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The impact of changes in HIV management guidelines on time to treatment initiation in Australia

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Between 1984 and 2015, 36 171 cases of HIV infection were diagnosed in Australia, with 1025 notified cases last year [1]. By 2014, an estimated 9 900–11 000 of these patients has died as a direct consequence of their HIV infection. Since combination antiretroviral therapy (ART) was first introduced 20 years ago, significant progress has been made in treatment of HIV infection, greatly reducing HIV-associated mortality by reconstituting and preserving immune function and effectively preventing HIV transmission by virological control of HIV [2].

Despite longer term trends to earlier treatment, the question of when to initiate ART has only been definitively answered recently. Since 2012, the US Panel on Antiretroviral Guidelines for Adults and Adolescents (from which Australian guidelines are usually adapted) has recommended initiating ART in all HIV-infected individuals. The strength of this recommendation differed by CD4 count stratum [3]. In Australia, this recommendation was initially only partially adopted as the Pharmaceutical Benefits Scheme (PBS)-subsidized funding limited initiation of first-line ART to those with a CD4 count < 500 cells/mL. This CD4 count criterion was subsequently removed in April 2014. Following two large randomized controlled trials that addressed the optimal time to initiate ART [4], the recommendation of the US panel in July 2015 to increase the strength and evidence rating to ‘strong’ for all HIV-positive individuals, regardless of CD4 cell count [3], was extended to Australia in August 2015.

To assess the impact of these two changes in treatment guidelines on clinical practice, we assessed newly diagnosed HIV-infected patients in the Australian HIV Observational Database (AHOD). AHOD is an observational cohort study of 4270 HIV-positive patients under routine clinical care at 30 treatment sites in Australia and New Zealand prospectively collecting patient data since 1999. Ethics approval was obtained from the Institutional

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Conflicts of interest: ML has received consultancy and teaching fees from Gilead Sciences, and DSMB sitting fees from Sirtex PtyLtd. All remaining authors have no funding or conflicts of interest to disclose.

Review Boards (IRBs) at participating sites and the University of New South Wales (UNSW) Australia Human Research Ethics Committee, and written informed consent was obtained from all patients.

We identified 135 AHOD patients from 14 treatment sites in Australia who were diagnosed with HIV infection from December 2012 to April 2016. Of these, 62 were diagnosed between December 2012 and March 2014, 53 between April 2014 and July 2015, and 20 between August 2015 and April 2016. Patient characteristics were similar in all three periods, with no significant differences in age, sex, and CD4 count and HIV viral load at diagnosis (Table 1). Median time to treatment initiation decreased from 84 days [interquartile range (IQR) 31–397 days] in the first period to 60 days (IQR: 28–156 days) in the second period and significantly to 19 days (IQR: 6–27) for those most recently diagnosed.

Explicit treatment guidelines have been shown to improve clinical practice in many fields [5]. In light of the now proven benefits of early treatment initiation, our findings – with the caveat of a small sample size – further highlight the benefit of such guidelines in HIV patient care. Early diagnosis and treatment are essential to achieve the Australian national goal of elimination of transmission of HIV by 2020.

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Appendix 1: AHOD study group members

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*Indicates steering committee membership

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Table 1

Patient characteristics and time to treatment initiation

	Date of HIV diagnosis			
	December 2012 to March 2014	**April 2014 to July 2015**	**August 2015 to April 2016**	***P*-value**
n	62	53	20	
Male [*n* (%)]	55 (88.7)	47 (88.7)	18 (90.0)	1.00
Age (years) [median (range)]	36 (17–74)	33 (19–71)	35 (20–67)	0.84
CD4 count at diagnosis *				
n	45	43	20	
Median (IQR) (cells/μL)	400 (252–560)	442 (250–587)	514 (278–637)	0.57
VL at diagnosis *				
n	46	40	20	
Median (IQR) [$\log_{10}$(copies/ml)]	4.8 (4.3–5.5)	4.7 (3.4–5.1)	4.7 (4.6–5.3)	0.29
CD4 count at treatment start †				
n	39	36	18	
Median (IQR) (cells/mL)	370 (195–510)	429 (279–563)	505 (273–624)	0.24
VL at treatment start †				
n	34	31	17	
Median (IQR) [$\log_{10}$(copies/ml)]	4.7 (4.0–5.1)	4.7 (3.9–5.1)	4.8 (4.6–5.3)	0.40
Never started treatment [*n* (%)]	5‡ (8.0)	1‡ (1.9)	1 (5.0)	0.31
Time to treatment start				
n	57	52	19	
Median (IQR) (days)	84 (31–397)	60 (28–156)	15 (6–27)	< 0.001

IQR, interquartile range; VL, viral load.

*Closest measurement to diagnosis within 28 days.

†Closest measurement within 28 days before and 14 after treatment start.

‡Lost to follow-up before starting treatment.