# Depressive Symptoms at the Muhimbili National Hospital MAT Clinic, Dar Es Salaam, Tanzania: A Cross-Sectional Study

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## ABSTRACT

**Background** Globally, the number of people who use substances has rapidly increased over the past decade and has become a public health problem. Co-morbidity of mental disorders and substance use disorder has been well documented with disproportionately higher diagnosis for depression been made in patients with substance use disorders including heroin users. Limited number of studies have examined the phenomenon of symptoms of depression among MAT clients in Tanzania setting and none has proposed the probable interventions.

**Broad objective** To determine the prevalence and factors associated with depressive symptoms among methadone using clients attending MAT clinic at Muhimbili National Hospital in Dar es Salaam, Tanzania.

**Methods** Hospital based cross-sectional study was conducted using quantitative methods and utilizing the Patient Health questionnaire-9 (PHQ-9) as screeners for depressive symptoms, a semi-structured questionnaire for socio-demographic information and clinical characteristics, Adverse Childhood Experiences-10 (ACE-10) for adverse childhood experiences (ACEs) and Multidimensional Scale of Perceived Social Support (MSPSS) for perceived social support. A total of 341 methadone using clients were recruited via systematic and stratified sampling techniques. Analysis was conducted using statistical package for social sciences (SPSS) version 23. Univariate analysis, logistic regression for Bivariate and Multivariate analysis presented as Odds ratios with 95% confidence interval and $p<0.05$ were conducted.

**Results** Overall, 310 (90.9%) participants were males. Mean age was 39.37 (SD□7.42) years. Prevalence of depressive symptoms was 36.7%. Risk of depressive symptoms increased by having a history of incarceration [aOR=2.87, 95%CI (1.70–4.86), ρ=0.000] and low perceived social support [aOR=4.03, 95%CI (1.78–9.15), ρ=0.001].

**Conclusion** Prevalence of depressive symptoms is high among clients taking methadone at the MAT clinic at Muhimbili National Hospital, Dar es Salaam, Tanzania. Those with a history of incarceration and low perceived social support are more likely to experience depression. Screening of depressive symptoms among MAT clients is essential as is the need to develop integrated psychosocial interventions tailored to their needs.

**Keywords:** Depressive symptoms, Medically Assisted Treatment (MAT), Substance use, comorbidity

## BACKGROUND

Substance use is currently one of the major issues to public health and its adverse effects are more emotive and widespread than previously thought. Reports note that over 35 million people suffer from substance related problems and only 10% receive treatment. Between 2016 and 2018, among those 15-64 years old, the global prevalence of heroin doubled from 0.5% to 1.2%.[1]

Heroin use in in Sub-Saharan Africa is increasing rapidly as the Southern heroin trafficking route expands

beyond its earlier Swahili Coast to South Africa connection to incorporate Madagascar and more people in poverty become disaffected and heroin involved.[2] People who use heroin face threats of overdose, accidental injuries, increased risk of HIV and hepatitis, high rates of TB, stigma, lack of social support, and legal problems more than those who use other drugs.[1 3]

Methadone has been used as the effective substitution treatment option in individuals suffering from opioid use disorders due to its peculiar pharmacological features such as long-acting effect on μ-opioid receptor and single daily administration that render it useful to treat opioids withdrawal symptoms without a risk of intoxication.[4 5] When provided as an opioid substitution therapy it, along with buprenorphine or naltrexone extended release, is called Medically Assisted Treatment (MAT).[6]

Due to its affordability, only methadone was initially available as a Medically Assisted Treatment (MAT) in Tanzania. Tanzania was the first sub-Saharan African country to launch free publicly available MAT as a part of the comprehensive package for HIV services.[7] This CDC/PEPFAR-funded initiative focused on combating HIV transmission among people who injected heroin who their initial rates of HIV seroprevalence was 42% in 2005.[7] Currently, medical treatment with methadone among the clients that attend MAT clinics have proven to be effective due to several indicators such as ability to help users to cease using heroin, decrease in criminality, decrease in HIV-, HBV- and HCV- related risk behaviors, treatment for TB, as well as improvement in physical health and psychosocial functioning including productivity.[8]

Globally, comorbidity of mental disorders among individuals with opioid use disorders (OUDs) reported to accounts for 7.4% (6.2–8.6) of all DALYs with disproportionately high diagnoses for depression been made in patients with substance use disorders.[9 10] These comorbid conditions pose challenges during management and predict poor outcomes as they tend to leave individuals with severe psychopathologies and many psychosocial impairments.[11] While maintenance on MAT programs significantly reduces opioids use and chances of developing anxiety and depression as well as improving psychosocial functioning;[12] successful management requires identification of these comorbid conditions and application of evidence-based treatments strategies such as psychotherapies, behavioral and pharmacological interventions in addition to methadone.[13]

A limited number of studies have been conducted among MAT clients in Tanzania to study symptoms of common mental disorders. [14 15 16] To the best of my knowledge, this is the first study to determine the prevalence and associated factors of depression among such a population and the proposed interventions thereof.

## METHODS

### Study design and settings

This cross-sectional study was conducted between August and September 2021 at the Medically Assisted Therapy (MAT) Clinic which operates under the Department of Psychiatric and Mental Health of Muhimbili National Hospital (MNH). MNH is the national referral and MUHAS teaching hospital located at Ilala municipality in Dar es Salaam, Tanzania. From MAT database, data obtained during February 2021 showed a total of 1386 clients received methadone daily. [17]

### Participants and sample size

Adult (aged 18 years and above) clients taking methadone at this MAT clinic during February 2021 and who met inclusion criteria were invited into the study. The minimum estimated sample size (N=341) was calculated using Yamane's formula for finite population.[18] MS referred back to data obtained in February 2021 which showed a total of 1386 clients attended the MAT clinic daily to obtain a prevalence figure.[17]

Participants selected were adults, available at clinic during the day of data collection and who were able to provide informed consent either through signature or fingerprint. Excluded were those enrolled on program less than two (2) months, who were on buprenorphine and psychotropic medications. Individuals were stratified into males and females forming two sampling frames in which a systematic sample of one in four was recruited until a total sample size was achieved. These sampling methods were preferred to ensure representativeness of both sex as well as giving clients equal chance of being selected into the study. This is due to significant male-female sex disproportion among clients attending MAT clinic, with majority being males (96%).[17]

**Data collection and variables**

Independent variables of interest were age, sex, education level, marital status, employment status, living arrangements, incarceration history, duration in MAT program, methadone dosage, concurrent substance use, physical health status, perceived social support and adverse childhood experiences (ACEs). The dependent variable in this study was depressive symptoms.

The collection of data was performed by the principal investigator and two registered nurses working at MAT clinic who had prior experience in mental health and public health research. Data collection tools were piloted, pre-tested, and modified accordingly. This helped the research team plan for the number of interviews to be conducted by one data collector per day while minimizing interference to the provision of clinical services. Eligible and interested participants were escorted to a private research office where they completed the informed consent procedure and the study survey. Participants were not financially compensated for their participation. All interviews were conducted in Swahili.

**Measures**

Data was collected through a survey comprised of a semi-structured questionnaire, Multidimensional Scale of Perceived Social Support (MSPSS), Adverse Childhood Experiences (ACE) questionnaire and Patient Health Questionnaire (PHQ-9).

**A semi-structured questionnaire**

A semi-structured questionnaire developed in English and then translated in Swahili language was used to collect the socio-demographic characteristics such as age, sex, marital status, education level, employment status, living arrangements, sexual risk behaviors, history of incarceration, and clinical characteristics. Clinical characteristics included concurrent substance use, duration on MAT program, methadone dosage and physical health status.

**Multidimensional Scale of Perceived Social support (MSPSS)**

We used the Multidimensional Scale of Perceived Social support (MSPSS) to assess perceived social support. This tool measures the level of social support using a Likert scale with 7-response options (from 1=very strongly disagree to 7=very strongly agree) for each of the 12 items assessed. The items are organized in three subscales assessing sources of social support i.e., from family members, friends or significant others. Subscale scores are obtained by adding all subscale score and dividing by 4, while total scale score is calculated by adding all items scores and dividing by 12. Perceived social support is considered good the higher the score. For example, a mean score of 5.1 to 7 indicates high support 3 to 5 moderate support, and 1 to 2.9 low support, and.[19] This tool has been validated for use in low-income countries, in Malawi[20] and Uganda it showed good internal consistency as demonstrated by a Cronbach's α of 0.83.[21]

**Adverse childhood experiences (ACE) questionnaire**

Participants' experience with childhood adversities was measured by 10-items Adverse Childhood Experiences (ACE-10) questionnaire that checks for the subject's recall of pre-age 19 years exposure to psychological, physical, and sexual abuse as well as household dysfunction including domestic violence, substance use, and

incarceration.[22] Each of 10 items has a Yes/No response. Scores range from minimum of 0 to a maximum of 10 with the higher scores indicating greater adverse childhood exposure and therefore the risk for negative health consequences. An individual who score four or more on ACE-10 has 4 to 12-fold increased possibility of health risks compared to those with lower scores.[22] This tool has not been validated in Tanzania though similar set of questions has been used in the national survey on violence against children,[23] also an 8-items Likert-type question adapted from the ACE study was used among street children in northern Tanzania.[24] The ACE-10 questionnaire has good psychometric properties and performs well with study populations in cross-cultural applications.[22]

**Patient Health Questionnaire (PHQ-9)**

We used the Patient Health Questionnaire 9 (PHQ-9) as a screening tool for depressive symptoms.[25] It has been previously translated to Swahili[26]and validated in the Tanzanian context showing very good psychometric properties.[27] The PHQ-9 comprises 9 items which match the Diagnostic and Statistical Manual of Mental Disorders version 5 (DSM 5) criteria, whereby each item can be scored from 0 (no symptoms at all) to 3 (symptoms nearly every day) with a maximum score of 27. The scores are interpreted as minimal depression (0–4), mild depression (5–9), moderate depression (10–14), moderately severe depression (15-19) and severe depression (20–27). The tool has been used for assessment of depression in various population including MAT clients in China with Cronbach's alpha of 0.89 with a cut off points of 5, which we used in this study.[28 29]

**Data management and analysis**

Data were analyzed using SPSS (v.23). Descriptive data was collected, organized, and summarized as; continuous data through frequencies, means and standard deviations and categorical data through frequencies. Bivariate analysis was done to check for significant association between the outcome of interest and independent variables. Multivariate analysis was conducted using all variables that showed significant association (including those with $\rho<0.25$) from and the bivariate analysis and adjusted to control for confounders; hence determining independent associations between anxiety and depressive symptoms, and the associated factors. Crude and adjusted odds ratios with corresponding 95% confidence intervals and p-values were reported. A two-sided $\rho<0.05$ was considered statistically significant.

**Ethical considerations**

Ethical clearance to conduct this study was sought from the Muhimbili University of Health and Allied Sciences (MUHAS) Senate's Research and Publication Committee (SRPC) (protocol number: MUHAS-REC-07-769). All participants gave written informed consent; if non-literate, participants gave a thumbprint to signify consent in presence of a data collector and another witness.

## RESULTS

**Socio-demographic, clinical and psychological characteristics of the study participants**

This study enrolled 341 participants, majority of them being males 310 (90.9%). The mean age of the sample was 39.37 years (SD□7.42) with nearly half 157 (46.0%) falling into 36–45 years age group. Majority of participants 250 (73.3%) had attained primary or lower level of education and about two-thirds 217 (63.6%) were unemployed. More than a half 179 (52.5%) of the participants had partners. About three-quarters 248 (72.7%) had stable living arrangements (not homeless) in the past year. More than two-third of the participants 238 (69.8%) did not report HIV risk behaviors for the past six months. Nearly three-quarters 243 (71.3%) had no history of incarceration. Slightly less than two third of participants 211 (61.9%) had been on the MAT program for at least 24 months and about a half 164 (48.1%) were on more than 120mg of methadone dose daily. Almost two third of participants 223 (65.4%) had used substances in the past 30 days where by tobacco 104 (30.5%) was the commonly used followed by polysubstance 74 (21.7%). Nearly three quarters of

participants 249 (73.0%) were HIV negative while majority 264 (77.4%) and 276 (80.9%) were negative for hepatitis and TB infections respectively. Slightly below two thirds of participants 211 (61.9%) had moderate perceived social support and more than half of participants 202 (59.2%) had low risk of ACEs (see table 1).

**Table 1: Descriptive statistics of the socio-demographic, clinical and psychological characteristics of the study participants (N=341)**

| Variable | Frequency (%) | Mean | SD |
|---|---|---|---|
| **Age (years)** | | **39.37** | **7.42** |
| 35 and below | 119 (34.9) | | |
| Between 36–45 | 157 (46.0) | | |
| 46 and above | 65 (19.1) | | |
| **Sex** | | | |
| Male | 310 (90.9) | | |
| Female | 31 (9.1) | | |
| **Level of education** | | | |
| Primary or lower | 250 (73.3) | | |
| Higher than primary | 91 (26.7) | | |
| **Marital status** | | | |
| Without partners | 179 (52.5) | | |
| With partners | 162 (47.5) | | |
| **Living arrangement (past year)** | | | |
| Homeless | 93 (27.3) | | |
| Not homeless | 248 (72.7) | | |
| **Employment status (past year)** | | | |
| Unemployed | 217 (63.6) | | |
| Employed | 124 (36.4) | | |
| **HIV risk behaviors (past 6 months)** | | | |
| Yes | 103 (30.2) | | |
| No | 238 (69.8) | | |

| | | | |
|---|---|---|---|
| **Incarceration history** | | | |
| Yes | 98 (28.7) | | |
| No | 243 (71.3) | | |
| **Duration at MAT program (months)** | | **45.86** | **33.02** |
| 24 and below | 130 (38.1) | | |
| More than 24 | 211 (61.9) | | |
| **Methadone dosage (milligrams)** | | | |
| Less than 80 | 76 (22.3) | | |
| Between 80–120 | 101 (29.6) | | |
| More than 120 | 164 (48.1) | | |
| **Current substance use (past 30 days)** | | | |
| Yes | 223 (65.4) | | |
| No | 118 (34.6) | | |
| **Type of substance used (past 30 days)** | | | |
| Tobacco | 104 (30.5) | | |
| Alcohol | 45 (13.2) | | |
| Polysubstance use | 74 (21.7) | | |
| **HIV status** | | | |
| Positive | 92 (27.0) | | |
| Negative | 249 (73.0) | | |
| **Hepatitis status** | | | |
| Positive | 77 (22.6) | | |
| Negative | 264 (77.4) | | |
| **TB status** | | | |
| Positive | 65 (19.1) | | |
| Negative | 276 (80.9) | | |

| | | | |
|---|---|---|---|
| **Perceived social support** | | | |
| Low | 58 (17.0) | | |
| Moderate | 211 (61.9) | | |
| High | 72 (21.1) | | |
| **Adverse childhood experiences (ACE)** | | | |
| Low risk | 202 (59.2) | | |
| High risk | 139 (40.8) | | |

Key: MAT=Medically Assisted Therapy, SD=Standard deviation

**Prevalence of depressive symptoms among study participants**

The prevalence of depressive symptoms was 36.7% (n=125) (table 2) where-by 88 (25.8%) had mild, 22 (6.5%) moderate, 10 (2.9%) moderately severe and 5 (1.5%) severe symptoms.

**Table 2: Prevalence of depressive symptoms over the past 2 weeks according to PHQ-9 among study participants (N=341)**

| **Variable** | **Outcome** | **n (%)** | **Severity** | |
|---|---|---|---|---|
| **Depressive symptoms** | No | 216 (63.3) | None | 216 (63.3) |
| | Yes | 125 (36.7) | Mild | 88 (25.8) |
| | | | Moderate | 22 (6.5) |
| | | | Moderately severe | 10 (2.9) |
| | | | Severe | 5 (1.5) |

**Factors associated with depressive symptoms among study participants**

The likelihood of having depressive symptoms was almost three times more likely among participants who reported a history of incarceration [aOR=2.87, 95%CI (1.70–4.86), ρ=0.000] (table 4). Additionally, those experiencing low perceived social support had more than four times the odds of having depressive symptoms [aOR=4.03, 95%CI (1.78–9.15), ρ=0.001] than those with high perceived social support.

**Table 4: Bivariate and multivariate analysis of factors associated with depressive symptoms among study participants (N=341)**

| Variables | Depressive Symptoms n (%) | cOR (95% CI) | p-value | aOR (95% CI) | p-value |
|---|---|---|---|---|---|
| Age (years) | | | | | |
| 35 and below | 39 (32.8) | Ref | — | Ref | — |
| 36–45 | 59 (37.6) | 1.24 (0.75–2.04) | 0.409 | 1.14 (0.65–2.01) | 0.643 |
| 46 and above | 27 (41.5) | 1.46 (0.78– | 0.237 | 1.30 (0.64– | 0.472 |

| | | | | | |
|---|---|---|---|---|---|
| | | 2.72) | | 2.62) | |
| Sex | | | | | |
| Male | 115 (37.1) | Ref | — | — | — |
| Female | 10 (32.3) | 0.81 (0.37–1.78) | 0.595 | — | — |
| Level of Education | | | | | |
| Primary or lower | 101 (40.4) | 1.89 (1.11–3.21) | 0.018* | 1.59 (0.88–2.87) | 0.121 |
| Higher than primary | 24 (26.4) | Ref | — | Ref | — |
| Marital Status | | | | | |
| Without partners | 64 (35.8) | 0.92 (0.59–1.43) | 0.716 | — | — |
| With partners | 61 (37.7) | Ref | — | — | — |
| Living Arrangement (past year) | | | | | |
| Homeless | 35 (37.6) | 1.06 (0.65–1.73) | 0.819 | — | — |
| Not homeless | 90 (36.3) | Ref | — | — | — |
| Employment Status (past year) | | | | | |
| Unemployed | 80 (36.9) | 1.03 (0.65–1.62) | 0.915 | — | — |
| Employed | 45 (36.3) | Ref | — | — | — |
| HIV Risk Behaviors (past 6 months) | | | | | |
| Yes | 43 (41.7) | 1.27 (0.63–2.56) | 0.510 | — | — |
| No | 82 (34.5) | Ref | — | — | — |
| Incarceration History | | | | | |
| Yes | 53 (54.1) | 2.80 (1.73–4.54) | 0.000* | 2.87 (1.70–4.86) | 0.000* |
| No | 72 (31.4) | Ref | — | Ref | — |
| Duration on MAT Program (months) | | | | | |
| ≤ 24 | 40 (30.8) | Ref | — | Ref | — |
| > 24 | 85 (40.3) | 1.52 (0.96–2.41) | 0.077 | 1.52 (0.90–2.56) | 0.119 |

| | | | | | |
|---|---|---|---|---|---|
| Methadone Dosage (mg) | | | | | |
| < 80 | 23 (30.3) | Ref | — | Ref | — |
| 80–120 | 32 (31.7) | 1.07 (0.56–2.04) | 0.840 | 1.08 (0.53–2.20) | 0.827 |
| > 120 | 70 (42.7) | 1.72 (0.96–3.06) | 0.068 | 1.65 (0.87–3.12) | 0.126 |
| Current Substance Use (past 30 days) | | | | | |
| No use | 45 (38.1) | Ref | — | Ref | — |
| Tobacco | 32 (30.8) | 0.72 (0.41–1.26) | 0.251 | 0.72 (0.39–1.34) | 0.297 |
| Alcohol | 23 (51.1) | 1.70 (0.85–3.39) | 0.135 | 1.70 (0.80–3.62) | 0.170 |
| Polysubstance use | 25 (33.8) | 0.83 (0.45–1.52) | 0.542 | 0.74 (0.37–1.47) | 0.384 |
| HIV Status | | | | | |
| Positive | 37 (40.2) | 1.23 (0.75–2.01) | 0.407 | — | — |
| Negative | 88 (35.3) | Ref | — | — | — |
| Hepatitis Status | | | | | |
| Positive | 29 (37.7) | 1.06 (0.63–1.79) | 0.835 | — | — |
| Negative | 96 (36.4) | Ref | — | — | — |
| TB Status | | | | | |
| Positive | 19 (29.2) | 0.66 (0.37–1.19) | 0.269 | — | — |
| Negative | 106 (38.4) | Ref | — | — | — |
| Perceived Social Support | | | | | |
| Low | 38 (65.5) | 5.30 (2.50–11.26) | 0.000* | 4.03 (1.78–9.15) | 0.001* |
| Moderate | 68 (32.2) | 1.33 (0.73–2.41) | 0.355 | 1.27 (0.66–2.44) | 0.480 |
| High | 19 (26.4) | Ref | — | Ref | — |
| Adverse Childhood Experiences (ACE) | | | | | |
| Low risk | 64 (31.7) | Ref | — | Ref | — |
| High risk | 61 (43.9) | 1.69 (1.08– | 0.022* | 1.54 (0.92– | 0.101 |

| | | | | | |
|---|---|---|---|---|---|
| | | 2.64) | | 2.57) | |

Key: CI=Confidence Interval, cOR= crude Odds Ratio, aOR= adjusted Odds Ratio, ρ=Pearson value,*=ρ<0.05, **=ρ<0.25 (variables to be entered in Multivariate analysis)

## DISCUSSION

### Prevalence of depressive symptoms among study participants

Our findings suggest that depressive symptoms are highly prevalent amongst methadone using clients attending MAT clinic in Tanzania. Approximately one in three (36.7%) had depressive symptoms. This high rate could be explained by the effects of prolonged use substances that leads to changes in the brains making it susceptible to mental illnesses.[33] It is also highly likely their experiences of depression led them to use substances. An alternative explanation could be the use of cut cut-off points of 5 for PHQ-9 instead of the commonly used cut off points of 9. The cut-off points of 5 incorporate the mild symptoms of depression.

These findings on prevalence of depressive symptoms in our study (36.7%) also mirrored the findings of two studies in China which had prevalence of 33.7% and 38.3%) and also another study in Taiwan with the prevalence of 33%.[36 34 37] Two studies in Tanzania reported around half the prevalence which were 18% and 19% as compared to this study.[14 15]

High prevalence depressive symptoms are reported from various studies in China 75.4%,[28] India 74.3%,[29] Egypt 59.2%,[38] USA 59.7%,[39] Canada 41.4%,[40] Europe 48%[41] and Australia 53.3%.[42] Some research indicate relatively lower prevalence of these symptoms, this includes one study from Iran with depressive symptoms (3.5%).[43]

### Factors associated with depressive symptoms among study participants

Among the factors that showed significant association with depressive symptoms were history of incarceration and low perceived social support. Stressful life events such as incarceration are well known to be important factors to be highly related mental health conditions such as depression. Individuals who use substances and attend treatment centers for instance MAT clinics commonly interact with the carceral state as a result of seeking illicit substances.

One study in Spain, also found that incarceration among MAT clients was associated with the increased likelihood of having depressive symptoms.[41] In addition, participants who reported low perceived social support had higher risk of having depressive symptoms in contrast to those who had high perceived social support. These findings were also in-keeping with other studies in Malaysia, China and Nepal.[45 46 47] Some studies from Spain, India and China did not show the association between history of incarceration and perceived social support.[35 41 47 49]

The discrepancy in findings between this study and others could be explained by the differences in ethnic and cultural backgrounds, study designs, use of different investigation tools, different settings and samples.

This study's findings should be cautiously interpreted due to some limitations. Because of the cross-sectional nature of the study, it was not possible to explain direction of causality. Self- reported information may be predisposed to social desirability and recall bias where, participants could under- or over-report, causing wrong estimation of some variables. Additionally, it should be noted that women weren't really represented in study. Lastly, co-existing substances' withdrawal or intoxication symptoms mighty have led to over-reporting of depressive symptoms.

# CONCLUSIONS

Prevalence of depressive symptoms among study participants was relatively high; similar to findings from studies conducted in other lower- and middle-income countries and lower compared to studies from high income countries. History of incarceration and low perceived social support were found to be predictors of depressive symptoms.

The data obtained from this study will contribute to growing body of literature in African research and will also provide a basis for further analytical research targeting more causality and implementation of interventions proposed.

# RECOMMENDATIONS

Routine screening depressive symptoms should be strengthened at MAT clinics as part of mental health service integration. Brief manualized screening tools should be provided to MAT clinicians to ensure convenience in screening for potential diagnosis and therefore choice of the appropriate interventions. A need of specific psychosocial interventions such as trauma focused cognitive behavioral therapies (CBT) and social skills training are particularly highlighted. Longitudinal studies are required to observe patterns of symptoms depression among a cohort of MAT clients over a longer period of time. Also, qualitative studies are needed to assess understanding of mental health issues around these symptoms quality of care and stigma related to MAT recovery. This could attempt to inform on gaps in current management from the clients' perspective.

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**Availability of data and materials**

All data used to write this paper is summarized in tables, graphs, or within text in the paper.

**Authors' contributions**

MS and JM contributed to the design of the study. MS analyzed the data with support from JM. MS wrote the first draft. All authors contributed to the interpretation of the findings and reviewed the full draft of the paper. All authors approved the final manuscript

**Competing interests**

The authors declare that they have no competing interests.

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