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Protective Factors for Mortality among HIV-Positive People Who Inject Drugs (PWID) in Malaysia

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ABSTRACT

Introduction: People who inject drugs (PWID) have long been associated with HIV transmission in the community. In many countries, Methadone Maintenance Therapy (MMT) programme has been regarded as a critical platform to ensure HIV-positive PWID receive appropriate antiretroviral treatment. Despite treatment availability and accessibility in Malaysia, mortality was extensively observed, and the protective factors are still scarcely studied in this population. This study investigated the protective factors for mortality among HIV-positive PWID in Malaysia's two mainstream treatment settings.

Method: This was a retrospective cohort study. The data was collected from one HIV Clinic of a tertiary hospital and six (6) MMT programs of primary care clinics in the district of Kuantan, Pahang, from 2006-2019. The patients were categorised into three different subgroups. The mortality was recorded until the end of the study period. The survival rate was analysed using one-way ANOVA, and the associated factors were analysed using Cox proportional hazard regression analysis.

Results: In total, 141 records were found to have met the inclusion and exclusion criteria. Fifteen HIV-related mortalities were recorded throughout the study period. There were significant differences in survival years between the MMT-only group versus MMT + ART and the MMT-only group versus the ART-only group (p-value <0.001 and 0.003, respectively). A longer ART duration was significantly associated with improved survival of PWID (HR=0.5, 95% CI=0.28-0.88). Extended duration in MMT program (HR= 0.50, 95% CI=0.33 – 0.78), started on ART (HR= 0.21, 95% CI=0.04 – 0.97) and received ART counselling (HR= 0.13, 95% CI=0.02 – 0.85) were significantly identified as protective factors for mortality among PWID on MMT.

Conclusion: Three factors were identified as protective factors for mortality among HIV-positive PWID in Malaysia. Extended retention in the MMT programme, initiation of ART, and regularly receiving HIV-related counselling were the significant factors contributing to reduced mortality rates among the patients.

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Introduction

Globally, around 11 million people inject drugs, and approximately 1 in 8 (or 1.4 million) live with HIV (UNODC, 2020). In Malaysia, it was estimated that the number of active PWID population in 2014 was about 153,000 patients, and in the year 2017, the number steadily increased to approximately 156,000 patients. At the end of 2018, it is estimated that 87,041 people were living with HIV (PLHIV) in Malaysia (Hiebert et al., 2020). In the initial years of encounters, PWID has been strongly associated with HIV risk transmission primarily via the sharing of injecting paraphernalia (Cheong et al., 1997, Rusli et al., 1995). However, the country observed gradual changes in the HIV epidemic landscape in the past decade from predominantly PWID to more sexual transmission. The proportion of sexual transmission has increased to more than 90% in 2019 (Suleiman, 2019). Nevertheless, it is still relevant to treat PWID with appropriate treatment or harm reduction modalities (Osornprasop et al., 2018; Reddon et al., 2019). Methadone maintenance therapy has been regarded as a harm reduction approach to preventing HIV transmission from PWID to the community other than needle/syringe exchange programs (NSPs), condom distribution, and outreach programs. Highly active antiretroviral therapy (HAART) is the mainstay treatment among HIV-positive PWID unless contraindicated (Osornprasop et al., 2018; Myers et al., 2012). The initiation of HAART is based on the symptoms or CD4 counts. Starting with an ART regimen is highly recommended in symptomatic patients, especially those already with an opportunistic infection. In asymptomatic patients, the treatment is recommended in patients with a CD4 count of less than 350cell/ml (MOH, 2011).

The government has adopted Methadone Maintenance Therapy (MMT) Program since 2006 as one of the harm reduction approaches to reduce the HIV seroprevalence rates. In many countries, MMT has been regarded as one of the essential platforms to ensure that HIV-positive PWID receives appropriate antiretroviral treatment. However, abstinent patients may also enrol on the Infectious Disease Clinic of a public hospital. People who inject drugs have an elevated risk of death, although mortality rates vary across different settings. Any comprehensive approach to improving health outcomes in this group must include efforts to reduce HIV infection and other causes of death, particularly drug overdose (Mathers et al., 2013). There are many predictors of all causes of mortality and premature death among PWID living with HIV AIDS. Among the identified factors were untreated concomitant infectious diseases such as tuberculosis, HIV AIDS and viral hepatitis; developing acute toxicity, especially in the case of overdose; unstable house conditions or homelessness; being sex workers; polydrug users, lack of regular employment, and poor retention rate at a drug substitution treatment (Davis et al., 2017.; Vinh et al., 2021; Zivanovic et al., 2015). Whereas for protective factors, opioid substitution therapy such as MMT and initiation of HAART were found to independently and significantly protect against HIV-related death, drug-related death and death due to other causes (Nosyk et al., 2015). In Malaysia, despite wide treatment accessibility, mortality was still being observed, and the protective factors were still scarcely investigated among the Malaysian population (Ngah et al., 2019; Bazazi et al., 2018; Lubis et al., 2013). This study aimed to investigate the mortality rate and its protective factors among the HIV-positive PWID from the two mainstream treatment settings in Malaysia.

Methodology

This study was designed as a retrospective cohort. It has received prior ethics committee approval by the Medical Research and Ethics Committee, Ministry of Health Malaysia (NMRR-18-3067-43939). The data was collected from the available patients' records at an Infectious Disease (ID) HIV Clinic of a tertiary hospital (Hospital Tengku Ampuan Afzan or HTAA) and MMT Programs of six (6) Primary Care Clinics in the district of Kuantan, Pahang. The timeframe for the collected data was from 2006-2019 using a data collection form. The patients' records were screened for the inclusion and exclusion criteria. The inclusion criteria include 1) HIV-positive patients diagnosed upon enrolment or at any time during MMT or ID HIV Clinic, 2) Categorised under PWID – used to or still injecting drugs, and 3) Available demographic and baseline data. The data will be excluded if there are prominent missing/incomplete data. The HIV-positive PWID's records were divided into three different categories based on their antiretroviral treatment (ART) / methadone maintenance therapy (MMT) programme; 1) MMT only; 2) MMT + ART, and 3) ART only. All demographic, baseline data, patients' progress and HIV-related mortality were obtained from the medical records and treated strictly. The flow of the data collection process is summarised in Figure 1. The analysis was conducted using SPSS ver 24. The descriptive baseline data was analysed and tabulated. The mortality rate and years of survival were explored using One-way ANOVA, and the associated factors were analysed using Cox proportional hazard regression analysis.

Results

In total, 141 records were found to have met the inclusion criteria and are appropriate for further analysis. There were 29 (20.6%) patients on MMT only, 41 (29.1%) were receiving MMT +ART, and most of the records retrieved were those receiving ART only, 71 (50.4%). Table 1 summarises the baseline data collection.

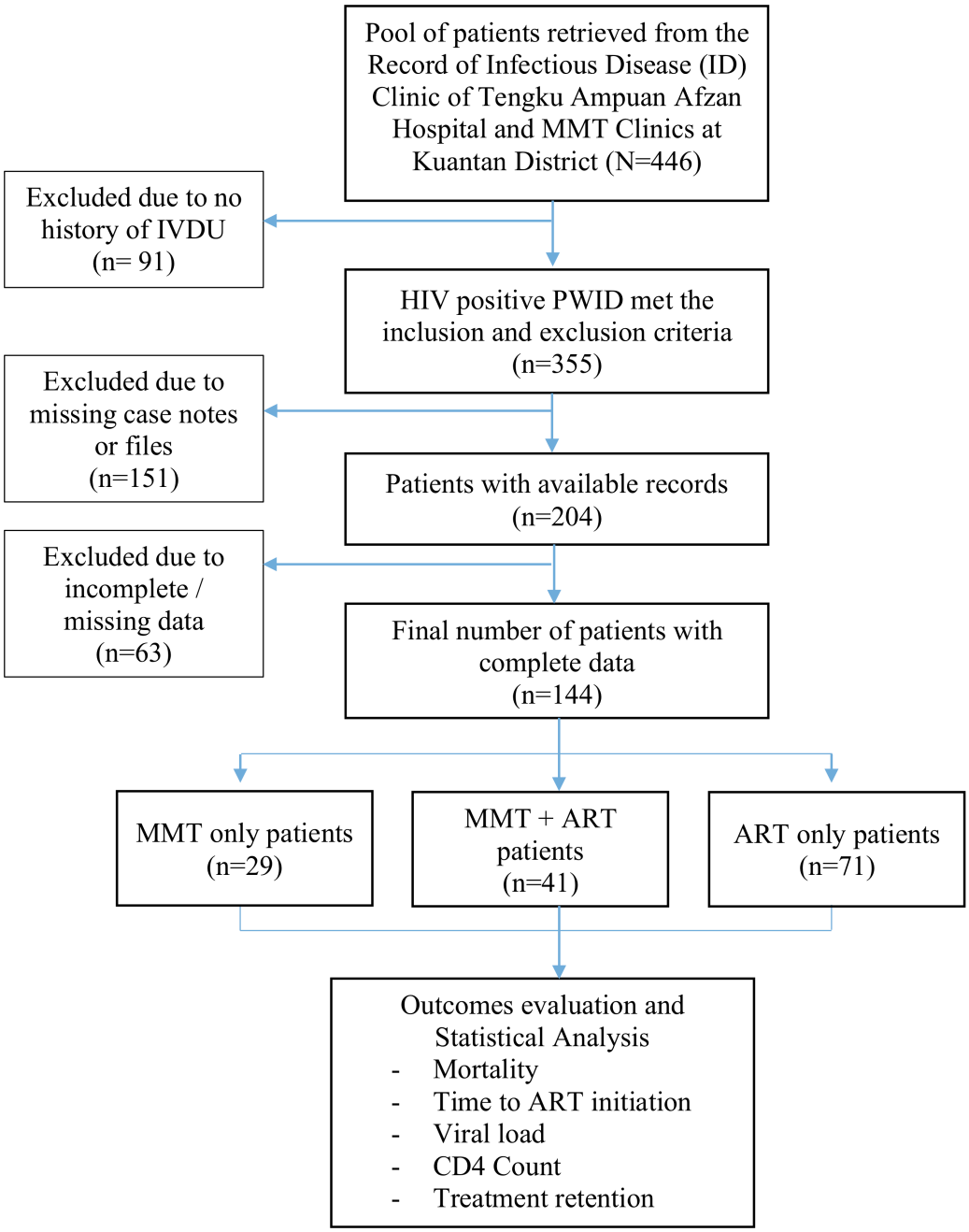

Figure 1: Flow Chart of Data Collection Process.

Table 1: Patients' Demographic Characteristics.

Patients' Characteristics	Number, n (%) of patients				P-value
	TOTAL 141	MMT only 29 (20.6)	MMT+ART 41(29.1)	ART only 71(50.4)	
Gender					
Male	136 (96.5)	29 (100)	41 (100)	66 (93)	0.124
Female	5 (3.5)	-	-	5 (7.0)	
Age					0.221[a]
Mean (SD) years	37 (6.4)	37 (4.1)	34 (4.3)	38 (7.6)	
Marital status					
Single	69 (48.9)	13 (44.8)	22 (53.7)	34 (47.9)	0.737
Married	53 (37.6)	12 (41.4)	13 (31.7)	28 (39.4)	
Divorced	17 (12.1)	3 (10.3)	5 (12.2)	9 (12.7)	
Widow	2 (1.4)	1 (3.5)	1 (2.4)	-	
Work					
Yes	94 (66.7)	22 (75.9)	29 (70.7)	43 (60.6)	0.297
No	47 (33.3)	7 (4.9)	12 (29.3)	28 (39.4)	

Note: The statistical test used is Fisher's Exact test unless stated otherwise, [a]One-Way ANOVA, Independent t-test SD: Standard deviation

Mortality and years of survival

At the end of the study period, the number of HIV-related mortality was 15 subjects (10.6%). Table 2 compares mortality (death) and years of survival between groups of PWID. The number of fatalities was significant between the MMT-only group and the ART-only group, with a p-value < 0.001 (Fisher's exact test). The mean (SD) survival years were the shortest among the MMT-only group, which was 3.6 (SD=2.7) years. There were significant differences in survival years between the MMT only group versus MMT + ART and MMT only group versus ART only group with p-value <0.001 and 0.003, respectively (Independent t-test).

Protective factors for mortality among PWID initiated on ART

A total of 14 independent variables were analysed with univariate Cox proportional hazards regression analysis, and only duration on ART was found to be significantly associated with improved survival of PWID (HR=0.5, 95% CI=0.28-0.88). The longer the patient was on ART, the risk of death was found to be reduced by 50%. Table 3 summarises the results.

The Protective factors for mortality among patients on MMT

Three independent variables were chosen to predict mortality among the MMT subjects in this study. All significant variables were incorporated in the multivariate analysis. The final model showed that the extended duration in MMT program (HR= 0.51, 95% CI=0.33 – 0.78), started on ART (HR= 0.21, 95% CI=0.04 – 0.97) and received ART counselling (HR= 0.13, 95% CI=0.02 – 0.85) were significantly identified as protective factors for mortality among PWID on MMT. The results are tabulated in Table 4.

Discussion

The mortality rate among HIV-infected PWID

High mortality rates among HIV-infected people who inject drugs (PWID) have been well studied. High-risk behaviour of the PWID population who practised needle sharing, unprotected sex and substance abuse, the risk for blood-borne infections, sexually transmitted disease, and a high rate of substance overdose were among the top contributing factors identified (Farhadian et al., 2021). Blood-borne infections mainly include HIV, HBV and HCV. HCV was one of the common co-infection in the

Table 2: Mortality and years of survival among PWID.

Characteristics	Number, n (%) of patients				
	TOTAL 141	MMT only 29 (20.6)	MMT+ART 41(29.1)	ART only 71(50.4)	P-value
Death	15	8 (53.3)	5 (33.3)	2 (13.3)	<0.001[a]
Survival, mean (SD) years	5.5 (3.5)	3.6 (2.7)	6.6 (3.2)	5.6 (3.6)	<0.001[b]

[a]Fisher's Exact test. [b]One-Way ANOVA

PWID population, and it definitely increases the mortality threshold in this population (Ali et al., 2018; Draper & McCance-Katz, 2005; Mehta et al., 2010; Teoh et al., 2018). From another perspective, suboptimal access to HIV care was also found to lead to mortality in the sub-population [Des Jarlais et al., 2018]. In this study, The patients who were not on ART had the shortest survival rate compared to those treated with ART. This result is consistent with other studies since ART is expected to restore immune function and improve patients' survival (Hogg et al., 1998; Manosuthi et al., 2021; Trickey et al., 2017).

ART initiation as a protective factor for mortality among HIV-positive PWID

This study showed that those patients who started with ART have a protective factor towards mortality compared to those without/not started, regardless of their treatment setting (MMT or without MMT). This finding is supported by many other studies emphasising the important role of ART in reducing the mortality rate among the PWID population (Kitahata et al., 2009; Liu et al., 2013; Wood et al., 2008; Zhao et al., 2017). In a study applying multivariable extended Cox regression analyses of all-cause mortality, those receiving ART and having undetectable VL (<50 copies/mL) had a 42% lower all-cause mortality hazard among both men and women as compared to those who did not receive ART (Brattgård et al., 2022; Shoko & Chikobvu, 2019). Those receiving ART but having detectable VL did not have a significantly lower risk of death (Croxford et al., 2017; Elvstam et al., 2021). The duration also plays a significant role in predicting mortality among the HIV PWID without MMT, where the more extended the ART duration resulted in better survival (Bogdanić et al., 2021). The time for ART treatment initiation is also crucial, and the treatment delay has been associated with increased mortality (Ramlan et al., 2019).

Extended MMT programme retention as a protective factor for mortality among HIV-positive PWID under the MMT programme

In MMT-treated PWID, it was found that other than the initiation of ART, a more extended period of MMT programme retention and attending the ART counselling sessions were the protective factors that have been significantly associated with improved survival and reduced mortality among patients. These findings are coherent with a study in China (Zhao et al., 2013a). PWID who was not in the MMT program had a higher mortality rate than those in the MMT program, although both groups were initiated on ART.

Findings in a few other studies supported that enrolment into the opioid-substitution program will improve access to HIV care and facilitate the early initiation of ART (Hogg et al., 2011; Montaner & Wood, 2011; Liu et al., 2013; Mukandavire et al., 2017; Pham et al., 2017). However, from a local study, about 33% of the MMT patients defaulted to the program due to negative perceptions and poor patient satisfaction (Ali et al., 2018), which needs improvement. The low mortality rate among the MMT + ART group indicated that both MMT and ART effectively reduced the mortality rate.

Regular Attendance to HIV and ART Counselling Sessions as protective factors for mortality among the HIV-positive PWID

The counselling session is prescribed to improve patients' understanding of the disease and the related treatment. The results from this study are consistent with other studies on the essential roles of counselling sessions in improving medication adherence, treatment outcomes and reducing the rate of mortality among patients (Go et al., 2017; Hussain et al., 2022).

Table 3: The Cox proportional hazards regression analysis on protective factors for mortality among PWID initiated on ART.

Variables	Univariate analysis			Multivariate analysis		
	HR	HR 95% CI	p	HR	HR 95% CI	p
Age (years)	1.00	0.87 – 1.14	0.946			
Working Yes No (ref)	0.31	0.07 – 1.38	0.123			
Married Yes No (ref)	0.50	0.10 – 2.60	0.411			
Ever had a positive urine test Yes No (ref)	0.29	0.07 – 1.31	0.108			
Ever been detained or prisoned Yes No (ref)	0.39	0.05 – 3.21	0.380			
CD4 baseline (cells/mm$^{3)}$	1.00	0.99 – 1.01	0.593			
CD4 post ART (>6 months (cells/mm^3)	0.99	0.97 – 1.01	0.388			
Start ART from diagnosis (year)	1.14	0.96 – 1.37	0.141			
Start ART from the eligible date (year)	1.03	1.01 – 1.05	0.001*	1.00	0.97 – 1.03	0.928
Duration on ART (year)	0.60	0.41 – 0.88	0.008*	0.50	0.28 – 0.88	0.016*
Existing OI	1.83	0.35 – 9.48	0.471			
OI after ART	4.05	0.78 – 20.90	0.095			
HIV related counselling Yes No (ref)	0.10	0.02 – 0.43	0.002*	17.19	0.92 – 320.9	0.06
RVD treatment centre Hospital Health clinic (ref)	0.20	0.04 – 0.92	0.038*	2.00	0.13 – 31.02	0.62

Note: ref = Reference group, HR = Hazard ratio, *significant when $p < 0.05$

Table 4: Cox proportional hazards regression analysis on protective factors for mortality among PWID on MMT.

Variables	Univariate analysis			Multivariate analysis		
	HR	HR 95% CI	p	HR	HR 95% CI	p
Age (year)	1.20	1.06 – 1.38	0.006			
Working Yes No (ref)	1.03	0.286 – 3.80	0.960			
Married Yes No (ref)	0.51	0.14 – 1.84	0.301			
Ever had a positive urine test Yes No (ref)	1.08	0.38 – 3.56	0.903			
Ever been detained or prisoned Yes No (ref)	1.53	0.50 – 4.740	0457			
Duration on MMT (year)	0.60	0.46 – 0.79	<0.001	0.51	0.33 – 0.78	0.002*
MMT dose (mg)	0.99	0.97 – 1.01	0.279			
MMT compliance Yes No (ref)	0.69	0.19 – 2.52	0.574			
Start ART Yes No (ref)	0.21	0.07 – 0.66	0.008	0.21	0.04 – 0.97	0.046*
CD4 baseline (cells/mm$^{3)}$	1	0.998 – 1.002	0.883			
Existing OI	1.592	0.528 – 4.803	0.409			
ART counselling Yes No (ref)	0.12	0.03 – 0.56	0.007	0.13	0.02 – 0.85	0.033*

Note: ref = Reference group, HR = Hazard ratio, *significant when $p < 0.05$

Conclusion

Three factors were identified as protective factors for mortality among HIV-positive PWID in Malaysia. Extended retention in the MMT programme, initiated on ART and regularly receiving HIV- & ART-related counselling were the significant protective factors in reducing the mortality rate among the patients.

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Conflict of Interest

We would like to declare that we do not have any conflict of interest in conducting this study.

References

Ali, N., Aziz, S. A., Norliza, C., & Abdullah, N. (2018). *Malaysian Methadone Treatment Outcome Study (MyTS) 2016. Ministry of Health. March*, 94.

Bogdanić, N., Bendig, L., Lukas, D., Zekan, Š., & Begovac, J. (2021). Timeliness of antiretroviral therapy initiation in the era before universal treatment. *Scientific Reports*, *11*(1). https://doi.org/10.1038/S41598-021-90043-7

Brattgård, H., Björkman, P., Nowak, P., Treutiger, C. J., Gisslén, M., & Elvstam, O. (2022). Factors associated with low-level viraemia in people with HIV starting antiretroviral therapy: A Swedish observational study. *PLOS ONE*, *17*(5), e0268540. https://doi.org/10.1371/JOURNAL.PONE.0268540

Cheong, I., Lim, A., Lee, C., Ibrahim, Z., & Sarvanathan, K. (1997). Epidemiology and clinical characteristics of HIV-infected patients in Kuala Lumpur. *The Medical Journal of Malaysia*, *52*(4), 313–317.

Croxford, S., Kitching, A., Desai, S., Kall, M., Edelstein, M., Skingsley, A., Burns, F., Copas, A., Brown, A. E., Sullivan, A. K., & Delpech, V. (2017). Mortality and causes of death in people diagnosed with HIV in the era of highly active antiretroviral therapy compared with the general population: an analysis of a national observational cohort. *The Lancet Public Health*, *2*(1), e35–e46. https://doi.org/10.1016/S2468-2667(16)30020-2

Davis, J. M., Suleta, K., Corsi, K. F., & Booth, R. E. (n.d.). *A Hazard Analysis of Risk Factors of Mortality in Individuals Who Inject Drugs in Denver CO*. https://doi.org/10.1007/s10461-016-1660-y

Draper, J. C., & McCance-Katz, E. F. (2005). Medical illness and comorbidities in drug users: Implications for addiction pharmacotherapy treatment. *Substance Use and Misuse*, *40*(13–14), 1899–1921. https://doi.org/10.1080/10826080500294775

Elvstam, O., Marrone, G., Medstrand, P., Treutiger, C. J., Sönnerborg, A., Gisslén, M., & Björkman, P. (2021). All-Cause Mortality and Serious Non-AIDS Events in Adults With Low-level Human Immunodeficiency Virus Viremia During Combination Antiretroviral Therapy: Results From a Swedish Nationwide Observational Study. *Clinical Infectious Diseases*, *72*(12), 2079–2086. https://doi.org/10.1093/CID/CIAA413

Farhadian, N., Karami Matin, B., Farnia, V., Zamanian, M. H., Najafi, F., & Farhadian, M. (2021). *The prevalence of people who inject drugs among those with HIV late presentation: a meta-analysis*. https://doi.org/10.1186/s13011-022-00439-5

Fighting HIV effectively, efficiently in Malaysia. (n.d.). Retrieved July 4, 2022, from https://blogs.worldbank.org/eastasiapacific/fighting-hiv-effectively-efficiently-malaysia

Go, V. F., Frangakis, C., le Minh, N., Ha, T. V., Latkin, C. A., Sripaipan, T., Zelaya, C. E., Davis, W. W., Celentano, D. D., & Quan, V. M. (2017). Increased survival among HIV-infected PWID receiving a multi-level HIV risk and stigma reduction intervention: results from a randomized controlled trial. *Journal of Acquired Immune Deficiency Syndromes (1999)*, *74*(2), 166. https://doi.org/10.1097/QAI.0000000000001245

Hiebert, L., Azzeri, A., Dahlui, M., Hecht, R., Mohamed, R., Hana Shabaruddin, F., & McDonald, S. A. (2020). Estimating the Population Size of People Who Inject Drugs in Malaysia for 2014 and 2017 Using the Benchmark-Multiplier Method. *Substance Use & Misuse*, *55*(6), 871–877. https://doi.org/10.1080/10826084.2019.1708943

Hogg, R. S., Ma, K. v, Heath, B., Yip, K. J. P., Craib, M. ;, Merck, D., Co, P.-C., Reprints, D., & Montaner, J. S. G. (n.d.). *Improved Survival Among HIV-Infected Individuals Following*

Initiation of Antiretroviral Therapy. https://jamanetwork.com/

Hogg, R. S., Montaner, J. S. G., & Wood, E. (2011). Methadone Maintenance Therapy Promotes Initiation of Antiretroviral Therapy Among Injection Drug. *Addiction*, *105*(5), 907–913. https://doi.org/10.1111/j.1360-0443.2010.02905.x.METHADONE

Hussain, A., Rahim, A., Sheikh, A., & Jiwani, A. (2022). The Effects of live-in rehabilitation on ARV adherence, abstinence from drugs and lifestyle modification in people who inject drugs (PWID) Living with HIV – A clinic review. *Pakistan Journal of Medical Sciences*, *38*, 411–416. https://doi.org/10.12669/PJMS.38.ICON-2022.5780.

Ismail R, Doi S, Naganathna N. HIV infection in Malaysia: a report of cases seen at the University Hospital, Kuala Lumpur. Med J Malaysia. 1995 Dec;50(4):298-301. PMID: 8668046.

Kitahata MM, Gange SJ, Abraham AG, E. Al. (2009). Effect of early versus deferred antiretroviral therapy for HIV on survival. *N Engl J Med.*, *360*(18), 1815–1826. https://doi.org/10.1056/NEJMoa0807252.Effect

Liu, E., Rou, K., McGoogan, J. M., Pang, L., Cao, X., Wang, C., Luo, W., Sullivan, S. G., Montaner, J. S. G., Bulterys, M., Detels, R., & Wu, Z. (2013). Factors associated with mortality of HIV-positive clients receiving methadone maintenance treatment in China. *Journal of Infectious Diseases*, *208*(3), 442–453. https://doi.org/10.1093/infdis/jit163

Manosuthi, W., Charoenpong, L., & Santiwarangkana, C. (2021). A retrospective study of survival and risk factors for mortality among people living with HIV who received antiretroviral treatment in a resource-limited setting. *AIDS Research and Therapy*, *18*(1), 1–10. https://doi.org/10.1186/S12981-021-00397-1/FIGURES/3

Mathers, B. M., Degenhardt, L., Bucello, C., Lemon, J., Wiessing, L., & Hickman, M. (2013). Systematic reviews Mortality among people who inject drugs: a systematic review and meta-analysis. *Bull World Health Organ*, *91*, 102–123. https://doi.org/10.2471/BLT.12.108282

Mehta, S. H., Kirk, G. D., Astemborski, J., Galai, N., & Celentano, D. D. (2010). Temporal Trends in Highly Active Antiretroviral Therapy Initiation among Injection Drug Users in Baltimore, Maryland, 1996–2008. *Clinical Infectious Diseases*, *50*(12), 1664–1671. https://doi.org/10.1086/652867

Mukandavire, C., Low, A., Mburu, G., Trickey, A., May, M. T., Davies, C. F., French, C. E., Looker, K. J., Rhodes, T., Platt, L., Guise, A., Hickman, M., & Vickerman, P. (2017). Impact of opioid substitution therapy on the HIV prevention benefit of antiretroviral therapy for people who inject drugs. *Aids*, *31*(8), 1181–1190. https://doi.org/10.1097/QAD.0000000000001458

Myers, B., Petersen, Z., Pithey, A., & Pasche, S. (2012). *Barriers to antiretroviral therapy use among people who inject drugs: A systematic review*. https://www.unodc.org/documents/hiv-aids/publications/People_who_use_drugs/D01_BarriersART_2012_EN.pdf

Nosyk, B., Min, J. E., Evans, E., Li, L., Liu, L., Lima, V. D., Wood, E., & Montaner, J. S. G. (2015). *The Effects of Opioid Substitution Treatment and Highly Active Antiretroviral Therapy on the Cause-Specific Risk of Mortality Among HIV-Positive People Who Inject Drugs*. https://doi.org/10.1093/cid/civ476

Pham, L. T. T., Kitamura, A., Do, H. M., Lai, K. A., Le, N. T., Nguyen, V. T. T., & Kato, M. (2017). Retrospective analysis of antiretroviral therapy uptake and retention of male clients receiving methadone maintenance therapy in two provinces in Vietnam: Potential synergy of the two therapies. *Harm Reduction Journal*, *14*(1). https://doi.org/10.1186/s12954-017-0133-6

Reddon, H., Marshall, B. D. L., Milloy, M.-J., & Reddon, H. (n.d.). *Elimination of HIV transmission through novel and established prevention strategies among people who inject drugs*. https://doi.org/10.1016/S2352-3018(18)30292-3

Shoko, C., & Chikobvu, D. (2019). A superiority of viral load over CD4 cell count when predicting mortality in HIV patients on therapy. *BMC Infectious Diseases*, *19*(1), 1–10. https://doi.org/10.1186/S12879-019-3781-1/TABLES/5

Suleiman, A. (2019). *Malaysia Global AIDS Reporting 2020 2 MALAYSIA 2020*.

Teoh, J., Yee, A., & Danaee, M. (2018). Predictors of retention and mortality among patients on methadone maintenance therapy. *Heroin Addiction and Related Clinical Problems*, *20*(4), 19–28.

Trickey, A., May, M. T., Vehreschild, J. J., Obel, N., Gill, M. J., Crane, H. M., Boesecke, C., Patterson, S., Grabar, S., Cazanave, C., Cavassini, M., Shepherd, L., Monforte, A. d. A., van Sighem, A., Saag, M., Lampe, F., Hernando, V., Montero, M., Zangerle, R., … Sterne, J. A. C. (2017). Survival of HIV-positive patients starting antiretroviral therapy between 1996 and 2013: a collaborative analysis of cohort studies. *The Lancet HIV*, *4*(8), e349–e356. https://doi.org/10.1016/S2352-3018(17)30066-8

Vinh, V. H., Vallo, R., Giang, H. T., Huong, D. T., Oanh, K. T. H., Khue, P. M., Thanh, N. T. T., Quillet, C., Rapoud, D., Michel, L., de Perre, P. van, Feelemyer, J., Moles, J. P., Cournil, A., Jarlais, D. des, Laureillard, D., & Nagot, N. (2021). A cohort study revealed high mortality among people who inject drugs in Hai Phong, Vietnam. *Journal of Clinical Epidemiology*, *139*, 38–48. https://doi.org/10.1016/J.JCLINEPI.2021.07.007

Wood, E., Hogg, R. S., Lima, V. D., Kerr, T., Yip, B., Marshall, B. D. L., & Montaner, J. S. G. (2008). Highly Active Antiretroviral Therapy and Survival in HIV-Infected Injection Drug Users. *Journal of American Medical Association*, *300*(5), 550. https://doi.org/10.1001/jama.300.5.550

Zhao, Y., Shi, C. X., Mcgoogan, J. M., Rou, K., & Wu, Z. (2013). *Methadone maintenance treatment and mortality in HIV-positive people who inject opioids in China*. *June 2012*, 93–101. https://doi.org/10.2471/BLT.12.108944

Zhao, Y., Zhang, M., Shi, C. X., Huang, J., Zhang, F., Rou, K., & Wu, Z. (2017). Mortality and virological failure among HIV-infected people who inject drugs on antiretroviral treatment in China: An observational cohort study. *Drug and Alcohol Dependence*, *170*, 189–197. https://doi.org/10.1016/j.drugalcdep.2016.11.011

Zivanovic, R., Milloy, M. J., Hayashi, K., Dong, H., Sutherland, C., Kerr, T., & Wood, E. (2015). *Impact of unstable housing on all-cause mortality among persons who inject drugs*. https://doi.org/10.1186/s12889-015-1479-x