Factors Affecting the Decision to Initiate Antiretroviral Therapy in the Era of Treatment-as-Prevention: Synthesis of Evidence from Qualitative Research in High-Income Settings

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ABSTRACT

The emergence of treatment-as-prevention has made early initiation of antiretroviral treatment (ART) a “universal” policy. This review synthesizes qualitative research findings on barriers and facilitators of ART initiation in Organisation for Economic Co-operation and Development (OECD) countries published since 2010. Ten articles describing seven research studies were included in the review. Findings confirmed ART initiation as a complicated process involving careful deliberation of the personal risks and benefits of treatment within the broader contexts of everyday life for people living with HIV (PLHIV). They also highlight interpersonal dynamics and concern for the public as increasingly important factors in shaping the decision to initiate treatment. The review provides valuable information for understanding treatment behaviour and maximizing treatment options brought forth by new biomedical advances.

KEYWORDS

HIV/AIDS; ART; TasP; initiation; treatment-as-prevention; qualitative
Introduction

The emergence of treatment-as-prevention (TasP) has made the early initiation of ART a “universal” treatment policy since 2015 (World Health Organization, 2016). This review explores the impact of TasP discourse on PLHIV’s decision to initiate ART. It synthesizes qualitative research conducted among PLHIV in OECD countries, published following the release of TasP policy.

Methods

Search Strategy

Systematic database searches were undertaken using PubMed, CINAHL/Medline, Embase and Scopus. The searches were confined to research published since 2010 - the year TasP entered mainstream policy discussion (Cohen et al., 2011; Cohen et al., 2012). Reference lists were cross-checked to identify additional articles.

Selection Criteria

For inclusion, the study had to:

1. Be conducted in one or more OECD countries;
2. Report evidence on ART initiation;
3. Employ qualitative research methods;
4. Be published in 2010 or later; and
5. Utilize research data collected in 2010 or later.

The screening was conducted by five authors (OH, CWL, AM, JD and LF). Any disagreements, were discussed and resolved among the authorship team.
Data Extraction and Synthesis

A standardized form was used to extract data, which were then examined to identify common themes.

Results

Of the initial 1,181 articles identified, ten articles, representing seven studies, met the inclusion criteria (Figure 1).

Figure 1: PRISMA flow diagram of the literature search and screening process
Table 1 outlines the details of the included studies. Two-hundred and eleven PLHIV participated in the seven studies (Table 2). Nearly half (95, 45.0%) had not initiated ART; however, 83 (39.3%) of the total sample were recently diagnosed and may still have been contemplating treatment. Four key themes were identified.
| Author (Year) | Country | Data Collection and Analysis Methods | Sample | Key Research Questions | Theoretical Framework |
|--------------|---------|-------------------------------------|--------|------------------------|-----------------------|
| Beer et al. (2012) | USA | In-depth interview Thematic analysis | PLHIV who had not received HIV medical care (n=48) | Perceptions of HIV medical care of PLHIV who have never been in HIV care (and non-ART users) | General inductive approach for data collection and analysis |
| Christopoulos et al. (2015) | USA | Repeated in-depth interviews at 2 time points Dyadic analysis | Adults eligible for but not taking ART (n=20) HIV care providers (n=15) | Reasons for lack of ART usage in PLHIV retained in HIV care, motivations for HIV primary care attendance in the absence of ART | General inductive approach for data collection and analysis |
| Down et al. (2014) | Australia | In-depth interviews Thematic analysis | Newly diagnosed (<2 years) men who identify as gay (n=53) | Perceptions, understandings and expectations of recently diagnosed gay men, influences on decisions and attitudes toward ART initiation | General inductive approach for data collection and analysis |
| *Grace, Chown et al. (2015) | Canada | Repeated in-depth interviews at 4 time points Thematic analysis | Newly diagnosed MSM (n=25) | Longitudinal sex life narratives following HIV diagnosis and factors informing sexual behaviour. Negotiations of risk management, sexual decision making and changes in sex lives | General inductive approach for data collection and analysis |
| *Grace, Steinberg et al. (2015) | Canada | In-depth interview (baseline interview of Grace, et al. 2015a) Thematic analysis | Newly diagnosed MSM (n=25) | PLHIV narratives of HIV testing technologies in action | General inductive approach for data collection and analysis |
| *Newman, Mao et al. (2015) | Australia | Semi-structured interview Thematic analysis | Adults with HIV who do not take ART (n=27) | PLHIV accounts for non-ART use. Underlying views about ART and ideal conditions to initiate | General inductive approach for data collection and analysis |
| Author(s) and Year | Location | Methodology | Study Population | Research Focus | Methodological Approach |
|--------------------|----------|-------------|-----------------|---------------|------------------------|
| Newman, de Wit et al. (2015) | Australia | Semi-structured interview, Thematic analysis | Adults with HIV who do not take ART (n=27) | Critical remarks on TasP and perceptions on its role in preventing HIV transmission of PLHIV not using ART | General inductive approach for data collection and analysis |
| Persson et al. (2016) | Australia | Semi-structured interview, Thematic analysis | Adults with HIV who do not take ART (n=27) | PLHIV perceptions of community attitudes toward treatment non-use and significance to pharmaceutical citizenship | Inductive design using “pharmaceutical citizenship” (Ecks, 2005) as a sensitizing concept |
| Persson (2015) | Australia | Semi-structured interview, Thematic analysis | Serodiscordant couples (n=13) and individual partners of serodiscordant relationship (n=12) | Exploration of TasP in relation to serodiscordant sexuality and perceptions of infectiousness and transmission risk. | Inductive design using “pharmaceutical citizenship” (Ecks, 2005) as a sensitizing concept |
| Sevelius et al. (2014) | USA | In-depth interviews and focus group (FG) meetings, Thematic analysis | Transgender women (n=20 interview; n=38 FG) | Barriers and facilitators to engagement and retention in HIV care. | Inductive design guided by the Model of Gender Affirmation and Health Care Empowerment |

* Articles reporting findings from the same research project
### Table 2: Demographic and HIV care profiles of the participants

| Participant Characteristics/Studies | Beer et al. (2012) | Christopoulos et al. (2015) | Down et al. (2014) | Grace et al. (2015; 2015) | Newman et al. (2015; 2015); Persson et al. (2016) | Persson (2015) | Sevelius et al. (2014) | Subtotal (%) |
|-------------------------------------|-------------------|-----------------------------|-------------------|--------------------------|-------------------------------------------------|----------------|--------------------------|-------------|
| **Number of Participants**          | 48                | 20                          | 53                | 25†                      | 27                                              | 18             | 20*                      | 211 (100)   |
| **Gender Identity**                 |                   |                             |                   |                          |                                                 |                |                          |             |
| Male                                | 36                | 17                          | 53                | 25                       | 23                                              | -              | -                        | 154 (73.0)  |
| Female                              | 11                | 3                           | -                 | -                        | 4                                               | -              | -                        | 18 (8.5)    |
| Transgender                         | 1                 | -                           | -                 | -                        | -                                               | -              | 20                       | 21 (10.0)   |
| Not specified                       | -                 | -                           | -                 | -                        | 18                                              | -              | 18                       | 18 (8.5)    |
| **Sexual Identity**                 |                   |                             |                   |                          |                                                 |                |                          |             |
| Gay                                 | 17                | 12                          | -                 | 24                       | -                                               | -              | -                        | 53 (25.1)   |
| Bisexual                            | 8                 | -                           | -                 | 1                        | -                                               | -              | -                        | 9 (4.3)     |
| Gay or bisexual                     | -                 | -                           | 53                | -                        | 23                                              | -              | -                        | 76 (36.0)   |
| Heterosexual                        | 23                | 3                           | -                 | -                        | 4                                               | -              | -                        | 30 (14.2)   |
| Not specified                       | -                 | 5                           | -                 | -                        | 18                                              | 20             | -                        | 43 (20.4)   |
| **Recently Diagnosed (<2 years)**   |                   |                             |                   |                          |                                                 |                |                          |             |
| Yes                                 | -                 | -                           | 53                | 25                       | 5                                               | -              | -                        | 83 (39.3)   |
| No                                  | -                 | -                           | -                 | -                        | 22                                              | -              | -                        | 22 (10.4)   |
| Not specified                       | 48                | 20                          | -                 | -                        | 18                                              | 20             | -                        | 106 (50.2)  |
| **Engaged in HIV Care**             |                   |                             |                   |                          |                                                 |                |                          |             |
| Yes                                 | -                 | -                           | 20                | -                        | -                                               | -              | -                        | 20 (9.5)    |
| No                                  | 48                | -                           | -                 | -                        | -                                               | -              | 48                       | 48 (22.7)   |
| Not specified                       | -                 | -                           | 53                | 25                       | 27                                              | 18             | 20                       | 143 (67.8)  |
| **Initiated ART**                   |                   |                             |                   |                          |                                                 |                |                          |             |
| Initiated and sustained use         | -                 | -                           | 24                | -                        | -                                               | -              | 16                       | 40 (19.0)   |
| Previously initiated but stopped    | -                 | 10                          | -                 | -                        | 17                                              | -              | -                        | 27 (12.8)   |
| Never initiated                     | 48                | 10                          | 23                | -                        | 10                                              | -              | 4                        | 95 (45.0)   |
| Unstated                            | -                 | -                           | 7†               | 25                       | -                                               | 18             | -                        | 50 (23.7)   |

*PLHIV participants only (provider participants excluded)

* Interview participants only (focus group participants excluded)

† Down et al. (2014) reported they were unsure whether seven of the participants had begun treatment or not (p. 201). We suspect this was a typo as the number does not add up to a total of 53. However, we reported the figure as stated by the authors here.
Perceptions and beliefs about treatment

Concerns about side-effects, interactions of treatment with other medications, and viral resistance were frequently identified by those who declined or delayed initiation (Beer et al., 2012; Christopoulos et al., 2015; Down et al., 2014; Newman, Mao, et al., 2015; Persson et al., 2016; Sevelius et al., 2014). PLHIV perceived an association between initiation and a decline in their health status (Beer et al., 2012; Christopoulos et al., 2015; Newman, de Wit, et al., 2015; Newman, Mao, et al., 2015). Participants were concerned side effects reduced their capacity to perform work or family roles and were cautious about “giving in” to the virus or taking medications that may upset their health/life balance (Beer et al., 2012; Down et al., 2014; Newman, Mao, et al., 2015; Persson et al., 2016).

Participants were concerned about the long-term effects of ART or were suspicious of the rapid changes in HIV medicine (Beer et al., 2012; Down et al., 2014; Newman, de Wit, et al., 2015). Many reported a distrust of medicines or a preference for alternative therapies (Beer et al., 2012; Christopoulos et al., 2015; Newman, Mao, et al., 2015; Persson et al., 2016; Sevelius et al., 2014). Sevelius and colleagues (2014) reported transgender women’s worries that treatment may interact with hormone therapy. The diversity of information sources contributed to confusion about the optimal time to start treatment (Down et al., 2014; Grace, Chown, et al., 2015).

Interaction with healthcare professionals and services

Although 67.8% (143) of participants had not specified whether they were engaged in HIV care, their reports/quotes suggested such interactions were common. Some PLHIV
initiated ART following advice from their healthcare provider (Christopoulos et al., 2015; Down et al., 2014; Grace, Chown, et al., 2015; Grace, Steinberg, et al., 2015; Sevelius et al., 2014). There were also reports that many refused treatment with the awareness or endorsement of health professionals (Christopoulos et al., 2015; Down et al., 2014; Newman, de Wit, et al., 2015; Newman, Mao, et al., 2015; Persson et al., 2016). Some recently diagnosed participants still believed commencement of medication should be based on clinical presentation (Down et al., 2014).

Distrust of health professionals or clinical environments had stopped PLHIV attending services (Beer et al., 2012; Christopoulos et al., 2015; Newman, de Wit, et al., 2015). Stigma of being seen in an HIV clinic was a barrier to ART uptake, attending appointments or refilling prescriptions (Down et al., 2014; Newman, Mao, et al., 2015; Sevelius et al., 2014).

**Competing concerns, supportive services and networking**

Work and family commitments, homelessness, substance use, discrimination, chronic pain and mental illness were competing concerns that took precedence over ART initiation and prevented PLHIV accessing care (Beer et al., 2012; Christopoulos et al., 2015; Down et al., 2014; Grace, Chown, et al., 2015; Newman, Mao, et al., 2015; Sevelius et al., 2014). The cost and challenges of lifelong adherence were also considered before initiation (Beer et al., 2012; Christopoulos et al., 2015; Down et al., 2014; Newman, Mao, et al., 2015).

Diagnosis and subsequent referral to HIV care services helped PLHIV address ongoing life challenges (Christopoulos et al., 2015; Down et al., 2014; Grace, Chown, et
al., 2015; Grace, Steinberg, et al., 2015) and counselling facilitated uptake of ART for some participants (Christopoulos et al., 2015; Down et al., 2014; Grace, Chown, et al., 2015; Grace, Steinberg, et al., 2015).

Findings revealed being part of an HIV-positive community resulted in an exchange of support, information and involvement in discussions about ART (Down et al., 2014; Grace, Chown, et al., 2015). Christopoulos et al. (2015) and Sevelius et al. (2014) found that having a supportive person to disclose their diagnosis to was a facilitator of initiation.

The desire to protect partners and the public

A desire to protect partners prompted PLHIV to start treatment (Christopoulos et al., 2015; Down et al., 2014; Grace, Chown, et al., 2015; Grace, Steinberg, et al., 2015; Newman, Mao, et al., 2015; Persson, 2015; Persson et al., 2016). Treatment represented a new layer of protection and made it easier to disclose their HIV status to partners (Down et al., 2014; Grace, Chown, et al., 2015). Participants in long-term serodiscordant relationships discussed using ART as an alternative to condoms (Persson, 2015).

Newman and colleagues (2015; 2015) found that the absence of a partner was a reason to postpone initiation. This picture becomes more complicated when considering treatment as a means to prevent transmission in the community. Many agreed with the importance of ART as a means to protect the public (Down et al., 2014; Grace, Chown, et al., 2015; Newman, de Wit, et al., 2015; Persson, 2015; Persson et al., 2016) and that initiation was the right thing to do (Down et al., 2014; Grace, Chown, et al., 2015; Persson, 2015). Nonetheless, some reported feeling pressure to start treatment following the rise
of discourse surrounding TasP (Down et al., 2014; Newman, de Wit, et al., 2015; Persson et al., 2016). PLHIV who had not initiated felt their decision was not well-understood and expressed concerns about marginalization (Newman, de Wit, et al., 2015; Persson et al., 2016).

Discussion

The rise in ART has altered the landscape of life and care with HIV over the past decade (Cohen et al., 2012; Young, Flowers, & McDaid, 2015). This review identified a number of factors that continue to shape treatment initiation in the era of TasP. Personal beliefs and concerns about ART, which are inextricably linked to the structural problems PLHIV face in everyday life, continue to play an important role in initiation (Alfonso, Bermbach, Geller, & Montaner, 2006; Bolsewicz, Debattista, Vallely, Whittaker, & Fitzgerald, 2015; Gold & Ridge, 2001; Kremer, Ironson, Schneiderman, & Hautzinger, 2006; Prentice et al., 2011; Vervoort, Borleffs, Hoepelman, & Grypdonck, 2007).

Initiation decisions are seldom made on an ad-hoc basis or out of irrational fear, as indicated by the fact that many non-initiators had consulted and received support from health providers (Christopoulos et al., 2015; Down et al., 2014; Newman, de Wit, et al., 2015; Newman, Mao, et al., 2015; Persson et al., 2016). Given many participants were diagnosed before the advent of TasP, the advice they received may not reflect current treatment guidelines. Nevertheless, this highlights the importance of continuing to educate PLHIV and the wider community on the benefits of early treatment.
The findings reveal that interpersonal dynamics and concern for the public are increasingly important considerations in ART initiation decisions (Down et al., 2014; Grace, Chown, et al., 2015; Grace, Steinberg, et al., 2015; Persson, 2015). However, it remains unclear whether desire to protect the public can independently motivate PLHIV to begin treatment (Down et al., 2014; Grace, Chown, et al., 2015; Newman, de Wit, et al., 2015; Persson, 2015; Persson et al., 2016). Many expressed concerns regarding social pressure to initiate treatment (Down et al., 2014; Newman, de Wit, et al., 2015; Persson et al., 2016). As Persson and colleagues (2015; 2016) observed, public discourse moralizing the responsibility of PLHIV to prevent transmission could lead to marginalization, stigma and violence. Strategies to increase initiation should acknowledge this unintended consequence of TasP and ensure principles of anti-stigma/discrimination and empowerment are embedded in interventions.

A limitation of this review is our focus only on OECD countries. The findings, however, highlight the value of qualitative data and the importance of a social lens in understanding biomedicalization of HIV prevention and its implications.

**Declaration of Interest**

No author has any conflicts of interest regarding this manuscript.
References

Alfonso, V., Bermbach, N., Geller, J., & Montaner, J. S. (2006). Individual variability in barriers affecting people's decision to take HAART: a qualitative study identifying barriers to being on HAART. AIDS Patient Care & STDS, 20(12), 848-857. doi: 10.1089/apc.2006.20.848

Beer, L., Fagan, J. L., Garland, P., Valverde, E. E., Bolden, B., Brady, K. A., . . . Bertolli, J. (2012). Medication-related barriers to entering HIV care. AIDS Patient Care & STDS, 26(4), 214-221. doi: 10.1089/apc.2011.0407

Bolsewicz, K., Debelltista, J., Varella, A., Wittkaker, A., & Fitzgerald, L. (2015). Factors associated with antiretroviral treatment uptake and adherence: a review. Perspectives from Australia, Canada, and the United Kingdom. AIDS Care, 27(12), 1429-1438. doi: 10.1080/09540121.2015.1114992

Christopoulos, K. A., Olenader, S., Lopez, A. M., Lekas, H. M., Jaiswal, J., Mellman, W., . . . Koester, K. A. (2015). Retained in HIV Care But Not on Antiretroviral Treatment: A Qualitative Patient-Provider Dyadic Study. PLoS Medicine, 12(8), e1001863. doi: 10.1371/journal.pmed.1001863

Cohen, M. S., Chen, Y. Q., McCauley, M., Gamble, T., Hosseinipour, M. C., Kumarasamy, N., . . . Fleming, T. R. (2011). Prevention of HIV-1 infection with early antiretroviral therapy. New England Journal of Medicine, 365(6), 493-505. doi: 10.1056/NEJMoa1105243

Cohen, M. S., Holmes, C., Padian, N., Wolf, M., Hirnschall, G., Lo, Y., & Goosby, E. (2012). HIV treatment as prevention: How scientific discovery occurred and translated rapidly into policy for the global response. Health Affairs, 31(7), 1439-1449. doi: 10.1377/hlthaff.2012.0250

Down, I., Prestage, G., Triffitt, K., Brown, G., Bradley, J., & Ellard, J. (2014). Recently diagnosed gay men talk about HIV treatment decisions. Sexual Health, 11(2), 200-206

Ecks, S. (2005). Pharmaceutical citizenship: Antidepressant marketing and the promise of demarginalization in India. Anthropology and Medicine, 12, 239–254

Gold, R. S., & Ridge, D. T. (2001). "I will start treatment when I think the time is right": HIV-positive gay men talk about their decision not to access antiretroviral therapy. AIDS Care, 13(6), 693-708. doi: 10.1080/09540120120076869

Grace, D., Chown, S., Kwag, M., Steinberg, M., Lim, E., & Gilbert, M. (2015). Becoming Undetectable: Longitudinal Narratives of Gay Men's Sex Lives After a Recent HIV Diagnosis. AIDS Education and Prevention, 27(4), 333-349

Grace, D., Steinberg, M., Kwag, M., Chown, S. A., Doupe, G., Trussler, T., . . . Gilbert, M. (2015). Diagnostic Technologies in Practice: Gay Men's Narratives of Acute or Recent HIV Infection Diagnosis. Qualitative Health Research, 25(2), 205-217. doi: 10.1177/1049732314549813

Kremer, H., Ironson, G., Schneiderman, N., & Hautzinger, M. (2006). To take or not to take: decision-making about antiretroviral treatment in people living with HIV/AIDS. AIDS Patient Care STDS, 20(5), 335-349. doi: 10.1089/apc.2006.20.335

Newman, C. E., de Wit, J., Persson, A., Holt, M., Slavin, S., Kidd, M. R., . . . Mao, L. (2015). Understanding Concerns About Treatment-as-Prevention Among People with HIV who are not Using Antiretroviral Therapy. AIDS and Behavior, 19(5), 821-831. doi: 10.1007/s10461-014-0959-9

Newman, C. E., Mao, L., Persson, A., Holt, M., Slavin, S., Kidd, M. R., . . . de Wit, J. (2015). ‘Not Until I'm Absolutely Half-Dead and Have To:’ Accounting for Non-Use of Antiretroviral Therapy in Semi-
Structured Interviews with People Living with HIV in Australia. *AIDS Patient Care & STDS, 29*(5), 267-278. doi: 10.1089/apc.2014.0301

Persson, A. (2015). 'The world has changed': Pharmaceutical citizenship and the reimagining of serodiscordant sexuality among couples with mixed HIV status in Australia. *Sociology of Health & Illness*. doi: 10.1111/1467-9566.12347

Persson, A., Newman, C. E., Mao, L., & de Wit, J. (2016). On the Margins of Pharmaceutical Citizenship: Not Taking HIV Medication in the "Treatment Revolution" Era. *Medical Anthropology Quarterly*. doi: 10.1111/maq.12274

Prentice, T., Mill, J., Archibald, C. P., Sommerfeldt, S., Worthington, C., Jackson, R., & Wong, T. (2011). Aboriginal Youth Experiences of Accessing HIV Care and Treatment. *Journal of HIV/AIDS & Social Services, 10*(4), 395-413. doi: 10.1080/15381501.2011.623903

Sevelius, J. M., Patouhas, E., Keatley, J. G., & Johnson, M. O. (2014). Barriers and Facilitators to Engagement and Retention in Care among Transgender Women Living with Human Immunodeficiency Virus. *Annals of Behavioral Medicine, 47*(1), 5-16. doi: 10.1007/s12160-013-9565-8

Vervoort, S. C., Borleffs, J. C., Hoepelman, A. I., & Grypdonck, M. H. (2007). Adherence in antiretroviral therapy: a review of qualitative studies. *Aids, 21*(3), 271-281. doi: 10.1097/QAD.0b013e328011cb20

World Health Organization. (2016). *Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: Recommendations for a public health approach (Second edition)*. Geneva.

Young, I., Flowers, P., & McDaid, L. (2015). Can a pill prevent HIV? Negotiating the biomedicalisation of HIV prevention. *Sociology of Health and Illness*. doi: 10.1111/1467-9566.12372