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Expansion of ART and progressive declines in all-cause mortality in British Columbia, Canada

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Background

- Expansion of ART programs in recent years has been promoted as a means to reducing the further spread of new HIV infections.
- We examined the effect of such an expansion in British Columbia (BC), Canada on ***all-cause and cause specific mortality*** among participants in the provincial HIV/AIDS Drug Treatment Program (DTP).

Methods

- We analyzed data from participants aged ≥18 in the BC DTP to measure two-year mortality and causes of death from January 1, 2001to December 31, 2012.
- Deaths were identified through record linkages with the BC Vital Statistics Agency and we used ICD-10 codes for the underlying cause of death.
- We conducted tests of trend and compared DTP participant characteristics by dividing the study time into two-year time periods for the entire study period.
- We used Cox proportional hazard models to determine the risk of death for participants who had received ART for at least 3 months.

Results

- A total of 4412 new participants initiated ART and a total of 8185 received ART during the study period.
- Overall mortality in the DTP declined from 257/4002 (6.4%) of DTP participants in 2001-2002 to 224/6244 (3.6%) in 2011-2012 (p= 0.018 for test of trend).
- HIV-related deaths decreased (3.9% to 0.9% of DTP participants, p= 0.021) and similar decreases were observed in deaths due to chronic liver disease, cardiovascular disease, and suicides (p= 0.015, 0.021, and 0.002; respectively).
- Multivariate models, adjusted for age, gender, history of injection drug-use and adherence to therapy demonstrated that reductions in the risk of mortality was independently associated with ART initiation in all periods after 2001 – 2002

Table 1. Summary of reported causes of death by calendar year among DTP participants (irrespective of the year in which they started ART)

ERA	2001-2002		2003-2004		2005-2006		2007-2008		2009-2010		2011-2012		Total (2001-2012)		p-value[2]
	N=4002		N=4268		N=4577		N=5064		N=5669		N=6244		N=8185		
	n (%)	Mortality rate (per 100 person years)	n (%)	Mortality rate (per 100 person years)	n (%)	Mortality rate (per 100 person years)	n (%)	Mortality rate (per 100 person years)	n (%)	Mortality rate (per 100 person years)	n (%)	Mortality rate (per 100 person years)	n (%)	Mortality rate (per 100 person years)	
Any death (%)	257 (6.42)	3.88	294 (6.89)	4.16	318 (6.95)	4.24	240 (4.74)	2.94	228 (4.02)	2.46	224 (3.59)	2.15	**1561 (19.07)**	**4.84**	0.018*
HIV related (%)	155 (3.87)	2.34	175 (4.1)	2.47	208 (4.54)	2.77	136 (2.69)	1.67	93 (1.64)	1.00	58 (0.93)	0.56	**825 (10.08)**	**2.56**	0.021*
Other infectious and parasitic disease (%)	4 (0.1)	0.06	9 (0.21)	0.13	5 (0.11)	0.07	6 (0.12)	0.07	3 (0.05)	0.03	3 (0.05)	0.03	**30 (0.37)**	**0.09**	0.157
Cancer (non-AIDS) (%)	12 (0.3)	0.18	20 (0.47)	0.28	18 (0.39)	0.24	18 (0.36)	0.22	36 (0.64)	0.39	21 (0.34)	0.20	**125 (1.53)**	**0.39**	0.589
Cardiovascular disease (%)	16 (0.4)	0.24	16 (0.37)	0.23	15 (0.33)	0.20	19 (0.38)	0.23	8 (0.14)	0.09	5 (0.08)	0.05	**79 (0.97)**	**0.25**	0.021*
Chronic respiratory diseases (%)	3 (0.07)	0.05	1 (0.02)	0.01	3 (0.07)	0.04	5 (0.1)	0.06	5 (0.09)	0.05	4 (0.06)	0.04	**21 (0.26)**	**0.07**	0.490
Chronic Liver Disease (%)	13 (0.32)	0.20	12 (0.28)	0.17	10 (0.22)	0.13	7 (0.14)	0.09	4 (0.07)	0.04	9 (0.14)	0.09	**55 (0.67)**	**0.17**	0.015*
Unintentional Injuries (%)	6 (0.15)	0.09	9 (0.21)	0.13	2 (0.04)	0.03	5 (0.1)	0.06	9 (0.16)	0.10	0 (0)	0	**31 (0.38)**	**0.10**	0.228
Suicide (%)	31 (0.77)	0.47	25 (0.59)	0.35	21 (0.46)	0.28	25 (0.49)	0.31	13 (0.23)	0.14	0 (0)	0	**115 (1.41)**	**0.36**	0.002*
Other causes of death (%)	17 (0.42)	0.26	27 (0.63)	0.38	36 (0.79)	0.48	19 (0.38)	0.23	57 (1.01)	0,61	124 (1.99)	1.19	**280 (3.42)**	**0.87**	0.076

1. For each time period, for calculation of proportion, DTP participants required to start ARV at least 3 months before the end of that period
2. p-values are calculated for trend analysis based on incidence rates of every two year period, total column not included in analysis.

Table 2
Cox proportional hazards modelling of time-to-death among DTP participants who initiated therapy between 2001 - 2012

	Unadjusted		Adjusted	
Variable	HR (95% CI)	p-value	HR (95% CI)	p-value
Year of initiation of ART		<0.001		<0.001
2001-2002	1.00 (-)		1.00 (-)	
2003-2004	0.8 (0.61, 1.05)		0.73 (0.56, 0.96)	
2005-2006	0.64 (0.48, 0.86)		0.6 (0.45, 0.81)	
2007-2008	0.55 (0.41, 0.75)		0.57 (0.42, 0.77)	
2009-2010	0.44 (0.3, 0.64)		0.54 (0.37, 0.79)	
2011-2012	0.32 (0.16, 0.62)		0.46 (0.23, 0.9)	
Age at ART initiation	1.04 (1.03, 1.05)	<0.001	1.06 (1.05, 1.07)	<0.001
Female gender	1.44 (1.16, 1.78)	0.001	1.37 (1.09, 1.72)	0.007

	Unadjusted		Adjusted	
		p-value		p-value
Adherence to therapy in first year (per 10% increment)	0.85 (0.83, 0.88)	<0.001	0.84 (0.81, 0.86)	<0.001
History of injection drug use		<0.001		<0.001
No	1.00 (-)		1.00 (-)	
Yes	2.99 (2.38, 3.75)		2.57 (2.01, 3.28)	
Unknown	1.82 (1.32, 2.49)		2.15 (1.56, 2.96)	
Baseline CD4 (per 100 cells)	0.83 (0.78, 0.89)	<0.001	0.84 (0.78, 0.91)	<0.001
Baseline VL (log10 c/mL)	1.18 (0.99, 1.41)	0.060	Not selected	
AIDS defining illness before ART	1.42 (1.12, 1.8)	0.004	1.22 (0.95, 1.57)	0.124

Conclusions

- We observed **decreases in overall mortality and reductions in HIV-related deaths** among participants in the BC DTP over the study period.
- However, we also observed declines in ***cardiovascular, liver-related deaths and suicides.***
- These changes parallel a secondary expansion of ART in BC which suggests **broader clinical benefits to HIV treatment expansion** beyond classically-defined HIV-related conditions.

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