

Received Date : 21-Dec-2016

Accepted Date : 07-Jan-2017

Article type : Letter to the Editor

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

1 Between 1984 and 2015, 36171 cases of HIV infection were diagnosed in Australia
2 with 1025 notified cases last year (1). By 2014 an estimated 9900-11000 of these
3 patients have died as a direct consequence of their HIV infection. Since combination
4 antiretroviral therapy (ART) was first introduced 20 years ago, significant progress
5 has been made in treatment of HIV infection greatly reducing HIV-associated
6 mortality by reconstituting and preserving immune function and effectively preventing
7 HIV transmission by virological control of HIV (2).

8 Despite longer term trends to earlier treatment, the question of when to initiate ART
9 has only been definitively answered recently. Since 2012, the US Panel on
10 Antiretroviral Guidelines for Adults and Adolescents (from which Australian
11 guidelines are usually adapted) has recommended initiating ART in all HIV-infected
12 individuals. The strength of this recommendation differed by CD4 count strata (3). In
13 Australia this recommendation was initially only partially adopted as the
14 Pharmaceutical Benefits Scheme (PBS)-subsidised funding limited initiation of first-
15 line ART to those with a CD4 count below 500cells/mm³. In April 2014, this CD4+
16 criterion was subsequently removed. Following two large randomized controlled trials

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the [Version of Record](#). Please cite this article as [doi: 10.1111/hiv.12504](https://doi.org/10.1111/hiv.12504)

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17 that addressed the optimal time to initiate ART (4), the recommendation of the US
18 panel from July 2015 to increase the strength and evidence rating to 'strong' for all
19 HIV-positive individuals, regardless of CD4 cell count (3), was extended to Australia
20 in August 2015.

21 To assess the impact of these two changes in treatment guidelines on clinical
22 practice, we assessed newly diagnosed HIV patients from the Australian HIV
23 Observational Database (AHOD). AHOD is an observational cohort study of 4270
24 HIV-positive patients under routine clinical care at 30 treatment sites in Australia and
25 New Zealand prospectively collecting patient data since 1999. Ethics approval was
26 obtained from the Institutional Review Boards (IRBs) at participating sites and the
27 UNSW Australia Human Research Ethics Committee, and written informed consent
28 was obtained from all patients.

29 We identified 135 AHOD patients from 14 treatment sites in Australia who were
30 diagnosed with HIV from December 2012 to April 2016. Of these, 62 were diagnosed
31 between December 2012 and March 2014, 53 between April 2014 and July 2015,
32 and 20 from August 2015 to April 2016. Patient characteristics were similar in all
33 three periods with no significant differences in age, sex, and CD4 count and HIV viral
34 load at diagnosis (Table 1). Median time to treatment initiation decreased from 84
35 days (interquartile range (IQR) 31-397 days) in the first period to 60 days (IQR 28-
36 156 days) and significantly to 19 days (IQR 6-27) for those most recently diagnosed.

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

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Table 1. Patient characteristics and time to treatment initiation

	Date of HIV diagnosis			P value
	Dec 2012 – Mar 2014	Apr 2014 – July 2015	Aug 2015 – Apr 2016	
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 at diagnosis [°] (cells/mm ³)				
n	45	43	20	
median (IQR)	400 (252-560)	442 (250-587)	514 (278-637)	0.57
VL at diagnosis [°] (log ₁₀ (copies/ml))				
n	46	40	20	
median (IQR)	4.8 (4.3-5.5)	4.7 (3.4-5.1)	4.7 (4.6-5.3)	0.29
CD4 at treatment start [†] (cells/mm ³)				
n	39	36	18	
median (IQR)	370 (195-510)	429 (279-563)	505 (273-624)	0.24
VL at treatment start [†] (log ₁₀ (copies/ml))				
n	34	31	17	
median (IQR)	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 (days)				
n	57	52	19	
median (IQR)	84 (31-397)	60 (28-156)	15 (6-27)	<0.001

* lost to follow-up before starting treatment

[°] closest measurement to diagnosis within 28 days

[†] closest measurement within 28 days before and 14 after treatment start

Abbreviations: IQR, interquartile range; VL, viral load



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Title:

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Date:

2017-10

Citation:

Puhr, R., Petoumenos, K., Youds, D., Law, M. G., Templeton, D. J. & Australian HIV Observational Database (AHOD) study group, (2017). The impact of changes in HIV management guidelines on time to treatment initiation in Australia.. HIV Med, 18 (9), pp.701-703. <https://doi.org/10.1111/hiv.12504>.

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File Description:

Accepted version