The Economic Burden of CLL in Canada Associated with the Adoption of Oral Targeted Therapy.

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Disclaimer

- Jean Lachaine and Catherine Beauchemin are partners at PeriPharm, a company that has served as a consultant to AbbVie and has received funding from AbbVie.
- Jean Lachaine, Catherine Beauchemin, Kimberly Guinan, and Philippe Thebault, from PeriPharm, have participated in the study conduct, data interpretation and the approval of the abstract.
- Dr. Andrew Aw has received honoraria into a separate account within the Ottawa Hospital Research Institute, for research/academic use only. Dr. Versha Banerji has received research funding from CIHR, CancerCare Manitoba, Research Manitoba, Janssen and Abbvie and has served as a consultant to Abbvie, Janssen AstraZeneca, Gilead, Roche, and Lundbeck. Dr. Isabelle Fleury has provided advisory consultations for Abbvie, AstraZeneca, BMS, Gilead, Janssen, Merck, Novartis, Roche and Seattle Genetics and has given presentations for Abbvie, Janssen, Novartis, Roche. Dr. Carolyn Owen has received honoraria from Abbvie, Janssen, Roche, Gilead, Merck, AstraZeneca, and Teva.
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Introduction

- For a number of CLL patients, watchful waiting may be an appropriate treatment approach.
- Until recently, chemoimmunotherapy (CIT) regimens were the standard first-line treatments for patients with CLL.
- In 2015, Health Canada approved two oral targeted therapies (OTT):
 Ibrutinib for relapsed/refractory CLL patients with del (17p)
 - o Idelalisib in combination with rituximab for patients with relapse/refractory CLL.
- The higher cost of OTT in comparison to CIT treatments suggests a significant impact on the budget of public and private payers, and on patient co-payments

Objective

• The objective of this study was to predict the future direct costs, as well as the number of CLL treated patients in the era of OTT in Canada.

- The economic burden of OTT compared to CIT for treating patients with CLL was assessed from 2011 to 2025.
- Intervention & comparator
 - <u>CIT Scenario</u>: CIT remained the standard of care over time
 - <u>OTT Scenario</u>: CIT was considered the standard of care before 2015, while OTT was considered for fludarabine ineligible CLL patients and those with a 17-p deletion starting in 2015.

• Population:

- Patients were stratified according to age, phase of CLL treatment ((WW), firstline or relapse), fitness level as well as mutation status.
- The study population in 2011 was defined based on incident cases from 2000 to 2010.

• **Model Structure:** A Markov model was developed including four health states: watchful waiting, first-line treatment, relapse and death.



- Costs: costs of therapy, follow-up/monitoring and adverse event management were included.
- Perspective: public healthcare perspective
- Time Horizon: 15 years (2011-2025)
- Clinical Effectiveness:
 - Health-state transition probabilities were estimated based on PFS and OS from pivotal clinical trials and Canadian all-cause mortality rates.
 - The trials were selected based on the best evidence available for the most widely used treatment regimens in clinical practice, referring to product monographs, clinical guidelines as well as key opinion leaders.

Patients living with CLL will increase over time



- The number of patients living with CLL will increase with time and will increase further with improved treatment options especially the ability to treat chemo ineligible and 17p deletion patients
- OTT scenario: CLL patients treated projected to increase from 8,301 in 2011 to 14,654 by 2025 (77% increase).
- CIT scenario: the number of CLL patients treated would increase from 8,248 to 12,521 (52% increase), by 2025.

*Excluding watchful waiting patients



- **OTT scenario:** total annual costs of CLL management will increase from Can\$60.8 million to Can\$957.5 million from 2011 to 2025, respectively (15.7-fold increase).
- **CIT scenario:** would also increase, but less drastically, reaching Can\$107.6 million (1.76-fold increase) in 2025. When comparing both scenarios, OTT would result in additional expenditures of Can\$3.6 billion, from 2014 to 2025.

Conclusions

- The projected significant cost increase from 2011 to 2025 are explained by:
 - Increased number of CLL patients eligible for therapy
 - Increased survival of CLL patients due to more effective therapy
 - Increased treatment costs per patients
- Changes in clinical strategies, such as implementation of a fixed OTT treatment duration, would help alleviate financial burden.

Impact of patient-targeted financial incentives on healthcare costs: A systematic review of randomized controlled trials

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Disclosure

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No funding was received for this study.

Background

- In this era of rising healthcare costs, there is a growing interest in understanding how health insurance policies can be used to support effective, efficient, affordable and accessible care.
- The costs borne by individuals may affect what services they will seek out or use.

Background

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- The costs borne by individuals may affect what services they will seek out or use.

We do not have a comprehensive understanding of the research that has been conducted on patient-targeted financial incentives in a randomized experimental environment.

Objective

• To describe the evidence landscape on the use of patienttargeted financial incentives in randomized controlled trials (RCTs).

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• To describe the evidence landscape on the use of patienttargeted financial incentives in randomized controlled trials (RCTs).

Today I will present preliminary findings regarding the impact of patient-targeted financial incentives on healthcare costs.

- Systematic review conducted according to PRISMA guidelines.
- Searched electronic databases, clinical trial registries, and websites of health economic organisations to identify RCTs in which a <u>patient-</u> <u>targeted financial incentive was provided within a healthcare system.</u>
- Two reviewers independently reviewed titles, abstracts and full texts to assess study eligibility.
- Data was abstracted using a piloted form.

Methods Data extraction form

Trial characteristics

- First author
- Year
- Country
- Jurisdiction
- Context (rural, urban, mixed)
- Population of interest
- Randomization procedure
- Unit of randomization
- Type and magnitude of intervention
- Type and magnitude of comparator
- Time horizon
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Outcome characteristics

- Outcome
- Definition
- Analysis approach
- Time point of analysis
- Measure of outcome
- Result
- P-value
- 95% confidence interval

Results



Results



25 records with outcome data that was categorized as a healthcare cost

Results Costs to Payers

- 17 records that measured costs from the perspective of healthcare payers.
 - 10 (58.8%) found no difference and 4 (23.5%) an increase in total healthcare costs.
 - 9 articles (52.9%) found an increase in costs associated with the intervention when evaluating specific cost components.

Results Costs to Patients

- 10 records that measured the costs to patients.
 - 6 (60.0%) found a significant decrease and 4 (40.0%) no difference in out-of-pocket costs.

Thank you

Michael Zoratti Andrew Irwin Zhou Ting Nora Chen Feng Xie

Questions?

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EARLY HIV TREATMENT AS PREVENTION (TasP) AMONG FEMALE SEX WORKERS IN COTONOU, BENIN, WEST AFRICA

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Introduction

Western and central Africa

- The second most affected region by the HIV epidemic
- 5 million people living with HIV (PLHIV) in 2018
- HIV testing and antiretroviral therapy (ART) coverage are among the lowest worldwide¹
- UNAIDS 2020 targets remain low
- 42% of PLHIV knowing their status
- -35% of those who know their status are on ART
- Only 25% of those on ART suppress their viral load¹

• FSWs contributed to between

- 32–84% of HIV prevalent cases among men²
- 18% in the general population of women³
- Female sex workers (FSWs) and their clients play a central role in the HIV transmission dynamics⁴
- No special programs to facilitate FSWs to access and retain in ART
- FSWs ideal target for TasP/PrEP

King et al., J Infect Dis. 2017; Kane et al. Int J STD AIDS. 2009; Alary et al., AIDS 2004

Objectives

In line with UNAIDS recommendations extending ART to all HIV-infected individuals, we conducted this demonstration project on immediate treatment as prevention (TasP) among FSWs in Cotonou, Benin, West Africa

Specific Objective included assessing:

 \checkmark The retention rate

- \checkmark The adherence to treatment
- \checkmark Restoration of CD4 count
- \checkmark Viral response to treatment
- ✓ Development of drug resistance

Study Design

This was a cohort study (Participants followed up between 12 and 24 months)

Study Population

- Female sex workers (FSWs)
- Greater Cotonou area and suburbs

Eligibility criteria

- Professional FSWs (whose income come from sex work)
- Aged 18 and over
- Confirmed HIV-positive
- ART-naive

Results (1)

Cascade of follow up

- -7 (6.5%) participants withdrew
- -15 (14.0%), went back to their country of origin
- -19(17.8%), traveled to others cities
- One died
- One got married and left sex work
- Retention rate of 59.8%

Population Characteristics

Variable	n	(%)
Country of origin	107	100%
Benin	56	52.3%
Other countries	51	47.7%
Age (in years)	107	100%
18-34	48	44.8%
35-44	40	37.3%
≥45	19	17.7%
Marital status	107	100%
Married	2	1.8%
Divorced or Widowed	76	70.9%
Single	29	27.1%
Parity	105	98.1%
0 child	9	8.5%
1-3 children	64	60.9%
4-5 children	24	22.8%
>5 children	8	7.6%
Number of clients/14 days	97	90.6%
0	11	10.3%
1-9	18	26.1%
10-49	47	43.80
\geq 50	11	10.3%
Monthly income in USD	103	96.2%
≤200	36	34.9%
200 à 350	41	39.8%
>350	26	25.2%
Sexually transmitted infecti	ons (STIs ^d)	
N. gonorrhoeae	104	97.2%
positive	6	5.7%
C. trachomatis	104	97.2%
positive	3	2.8%
Trichomonas vaginalis	104	97.2%
positive	1	0.9%
Vaginal Candidiasis	104	97.2%
positive	8	7.2%

Results (2)

Fig 1: Changes in CD4 count



Mean CD4 count increased progressively from baseline to Month9 then reached a plateau, while % tage of CD4 count < 500, as well as number of partcipants decreased over time

Both % tage of suppressed and undetectable viral loads decreased over time even in those with final visits

Results (3)

Viral suppression vs adherence

Adherence levels (self-reported)	Prevalences	PR ^a	R ^a 95%CI ^b		p value	p trend ^c
Suppressed viral load						
\geq 90% (Pill missed \leq 3)	129/155 (83.2%)	1.4	1.0	2.0	0.04	
75-89% (Pill missed = 4-7)	16/19 (84.2%)	1.4	0.9	2.2	0.10	
50-74% (Pill missed 8-15)	9/11 (81.8%)	1.4	0.9	2.2	0.12	0.06
<50% (Pill missed >15)	13/22 (59.1%)	1	-	-	(Reference)	
missing ^d	5/10 (50.0%)					
Undetectable viral load						
\geq 90% (Pill missed \leq 3)	114/155 (73.5%)	3.2	1.5	6.8	0.002	
75-89% (Pill missed = 4-7)	14/19 (73.7%)	3.3	1.5	7.0	0.003	
50-74% (Pill missed 8-15)	8/11 (72.7%)	3.3	1.5	7.1	0.003	0.003
<50% (Pill missed >15)	5/22 (22.7%)	1	-	-	(Reference)	
missing ^d	4/10 (40.0%)					

^aPR: Prevalence ratio

b95%CI: 95% Confidence Interval *cp trend*: trend in the prevalence ratio

^dMissing: No data available for self-reported adherence for these subjects

Summary of drug resistance

Table 1: Pre-ART drug resistance

Table 2: Emerging drug resistance

Pre-ART resistance	Prevalence	Mutations	Emerging resistance	Prevalence	Mutations
Total prevalence	10.8% (12/111)		Total prevalence	16,7% (2/12)	
NRTIs	(3.6%)	M41L, M184V, T215TS, M184I	NRTIs	20%	M41L, M184V, T215TS, M184I
NNRTIs	(10%)	K103N, Y181C, Y188L, Y181S	NNRTIs	20%	K103N, Y181C, Y188L, Y181S
PIs	0,9%	L90M, L33F, K20I and L10V	PIs	NA	NA

Note:

- All samples included at baseline were tested for drug resistance
- Most of patients with pre-ART resistance did not show clinical resistance during follow up, showed increased CD4 count, and viral suppression
- At the end of the follow up, 12 samples showed viral load ≥1000 copies/ml, only 2 exhibited mutations associated with resistance to NNRTI or NRTI

Discussion

- First study on TasP/PrEP in the West and Central Africa region
- TasP was accepted by the majority of HIVinfected FSWs (96.4%)
- Feasibility was highly affected by mobility (about 40.2% dropped out between recruitment and the end of the study)
- FSWs could also face individual, social, or structural barriers, including anxiety, stigmatization, lack of social support, violence, or discrimination from medical staff, which could prevent them from being fully adherent

 Despite mobility and other barriers, 73.5%-83.2% of participants achieved adherence levels above ≥90%

- Viral load<1000 (<40) was attained in 73.1% (64.6%) of participants at month-6; 84.8% (71.2%) at month-12, and; 80.9% (65.1%) at final visit, respectively.
- TasP coupled with good adherence resulted in CD4 count restoration, increased viral suppression, and low emergence of drug resistance

Conclusion

- Immediate HIV treatment initiation following diagnosis is widely accepted and should be implemented in this region
- Mobility and adherence should be seriously addressed in future interventions programs
- Regional collaboration between FSW-friendly clinics is needed for sustained treatment implementation.
- We fell short of the UNAIDS objective of 90% viral suppression among those treated
- Need for better programs for enhancing treatment adherence, including structural interventions for reducing stigma and discrimination towards female sex workers and HIV-infected individuals

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- -Dr Michel Alary and his team at Hôpital du Saint-Sacrement,
- -The CHU de Québec-Université Laval
- -The statistician of the SP-POS
- -The team of the IST-clinic in Cotonou, Benin

Thank you for your attention

Welcome Questions

Summary of Pre-ART Drug resistance

D						D				
Baseline	CD4 arrest	Vinal la a d	Mutations			Resistance leve	IS		AK1 regimen	HIV Subtypes
Samuela ID			NIDTTI	NINTERT	DI-c	NIDTT	NINIDAT	DI-	Mala and an	
Sample ID	(cell/µ)	(copies/mi)	NK11ª	ININK I I"	PIS	NKII	NNKII	P18	Molecules	
CD009			M41L, D67N, T69D, 70R,	K103N, V179E	NA	Intermediate to	High	NA	3TC, ABC, AZT, D4T, DDI, FTC, TDF, EFV, NVP, ETR, RPV	
	321	11220	M184V, T215F, K219Q			High				G/CRF02_AG
CD011				K103N Y181C	NA		Intermediate to High	NA	ABC, AZT, D4T, DDI, FTC, 3TC, TDF, EFV, NVP, ETR, RPV	CRF02_AG/CRF02_AG
CDUII	700	6309					interinediate to fingi			
CD068	305	2800	T215TS	Y181YF, G190A	NA	low	Low to High	NA	AZT, D4T, DDI, EFV, NVP, ETR, RPV	G/CRF02_AG
CD083	506	2786	T215S	A98G V179E Y188L	NA	Low	High	NA	ABC, DDI, AZT, D4T, EFV, NVP, RPV, ETR	CRF02_AG/CRF02_AG
					NA			NA	ABC, AZT, D4T, DDI, FTC, 3TC, TDF, EFV, ETR NVP, RPV,	CRF02_AG/CRF02_AG
CD140	395	140000		Y181YF			Intermediate to High		NFV	
					NA			NA	ABC, AZT, D4T, DDI, FTC, 3TC, TDF, EFV, ETR, NVP, RPV,	CRF02_AG/CRF02_AG
CD191	90	36 000		Y181YF			Low to High		NFV	
CD244	720	1900		K103N, P225H	NA		High	NA	ABC, AZT, D4T, DDI, FTC, 3TC, TDF, EFV, NVP	CRF02_AG/CRF02_AG
							8			
CD330				Y181S	NA		Low to High	NA	ABC, AZT, D4T, DDI, FTC, 3TC, TDF, NVP, EFV, ETR, RPV	CRF02_AG/CRF02_AG
	78	100968								
D333	686	3466	M184I	Y181F	NA	Low to high	Low to High	NA	FTC, 3TC, DDI, ABC. NVP, NFV EFV, ETR RPR	CRF11-cpx/CRF02_AG
CD343	448	2044		K103N	NA		High	NA	ABC, AZT, D4T, DDI, FTC, 3TC, TDF. EFV, NVP, ETR, RPR	CRF02_AG/CRF02_AG
CD371	1365	1000		Y181YF	NA		Low to High	NA	ABC, AZT, D4T, DDI, FTC, 3TC, TDF. NVP, EFV, ETR, RPV	CRF02_AG/CRF02_AG
					L90M, K20I,			High	ABC, AZT, D4T, DDI, FTC, 3TC, TDF,	
CD314	590	12657	Inhibitory bNNTT, No.Nucl	agaida Davanaa Transarint	L33E:Literes	DIg. Duotoogo Inh	hitom		ATV/r, FPV/r, LPV/r, IDV/r, SOV/r, NFV	CRF02 AG/CRF02 AG

^aNRTI: Nucleoside Reverse Transcriptase Inhibitors; ^bNNTI: NoNucleoside Reverse Transcriptase filhibitors; ^ePIs: Protease Inhibitors:

Class of drugs NRTIs: Lamivudine (3TC), Abacavir (ABC), Emtricitabine (FTC), zidovudine (AZT), Stavudine (DDI), Tenofovir (TDF), NNRTIs: Efavirenz (EFV), Nevirapine (NVP), Rilpivirine (RPV) Etravirine (ETR), PIs : Atazanavir/Retronavir (ATV/r), Lopinavir/Retronavir (LPV/r), Indinavir/Retronavir (IDV/r), Saquinavir/Retronavir (SQV/r), Fosamprenavir/Ritonavir (FPV/r), Nelfinavir (NFV). HIV Subtypes: CRF02_AG, G/CRF02_AG and CRF11-cpx/CRF02_AG



Canadian Association for Population Therapeutics/ Association Canadienne pour la Thérapeutique des Populations Annual Conference

Systemic Sclerosis (SSc) with Interstitial Lung Disease (SSc-ILD) in Canada's Largest Province: An Estimate of the Prevalence and Survival of SSc and SSc-ILD in Ontario

Presenter: Kobina Quansah, Boehringer- Ingelheim (Canada) Limited

Co-authors: Dr. Janet E. Pope, Dr. Martin Kolb, Jason Flavin and Dr. Kris Garlick

DISCLOSURES

I am an employee of Boehringer-Ingelheim (Canada) Limited

BACKGROUND

- Systemic sclerosis is a rare, chronic and complex autoimmune disease, characterised by extensive vascular injury and progressive fibrosis (scarring) of the skin thickening and internal organ damage.¹
- When fibrosis occurs in the lungs, it is generally known as Interstitial Lung Disease (ILD) a frequent complication of SSc (SSc-ILD). The ILD usually leads to dyspnea (shortness of breath) caused by stiffening of the lungs.
- After diagnosis with SSc-ILD, some patients may experience a rapid pulmonary decline in the first 3 years of disease.²
- SSc-ILD is generally associated with increased morbidity and mortality.³ The median survival of patients with SSc-ILD is as low as 5 years.²
- To date, no published study has generated population based estimates of the prevalence and survival of SSc-ILD in Canada.

Source: 1. Fisher et al (2017). Humanistic and cost burden of systemic sclerosis: A review of the literature. Autoimmunity Reviews, 1147-1154.

^{2.} Herzog et al. (2014). Interstitial Lung Disease Associated With Systemic Sclerosis and Idiopathic Pulmonary Fibrosis: How Similar and Distinct. Arthritis Rheumatol, 1967-1978

^{3.} Schonefeld et al (2014). Interstitial Lung Disease in Scleroderma. Rheumatic Diseases Clinics of North America, 237-48.

OBJECTIVES

- Estimate the prevalence of SSc and SSc-ILD in Ontario
- Describe the demographic profile of SSc and SSc-ILD in Ontario
- Estimate the survival of SSc and SSc-ILD patients in Ontario

STUDY DESIGN AND POPULATION

Retrospective Cohort study using administrative data

- Inpatient hospitalization and day surgery data [Discharge Abstract Database (DAD)]
- Ambulatory care, emergency department and outpatient hospital clinic data [National Ambulatory Care Reporting System (NACRS)]
- ICD 10 CA codes were used to identify patients

Population-Inclusion Criteria

- Ontario adult residents (\geq 18 years of age)
- Valid health card on the first day of the fiscal year (s) of interest (April 1)
- Date of last contact with the health care system within 7 years prior to the first day of the fiscal year of interest (April 1)
- Eligible for the provincial insurance plan on the first day of the fiscal year (s) of interest (April 1)
- Patient identified with a diagnosis between April 1, 2008 to March 31, 2018

COHORT DEFINITIONS- PREVALENCE

- Prevalent SSc: defined using M34 codes to identify Systemic Sclerosis (M34.0, M34.1, M34.2, M34.8 and M34.9)
- Prevalent SSc-ILD: Any Systemic Sclerosis (any M34 code from above) only if followed by an occurrence of <u>any</u> of these codes:
 - J84.1 Other interstitial pulmonary disease with fibrosis
 - J84.8 Other specified interstitial pulmonary diseases
 - J84.9 Interstitial pulmonary disease; unspecified
 - J99.1 Respiratory disorders in the other diffuse connective tissue disorders

F

RESULTS- COHORT DEMOGRAPHICS

Variable	SSc Patients	SSc-ILD Patients
Ν	3,111	519
Mean age at index date (years)	57.4 ± 14.3	57.9 ± 12.2
Females	84.2%	80.2%

Baseline characteristics of patients between 2008 and 2018



RESULTS- PREVALENCE FOR SSc

Crude estimate of SSc (per 100,000)

Fiscal Year	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	Overall*
Overall	5.02	8.19	10.53	11.99	13.7	14.99	16.31	17.63	18.31	19.12	13.73
Age Group, n(%)											
18-29	0.55	0.96	1.21	1.66	2.45	2.68	2.87	3.21	3.44	3.59	2.29
30-50	2.77	4.85	6.44	7.6	8.75	9.69	11.05	12.46	13.25	14.1	9.04
51-64	8.11	13.02	16.84	19.19	21.23	22.75	24.54	26.11	27.14	28.79	21.21
65+	11.15	17.27	21.18	22.76	25.53	27.57	28.59	29.66	29.54	29.4	24.79
Sex n(%)											
Female	8.09	13.51	17.43	19.94	22.54	24.77	27	29.01	30.06	31.19	22.61
Male	1.77	2.56	3.21	3.57	4.33	4.6	4.94	5.52	5.81	6.24	4.31

* Overall represents the average prevalence over the 10 year period



RESULTS- PREVALENCE FOR SSc-ILD

Crude estimate of SSc-ILD (per 100,000)

Fiscal Year	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	Overall°
Overall	1.19	1.77	2.23	2.54	2.69	2.71	2.69	2.73	2.56	2.32	2.36
Age Group, n(%)											
18-29	*0.05 - 0.27	*0.05 - 0.27	*0.05 - 0.26	*0.05 - 0.26	*0.05 - 0.26	*0.05 - 0.25	*0.05 - 0.25	*0.05 - 0.25	0	0	*0.05 - 0.26
30-50	*0.44 - 0.53	*1.02 - 1.12	*1.37 - 1.47	*1.52 - 1.62	*1.53 - 1.63	*1.52 - 1.61	*1.65 - 1.75	*1.79 - 1.90	1.88	1.65	1.48
51-64	2.48	3.35	4.21	4.56	4.74	4.75	4.83	4.61	4.44	4.22	4.26
65+	2.31	3.04	3.61	4.42	4.9	4.9	4.29	4.38	3.75	3.21	*3.78 - 3.97
Sex n(%)											
Female	1.85	2.83	3.49	3.97	4.1	4.27	4.29	4.3	3.97	3.61	3.69
Male	0.5	0.66	0.89	1.02	1.2	1.07	1	1.07	1.07	0.95	0.95

* Exact counts suppressed for privacy reasons

°Overall represents the average prevalence over the 10 year period

RESULTS- SSc SURVIVAL

The survival rates at one, five and ten years after diagnosis were 85.0%, 64.5% and 44.9%, respectively



RESULTS- SSc-ILD SURVIVAL

The survival rates at one, five and ten years after diagnosis were 77.1%, 44.4% and 22.0%, respectively



CONCLUSIONS

- SSc prevalence rates found in this study are in line with findings from a recent systematic review
 of published literature based on North American results (13.5 44.3 per 100,000 persons).³
- Survival rates for SSc at 1, 5 and 10 years are similar to findings from a comprehensive SR and MA of the published literature.⁴
- SSc-ILD prevalence and survival rates could not be compared with the literature due to lack of published results.
- This study suggest a lower survival rate for SSc-ILD than for SSc. The 5-year survival for SSc-ILD is similar to that of multiple myeloma.⁵
- Results confirm that the prevalence of SSc-ILD may fall within a Canadian threshold for drugs for 'other' rare disease.⁶

Source: 3. Bergamasco et al. (2019). Epidemiology of Systemic Sclerosis and Systemic Sclerosis- Asoociated Interstitial Lung Disease. Clinical Epidemiology, 257-273.

^{4.} Rubio-Rivas et al. (2014)-Mortality and survival in systemic sclerosis: systematic review and meta-analysis. Seminars in Arthritis and Rheumatism, 208-219

^{5.} Canadian Cancer Statistics Advisory Committee. Canadian Cancer Statistics 2019. Toronto, ON: Canadian Cancer Society; 2019. Available at: cancer.ca/Canadian-Cancer-Statistics-2019-EN [accessed (October 17, 2019)]

^{6.} Richter et al. (2018). Characteristics of drugs for ultra-rare diseases versus drugs for other rare diseases in HTA submissions made to the CADTH CDR, Orphanet Journal of Rare Diseases, 23:25

FUTURE INVESTIGATIONS

 Potential "second look" can include looking at a community-definition using physician and diagnostic procedure codes to capture a population diagnosed outside of the hospital

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QUESTIONS?