agency for Drugs and Technologies in Health. Optimal use report 2013. Optimal use recommendations for second- and third-line therapy for people with type 2 diabetes. Available at: https://www.cadth.ca/media/pdf/OP0512_Diabetes_RecsReport_2nd_3rd-line_e.pdf [Last accessed April 24, 2020]

Diabetes Canada. Paying for your glucose monitoring device November 28, 2019. Available at: https://www.diabetes.ca/managing-my-diabetes/stories/paying-for-glucose-monitoring-devices [Last accessed April 28, 2020]

Canadian Institute for Health Information. Patient cost estimator. Available at: https://www.cihi.ca/en/patient-cost-estimator [Last accessed April 24, 2020]

Economic Model

- The analysis was performed using the IQVIA CORE Diabetes Model (CDM, version 9.0 E360).
- The CDM is a published and validated computer simulation model able to project long-term clinical and economic outcomes for either type 1 or type 2 diabetes.
- Validation of the model has been previously described in detail in publications by Palmer et al. (2004), and McEwan et al (2014).
- Outputs provided by the CDM include:
  - Life expectancy and quality-adjusted life expectancy.
  - Cumulative incidence of long-term complications including cardiovascular, cerebrovascular, renal, ophthalmic and diabetic foot complications, mean time to onset of complications.
  - Direct and indirect costs and the incremental cost-effectiveness ratio (ICER).

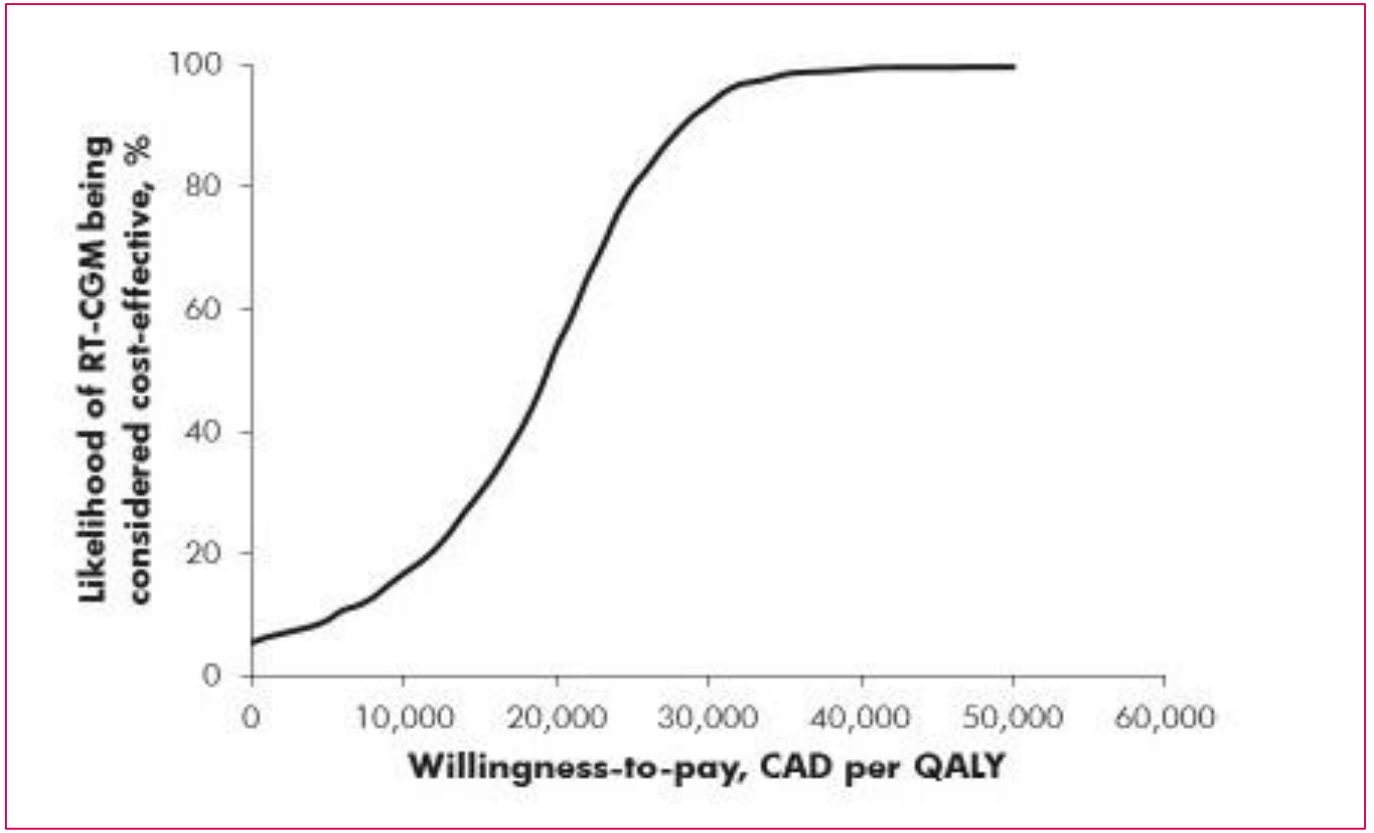
Palmer AJ, Roze S, Valentine WJ, Minshall ME, Foos V, Lurati FM, Lammert M, Spinas GA. Validation of the CORE Diabetes Model against epidemiological and clinical studies. Curr Med Res Opin. 2004 Aug;20 Suppl 1:S27-40

McEwan P, Foos V, Palmer JL, Lamotte M, Lloyd A, Grant D. Validation of the IMS CORE Diabetes Model. Value Health. 2014 Sep;17(6):714-24

Results – Base Case Analysis

Base Case Analysis	G6	SMBG	Difference
Total direct cost, CAD	227,357	192,004	35,353
Treatment costs	87,153	29,416	57,737
Management costs	9,365	9,234	131
Cardiovascular complications	15,993	16,497	−504
Renal complications	65,763	80,779	−15,016
Ulcer/amputation/neuropathy complications	13,692	14,478	−786
Ophthalmic complications	33,163	35,230	−2,067
Severe hypoglycemia	2,229	6,372	−4,143
Quality-adjusted life expectancy, QALYs	15.517	13.429	2.088
ICER, CAD per QALY gained	**16,931**		
Likelihood of cost-effective at WTP threshold of CAD 50,000 per QALY	%99.7		

Results – Willingness to Pay Threshold



Conclusions

Overall, findings of long-term cost-effectiveness analysis suggest that for adult patients with T1D in Canada, the Dexcom G6 system is cost-effective relative to SMBG.

The Dexcom G6 system improves glycemic control and reduces the risk of costly long-term diabetes-related complications, providing a cost-effective disease management option (relative to SMBG) based on a willingness-to-pay threshold of CAD 50,000 per QALY gained.

Non-Steroidal Anti-Inflammatory Drug Use Does Not Adhere To Prescribing Guidelines For Older Men Or Women With Dementia

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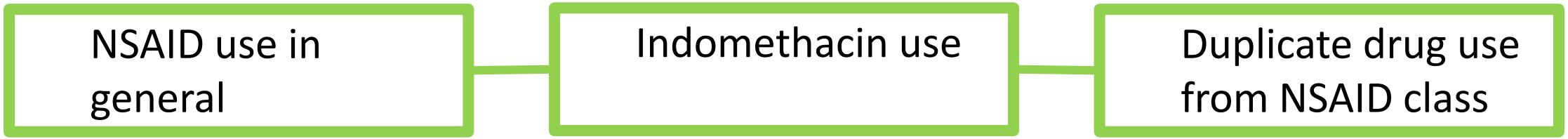
https://www.dreamstime.com/illustration/joint-older-pain-person.html

Introduction

- Pain is a potential contributor to responsive behaviours for older adults with dementia
- One option for pain treatment is non-steroidal ani-inflammatory drugs (NSAIDs)
- Best practice guidelines for prescribing in older adults recommend short-term NSAID use (less than 90 days), avoidance of indomethacin, and two or more NSAIDs should not be used at a time

Objective

- To complete a drug utilization review, with attention to prescribing guidelines, and a sex-based analysis of NSAID use in older adults with dementia in Nova Scotia, Canada.

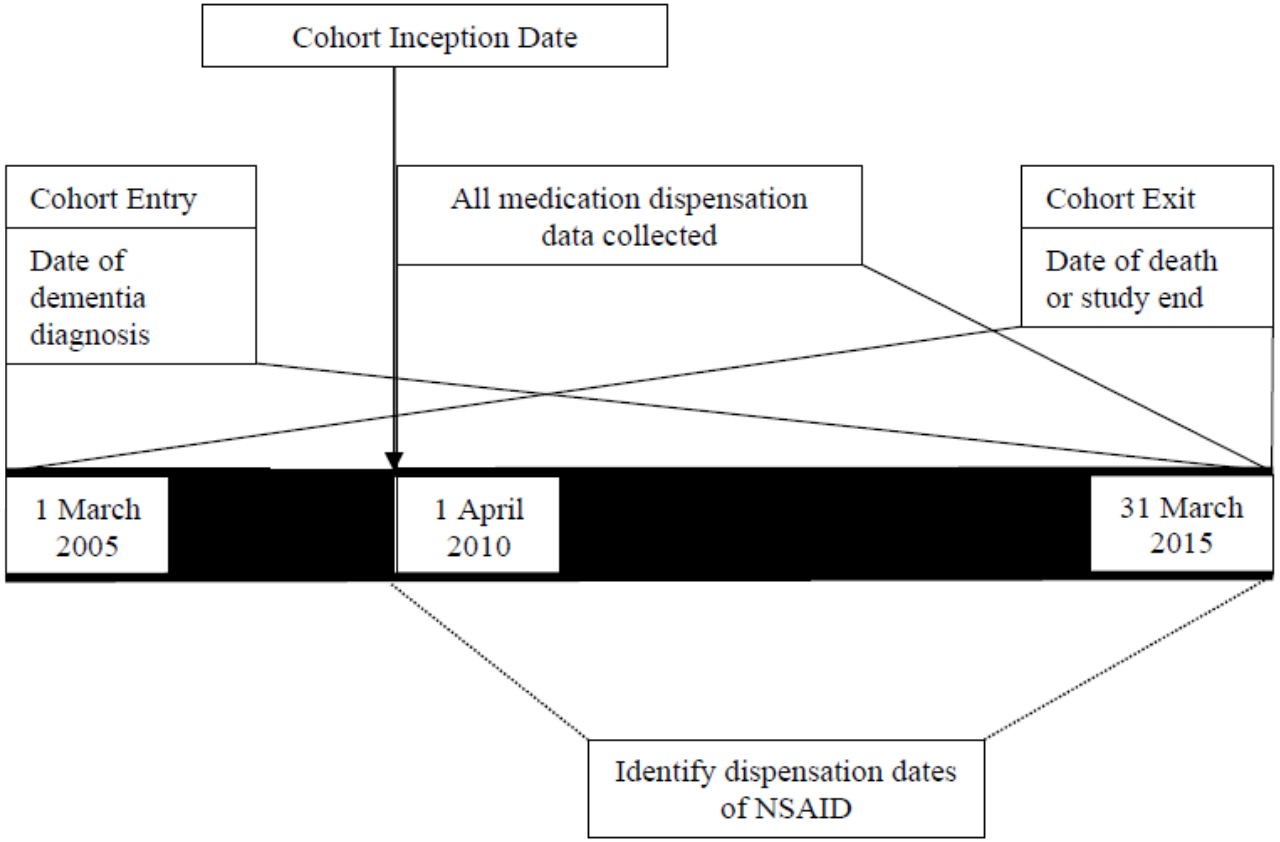


Methods

- We examined NSAID use in a cohort of adults aged 65 years and older with dementia in Nova Scotia, Canada
- Nova Scotia Seniors' Pharmacare Beneficiaries with dementia prescription data was examined from April 1, 2010 to March 31, 2015
- Concordance with prescribing guidelines was compared for men and women using descriptive statistics
- Analyses included:
  - t-tests for pairwise comparisons
  - unadjusted odds ratios for associations

Description	ICD-9	ICD-10
Alcohol-induced persisting amnestic disorder	290.x	F01.x, F05.1
Alcohol-induced persisting dementia	291.1	F10.6
Amnestic disorder in conditions classified elsewhere	291.2	F10.7
Dementia in conditions classified elsewhere	294.0	F04.x
Other cerebral degenerations ***Includes***: *Alzheimer's disease; Frontotemporal dementia; Senile degeneration of the brain; Communicating hydrocephalus; Idiopathic normal pressure hydrocephalus; Cerebral degeneration in diseases classified elsewhere; dementia with Lewy's bodies; Dementia with Parkinsonism; Cerebral degeneration, unspecified.* ***Excludes***: *Obstructive hydrocephalus; Reye's syndrome*	331.0-331.3, 331.5-331.7, 331.82, 331.83, 331.89, 331.9	G30.x, G31.0, G31.1, G31.8, G31.9, G32.8, G91.0, G91.2-G91.3, G91.8, G91.9, G94.x
Senility without mention of psychosis	797	R54.x

Cohort Identification



Detailed drug utilization of NSAID use by NSSPBD over period of 1 April 2010 to 31 March 2015

NSAID	Total NSSPBD	Men	Women
Total Rx dispensed	37,916	10,049 (26.5%)	25,244 (66.6%)
NSSPBD receiving at least one Rx	6,119 (21.1%)	1,850 (30.2%)	3,741 (61.1%)
Age at diagnosis (years (SD))	79.4 (7.7)	77.2 (7.2)	80.3 (7.8)
Age at first NSAID Rx (years (SD))	80.0 (7.6)	78.0 (6.9)	81.3 (7.7)
Duration (days (SD))	207.7 (360.4)	186.7 (334.2)	220.0 (372.4)

Results

- Duration of use was longer in women than in men (220.0 days versus 186.7 days, p=0.0006), though notably the mean duration of use for both men and women exceeded the recommendation for less than 90 days.
- NSAID use exceeding 90 days occurred in 2,170 NSSPBD (35.5% of NSAID users).

NSAID		Total NSSPBD				Men				Women			
Generic Name	ATC code	# Rx	NSSPBD receiving at least one Rx	Age at first NSAID Rx (years (SD))	Dura-tion (days (SD))	# Rx	NSSPBD receiving at least one Rx	Age at first NSAID Rx (years (SD))	Duratio n (days (SD))	# Rx	NSSPBD receiving at least one Rx	Age at first NSAI D Rx (years (SD))	Dura-tion (days (SD))
indometh-acin	M01AB01	1,404 (3.7%)	521 (8.5%)	80.0 (7.7)	53.7 (132.4)	659 (1.8%)	232 (3.8%)	78.6 (7.1)	55.0 (112.4)	582 (1.5%)	242 (4.0%)	81.8 (7.9)	51.9 (154.4)

Results

- Indomethacin was used by 521 older adults with dementia in the cohort (1.7%) with higher use in males (OR 0.46, 95% CI [0.38-0.56]).

Drug 2 \ Drug 1	indomethacin	sulindac	diclofenac	diclofenac, combinations	meloxicam	ibuprofen	naproxen	ketoprofen	tiaprofenic acid	celecoxib	Total
indomethacin			1	5	1		2			4	**13**
sulindac			1				1				**2**
diclofenac				3		3	6			2	**14**
diclofenac, combinations		1			2	4	2	1		11	**21**
piroxicam							1				**1**
meloxicam				1		1	4			1	7
ibuprofen			1	1			4	1		4	**11**
naproxen	1		1	3	4				1	11	**21**
ketoprofen									1		**1**
celecoxib			2	3	2	2	1				**10**
Total	**1**	**1**	**6**	**16**	**9**	**10**	**21**	**2**	**2**	**33**	**101**

Results

- There was concurrent use of NSAIDs in 317 NSSPBD.
- Overlap varied in duration from 1-419 days with a mean of 32.4 days.
- Limiting overlap to more than 30 days identified 101 cases of NSAID duplication with an average period of duplication of 75.6 days.
- Duplicate NSAID use showed no sex difference (OR 1.01, 95% CI [0.66-1.55]).

Discussion

- 101 NSSPBD with concurrent NSAID use of more than 30 days
- NSAID duplication was studied in Korea (S.-Y. Jung et al., n.d.; Kang et al., 2016)
  - In 59,636,222 NSAID prescriptions 13.3% involved NSAID duplication over 3 months of 2011 (Kang et al., 2016)
  - Follow-up in Korea showed NSAID duplication fall to 5.6% (S.-Y.Jung et al., n.d.) after implementation of a nationwide drug utilization monitoring program
- NSAID use was associated with frailty in a study of 12,405 community dwelling adults, aged 58-73 years in France (Martinot et al., 2018) even though frailty may increase risks of NSAID use
- Unable to report on over the counter NSAID use or aspirin use
- An educational intervention by community pharmacists for NSAID discontinuation was less costly and more effective than standard care (Sanyal et al., 2020) when considering adverse events prevented

Conclusions

- NSAID use was similar in men and women
- Duration of NSAID use was longer in women
- Indomethacin use was more common in men
- Duplicate NSAID use was similar in men and women
- Interventions to reduce NSAID use for older adults with dementia are needed

Questions?

Thank you for your attention

Acknowledgements:

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Disclaimer:

The data (or portions of the data) used in this report were were made available by Health Data Nova Scotia of Dalhousie University. Although this research is based on on data obtained from the Nova Scotia Department of of Health and Wellness, the observations and opinions opinions expressed are those of the authors and do not not represent those of either Health Data Nova Scotia or or the Department of Health and Wellness.

Examining Self-Monitoring of Blood Glucose in the Nova Scotia Public Pharmacare Program

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October 27/2020

Background

- Prevalence of type 2 diabetes (T2DM) in NS is above the Canadian average.
  - 11% in 2019
  - Projected to rise to 14% by 2029
- Complications related to T2DM are numerous
  - Ex: cardiovascular disease, vision loss, end stage renal disease
  - Cardiovascular disease is the largest contributor to direct and indirect T2DM costs
  - However, novel cardiovascular disease treatments for T2DM with no hypoglycemic risk exist and reduced cardiovascular events

Self monitoring of Blood glucose (SMBG)

- Little effectiveness in:
  - long term blood sugar control
  - Improved of quality of life
  - Patient satisfaction
  - Reduction of long term complications

- For these reasons, SMBG is controversial in patients not using medications with hypoglycemic risk

Efficacy of Test strip limits

- Recommendation from CADTH
  - Maximum 14 test strips/week for those using insulin
  - No test strips for others
- Recommendation from CDA
  - Personalized for those using insulin
  - 30/month for those using drugs with increased hypoglycemic risk
  - 15/month for those using low hypoglycemic risk drugs
- Research from Ontario and BC show cost of $100 million, and $23 million over 5 years, respectively.

Objectives

- Describe the number, and cost of blood glucose test strips dispersed by the Nova Scotia public pharmacare program between 2014-17
- Examine costs stratified by:
  - Current pharmacotherapy
  - Presence of CVD
- Estimate potential cost savings to the program in subsequent years

Methods - Population

- Publicly funded prescriptions for blood glucose test strips for 2014-17
- Data stratified by:
  - Age 65
  - Presence of CVD according to the Canadian chronic disease surveillance system

Methods - Analysis

- Average number of test strips/person/year determined
  - Overall
  - Age stratified
  - CVD stratified
- Potential cost savings over the duration of the study period were estimated, along with 5 year projections

Methods – Restriction models

- Model 1: status quo
- Model 2 (CERC)
  - No restriction for insulin users
  - 100 strips/year for non-insulin users
- Model 3 (400/200)
  - No limitation for insulin users
  - 400 strips/year for individuals using higher risk medications
  - 200 strips/year for individuals using lower risk medications

Results

- In 2016, 24,625 beneficiaries were dispensed test strips
- Total cost (drug and dispensing) of $9.7 million.
- 35.7% of test strip users were dispensed insulin
- Over 75% were 65 years of age or older.

Results

- Average number of test strips dispersed/person/year by treatment:
  - Insulin → 699.5 (SD = 8.3)
  - High hypoglycemic risk medications → 320.4 (SD = 8.9)
  - Low hypoglycemic risk medications → 299.5 (SD = 7.0)
  - No medical therapy → 242 (SD = 0.8)

Results – Quantity Limits

		None	Non - hypoglycemia inducing	Hypoglycemia inducing*	Insulin
Status Quo	Total Costs	2,093,063.40	7,803,222.97	5,028,690.48	18,072,089.79
400/200	Total Savings	363,155.40	2,592,966.97	- 1,248,533.52	
CERC model	Total Savings	1,228,109.40	5,198,094.97	3,459,384.48	

Results - CVD subgroup

		Pharmaceutical Treatment			
		None	**Non-hypoglycemia inducing**	**Hypoglycemia inducing***	**Insulin**
Status Quo	Total	773,874.57	2,951,855.19	2,079,393.96	8,982,869.45
400/200	Total savings	139,644.57	1,001,489.19	- 522,254.04	
CERC Model	Total Savings	456,759.57	1,976,672.19	1,428,981.96	

Discussion

- Overall, millions of dollars could have been saved over the study period using test strip limitations as outlined
- Over the 5 years after the study period:
  - **$10.3 million could be saved amongst patients with CVD**
  - **$26.8 million over the Diabetic population studied!**

Discussion

- The findings of this study are in line with previously conducted Canadian research
- This study demonstrates potential cost savings due to blood glucose test strip limitations to the Nova Scotia health care system and patients alike
- Savings afforded by test strip limits could be re-directed toward more cost effective therapies that reduce hospitalizations, morbidity and death in Nova Scotians living with T2DM!!

Strengths and Limitations

- Limitations
  - Only three years of data were requested, which may have had an impact on the ability to estimate trends over time and extrapolate into the future
- Strengths
  - Quantitative analysis objectively demonstrating the potential for cost savings to the NSPPP should test strip limits be enforced and with potential for savings to all Nova Scotians in health care costs beyond T2DM

Conclusion

- This study demonstrates potential cost savings to the NS public pharmacare program, without negatively impacting complications related to type 2 diabetes

References:

1. The top 10 causes of death. Available at: https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death. (Accessed: 29th January 2020)
2. Canadian Diabetes Association. Diabetes Statistics in Canada | Canadian Diabetes Association. *Can. J. Diabetes* (2017).
3. Diabetes Canada. *Diabetes in Nova Scotia*. (2018).
4. Allan, G. M., Korownyk, C. & Ivers, N. Routine self-monitoring of blood glucose. *Can. Fam. Physician* **57**, 1015 (2011).
5. Matheus, A. S. D. M. *et al.* Impact of diabetes on cardiovascular disease: An update. *International Journal of Hypertension* **2013**, (2013).
6. Cardiovascular disease and risk management: Standards of medical care in Diabetesd2018. *Diabetes Care* **41**, S86–S104 (2018).
7. Diabetes Canada | Clinical Practice Guidelines - Chapter 9: Monitoring Glycemic Control. Available at: https://guidelines.diabetes.ca/cpg/chapter9. (Accessed: 28th January 2020)
8. Diabetes Initiative Panel – Atlantic Cardiovascular Society. Available at: http://ac-society.org/wp/en/initiatives/diabetes-initiative/diabetes-initiative-panel/. (Accessed: 29th January 2020)
9. Diabetes Canada | Clinical Practice Guidelines - Chapter 13: Pharmacologic Glycemic Management of Type 2 Diabetes in Adults. Available at: http://guidelines.diabetes.ca/cpg/chapter13. (Accessed: 28th January 2020)
10. Zinman, B. *et al.* Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. *N. Engl. J. Med.* **373**, 2117–2128 (2015).
11. Marso, S. P. *et al.* Liraglutide and cardiovascular outcomes in type 2 diabetes. *N. Engl. J. Med.* **375**, 311–322 (2016).
12. O'Kane, M. J. & Pickup, J. Self-monitoring of blood glucose in diabetes: Is it worth it? *Annals of Clinical Biochemistry* **46**, 273–282 (2009).
13. Clar, C., Barnard, K., Cummins, E., Royle, P. & Waugh, N. Self-monitoring of blood glucose in type 2 diabetes: Systematic review. *Health Technol. Assess. (Rockv).* **14**, 1–140 (2010).
14. Systematic Review of Use of Blood Glucose Test Strips for the Management of Diabetes Mellitus. *CADTH Technol. Overv.* **1**, (2010).
15. Malanda, U. L. *et al.* Self-monitoring of blood glucose in patients with type 2 diabetes mellitus who are not using insulin. *Cochrane Database Syst. Rev.* (2012). doi:10.1002/14651858.CD005060.pub3
16. Gomes, T. *et al.* Association of a blood glucose test strip quantity-limit policy with patient outcomes: A population-based study. *JAMA Intern. Med.* **177**, 61–66 (2017).
17. Xu, Y., Tan, D. H. Y. & Lee, J. Y. C. Evaluating the impact of self-monitoring of blood glucose frequencies on glucose control in patients with type 2 diabetes who do not use insulin: A systematic review and meta-analysis. *International Journal of Clinical Practice* **73**, (2019).
18. Cameron, C., Coyle, D., Ur, E. & Klarenbach, S. Cost-effectiveness of self-monitoring of blood glucose in patients with type 2 diabetes mellitus managed without insulin. *CMAJ* **182**, 28–34 (2010).
19. Ontario Drug Policy Research Network. *Blood Glucose Test Strip Quantity Limits Across Canada*. (2012).
20. Wu, J. H. Y. *et al.* Effects of sodium-glucose cotransporter-2 inhibitors on cardiovascular events, death, and major safety outcomes in adults with type 2 diabetes: A systematic review and meta-analysis. *Lancet Diabetes Endocrinol.* **4**, 411–419 (2016).
21. Verma, S., Jüni, P. & Mazer, C. D. Pump, pipes, and filter: do SGLT2 inhibitors cover it all? *The Lancet* **393**, 3–5 (2019).
22. McMurray, J. J. V. *et al.* Dapagliflozin in patients with heart failure and reduced ejection fraction. *N. Engl. J. Med.* **381**, 1995–2008 (2019).
23. *COMPUS Cost-Effectiveness of Blood Glucose Test Strips in the Management of Adult Patients with Diabetes Mellitus À l'appui des décisions éclairées*. (2009).
24. Information for Nova Scotians | novascotia.ca. Available at: https://novascotia.ca/dhw/pharmacare/nova-scotians.asp. (Accessed: 30th January 2020)
25. Public Health Infobase: Canadian Chronic Disease Surveillance System (CCDSS), PHAC. Available at: https://health-infobase.canada.ca/ccdss/data-tool/. (Accessed: 30th January 2020)
26. Knowles, S. R. *et al.* Self-Monitoring of Blood Glucose: Impact of Quantity Limits in Public Drug Formularies on Provincial Costs Across Canada. *Can. J. Diabetes* **41**, 138–142 (2017).

Persistence in Rheumatoid Arthritis Patients on Biosimilar and Bio-Originator Etanercept: A Pooled Analysis of Pan-Canadian Cohorts

CRISTIANO S MOURA

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I have no conflict of interest to disclose with respect to this presentation.

Introduction

- Biosimilars hold the potential to improve access to needed therapies at a reduced cost, theoretically enabling savings to be reallocated to other needs.
- Uptake of biosimilars in North America has been slow
  - Particularly true for products used in the treatment of autoimmune conditions, such as inflammatory arthritis (IA) and inflammatory bowel diseases (IBD)[1].
  - In 2017, only 4.0% of all infliximab sold in Canada was biosimilar; the equivalent number was 3.1% for biosimilar etanercept[2].
- Biosimilar etanercept (ETA-B) was recently introduced in Canada (2016) but real-world data descriptions of drug persistence (and comparisons with the originator product, ETA-O) are scarce.
  - Real-world data comparing biosimilars vs. equivalent bio-originator is needed.

[1]Sarpatwari A *et al.* 2020; Mansel K *et al.*, 2019
[2]PMPRB, 2019

Objective

To describe the recent use of etanercept biosimilar and to compare therapy persistence with its originator biologic medication in patients with rheumatoid arthritis (RA).

Our hypothesis is that therapy persistence is similar between the two medications.

Methods

- Data from four ongoing, prospective cohorts in Canada:
  - Canadian Early Arthritis Cohort (CATCH);
  - Rheumatoid Arthritis Pharmacovigilance Program and Outcomes Research in Therapeutics (RAPPORT);
  - Early Undifferentiated Polyarthritis (EUPA) cohort;
  - RHUMADATA® registry.
- Biologic-naïve and biologic-experienced RA adults initiating ETA-B or ETA-O between Jan. 2015 and Oct. 2019.
  - Switchers from ETA-O to ETA-B (or vice-versa) were included.
    - Those switching products could contribute person-time to new exposure category

Methods

- Outcomes: Persistence on therapy in the first 12 or 24 months, measured as time from therapy initiation (time zero) to discontinuation.

- Multivariable Cox regression models with each cohort dataset separately, following a common protocol.
  - Model variables included age, sex, comorbidity, past biologic use, and disease duration.

  - After testing for between-study heterogeneity, cohort-estimated hazard ratios (HR) were pooled using random effects meta-analysis.

Results

- We identified 262 episodes of etanercept use (118 ETA-B and 144 ETA-O) from 250 RA patients.
- Sex distribution and age were similar in all cohorts.
- We observed considerable variations in other aspects
  - RA duration at the time of etanercept initiation: 2.1±2.5 years for ETA-B in the EUPA cohort and 11.6±11.7 years in RHUMADATA and 2.7±2.6 years for ETA-O in CATCH and 11.6±15 years in RAPPORT.
  - Use of medications prior to etanercept: use of other biologic agents was as high as 68% in CATCH ETA-B users while 79% of ETA-O users in EUPA were previously exposed to oral corticosteroids.

Results

- Fig. 1: At 12 months, adjusted HR 0.82 (95% CI 0.42-1.60)
- Fig 2: at 24 months, adjusted HR 0.51 (95% CI, CI: 0.26-0.98)

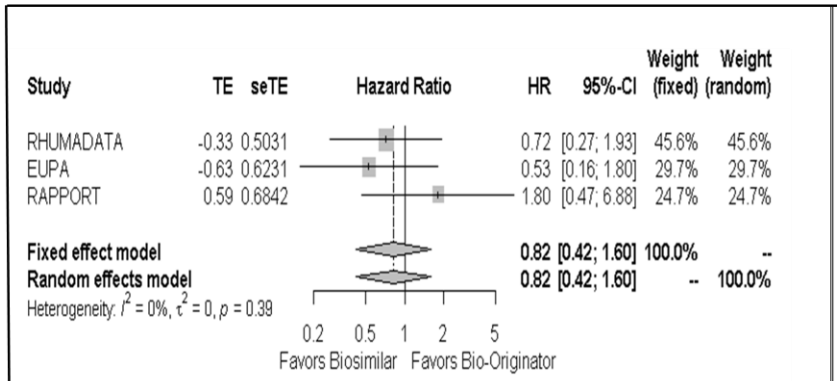

Figure 1 - Pooled adjusted Hazard Ratio [95% confidence interval (CI)] of discontinuation at 12 months for biosimilar versus bio-originator adjusted by sex, age, comorbidity, past biologic use, and disease duration.

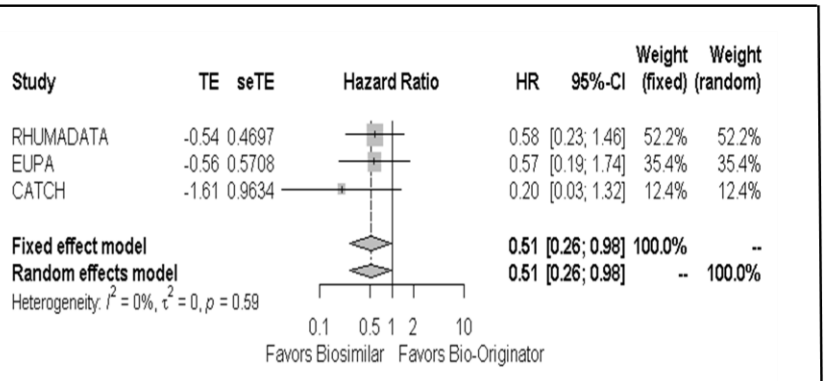

Figure 2 - Pooled adjusted Hazard Ratio [95% confidence interval (CI)] of discontinuation at 24 months for biosimilar versus bio-originator adjusted by sex, age, comorbidity, past biologic use, and disease duration.

Conclusions

- In pooled analyses, the adjusted HR point estimates for therapy discontinuation comparing ETA-B to ETA-O suggested less discontinuation with ETA-B versus ETA-O.
- Given the wide confidence intervals around our estimates, we were unable to establish clear differences in persistence with ETA-B versus ETA-O.
- We must also acknowledge that some of the observed associations may be related to residual confounding
  - E.g. disease activity, time-dependent effects of concomitant drugs) and/or survivorship bias (in patients transitioning from ETA-O to ETA-B).
- Still, our study hints that in the real world, bio-originators may indeed be associated with similar or even better drug persistence.

Participating cohorts

CATCH

INSTITUT de RHUMATOLOGIE de MONTRÉAL

EUPA
Early Undifferentiated Polyarthritis cohort

RAPPORT
Rheumatoid Arthritis Pharmacovigilance Program and Outcomes Research in Therapeutics

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CAN-AIM

CIHR IRSC
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Thank you

Mental health in the workplace

Economic costs of productivity losses due to presenteeism and sickness absence in Canadian workers having psychological distress

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CAPT, October 27th, 2020

Outline

1. CONTEXT AND OBJECTIVE

2. METHODS

3. RESULTS

4. DISCUSSION

5. CONCLUSION

Context

Mental health problems

- Largest contributor to global disability worldwide (1)
- Productivity losses are responsible for most of the total economic burden attributable to mental health problems
  - 54% of the total economic burden of depression in the US (2), 64% in Europe (3) and 86 to 98% in Japan (2, 4-6)

Ref.

1. WHO, Global Health Estimates, 2017
2. Johnston, 2009
3. Sobocki et al., 2006
4. Chang et al., 2012
5. Okumura et al., 2011
6. Sado et al., 2013

Productivity losses

- Sickness absence from work
- Presenteeism
  - Attending work but performing sub-optimally due to poor health or ill-being

Costs of productivity losses

- Sickness absence from work: well-documented

- Presenteeism: often omitted
  - Tend to cost more than sickness absence (7). Major underestimation of total costs of productivity losses.

Ref.

7. Kigozi et al., 2017

Costs of presenteeism associated with mental health problems

- ‘High’ and ‘increasing’
- 10 times higher than the costs of absenteeism, based on projections from eight countries in 2016

Costs of presenteeism associated with mental health problems (2)

Contributions are still needed. **There is a need to evaluate these costs:**

1. **In Canada**
   - A single study. Mean annual presenteeism cost per employee of $4,270(USD). High-risk for selection bias (10% participation at baseline).
2. **In 'older' workers (≥45 years-old)**
   - More frequently in vulnerable working situations. Widespread negative age stereotypes such as being less productive.
     - Potential pressure to perform leading to presenteeism.
3. **For early symptoms of MHP**
   - 1 in 4 workers in OECD countries. Strongly associated with the incidence of future depression.
     - Costs: pivotal role in convincing managers and stakeholders of the importance of developing prevention strategies targeting early symptoms.

Objective

To evaluate the average 12-month costs of presenteeism and sickness absences due to psychological distress (PD) among 1,472 female and male white-collar workers aged 45 years and older in Quebec City, Canada

Methods

Design and population

- Cross-sectional study part of the larger ‘Prospective Quebec study on Work and Health’ (8)
- Sample of 1,436 workers (50% women)
- White-collar occupations
- Mean age: 56 years-old

Ref.

8. Trudel X, Gilbert-Ouimet M *et al.*, 2018.

Main variables

Self assessed using validated questionnaires:

- **Psychological distress**
  - *Kessler-6*; 6 questions about depressive and anxiety symptoms in the past month
- **Presenteeism and sickness absence**
  - *Work Productivity and Activity Impairment*; 5 questions about workers' productivity in the past month

Main variables (2)

Mean annual costs of production losses estimated:

- using the human capital approach
- by multiplying the mean annual number of hours of presenteeism or sickness absence by the mean hourly gross wage (Statistics Canada)

Analyses

Generalized linear models to examine the mean annual a) number of hours lost and b) costs of production losses per worker, across mental health statuses

Results

Table 1. Mean annual hours of work lost to presenteeism and sickness absence and related mean annual costs per worker for women and men with and without psychological distress

	WOMEN		MEN	
	No psychological distress	**With psychological distress**	**No psychological distress**	**With psychological distress**
Presenteeism				
Mean annual hours ± SD	150.4 (12.1)	304.4 (21.2)	79.3 (7.9)	312.3 (19.1)
Mean annual cost ± SD	3840.7 (309.1)	7797.1 (541.9)	2366.2 (234)	9305 (569.6)
Sickness absence				
Mean annual hours ± SD	49.6 (9.9)	109.3 (17.1)	38.5 (8.7)	97.4 (20.8)
Mean annual cost ± SD	1272 (254)	2787.4 (440.7)	1144.9 (257.9)	2913.1 (620.9)

Key messages

Average cost of **presenteeism** per worker :

- 3,353$ and 6,66$ higher among women and men having psychological distress, respectively, compared to those without distress

Average cost of **sickness absences** per worker:

- 1,082$ and 1,787$ higher among women and men having psychological distress, respectively, compared to those without distress

Discussion

In brief

Workers with psychological distress : increased number of hours lost to presenteeism and sickness absence compared to workers without distress

Presenteeism : 2.5- to 3.5-fold the costs of sickness absence

Annual cost of presenteeism in men with psychological distress : almost 4000C$ higher than among women with psychological distress

Comparison with previous studies

Consistent with:

- Presenteeism tend to cost more than sickness absence (7)
- Mean annual presenteeism cost per employee with depression estimated at $4,270(USD) in Canada
  - A more severe outcome expected to lead to higher costs
- Men with depression are more stigmatized, less likely to consult a physician and, in turn, less likely to take a leave of absence
  - More presenteeism expected in men – higher costs

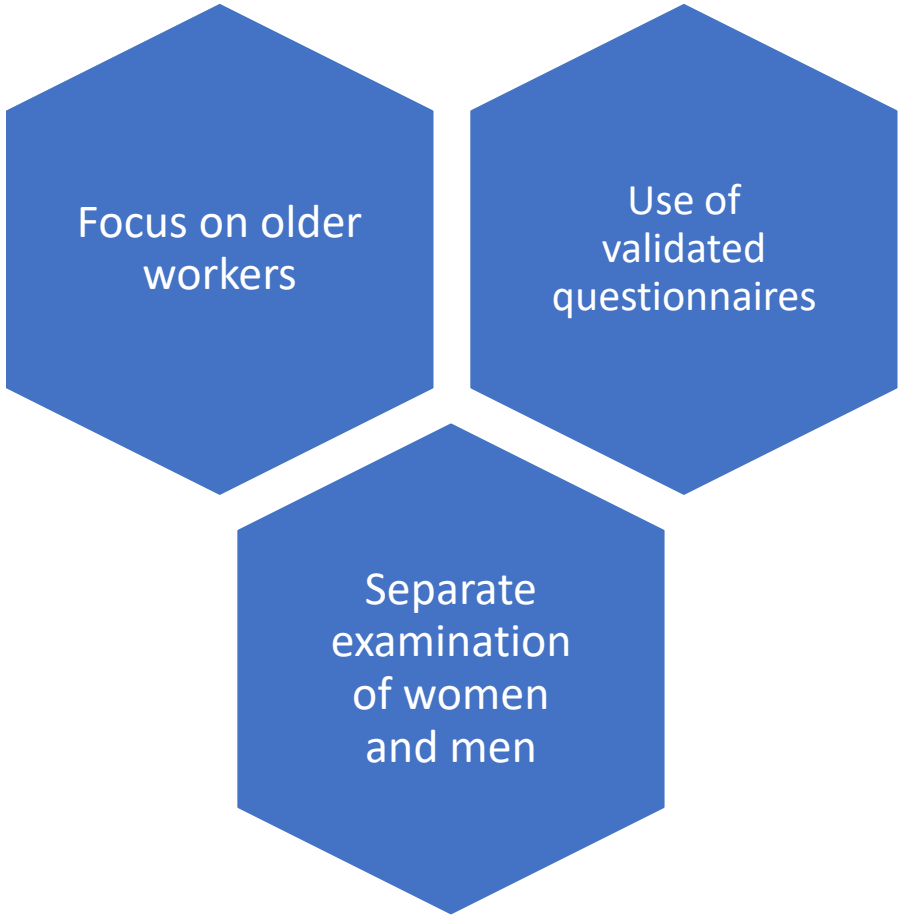
Ref.

7. Kigozi et al., 2017

Limitations

- Cross-sectional design
- Self-reported sickness absence limited to 4 weeks (potential underestimation)
- Sample limited to white-collar workers

Strenghts


Focus on older workers
Use of validated questionnaires
Separate examination of women and men

Conclusion

Primary prevention strategies aiming to reduce psychological distress might contribute to lower the economic burden associated with presenteeism and sickness absences in the Canadian aging workforce

What's next

Our team will examine the costs of depression, cardiovascular diseases and type 2 diabetes attributable to job stress over a 24-year period from a societal perspective

- Direct costs:
  - Physician fees: inpatient and outpatient physician visits (general practitioners and specialists)
  - Hospitalizations costs (inpatient)
  - Emergency visits costs
  - Medication costs (outpatient)
- Indirect costs:
  - Presenteeism
  - Sickness absence
  - Premature retirement and death

References

1. Organization WH. Depression and other common mental health disorders. Global Health Estimates. Geneva. 2017;Licence: CC BY-NC-SA 3.0 IGO.

2. Johnston K, Westerfield W, Momin S, Phillippi R, Naidoo A. The direct and indirect costs of employee depression, anxiety, and emotional disorders--an employer case study. Journal of occupational and environmental medicine. 2009;51(5):564-77.

3. Sobocki P, Jonsson B, Angst J, Rehnberg C. Cost of depression in Europe. J Ment Health Policy Econ. 2006;9(2):87-98.

4. Chang SM, Hong JP, Cho MJ. Economic burden of depression in South Korea. Social psychiatry and psychiatric epidemiology. 2012;47(5):683-9.

5. Okumura Y, Higuchi T. Cost of depression among adults in Japan. The primary care companion for CNS disorders. 2011;13(3).

6. Sado M, Takechi S, Inagaki A, Fujisawa D, Koreki A, Mimura M, et al. Cost of anxiety disorders in Japan in 2008: a prevalence-based approach. BMC psychiatry. 2013;13:338.

7. Kigozi J, Jowett S, Lewis M, Barton P, Coast J. The Estimation and Inclusion of Presenteeism Costs in Applied Economic Evaluation: A Systematic Review. Value Health. 2017;20(3):496-506.

8. Trudel X, Gilbert-Ouimet M et al. Cohort Profile: The PROspective Quebec (PROQ) Study on Work and Health. Int J Epidemiol. 2018.