ELSEVIER

Contents lists available at ScienceDirect

Drug and Alcohol Dependence Reports

journal homepage: www.elsevier.com/locate/dadr



Substance use referral, treatment utilization, and patient costs associated with problematic substance use in people living with HIV in Cape Town, South Africa



Jennifer M. Belus ^{a,b,c,*}, Kristen S. Regenauer ^c, Elizabeth Hutman ^d, Alexandra L. Rose ^c, Warren Burnhams ^e, Lena S. Andersen ^f, Bronwyn Myers ^{g,h,i}, John A. Joska ^j, Jessica F. Magidson ^c

- ^a Swiss Tropical and Public Health Institute, Department of Medicine, Basel, Switzerland
- b University of Basel, Basel, Switzerland
- ^c University of Maryland, Department of Psychology, College Park, MD, USA
- d University of Maryland, School of Public Health, College Park, MD, USA
- e City of Cape Town, Department of Health, Cape Town, South Africa
- ^f University of Copenhagen, Global Health Section, Department of Public Health, Copenhagen, Denmark
- g Curtin enAble Institute, Faculty of Health Sciences, Curtin University, Perth, WA, Australia
- h South African Medical Research Council, Alcohol, Tobacco, and Other Drug Research Unit, Cape Town, South Africa
- University of Cape Town, Division of Addiction Psychiatry, Department of Psychiatry and Mental Health, Cape Town, South Africa
- ^j University of Cape Town, HIV Mental Health Research Unit, Division of Neuropsychiatry, Department of Psychiatry and Mental Health, Cape Town, South Africa

ARTICLE INFO

Keywords: South Africa HIV Substance use referral Co-located treatment Matrix

ABSTRACT

Introduction: Despite efforts to detect and treat problematic substance use (SU) among people living with HIV (PLWH) in South Africa, integration of HIV and SU services is limited. We sought to understand whether PLWH and problematic SU were: (a) routinely referred to SU treatment, a co-located Matrix clinic, (b) used SU treatment services when referred, and (c) the individual amount spent on SU.

Methods: Guided by the RE-AIM implementation science framework, we examined patient-level quantitative screening and baseline data from a pilot clinical trial for medication adherence and problematic SU. Qualitative data came from semi-structured interviews with HIV care providers (N = 8), supplemented by patient interviews (N = 15)

Results: None of the screened patient participants (N = 121) who were seeking HIV care and had problematic SU were engaged in SU treatment, despite the freely available co-located SU treatment program. Only 1.5% of the enrolled patient study sample (N = 66) reported lifetime referral to SU treatment. On average, patients with untreated SU spent 33.3% (SD = 34.5%) of their monthly household income on substances. HIV care providers reported a lack of clarity about the SU referral process and a lack of direct communication with patients about patients' needs or interest in receiving an SU referral.

Discussion: SU treatment referrals and uptake were rare among PLWH reporting problematic SU, despite the high proportion of individual resources allocated to substances and the co-located Matrix site. A standardized referral policy between the HIV and Matrix sites may improve communication and uptake of SU referrals.

1. Introduction

HIV is a global problem and it carries most burden in sub-Saharan Africa. South Africa in particular has the greatest number of people living with HIV (PLWH), currently estimated to be 7.9 million people (Simbayi et al., 2019). In addition to HIV, problematic substance use (SU) is a co-occurring epidemic in many parts of South Africa, especially in the Western Cape Province. There is a significant burden of alcohol, cannabis, mandrax, methamphetamine ("tik"), and opiate use

(Dada et al., 2019; Harker et al., 2020). Between 13 – 37% of PLWH engage in problematic SU in the greater Cape Town area (Kader et al., 2014). In addition to the direct hazardous consequences of SU on health, such as increased risk of cirrhosis (Mann et al., 2003) and motor vehicle accidents (Derakhshanfar et al., 2012), problematic SU is associated with decreased engagement throughout the HIV care cascade, including lower antiretroviral therapy (ART) adherence, lower rates of viral suppression, and faster disease progression (Baum et al., 2010;

^{*} Corresponding author at: Swiss Tropical and Public Health Institute, Socinstrasse 57, Basel 4051, Switzerland. *E-mail address*: jennifer.belus@unibas.ch (J.M. Belus).

Velloza et al., 2020). Addressing problematic SU among PLWH must be a priority to improve the health outcomes of this population.

To address this health priority, there has been a growing emphasis on screening PLWH for problematic SU and providing evidence-based brief or extended brief interventions, which can range from as little as one 20-minute session to approximately six sessions of 60 minutes (Magidson et al., 2020; Myers et al., 2020, 2019a, 2018; Petersen Williams et al., 2020; Scott et al., 2020). These interventions can involve referring patients with more severe SU for further assessment and specialized treatment at stand-alone SU disorder treatment facilities, known as screening, brief intervention, and referral to treatment (SBIRT) programs. It is essential that PLWH who need SU treatment, whether a brief intervention or referral to stand-alone SU treatment, are able to receive it through existing healthcare channels and in a timely manner.

Although limited, there are affordable, stand-alone SU treatment options available where patients can be referred in South Africa (Myers et al., 2019b). In Cape Town, these include intensive outpatient programs using the Matrix model (City of Cape Town, 2021). The Matrix model is a 16-week, largely group-based intervention, that includes a primary focus on early recovery and relapse prevention. The Matrix model was originally developed in the U.S. to treat methamphetamine use and other stimulant use (Rawson et al., 1995) and has since been shown to improve SU outcomes, such as reducing the likelihood of a positive urine test for individuals who complete the treatment program (Rawson et al., 2021). The Matrix model has been implemented by the City of Cape Town's Health department to provide a freely available, evidence-based SU treatment program co-located in public primary care clinics that offer a range of health services, including HIV care (Gouse et al., 2016b; Magidson et al., 2017). In the context of limited treatment options in South Africa, Matrix has also been used to treat other types of substances, including opioids, alcohol, and cannabis use (Magidson et al., 2017). In a large study of over 2200 patients who attended a Matrix site in Cape Town, close to 1000 patients initiated treatment, defined as attending at least one individual or group session, and over half (54%) who completed urine toxicology had negative results at treatment exit for all substances (Gouse et al., 2016b).

In order to provide an integrated and holistic healthcare service that aids in eliminating transportation barriers, most Matrix sites are strategically co-located next to health clinics in Cape Town. However, there appears to be a lack of service integration across health and SU service settings due to low awareness of existing Matrix services (Magidson et al., 2019), which suggests there are barriers to Matrix utilization. Low awareness of where to refer patients has also been noted as a barrier to referral by SBIRT programs when implemented in HIV and other healthcare services. These SBIRT programs have consistently noted low rates of referral to stand-alone SU treatment after receipt of a brief intervention, although the reasons for this poor referral uptake are not well understood (Meade et al., 2015; Myers and Sorsdahl, 2014; Sorsdahl et al., 2012; van der Westhuizen et al., 2019). Improving the system of referrals to Matrix and other stand-alone SU treatment centers is critical in order for efficient integration of HIV and SU services.

To improve our understanding of SU treatment referrals and utilization in this context, and the potential impact on patients who have untreated SU, we sought to quantitatively investigate this by examining whether PLWH and problematic SU were: (a) routinely being referred to SU treatment, including a co-located Matrix program, (b) initiated and utilized SU treatment services when referred, and (c) individual costs spent on alcohol and substances when not engaged in treatment. We also sought to integrate qualitative feedback from the perspectives of HIV care providers to better understand the referral process at co-located HIV primary care and Matrix sites as well as identify barriers and possible solutions to referring patients to SU treatment when needed. This qualitative data with providers was supplemented with interview data from patients on their experience of SU referrals in the context of primary care. The overarching goal of this study was to improve continuity

of care for PLWH who needed SU treatment services by understanding current practices of SU referrals for patients receiving HIV services in primary care.

2. Methods

2.1. Participants and procedures

This study used a mixed methods approach integrating quantitative and qualitative data from two phases of a research study focused on investigating the integration of SU and HIV services for PLWH in a peri-urban community outside of Cape Town. Specifically, we utilized an embedded design (Creswell and Clark, 2017), where the quantitative results provided data on the extent to which SU referrals were occurring in the context of HIV primary care and the impact on patients, whereas the qualitative findings provided insights into the actual SU referral process. The parent study, where the data were derived, compared a 6-session behavioral activation and mindfulness intervention versus a referral to Matrix for PLWH who were in need of SU services (Magidson et al., 2021). We used RE-AIM (Glasgow et al., 1999), an implementation science framework, to guide the measures chosen for the current study, in order to align with the theoretical and implementation science frameworks of the parent study (Magidson et al., 2021) and because the overarching goal of the current study was to improve continuity of care for PLWH who were experiencing SU problems in a real-world clinical setting. All procedures were conducted in either English or isiXhosa, the dominant local language. For both phases of the larger study, participants were compensated with a grocery store gift card (ZAR 150, approximately \$11 USD at time of the study). Informed consent was completed with all participants and ethics approval was granted from the University of Cape Town Human Research Ethics Committee and from the City of Cape Town.

The study took place at an HIV clinic that was co-located with a Matrix site. The two clinics share one building, but the entrances are separate and can only be accessed from the outside (i.e., it is not possible to go between sites from the inside of the building). The quantitative data, which were used to quantify patient-reported referrals and individual costs of untreated SU, were taken from screening and baseline data collection from the clinical trial phase of the study (August 2018 - October 2019). Participants were those attending an HIV care clinic and met the following criteria: prescribed ART but non-adherent in the past 3 months¹; between 18 and 65 years old; and at least moderate SU according to the WHO Alcohol, Smoking, and Substance Involvement Screening Test (WHO ASSIST Working Group, 2002). A total of N = 175 were screened for the study and N = 121 met criteria for problematic SU based on the ASSIST of moderate or high-risk alcohol or other substance use. A total of N = 66 participants completed a baseline assessment. See Table 1 for the sample demographics. The majority of the sample used alcohol only. Of those who also had a moderate or high drug use risk score on the ASSIST, almost all used cannabis; some participants reported using amphetamines, sedatives, or cocaine. See Magidson et al. (2020) for more details on the methods.

We also conducted qualitative research to better understand the SU referral process between the primary care clinic and Matrix site and identify possible suggestions for improvement. Individual semi-structured interviews, which took place between October 2016 to February 2017, were conducted with N=8 HIV providers from two primary care clinics in the same area of Cape Town that the later clinical trial would take place. Providers were eligible if they were involved in HIV care at either of the primary care clinics, one of which was next door to a Matrix SU treatment center. Provider professions included nurses

¹ ART non-adherence was met by any of the following: (a) missing a pharmacy refill; (b) reinitiating first-line ART treatment or being on second-line ART treatment; or (c) having unsuppressed viral load (>400 copies/mL).

Table 1.Demographics of the Screening and Baseline Samples.

Characteristic	Screening sample($N = 121$)	Baseline sample($N = 66$)
Age, M (SD)	_	36.6 (9.7)
% (n) Women	55.4% (67)	54.6% (36)
% (n) Black African	_	98.5% (65)
Moderate or high substance use problems	_	_
% (n) Alcohol only	81.0% (98)	83.3% (55)
% (n) Drug only	6.6% (8)	3.0% (2)
% (n) Alcohol and drug	12.4% (15)	13.6% (9)
% (n) Tobacco ^a	61.2% (74)	57.6% (38)
ASSIST alcohol scoreb, M (SD)	25.0 (6.6)	26.3 (6.4)
ASSIST drug score ^b , M (SD)	15.0 (9.9)	17.4 (9.6)

Note.

- ^a Participants were not enrolled in the study based on tobacco.
- $^{\rm b}\,$ Based on participants who were eligible for that substance.

(n=3), medical providers (n=2), community health workers (n=2), and an adherence counselor (n=1). Providers were 46.6 years on average (SD=6.3), all were female, and 75% were Black African. On average, providers had 13.3 years of job experience (SD=7.2) and worked 3.1 years at their current job (SD=1.6). This data was supplemented with semi-structured qualitative patient interviews to understand how HIV clinic staff engaged with patients on issues related to their SU. We enrolled N=15 patients who were attending HIV care and were struggling with SU. Patients were 39.4 years old on average (SD=8.7), 46.7% female, and 100% Black African.

In the present analysis, HIV providers responded to questions around how the clinic identifies SU among patients, how the clinic currently responds to SU among patients (including if and how they refer patients to SU treatment and follow-up on referrals), and the type of provider needed to deliver interventions for SU treatment and ART adherence. HIV patients responded to questions around if they had ever been referred to SU treatment. All interviews lasted about an hour, were digitally audiotaped, and followed semi-structured interview guides developed with open-ended questions and probes to further explore responses. Further details about qualitative procedures are described in prior papers (e.g., Magidson et al., 2019). All interviews were transcribed verbatim into English (the isiXhosa interviews were first translated). Two independent coders analyzed all transcripts in NVivo v.11. We used thematic analysis (Braun and Clarke, 2006) informed by grounded theory (Glaser and Strauss, 1967), which allowed us to deductively analyze themes from the interview guide while also identifying emerging themes. All transcripts were double-coded and interrater reliability was measured throughout coding, yielding a final Kappa score > 0.80.

2.2. Measures

Table 2 provides an overview of the concepts and the measurement strategies that were guided by RE-AIM (Glasgow et al., 1999). RE-AIM assesses the following components: reach, effectiveness, adoption, implementation, and maintenance of an intervention or implementation strategy. These components of RE-AIM can be evaluated using a variety of indicators, either at the patient, provider, or system level (depending on the indicator assessed). We assessed the percentage of the screened sample who were currently enrolled in SU treatment as our indicator of reach. Effectiveness, or the overall net positive impact of an intervention, in the current context relates to the burden experienced by patients when not receiving SU treatment (conceptualized as lack of effectiveness) and strategies to increase uptake of SU referrals. This was assessed using the average percentage of the baseline sample's income spent on SU in the past month as a measure of the economic burden of untreated SU. We also examined the percent of the randomized sample who received a Matrix referral and who subsequently attended the program at least once (as described in Magidson et al., 2021). Adoption was assessed at the patient level only, using the percentage of the baseline sample who had a lifetime referral to SU treatment. HIV provider and patient qualitative interview responses to questions around how providers identify and respond to SU among patients at the clinic were used to assess implementation in RE-AIM. Maintenance was not assessed in this study because we focused on early implementation outcomes; we will evaluate the maintenance dimension in future work.

3. Results

3.1. Quantitative

The quantitative results are presented in Table 2 and summarized below. We found that none of the 121 patients who were attending HIV appointments in primary care and who screened positive for problematic SU were currently engaged in SU treatment. Furthermore, only 1.5% of the baseline sample of N=66 reported a lifetime referral for SU treatment. With regard to the individual economic burden for patients, participants on average spent 33% of their household income on SU in the past month. Participants' average household income was ZAR 3675 (~US \$243) and 62% of the sample reported not having enough to eat at least once in the past month, highlighting the financial difficulties faced by this sample.

3.2. Qualitative

The qualitative data from providers revealed a lack of clarity on the SU referral process, and when referrals did take place, they lacked a patient-centered approach, defined as not giving patients appropriate autonomy to make healthcare decisions and/or not engaging patients in the process of SU referral and treatment. These themes were echoed in the experiences of patients who had interacted with HIV providers around their SU. Finally, providers gave suggestions such as providing SU services within the clinic and hiring peers to better communicate with patients about SU referrals as ways to address the current barriers to referral procedures.

Lack of clarity on SU referral process. Matrix, the co-located SU treatment clinic, was the only place that providers described referring patients to SU treatment, unless patients required a higher level of care. Despite this, providers noted a lack of clarity around how to make the SU referral at the clinic. Processes for making a referral varied across providers, and often depended on provider burden. For instance, one provider described the preferred method of walking patients over to the Matrix treatment site to enhance uptake of the referral, rather than just providing the patient with a referral letter. Yet, this was dependent on the provider having time to do so.

If I've got time, I'll take the patient myself [to co-located Matrix site]. But I don't have time, I'll just direct the patient where to go by, and

Table 2.RE-AIM concepts, definitions, and measurement strategies.

RE-AIM concept	Definition	Measurement strategy	Result
Reach	The percentage of individuals who received the intervention (e.g., Matrix or other SU services)	Percent of screened ample, all had problematic SU, who were enrolled in SU treatment	0% (0/121)
Effectiveness	The impact of the intervention, positive outcomes net negative outcomes (e.g., on increasing	-Individual patient-level economic burden of untreated SU, defined as percentage of household income spent	33.3% (<i>SD</i> =34.5) 100% of eligible participants referred
	referrals to SU treatment, reducing problematic SU and associated burden)	on SU, past month -Percent of clinical trial sample willing to receive Matrix referral and percent uptake of referral	and 80.6% (25/31) attended at least one session (Magidson et al., 2021)
Adoption	The percentage of individuals who received the referral (e.g., to Matrix) and/or other SU services	Percent of baseline sample who had a lifetime referral to SU treatment	1.5% (1/66)
Implementation	Evaluates the delivery of the intervention (i.e., of the referral process)	Provider qualitative interviews asking: - How does the clinic identify (or become aware of) SU among patients? - How does the clinic currently respond to SU among patients? - Who do you think should deliver an intervention for ART adherence and SU? Patient qualitative interviews asking: - Has anyone at the clinic ever talked to you about your alcohol or drug use? Please explain. - Have you ever received a referral for alcohol or drug use? Please explain.	Primary themes were: lack of clarity on the SU referral process, lack of patient-centered approach to referrals, role of peers in enhancing the referral process
Maintenance	Examines the long-term sustainability of intervention delivery	Will be addressed in a subsequent larger trial following from the pilot study (Magidson et al., 2020)	-

I'll follow-up with the phone to find out if so-and-so did arrive... Provider 3 (Nurse, Black)

This was echoed by patient feedback of never having been referred to Matrix, as well as the quantitative results demonstrating low rates of referrals to Matrix. Several patients reported that their alcohol use was raised as an issue during their HIV appointments with the nurses, though they never received a referral for treatment or support.

No, I've never gone to any place [for substance use]. I've never received any, any treatment...I was told here at the clinic to stop using alcohol. And because of the things that were happening I then realized I really needed to stop using alcohol...[my viral load] was high. So, I was advised to stop using alcohol. Patient 1 (Female, Age 48)

Furthermore, several providers described that, although they referred patients to Matrix, they did not know much about the treatment that Matrix provided. One community health worker believed that patient attendance at Matrix after a referral was low because patients also did not have a good sense of what the treatment entailed. Providers suggested that if HIV care providers knew more about the treatment at Matrix, this would lead to better explanations and patients would be more willing to attend. One potential solution to address this issue was to deliver the Matrix (or other SU programming) at the HIV clinic.

Do [it] here at the clinic. I think it's better to try to come here at the clinic...after that they can get the educate, campaigns around the community...It's better because they [patients] come to fetch their medication [at the clinic as well]. They can do everything here. - Provider 4 (Community health worker, Black)

Lack of patient-centered approach in referrals. As described, the lack of a formalized referral process from the HIV clinic to Matrix meant that providers could choose how they referred patients. The examples of how providers approached referrals demonstrate how providers reduced patient autonomy for healthcare decisions and did not engage with patients in the referral process. For example, some providers described contacting the patient's family about the referral, rather than speaking directly to the patient about their need or desire for SU treatment.

I write a letter, and I rarely give it to the patient unless they ask for rehab. I give the letter to a caregiver and then they have the responsibility. I can't force much more than that. - Provider 1 (Medical Worker, White)

Indeed, providers shared that they often waited for patients to ask for referrals rather than identifying patients proactively who may need services. Furthermore, the provider's statement that she was unable to "force" any additional action hinted at a confrontational or adversarial nature of some provider-based referrals. This was echoed in another provider's statement that she referred patients to Matrix to "prove" their sobriety through a urine test:

I say, look, you say you are not using, and there is a problem and it really looks like you could be [using substances], so how about we do this [go to Matrix for a urine test], and then you can prove to me that you are not. - Provider 2 (Medical Worker, White)

While no patients reported being referred to Matrix, one patient reported receiving a referral to another primary care clinic in the community to meet with a doctor about their alcohol use.

I was once referred to [clinic name] but the doctor was not there, so I never went again...It was for this alcohol...I was told I am going for counselling so that I stop drinking alcohol, or something like that...The doctor was not there and I never went again. – Patient (Female, Age 43)

As the quote indicates, the provider was not there when the patient attempted to receive services, and as a result, they did not try to seek services again. It was unclear from the participant whether they had an appointment with the provider, or if it was a day when the provider was not working. Regardless, there did not appear to be follow-up from the original clinic that made the referral to check if the patient had attended. This highlights the importance of follow-up, which can be conceptualized as patient-centered care, rather than a perfunctory service.

Role of peers in enhancing the referral process. We asked providers (not patients) to suggest ways of enhancing the current referral strategies, which were not patient-centered. Incorporating peers was discussed as a strategy to better communicate and engage patients about the SU referral process. Providers explained that a peer may be able to better relate to what the patient is experiencing with their SU problems, and consequently, better able to explain to the patient why SU treatment may be beneficial. For instance, one HIV care provider shared:

I think what is missing a lot is...the essence of kind of a peer intervention person, because they [the patient] go from me as a health professional trying to explain why it's [important], to Matrix as pro-

fessionals but also trying. Yeah, I think that level is definitely what is missing at the moment. - Provider 2 (Medical Worker, White)

Results suggest that peers could serve in the role of intermediary between medical professionals and patients and improve the SU referral process.

4. Discussion

The goal of this study was to understand the extent to which PLWH with ongoing problematic SU were being referred and utilizing the public SU treatment services at the co-located Matrix site. Study results reveal that none of the patients who were receiving clinic-based HIV care were in SU treatment and that only 1.5% of the sample reported a lifetime referral to Matrix. The economic, patient-level burden of untreated SU was high, at about 33% of patients' household income. Qualitative data from providers, supplemented with patient data, illuminated the referral procedures between the two sites were not formalized, lacked clarity, and were not patient-centered.

The challenges cited regarding the lack of integration between the HIV clinic and co-located Matrix site are longstanding issues in the broader literature of integrating behavioral health services into primary care in resource-limited settings, both in sub-Saharan Africa as well as high-income countries such as the U.S. (Hall et al., 2015; Mendenhall et al., 2014). It is important to note that behavioral health services can be delivered using a range of approaches in the context of primary care settings. Coordinated services are those where a behavioral health referral is made to a specialist provider in a different setting than where the medical care is provided. Co-located services refer to medical and behavioral services that exist in the same physical space, whereas integrated services involve a combined treatment plan for medical and behavioral health (Blount, 2003). In the current study, HIV primary care and SU services were co-located. As the findings suggest, some coordination of these co-located services exist (i.e., referrals), but integration of services does not.

Yet, it is recognized that integrating SU and other mental health services into primary care settings is needed to overcome barriers to treatment, such as stigma and limited resources to attend visits in multiple locations (Alloh et al., 2018; Cubillos et al., 2020). To date, very few HIV and SU integrated services exist, particularly in sub-Saharan Africa (Haldane et al., 2017; Parcesepe et al., 2018). However, it is possible that small adjustments to the current system may result in a large impact on patients' healthcare. For example, providers mentioned the preferred method of walking patients over to Matrix for their referral, rather than just providing a letter and having the patient go on their own. Evidence from another co-located Matrix and primary care site in Cape Town demonstrates that HIV testing can be dramatically improved when Matrix staff walk patients over to the primary care clinic next door (Gouse et al., 2016a). In our group's pilot trial for SU and HIV medication adherence at this site, we used this 'warm handoff' approach for patients who were randomized to receive a Matrix referral, and found that about 80% of patients attended Matrix, indicating that this approach is feasible and likely efficacious to improve SU referral uptake (Magidson et al., 2020).

When referrals to Matrix did happen according to our qualitative findings, they lacked a patient-centered focus. High quality SU services in South Africa involve staff spending enough time with patients, providing patients with information on available treatment services, and involving patients in the treatment decision-making process (Myers et al., 2015). Yet, data from this study revealed that patients were excluded from the referral process at times, which also has the potential to reinforce stereotypes that people who use substances are not competent with regard to their health (Yang et al., 2017). Although including family members in SU treatment is recommended (Akram and Copello, 2013), it is not a replacement for engaging patients in their own healthcare decisions. Moreover, the very low lifetime referral rate observed in this

study may partially be explained by the fact that patients did not know they had been referred for treatment due to their exclusion in the pro-

Provider stigma towards patients with SU, which was observed in some provider interviews, is an ongoing problem and may lead patients to minimize or deny their SU, avoid clinics, or delay seeking or restarting care (e.g., Myers et al., 2016; Regenauer et al., 2020). Providers with SU stigma may also provide lower quality care to patients struggling with SU—for instance, spending less time with patients, being less likely to implement evidence-based care, and prioritizing a task-oriented versus collaborative approach towards these patients (van Boekel et al., 2013). Formative work from our team using the same patient interviews also highlighted that patients experienced stigma from healthcare providers regarding their SU when accessing HIV care (Magidson et al., 2019). Interventions aimed at reducing provider SU stigma are efficacious (Nyblade et al., 2019), though not yet part of regular training for clinicians in South Africa.

An additional strategy that may work to improve integration of services, reduce provider stigma towards SU, and deliver more patient-centered care is by including peers as service providers for SU. Peers are defined as individuals with lived substance use experience, who are trained to provide particular support services and incorporate their substance use experience into interactions with patients. In the U.S., the use of peer recovery specialists, who receive training and go through a certification process, deliver services such as linking patients to care, helping patients navigate health systems, and case management (Bassuk et al., 2016). Incorporating peers into existing healthcare teams can successfully increase patients' engagement in care and SU outcomes (e.g., Bassuk et al., 2016; Magidson et al., 2018). This cadre of healthcare worker does not yet exist in South Africa, though other researchers have advocated for this approach (Jack et al., 2020).

This study has several strengths and limitations that need to be acknowledged. Strengths include the use of mixed methods approach, which allows for an explanation of the quantitative results with qualitative data. Furthermore, the patient participants in the study represent an underserved group, with both ART adherence and SU challenges. Addressing the needs of this group is a high priority. Study limitations include the fact that the experience and rates of SU referral likely looks different in patients who demonstrate high levels of ART adherence or in patients who have fallen out of HIV care for a longer period of time. Our results are likely not generalizable beyond the current sample. Furthermore, our quantitative assessments were not conducted at the provider or health systems level; yet, successful implementation of evidence-based interventions is contingent on factors operating at these levels, such as having the structural procedures in place to support intervention delivery or provider adoption/uptake of an intervention. Our patient-level quantitative data only provides information on the implementation impact on patients, rather than the modifiable factors operating at the provider or system levels. Finally, we were also not able to assess the maintenance factor of RE-AIM, which needs to be evaluated in a future study over a longer period of time.

5. Conclusion

Although evidence-based SU treatments are publicly available in Cape Town, this study shows that PLWH who have problematic SU and who are accessing clinic-based HIV services rarely, if ever, receive referrals. Further, this study demonstrated that the economic burden of untreated problematic SU on patients in this sample totaled about 30% of their household monthly income. This is echoed by other research with methamphetamine users in Cape Town, which shows that the average monthly amount spent on SU well exceeds the median household income (Meade et al., 2015). Poverty and unemployment are high in this community, though prior research demonstrates that successful SU treatment can result in improved employment for some populations (Dunigan et al., 2014). Integrating HIV and SU services across clinical

sites and using more patient-centered referral approaches by HIV care providers, as well as potentially incorporating peers to provide SU referrals, are strategies that may lead to an increased number of referrals by providers, and ultimately, greater uptake by patients to reduce the economic and health burden of untreated problematic SU among PLWH.

Contributors

JMB conceptualized the research idea, conducted the analyses, and wrote the first draft of the methods, results, and discussion. KR supported the qualitative analyses and EH wrote the first draft of the introduction; both provided substantive edits on the manuscript. JFM secured funding for the project, contributed to the research idea, and provided substantive edits on the manuscript. ALR, WB, LSA, BM, JAJ, provided substantive edits on the manuscript. All authors have approved the final version of the manuscript.

Declaration of Competing Interest

All authors declare they have no competing interests to report.

Role of funding source

This study is funded by the National Institutes of Drug Abuse (K23DA041901, PI: Magidson). Some of the author time for Lena Andersen and John Joska was supported by National Institute of Mental Health (NIMH) grant R01MH103770 (PIs: Safren and O'Cleirigh), and for Bronwyn Myers by the South African Medical Research Council. Drs. Magidson and Myers are also supported by National Institute of Mental Health (R34MH122268) and National Institute of Drug Abuse (R21DA053212). The funding source had no role in study design or execution, analyses, manuscript writing, or decision to submit results.

References

- Akram, Y., Copello, A., 2013. Family-based interventions for substance misuse: a systematic review of reviews. Lancet 382, S24. doi:10.1016/S0140-6736(13)62449-6.
- Alloh, F.T., Regmi, P., Onche, I., Van Teijlingen, E., Trenoweth, S., 2018. Mental health in low-and middle income countries (LMICs): going beyond the need for funding. Heal. Prospect 17, 12–17. doi:10.3126/hprospect.v17i1.20351.
- Bassuk, E.L., Hanson, J., Greene, R.N., Richard, M., Laudet, A., 2016. Peer-delivered recovery support services for addictions in the United States: a systematic review. J. Subst. Abuse Treat. 63, 1–9. doi:10.1016/j.jsat.2016.01.003.
- Baum, M.K., Rafie, C., Lai, S., Sales, S., Page, J.B., Campa, A., 2010. Alcohol use accelerates HIV disease progression. AIDS Res. Hum. Retroviruses 26, 511–518. doi:10.1089/aid.2009.0211.
- Blount, A., 2003. Integrated primary care: organizing the evidence. Fam. Syst. Heal. 21, 121–133. doi:10.1037/1091-7527.21.2.121.
- Braun, V., Clarke, V., 2006. Using the matic analysis in psychology. Qual. Res. Psychol. 3, 77–101. doi: 10.1191/1478088706qp063oa.
- City of Cape Town, 2021. Help and treatment for your addiction [WWW Document].

 Creswell, J.W., Clark, V.L.P., 2017. Designing and Conducting Mixed Methods Research,
 3rd ed. Sage publications, Thousand Oaks, CA.
- Cubillos, L., Bartels, S., Torrey, W., Naslund, J., Uribe-Restrepo, J., Gaviola, C., Castro Díaz, S., John, D.T., Williams, M.J., Cepeda, M., Gómez-Restrepo, C., Marsch, L., 2020. The effectiveness and cost-effectiveness of integrating mental health services in primary care in low- and middle-income countries: systematic review. BJPsych. Bull. 1–13. doi:10.1192/bjb.2020.35.
- Dada, S., Burnhams, N.H., Erasmus, J., Lucas, W., Parry, C., Bhana, A., Pretorius, S., Weimann, R., Keen, H., 2019. South African community Epidemiology Network On Drug Use (SACENDU): Monitoring alcohol, Tobacco and Other Drug Use Treatment Admissions in South Africa. Tygerberg, South Africa.
- Derakhshanfar, H., Meibodi, M.K., Kariman, H., Arhamidolatabadi, A., Safari, S., 2012. Substance abuse among drivers of motor vehicle collisions. Trauma Mon. 17, 236–238. doi:10.5812/traumamon.4182.
- Dunigan, R., Acevedo, A., Campbell, K., Garnick, D.W., Horgan, C.M., Huber, A., Lee, M.T., Panas, L., Ritter, G.A., 2014. Engagement in outpatient substance abuse treatment and employment outcomes. J. Behav. Health Serv. Res. 41, 20–36. doi:10.1007/s11414-013-9334-2.
- Glaser, B.G., Strauss, A., 1967. The Discovery Grounded Theory. Aldine, Chicago, IL.
- Glasgow, R.E., Vogt, T.M., Boles, S.M., 1999. Evaluating the public health impact of health promotion interventions: the RE-AIM framework. Am. J. Public Health 89, 1322– 1327. doi:10.2105/AJPH.89.9.1322.
- Gouse, H., Joska, J.A., Lion, R.R., Watt, M.H., Burnhams, W., Carrico, A.W., Meade, C.S., 2016a. HIV testing and sero-prevalence among methamphetamine users seeking substance abuse treatment in Cape Town. Drug Alcohol Rev. 35, 580–583. doi:10.1111/dar.12371.

- Gouse, H., Magidson, J.F., Burnhams, W., Remmert, J.E., Myers, B., Joska, J.A., Carrico, A.W., 2016b. Implementation of cognitive-behavioral substance abuse treatment in sub-Saharan Africa: treatment engagement and abstinence at treatment exit. PLoS ONE 11, e0147900. doi:10.1371/journal.pone.0147900.
- Haldane, V., Cervero-Liceras, F., Chuah, F.L.H., Ong, S.E., Murphy, G., Sigfrid, L., Watt, N., Balabanova, D., Hogarth, S., Maimaris, W., Buse, K., Piot, P., McKee, M., Perel, P., Legido-Quigley, H., 2017. Integrating HIV and substance use services: a systematic review. J. Int. AIDS Soc. 20, 21585. doi:10.7448/IAS.20.1.21585.
- Hall, J., Cohen, D.J., Davis, M., Gunn, R., Blount, A., Pollack, D.A., Miller, W.L., Smith, C., Valentine, N., Miller, B.F., 2015. Preparing the workforce for behavioral health and primary care integration. J. Am. Board Fam. Med. 28, S41–S51. doi:10.3122/jabfm.2015.S1.150054.
- Harker, N., Lucas, W.C., Laubscher, R., Dada, S., Myers, B., Parry, C.D.H., 2020. Is South Africa being spared the global opioid crisis? A review of trends in drug treatment demand for heroin, nyaope and codeine-related medicines in South Africa (2012– 2017). Int. J. Drug Policy 83, 102839. doi:10.1016/j.drugpo.2020.102839.
- Jack, H.E., Myers, B., Regenauer, K.S., Magidson, J.F., 2020. Mutual capacity building to reduce the behavioral health treatment gap globally. Adm. Policy Ment. Heal. Ment. Heal. Serv. Res. 47, 497–500. doi:10.1007/s10488-019-00999-y.
- Kader, R., Seedat, S., Govender, R., Koch, J.R., Parry, C.D., 2014. Hazardous and harmful use of alcohol and/or other drugs and health status among South African patients attending HIV clinics. AIDS Behav. 18, 525–534. doi:10.1007/s10461-013-0587-9.
- Magidson, J.F., Gouse, H., Burnhams, W., Wu, C.Y.Y., Myers, B., Joska, J.A., Carrico, A.W., 2017. Beyond methamphetamine: documenting the implementation of the Matrix model of substance use treatment for opioid users in a South African setting. Addict. Behav. 66, 132–137. doi:10.1016/j.addbeh.2016.11.014.
- Magidson, J.F., Joska, J.A., Belus, J.M., Andersen, L.S., Regenauer, K.S., Rose, A.L., Myers, B., Majokweni, S., O'Cleirigh, C., Safren, S.A., 2021. Project Khanya: results from a pilot randomized type 1 hybrid effectiveness-implementation trial of a peer-delivered behavioural intervention for ART adherence and substance use in HIV care in South Africa. J. Int. AIDS Soc. 24 (S2), e25720. doi:10.1002/jia2.25720.
- Magidson, J.F., Joska, J.A., Myers, B., Belus, J.M., Regenauer, K.S., Anderson, L.S., Majokweni, S., O'Cleirigh, C., Safren, S.A., 2020. Project Khanya: a randomized, hybrid effectiveness-implementation trial of a peer-delivered behavioral intervention for ART adherence and substance use in Cape Town, South Africa. Implement. Sci. Commun. 1, 23. doi:10.1186/s43058-020-00004-w.
- Magidson, J.F., Joska, J.A., Regenauer, K.S., Satinsky, E., Andersen, L.S., Seitz-Brown, C.J., Borba, C.P.C., Safren, S.A., Myers, B., 2019. Someone who is in this thing that I am suffering from": the role of peers and other facilitators for task sharing substance use treatment in South African HIV care. Int. J. Drug Policy 70, 61–69. doi:10.1016/j.drugpo.2018.11.004.
- Magidson, J.F., Regan, S., Jack, H., Wakeman, S., 2018. Reduced hospitalizations and increased abstinence six months after recovery coach contact. Poster Presented at the American Society of Addiction Medicine (ASAM).
- Mann, R.E., Reginald, S.G., Govoni, R., 2003. The Epidemiology of alcoholic liver disease. Alcohol Res. Heal. 27, 209–219.
- Meade, C.S., Towe, S.L., Watt, M.H., Lion, R.R., Myers, B., Skinner, D., Kimani, S., Pieterse, D., 2015. Addiction and treatment experiences among active methamphetamine users recruited from a township community in Cape Town, South Africa: a mixed-methods study. Drug Alcohol Depend 152, 79–86. doi:10.1016/j.drugalcdep.2015.04.016.
- Mendenhall, E., De Silva, M.J., Hanlon, C., Petersen, I., Shidhaye, R., Jordans, M., Luitel, N., Ssebunnya, J., Fekadu, A., Patel, V., Tomlinson, M., Lund, C., 2014. Acceptability and feasibility of using non-specialist health workers to deliver mental health care: stakeholder perceptions from the PRIME district sites in Ethiopia, India, Nepal, South Africa, and Uganda. Soc. Sci. Med. 118, 33–42. doi:10.1016/j.socscimed.2014.07.057
- Myers, B., Carney, T., Wechsberg, W.M., 2016. Not on the agenda": a qualitative study of influences on health services use among poor young women who use drugs in Cape Town, South Africa. Int. J. Drug Policy 30, 52–58. doi:10.1016/j.drugpo.2015.12.019.
- Myers, B., Govender, R., Koch, J.R., Manderscheid, R., Johnson, K., Parry, C.D.H., 2015. Development and psychometric validation of a novel patient survey to assess perceived quality of substance abuse treatment in South Africa. Subst. Abuse Treat. Prev. Policy 10, 44. doi:10.1186/s13011-015-0040-3.
- Myers, B., Lund, C., Lombard, C., Joska, J., Levitt, N., Butler, C., Cleary, S., Naledi, T., Milligan, P., Stein, D.J., Sorsdahl, K., 2018. Comparing dedicated and designated models of integrating mental health into chronic disease care: study protocol for a cluster randomized controlled trial. Trials 19, 185. doi:10.1186/s13063-018-2568-9.
- Myers, B., Parry, C.D.H., Morojele, N.K., Nkosi, S., Shuper, P.A., Kekwaletswe, C.T., Sorsdahl, K.R., 2020. Moving forward with life": acceptability of a brief alcohol reduction intervention for people receiving antiretroviral therapy in South Africa. Int. J. Environ. Res. Public Health 17, 5706. doi:10.3390/ijerph17165706.
- Myers, B., Petersen-Williams, P., van der Westhuizen, C., Lund, C., Lombard, C., Joska, J.A., Levitt, N.S., Butler, C., Naledi, T., Milligan, P., Stein, D.J., Sorsdahl, K., 2019a. Community health worker-delivered counselling for common mental disorders among chronic disease patients in South Africa: a feasibility study. BMJ Open 9, e024277. doi:10.1136/bmjopen-2018-024277.
- Myers, B., Sorsdahl, K., 2014. Addressing substance use within primary health care settings in South Africa: opportunities and challenges. Addicta Turk. J. Addict. 1, 80–94.
- Myers, B., Williams, P.P., Govender, R., Manderscheid, R., Koch, J.R., 2019b. A mixed-methods evaluation of the implementation of a performance measurement system for South Africa's substance use treatment services. J. Stud. Alcohol Drug. 131–138. doi:10.15288/jsads.2019.s18.131.
- Nyblade, L., Stockton, M.A., Giger, K., Bond, V., Ekstrand, M.L., Lean, R.M., Mitchell, E.M.H., Nelson, L.R.E., Sapag, J.C., Siraprapasiri, T., Turan, J., Wouters, E., 2019. Stigma in health facilities: why it matters and how we can change it. BMC Med. 17, 25. doi:10.1186/s12916-019-1256-2.

- Parcesepe, A.M., Mugglin, C., Nalugoda, F., Bernard, C., Yunihastuti, E., Althoff, K., Jaquet, A., Haas, A.D., Duda, S.N., Wester, C.W., Nash, D., 2018. Screening and management of mental health and substance use disorders in HIV treatment settings in low- and middle-income countries within the global IeDEA consortium. J. Int. AIDS Soc. 21, e25101. doi:10.1002/jia2.25101.
- Petersen Williams, P., Brooke-Sumner, C., Joska, J., Kruger, J., Vanleeuw, L., Dada, S., Sorsdahl, K., Myers, B., 2020. Young south African women on antiretroviral therapy perceptions of a psychological counselling program to reduce heavy drinking and depression. Int. J. Environ. Res. Public Health 17, 2249. doi:10.3390/ijerph17072249.
- Rawson, R., Glasner, S., Brecht, M.-.L., Farabee, D., 2021. A randomized comparison of 4 vs. 16 weeks of psychosocial treatment for stimulant users. J. Subst. Abuse Treat. 124, 108274. doi:10.1016/j.jsat.2020.108274.
- Rawson, R.A., Shoptaw, S.J., Obert, J.L., Mccann, M.J., Hasson, A.L., Marinelli-casey, P.J., Brethen, P.R., Ling, W., Minsky, S., Lopata, D., Casey, J., Molnar-Southon, D., Smith, M., Cho, F., Corrales NIDA, L., 1995. An Intensive Outpatient Approach for Cocaine Abuse Treatment The Matrix Model. J. Subst. Abuse Treat. 12, 117–127.
- Regenauer, K.S., Myers, B., Batchelder, A.W., Magidson, J.F., 2020. That person stopped being human": intersecting HIV and substance use stigma among patients and providers in South Africa. Drug Alcohol Depend. 216, 108322. doi:10.1016/j.drugalcdep.2020.108322.
- Scott, K., Sibeko, G., Cummings, B., Myers, B., Sorsdahl, K., Stein, D.J., Kuo, C., Becker, S.J., 2020. Training the addiction treatment workforce in HIV endemic regions: an overview of the South Africa HIV Addiction Technology Transfer Center initiative. Train. Educ. Prof. Psychol. 14, 78–85. doi:10.1037/tep0000286.

- Simbayi, L.C., Zuma, K., Zungu, N., Moyo, S., Marinda, E., Jooste, S., Mabaso, M., Ramlagan, S., North, A., van Zyl, J., Mohlabane, N., Dietrich, C., Naidoo, I., Team, S.V., 2019. South African National HIV Prevalence, Incidence, Behaviour and Communication Survey, 2017. HSRC Press, Cape Town, South Africa.
- Sorsdahl, K.R., Stein, D.J., Weich, L., Fourie, D., Myers, B., 2012. The effectiveness of a hospital-based intervention for patients with substance-use problems in the Western Cape [WWW Document]. SAMJ South African Med. J..
- van Boekel, L.C., Brouwers, E.P.M., van Weeghel, J., Garretsen, H.F.L., 2013. Stigma among health professionals towards patients with substance use disorders and its consequences for healthcare delivery: systematic review. Drug Alcohol Depend. 131, 23–35. doi:10.1016/j.drugalcdep.2013.02.018.
- van der Westhuizen, C., Myers, B., Malan, M., Naledi, T., Roelofse, M., Stein, D.J., Lahri, S., Sorsdahl, K., 2019. Implementation of a screening, brief intervention and referral to treatment programme for risky substance use in South African emergency centres: a mixed methods evaluation study. PLoS ONE 14, e0224951. doi:10.1371/journal.pone.0224951.
- Velloza, J., Kemp, C.G., Aunon, F.M., Ramaiya, M.K., Creegan, E., Simoni, J.M., 2020. Alcohol use and antiretroviral therapy non-adherence among adults living with HIV/AIDS in sub-Saharan Africa: a systematic review and meta-analysis. AIDS Behav. 24, 1727–1742. doi:10.1007/s10461-019-02716-0.
- WHO ASSIST Working Group, 2002. The alcohol, smoking and substance involvement screening test (ASSIST): development, reliability and feasibility. Addiction 97, 1183–1194. doi:10.1046/j.1360-0443.2002.00185.x.
- Yang, L.H., Wong, L.Y., Grivel, M.M., Hasin, D.S., 2017. Stigma and substance use disorders: an international phenomenon. Curr. Opin. Psychiatry 30, 378–388. doi:10.1097/YCO.00000000000000351.