

## ORIGINAL ARTICLE

# Effects of socio-demographic characteristics, premorbid functioning, and insight on duration of untreated psychosis in first-episode schizophrenia or schizophreniform disorder in Northern Malawi

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**Aim:** Long duration of untreated psychosis (DUP) is prevalent and has been shown to be associated with poorer prognosis. Thus, knowledge of its determinants may help to target early interventions to reduce DUP on the needed population. Previous studies seeking to understand determinants of DUP have been inconclusive. Therefore, this study aimed to investigate the effects of socio-demographic characteristics, premorbid functioning, and insight on DUP in patients with first-episode schizophrenia or schizophreniform disorder.

**Methods:** This cross-sectional study recruited 110 subjects (aged 18-65) during a pilot early intervention service for psychosis in Northern Malawi, between June 2009 and September 2012. Short DUP was defined as  $\leq 6$  months, whereas long DUP was defined as  $> 6$  months. Unadjusted and adjusted analyses were performed to identify determinants of DUP.

**Results:** Of the 110 subjects, 99 (90%) had schizophrenia. Median DUP was 27.5 months, while mean (SD) DUP was 71.24 (92.32) months. In addition, at least 75% had long DUP, which was associated with lower level of education, poor insight, younger age at onset, and at least one parent deceased.

**Conclusions:** Long DUP is prevalent in Northern Malawi. Thus, early interventions to reduce DUP are warranted in this population. Although having at least one parent deceased predicted long DUP in this study, this remains speculative because factors, such as timing of parents' death and grief reactions of the patients were not assessed. Therefore, further investigations incorporating these factors are needed to ascertain this result.

## KEYWORDS

cross-sectional study, early intervention, risk factors, schizophrenia, schizophreniform disorder

## 1 | INTRODUCTION

Duration of untreated psychosis (DUP) is an interval from onset of first psychotic symptoms to the initiation of adequate treatment (Marshall et al., 2005). A recent meta-analysis on DUP (Penttila, Jaaskelainen, Hirvonen, Isohanni, & Miettunen, 2014) showed that long DUP in schizophrenia has been prevalent with mean DUP of

61.3 weeks and DUP ranging between 10.4 and 213.2 weeks. There has been growing evidence implying that longer DUP may result in poorer prognosis (Farooq, Large, Niessen, & Waheed, 2009; Marshall et al., 2005; Tang et al., 2014), and may be associated with patients inflicting harm on other people or themselves (Lincoln & McGorry, 1995; Melle et al., 2004). Thus, early interventions to reduce DUP have been postulated as necessary for not only successful secondary

preventive efforts but also reduction of the burden of suffering with the illness (Cechnicki et al., 2014; Hegelstad et al., 2012; Penttila et al., 2014). These would greatly benefit from an understanding of factors influencing DUP because they would guide in identifying targets for early detection of the disease (Souaiby, Gaillard, & Krebs, 2016). Results of studies exploring factors influencing DUP in various populations have thus far been inconclusive and; hence, it remains speculative what determines DUP in the general population. For example, in West London, older age, being unemployed, and living alone or being homeless was associated with a longer DUP (Barnes et al., 2000), while in Hong Kong, and in both London and Nottingham, living alone was not related to DUP (Chen et al., 2005; Morgan et al., 2006). In addition, in Singapore, long DUP was not associated with ethnicity, gender, and living situation of patients (Pek, Mythily, & Chong, 2006), whereas a recent systematic review of 10 studies found that although there was generally no evidence to suggest racial and ethnic differences in DUP, 3 of the 10 studies suggested that White patients were more likely to have longer DUP than Black patients generally, and Black-African patients specifically (Anderson, Flora, Archie, Morgan, & McKenzie, 2014).

The factors influencing DUP are complex, and investigations in different populations are needed in this field of science. In Malawi, the national prevalence of long DUP has not been reported. However, a pilot study of early intervention service for psychosis in Northern Malawi, observed a high prevalence of first-episode schizophrenia with long DUP (Chilale, Banda, Muyawa, & Kaminga, 2014), suggesting that a study on factors associated with long DUP could be most cost-efficient among patients with schizophrenia or schizophreniform disorder in this area.

## 2 | METHODS

### 2.1 | Subjects

This cross-sectional study used a sample from a group of patients who presented with psychosis to the Community Mental Health Care Team (CMHCT) of Saint John of God (SJOG) community services during a pilot study of early intervention service for psychosis in Northern Malawi between June 2009 and September 2012. Specifically, the sample was from a community setting, where the CMHCT conducted an awareness campaign about mental health disorders, and made an advertisement that people with mental disorders should come to them for assessment. Thus, people from the community brought suspected cases to the CMHCT for assessment. Inclusion criteria were diagnosed of schizophrenia or schizophreniform disorder by the Structured Clinical Interview for DSM-IV-TR Axis I Disorders (SCID-I), criteria (First, Spitzer, Gibbon, & Williams, 2002); being identified by CMHCT clinicians as experiencing first-episode psychosis (FEP), and having never had previous antipsychotic medication for a psychotic disorder; 18 to 65 years of age at first time receiving antipsychotic medication; and having given consent to participate in the study. Exclusion criteria were having an organic illness that causes psychosis, a learning disability, and a drug abuse disorder. Also, the focus of clinical attention was not on a reaction to the death of a

loved one. Thus, pathological bereavement was not calculated in this study. Permission to conduct this study was obtained from the National Health Sciences Research Committee (NHSRC) of the Ministry of Health in Malawi (NHSRC/577). Participants were given information about the study and their consent to participate was sought.

### 2.2 | Measures

DUP in this study was defined as the period from first psychotic symptoms until the initiation of first antipsychotic medication. This was measured using Beiser Scale (Beiser, Erickson, Fleming, & Iacono, 1993; Register-Brown & Hong, 2014). A previous 20-year follow-up study on DUP and the course of schizophrenia (Cechnicki et al., 2014), found that the optimal cut-off point for DUP was the 23rd week beyond which there are higher chances for poorer prognosis. Also, another 13-year follow-up study found that DUP of >6 months predicted poorer prognosis in psychosis (Tang et al., 2014). Nevertheless, thus far, there is no consensus on the cut-off point between short and long DUP (Marshall et al., 2005). However, in this study, the preceding suggestions were used to classify DUP as at most 6 months (short DUP) and >6 months (long DUP). This idea was also used in other previous studies (Addington et al., 2015; Qin et al., 2014; Ran et al., 2018). Moreover, some studies found median DUP of 2 months (Kalla et al., 2002; Qiu et al., 2017; Schimmelmann et al., 2008), and 4 months (O'Donoghue et al., 2016); while other studies dichotomized DUP using the cut-off point of 3 (Cotter, Zabel, French, & Yung, 2017; Devi Thakoor et al., 2016; González-Valderrama et al., 2015). Thus, the cut-off points of 2, 3, and 4 months were also considered in this study in order to see if results could be maintained.

Severity of psychosis symptoms was assessed using the scale for the assessment of positive symptoms (SAPS) (Andreasen, 1984) and the scale for the assessment of negative symptoms (SANS) (Andreasen, 1983). The SAPS is divided into four domains whereas the SANS is divided into five domains. Each domain has separate symptoms, each rated from 0 (absent) to 5 (severe), which form a basis for the global rating of the severity of the domain on a scale from 0 (absent) to 5 (severe). For both scales, the sum of the global scores of the domains was recorded.

The self-report Insight Scale (Birchwood et al., 1994) was used to measure insight. This scale measures three dimensions of insight, namely awareness of illness (2 items), awareness of symptoms (2 items), and awareness of the need for treatment (4 items). Each dimension has a total score ranging from 0 to 4. All participants in this study were not in hospital admission, hence item 4 (my stay in hospital is necessary) for the dimension, awareness of the need for treatment, was excluded (Cooke et al., 2007). Nonetheless, this dimension was still given equal weight as the other dimensions when calculating the total score (Cooke et al., 2007). A total score of at least 9 indicates good insight (Jonsdottir et al., 2008).

The premorbid adjustment scale (PAS) (Cannon-Spoor, Potkin, & Wyatt, 1982) was used to measure levels of functioning prior to the onset of psychosis. It has 36 items, which measure the domains: sociability and withdrawal, peer relationships, scholastic performance, adaptation to school, and capacity to establish socio-sexual relationships. These are assessed during four developmental periods in life:

childhood (up to 11 years), early adolescence (12-15 years), late adolescence (16-18 years), and adulthood (at least 19 years). Each item is scored from 0 to 6 with 0 indicating the best level of functioning and 6 the worst. A score for each developmental period is an average score calculated as total score divided by possible total score for the items rated. In the end, an overall score for the whole scale is obtained by averaging the developmental period scores for all the developmental periods rated for the patient. In this study, overall PAS scores for the social domain (sociability and withdrawal, peer relationships, and capacity to establish socio-sexual relationships), and academic domain (school performance and school adaptation) were analysed in relation to DUP. This was adopted following a suggestion that the PAS may essentially measure the preceding two domains of functioning (Melle et al., 2004; Silverstein, Mavrolefros, & Close, 2002).

In addition, socio-demographic characteristics, such as age at assessment, age at onset, sex, marital status, level of education, employment, family history of psychiatric disorders, first help seeking, and number of parents deceased were measured.

### 2.3 | Data analysis

Data were analysed using a Statistical Package for the Social Sciences (SPSS) Version 23.0 (IBM Corp, Armonk, New York) for Windows. The Shapiro-Wilk's test was used to test the normality of continuous data (Razali & Wah, 2011; Shapiro & Wilk, 1965). Unadjusted and adjusted logistic regression analyses were performed to identify the effects of explanatory variables on DUP. In the unadjusted analyses, explanatory variables whose *P* value was <0.1, and those which showed significant relationship with DUP (Lang, 2007), were tested for the multicollinearity assumption of logistic regression according to Midi, Sarkar, and Rana (2010). Then, all the non-collinear explanatory variables from this test were assessed using multivariable logistic regression analysis to see their adjusted effects on DUP. All statistical tests were two-tailed and the significance level was 0.05.

## 3 | RESULTS

### 3.1 | Sample characteristics

A total of 400 patients were referred to the CMHCT, of which 201 had psychosis. Among this group, 140 had first-episode psychosis based on the inclusion criteria and, additionally, 30 were excluded for not reporting schizophrenia or schizophreniform disorder. In the end, 110 subjects were selected for this study. Majority were male, had long DUP, had poor insight, were married, had attended more than primary education, were unemployed, had at least one parent deceased, had schizophrenia, and had first help from a traditional healer. Besides, the subjects were of the same tribe. Age at assessment ( $P = 0.001$ ), age at onset ( $P = 0.00002$ ), SANS ( $P < 0.001$ ), PAS social domain ( $P < 0.001$ ), PAS academic domain ( $P = 0.011$ ) and DUP ( $P < 0.001$ ) were not normally distributed (positively skewed). Thus, the mean of each of these variables was exaggerated by a few extremely large values, which makes it not a better representation of

the majority. In this regard, the mode and the three percentiles (25th percentile (Q1), median, 75th percentile (Q3)) would help to understand the general picture of these distributions. For example, with respect to age at onset, the mode, Q1, median, and Q3 would, respectively, mean that the majority had onset at the age of 27, a quarter at the age <24, half at the age <29.5, and three quarters at the age <36, which means a quarter had onset at the age  $\geq 36$ . A similar description can be used for the other skewed data. Table 1 displays more detail.

### 3.2 | Unadjusted effects of explanatory variables on DUP

Table 2 displays results of unadjusted analyses. Poor insight, at most primary level of education, and at least one parent deceased had about 3-fold significant effect on long DUP (>6 months). Similarly, at most primary level of education, and at least one parent deceased had about 3-fold significant effect on long DUP (>4 months); poor insight, and at most primary level of education had about 3-fold significant effect on long DUP (>3 months); and at most primary level of education had about 3-fold significant effect on long DUP (>2 months). Exceptionally, being single had about 12-fold significant effect on long DUP (>2 months). Besides, long DUP was 5% or 4% less likely to occur per unit increase in age at onset for all DUP cut-off points, except the cut-off point of 4. Also, long DUP was 2% less likely to occur per unit decrease in PAS social domain score for all the DUP cut-off points. Noteworthy, the PAS social domain was initially significant for all the four categories of long DUP (>2, >3, >4, and >6), but with abnormally large odds ratios (ORs) and wide 95% confidence intervals (CIs). Specifically, the ORs and 95% CIs were (OR = 15 742.39, 95%CI = 10.99-22 552 342.65,  $P = 0.009$ ), (OR = 726.92, 95%CI = 3.14-168 222.60,  $P = 0.018$ ), (OR = 426.48, 95%CI = 2.76-65 796.38,  $P = 0.018$ ), and (OR = 1461.47, 95%CI = 6.59-324 298.71,  $P = 0.008$ ) for long DUP categories, >2, >3, >4, and >6, respectively. This was enough reason to consider transforming this variable into something which would produce meaningful estimates (Kutner, Nachtsheim, & Neter, 2004). Therefore, knowing that the values of this variable ranged between 0.01 and 0.51 (Table 1), reciprocal transformation was considered as appropriate. That is, for each value  $x$  we obtained a corresponding value  $1/x$ . It should be noted that, before this transformation, the greater the PAS social domain score the poorer the premorbid social adjustment and, after transformation, the greater the transformed value the better the premorbid social adjustment. This is the case because when we divide 1 by a positive number closer to zero but <1 the answer is a bigger number, and when we divide 1 by a positive number closer to 1 but <1, the answer is a smaller number. For example,  $1/0.01 = 100$ , while  $1/0.51 = 2.0$ . Therefore, when interpreting the results of the transformed variable, we kept in mind that bigger transformed values corresponded to smaller PAS social domain scores and better premorbid social adjustment, while smaller transformed values corresponded to bigger PAS social domain scores and poorer premorbid social functioning.

**TABLE 1** Sample characteristics (N = 110)

|   |   |
|---|---|
| <b>Age at assessment</b>                          |   |
| Mean (SD), median (minimum-maximum), mode, Q1, Q3 | 37.09 (11.89), 35.50 (18-65), 25, 28, 45        |
| <b>Age at onset</b>                               |   |
| Mean (SD), median (minimum-maximum), mode, Q1, Q3 | 31.41 (10.49), 29.50 (16-65), 27, 24, 36        |
| <b>DUP score in months</b>                        |   |
| Mean (SD), median (minimum-maximum), mode, Q1, Q3 | 71.24 (92.32), 27.50 (0-370), 1, 5, 90.75       |
| <b>DUP, n (%)</b>                                 |   |
| ≤6  | 27 (24.55) <sup>a</sup>                         |
| >6  | 83 (75.45)                                      |
| <b>DUP, n (%)</b>                                 |   |
| ≤4  | 26 (23.60) <sup>a</sup>                         |
| >4  | 84 (76.40)                                      |
| <b>DUP, n (%)</b>                                 |   |
| ≤3  | 24 (21.80) <sup>a</sup>                         |
| >3  | 86 (78.20)                                      |
| <b>DUP, n (%)</b>                                 |   |
| ≤2  | 21 (19.10) <sup>a</sup>                         |
| >2  | 89 (80.90)                                      |
| <b>Positive symptoms (SAPS)</b>                   |   |
| Mean (SD)   | 8.18 (3.31)                                     |
| <b>Negative symptoms (SANS)</b>                   |   |
| Mean (SD), median (minimum-maximum), mode, Q1, Q3 | 4.71 (5.85), 2.50 (0-24), 0, 0, 8.25            |
| <b>Insight, n (%)</b>                             |   |
| Good  | 20 (18.18) <sup>a</sup>                         |
| Poor  | 90 (81.82)                                      |
| <b>PAS social domain</b>                          |   |
| Mean (SD), median (minimum-maximum), mode, Q1, Q3 | 0.14 (0.13), 0.10 (0.01-0.51), 0.04, 0.04, 0.21 |
| <b>PAS academic domain</b>                        |   |
| Mean (SD), median (minimum-maximum), mode, Q1, Q3 | 0.24 (0.15), 0.22 (0.00-0.75), 0.17, 0.14, 0.33 |
| <b>Sex, n (%)</b>                                 |   |
| Male  | 70 (63.64) <sup>a</sup>                         |
| Female  | 40 (36.36)                                      |
| <b>Marital status, n (%)</b>                      |   |
| Married or living with someone                    | 56 (50.91) <sup>a</sup>                         |
| Separated/divorced/widowed                        | 26 (23.64)                                      |
| Single  | 28 (25.45)                                      |
| <b>Level of education, n (%)</b>                  |   |
| Primary or less                                   | 43 (39.09) <sup>a</sup>                         |
| More than primary                                 | 67 (60.91)                                      |
| <b>Employment, n (%)</b>                          |   |
| Employed  | 17 (15.45) <sup>a</sup>                         |
| Unemployed  | 93 (84.55)                                      |
| <b>Number of parents deceased, n (%)</b>          |   |
| At least one                                      | 71 (64.55) <sup>a</sup>                         |
| None  | 39 (35.45)                                      |

**TABLE 1** (Continued)

|  |                         |
|--|-------------------------|
| <b>Age at assessment</b>                                 |                         |
| Previous family experience of psychotic disorders, n (%) |                         |
| No   | 53 (48.18)              |
| Yes  | 57 (51.82)              |
| <b>First help seeking, n (%)</b>                         |                         |
| Hospital   | 25 (22.70) <sup>a</sup> |
| Traditional healer                                       | 73 (66.40)              |
| Other  | 12 (10.90)              |
| <b>Type of diagnosis, n (%)</b>                          |                         |
| Schizophrenia  | 99 (90.00) <sup>a</sup> |
| Schizophreniform disorder                                | 11 (10.00)              |

DUP, duration of untreated psychosis; SANS, scale for the assessment of negative symptoms; SAPS, scale for the assessment of positive symptoms; Q1, 25th percentile; Q3, 75th percentile.

<sup>a</sup> P value <0.05,  $\chi^2$  test for homogeneity of proportions.

### 3.3 | Adjusted effects of the explanatory variables on DUP

In Table 2, all the significant explanatory variables ( $P$  value <0.05), and those whose  $P$  value was <0.1, were considered for the multivariable logistic regression analysis to assess the adjusted effect of each of them on DUP. Thus, these variables were tested for the multicollinearity assumption before running the multivariable logistic regression analysis. For the DUP cut-off points, 3, 4, and 6, the correlation matrix showed that there was no serious collinearity between all possible pairs of these explanatory variables ( $-0.28 \leq r \leq 0.20$ ). In addition, the variance inflation factor (VIF) was <5 for each predictor variable ( $1.01 \leq VIF \leq 1.16$ ), the condition index (10.6) corresponding to the smallest Eigenvalue (0.04) was <15, and there was exactly one highest variance proportion (0.72) of a predictor variable corresponding to the dimension of the smallest Eigenvalue. Thus, there was no multicollinearity problem. Similarly, for the DUP cut-off point of 2, the correlation matrix showed no serious collinearity between all possible pairs of these explanatory variables ( $-0.46 \leq r \leq 0.21$ ). Besides, the VIF was <5 for each predictor variable ( $1.06 \leq VIF \leq 1.64$ ), the condition index (11.72) corresponding to the smallest Eigenvalue (0.03) was <15, and there was exactly one highest variance proportion (0.90) of a predictor variable corresponding to the dimension of the smallest Eigenvalue. Therefore, there was no multicollinearity problem.

Results of multivariable logistic regression analysis in Table 3 analyse the reliability of the models in predicting DUP. Specifically, the models correctly classified 94.40% of those with long DUP (>2 months), 96.50% of those with long DUP (>3 months), 95.20% of those with long DUP (>4 months), and 94.00% of those with long DUP (>6 months). Also, the models correctly classified 33.30% of those with short DUP ( $\leq 2$  months and  $\leq 3$  months), 34.60% of those with short DUP ( $\leq 4$  months), and 40.70% of those with short DUP ( $\leq 6$  months). The overall success rate of correct prediction was 80.90% for the DUP cut-off scores, 4 and 6, and this was 82.70% for the DUP cut-off scores, 2 and 3. In addition, the models proved to have considerably high positive predictive values. That is, if someone has the related explanatory variables, the probability that this person has long DUP is 85.70% for the DUP cut-off score of 2, 83.80% for the DUP cut-off score of 3, 82.50% for the DUP cut-off score of

**TABLE 2** Unadjusted effects of explanatory variables on DUP

| Variable                         | Univariate logistic regression |                    |                   |                    |                   |                    |                   |                    |
|----------------------------------|--------------------------------|--------------------|-------------------|--------------------|-------------------|--------------------|-------------------|--------------------|
|                                  | DUP > 2 months                 |                    | DUP > 3 months    |                    | DUP > 4 months    |                    | DUP >6 months     |                    |
|                                  | OR (95%CI)                     | P value            | OR (95%CI)        | P value            | OR (95%CI)        | P value            | OR (95%CI)        | P value            |
| Age at assessment                | 1.00 (0.96-1.05)               | 0.855              | 1.02 (0.98-1.06)  | 0.446              | 1.03 (0.99-1.07)  | 0.226              | 1.02 (0.98-1.06)  | 0.293              |
| Age at onset                     | 0.95 (0.91-0.99)               | 0.014 <sup>a</sup> | 0.96 (0.92-0.99)  | 0.037 <sup>a</sup> | 0.94 (0.93-1.00)  | 0.079              | 0.96 (0.92-0.99)  | 0.045 <sup>a</sup> |
| Premorbid academic domain        | 0.10 (0.00-2.44)               | 0.158              | 0.10 (0.01-2.09)  | 0.137              | 0.14 (0.01-2.81)  | 0.201              | 0.24 (0.01-4.52)  | 0.341              |
| Premorbid social domain trans    | 0.98 (0.96-0.99)               | 0.016 <sup>a</sup> | 0.98 (0.96-0.99)  | 0.023 <sup>a</sup> | 0.98 (0.96-0.99)  | 0.042 <sup>a</sup> | 0.98 (0.96-0.99)  | 0.027 <sup>a</sup> |
| Insight                          |                                |                    |                   |                    |                   |                    |                   |                    |
| Good                             | Reference                      |                    | Reference         |                    | Reference         |                    | Reference         |                    |
| Poor                             | 2.14 (0.71-6.47)               | 0.177              | 3.08 (1.08-8.77)  | 0.035 <sup>a</sup> | 2.67 (0.95-7.49)  | 0.063              | 3.27 (1.18-9.09)  | 0.023 <sup>a</sup> |
| Sex                              |                                |                    |                   |                    |                   |                    |                   |                    |
| Female                           | Reference                      |                    | Reference         |                    | Reference         |                    | Reference         |                    |
| Male                             | 1.40 (0.53-3.69)               | 0.493              | 1.07 (0.42-2.72)  | 0.896              | 0.91 (0.36-2.28)  | 0.832              | 1.04 (0.42-2.56)  | 0.933              |
| Marital status                   |                                |                    |                   |                    |                   |                    |                   |                    |
| Married or living with someone   | Reference                      |                    | Reference         |                    | Reference         |                    | Reference         |                    |
| Separated/divorced/widowed       | 3.58 (0.95-13.53)              | 0.060              | 2.57 (0.77-8.59)  | 0.125              | 2.57 (0.77-8.59)  | 0.125              | 2.80 (0.84-9.31)  | 0.093              |
| Single                           | 12.08 (1.52-96.32)             | 0.019 <sup>a</sup> | 3.73 (0.99-14.06) | 0.052              | 2.06 (0.67-6.33)  | 0.208              | 2.24 (0.73-6.85)  | 0.158              |
| Education                        |                                |                    |                   |                    |                   |                    |                   |                    |
| More than primary                | Reference                      |                    | Reference         |                    | Reference         |                    | Reference         |                    |
| Primary or less                  | 3.32 (1.03-10.65)              | 0.044 <sup>a</sup> | 3.01 (1.03-8.80)  | 0.044 <sup>a</sup> | 3.47 (1.20-10.07) | 0.022 <sup>a</sup> | 2.82 (1.03-7.69)  | 0.044 <sup>a</sup> |
| Employment                       |                                |                    |                   |                    |                   |                    |                   |                    |
| Employed                         | Reference                      |                    | Reference         |                    | Reference         |                    | Reference         |                    |
| Unemployed                       | 1.38 (0.40-4.74)               | 0.614              | 1.62 (0.51-5.17)  | 0.413              | 1.99 (0.66-6.05)  | 0.224              | 1.87 (0.62-5.66)  | 0.268              |
| Number of parents deceased       |                                |                    |                   |                    |                   |                    |                   |                    |
| None                             | Reference                      |                    | Reference         |                    | Reference         |                    | Reference         |                    |
| At least one                     | 2.40 (0.91-6.30)               | 0.076              | 2.19 (0.87-5.49)  | 0.096              | 2.75 (1.12-6.78)  | 0.028 <sup>a</sup> | 3.07 (1.26-7.52)  | 0.014 <sup>a</sup> |
| Family history of mental illness |                                |                    |                   |                    |                   |                    |                   |                    |
| Yes                              | Reference                      |                    | Reference         |                    | Reference         |                    | Reference         |                    |
| No                               | 1.66 (0.63-4.40)               | 0.307              | 1.40 (0.56-3.50)  | 0.471              | 1.11 (0.46-2.69)  | 0.813              | 1.00 (0.420-2.39) | 0.997              |
| First help seeking               |                                |                    |                   |                    |                   |                    |                   |                    |
| Hospital                         | Reference                      |                    | Reference         |                    | Reference         |                    | Reference         |                    |
| Traditional healer               | 1.05 (0.34-3.30)               | 0.929              | 1.22 (0.42-3.59)  | 0.717              | 1.13 (0.39-3.29)  | 0.830              | 1.13 (0.39-3.29)  | 0.830              |
| Other                            | 1.25 (0.21-7.62)               | 0.809              | 0.95 (0.19-4.68)  | 0.947              | 0.63 (0.14-2.86)  | 0.551              | 0.44 (0.10-1.92)  | 0.276              |

DUP, duration of untreated psychosis; CI, confidence interval; OR, odds ratio.

<sup>a</sup> P value <0.05.

4, and 83.00% for the DUP cut-off score of 6. Thus, generally, these models have substantial qualities in predicting subjects with long DUP in this population.

Table 4 shows the four multivariable logistic regression models. All the 4 models indicated a significant adjusted effect of age at onset, education, and number of parents deceased on DUP. For example, long DUP was 7% (for the DUP cut-off points of 2, 3 and 4), or 8% (for the DUP cut-off point of 6) less likely to occur per unit increase in age at onset; having primary or less education was about 4 times (for the DUP cut-off points of 3 and 6), or 5 times (for the DUP cut-off points of 2 and 4) more likely to prolong DUP; and having at least one parent deceased was about 6 times (for the DUP cut-off point of 6), or 5 times (for the DUP cut-off points of 2 and 4), or 3 times (for the DUP cut-off point of 3) more likely to prolong DUP. Nevertheless, poor insight had about 4 times more likely to prolong DUP only when the DUP cut-off point was 6. The overall models indicated a significant improvement on an intercept only model (likelihood ratio test:

$\chi^2(6, N = 110) = 26.48$  and  $P < 0.001$  for DUP cut-off score of 2;  $\chi^2(5, N = 110) = 22.10$  and  $P = 0.001$  for DUP cut-off score of 3;  $\chi^2(5, N = 110) = 23.22$  and  $P < 0.001$  for DUP cut-off score of 4; and  $\chi^2(5, N = 110) = 27.18$  and  $P < 0.001$  for DUP cut-off score of 6). Also, the predictions made by these models fitted well with observed group memberships (goodness-of-fit test:  $\chi^2(8) = 10.64$  and  $P = 0.223$  for DUP cut-off score of 2;  $\chi^2(8) = 4.34$  and  $P = 0.825$  for DUP cut-off score of 3;  $\chi^2(8) = 7.54$  and  $P = 0.479$  for DUP cut-off score of 4;  $\chi^2(8) = 6.76$  and  $P = 0.563$  for DUP cut-off score of 6).

## 4 | DISCUSSION

To the best of our knowledge, this is the first study to examine the effects of socio-demographic characteristics, premorbid functioning, and insight on DUP in a sample of first-episode schizophrenia or schizophreniform disorder patients in Northern Malawi. We found that at

**TABLE 3** Assessment of predictive value of the four multivariable models

| Observed  | Predicted DUP cases |         | Percentage of correct predictions |
|---|---------------------|---------|-----------------------------------|
|   | DUP ≤ 2             | DUP > 2 |                                   |
| DUP ≤ 2   | 7                   | 14      | 33.3                              |
| DUP > 2   | 5                   | 84      | 94.4                              |
| Overall predicted correct percentage  |                     |         | 82.7                              |
| Sensitivity = 84/(84 + 5)% = 94.4%; specificity = 7/(7 + 14)% = 33.3%; false positive = 14/(14 + 84)% = 14.3%; false negative = 5/(5 + 7)% = 41.7%; positive predictive value = 84/(84 + 14)% = 85.7%; negative predictive value = 7/(7 + 5)% = 58.3% |                     |         |                                   |

  

| Observed  | Predicted DUP cases |         | Percentage of correct Predictions |
|---|---------------------|---------|-----------------------------------|
|   | DUP ≤ 3             | DUP > 3 |                                   |
| DUP ≤ 3   | 8                   | 16      | 33.3                              |
| DUP > 3   | 3                   | 83      | 96.5                              |
| Overall predicted correct percentage  |                     |         | 82.7                              |
| Sensitivity = 83/(83 + 3)% = 96.5%; specificity = 8/(8 + 16)% = 33.3%; false positive = 16/(16 + 83)% = 16.2%; false negative = 3/(3 + 8)% = 27.3%; positive predictive value = 83/(83 + 16)% = 83.8%; negative predictive value = 8/(8 + 3)% = 72.7% |                     |         |                                   |

  

| Observed  | Predicted DUP cases |         | Percentage of correct Predictions |
|---|---------------------|---------|-----------------------------------|
|   | DUP ≤ 4             | DUP > 4 |                                   |
| DUP ≤ 4   | 9                   | 17      | 34.6                              |
| DUP > 4   | 4                   | 80      | 95.2                              |
| Overall predicted correct percentage  |                     |         | 80.9                              |
| Sensitivity = 80/(80 + 4)% = 95.2%; specificity = 9/(9 + 17)% = 34.6%; false positive = 17/(17 + 80)% = 17.5%; false negative = 4/(4 + 9)% = 30.8%; positive predictive value = 80/(80 + 17)% = 82.5%; negative predictive value = 9/(4 + 9)% = 69.2% |                     |         |                                   |

  

| Observed   | Predicted DUP cases |         | Percentage of correct predictions |
|--|---------------------|---------|-----------------------------------|
|  | DUP ≤ 6             | DUP > 6 |                                   |
| DUP ≤ 6  | 11                  | 16      | 40.7                              |
| DUP > 6  | 5                   | 78      | 94.0                              |
| Overall predicted correct percentage   |                     |         | 80.9                              |
| Sensitivity = 78/(78 + 5)% = 94.0%; specificity = 11/(11 + 16)% = 40.7%; false positive = 16/(16 + 78)% = 17.0%; false negative = 5/(5 + 11)% = 31.3%; positive predictive value = 78/(78 + 16)% = 83.0%; negative predictive value = 11/(11 + 5)% = 68.8% |                     |         |                                   |

DUP, duration of untreated psychosis.

least 75% of the subjects had long DUP, which was associated with lower level of education, poor insight, younger age at onset, and at least one parent deceased.

Several limitations should be considered when interpreting the results of this study. First, some factors, such as mode of onset of psychosis, global functioning, household income, and childhood/adolescent maltreatment, which are potential confounders of DUP, were not assessed. It could be important to see how these could affect other variables in determining DUP. Second, the retrospective measurement of DUP may not be exact because participants had to recall the date

of the onset of psychosis, and their ability to recall correctly could be influenced by cognitive deficits due to psychosis, hence giving a possibility of exaggerated approximations of DUP. Finally, all the participants were patients with first-episode schizophrenia or schizophreniform disorder, 18-65 years old, from the same tribe (Tumbuka) who consented to participate in this study. Therefore, this may limit the findings from being generalized to other populations.

Despite the preceding limitations, this study has some strength. First, cultural uniqueness of this sample makes this study duly generalisable to other members of the same tribe and hence providing a reliable platform for planning early intervention services to reduce DUP specific for the tribe. Second, this is the first study in Malawi or perhaps until recently to show that having at least one parent deceased in first-episode schizophrenia or schizophreniform disorder was an important determinant of long DUP. Thus, this outcome opens up an area for further investigation, which is an examination of mechanisms that lead bereavement of a parent to be associated with long DUP. Third, results were maintained for the DUP cut-off points, 2, 3, 4, and 6, except for the variable, insight, which showed only for the DUP cut-off point of 6 that poor insight was associated with long DUP. Finally, the high prevalence of DUP >6 months in this study population, implied a high prevalence of first-episode schizophrenia or schizophreniform disorder patients at a higher risk for poorer prognosis, hence, justifying the need for early intervention for psychosis in the study area. Besides, the median DUP (27.5 months >2 years) of this sample was exceptionally longer than that of most similar studies, too numerous to acknowledge them here, in other populations. Just to state a few examples, a similar study in a community treatment setting in the United States found a median DUP of 74 weeks (about 19 months) (Addington et al., 2015); in Singapore a study found median DUP of 4 months in a sample from Early Psychosis Intervention Programme (Pek et al., 2006); in West London median DUP was 26 weeks (about 7 months), for a schizophrenia sample from a prospective clinical and neurobiological study (Barnes et al., 2000); in a sample from a psychiatric referral hospital in South Africa, the median was 6 weeks (about 2 months) (Burns, Jhazbhay, Esterhuizen, & Emsley, 2011); and a Zambian study, at the only psychiatric hospital, found median DUP of 1 month (Mbewe et al., 2006).

Among other reasons, the higher prevalence of long DUP in this study could possibly be explained by methodological differences in sample collection between this study and other related studies. For example, unlike in other related studies, where the sample was hospital based, targeting only those that have reported at the hospital, the sample of this study was obtained from people who responded to an awareness campaign about mental disorders in a community setting. This approach attracted even those people in the community who thought would not go to hospital to come for assessment, and this might have attracted a considerable proportion of patients with long DUP in the process. Also, it should be noted that, during assessment, it was anecdotally observed that people in the study area interpreted the symptoms of psychosis differently. For instance, those that experience hallucinations, such as hearing voices when actually no one is talking to them, would be interpreted as they were on the verge of becoming a traditional healer, "Kuthwasa." Nonetheless, it was only when they also exhibited violent behavior that the community would

**TABLE 4** Adjusted effects of the explanatory variables on DUP

| Variable                                   | Multivariable logistic regression |                     |                   |                    |                   |                     |                   |                     |
|--|-----------------------------------|---------------------|-------------------|--------------------|-------------------|---------------------|-------------------|---------------------|
|  | DUP > 2 months                    |                     | DUP > 3 months    |                    | DUP > 4 months    |                     | DUP >6 months     |                     |
|  | aOR (95%CI)                       | P value             | aOR (95%CI)       | P value            | aOR (95%CI)       | P value             | aOR (95%CI)       | P value             |
| Age at onset                               | 0.93 (0.87-0.99)                  | 0.030 <sup>a</sup>  | 0.93 (0.88-0.98)  | 0.008 <sup>a</sup> | 0.93 (0.88-0.98)  | 0.010 <sup>a</sup>  | 0.92 (0.87-0.97)  | 0.004 <sup>a</sup>  |
| Premorbid social domain trans              | 0.99 (0.97-1.01)                  | 0.380               | 0.99 (0.97-1.01)  | 0.263              | 0.99 (0.97-1.01)  | 0.384               | 0.99 (0.97-1.01)  | 0.349               |
| Insight                                    |                                   |                     |                   |                    |                   |                     |                   |                     |
| Good                                       | NA                                |                     | Reference         |                    | Reference         |                     | Reference         |                     |
| Poor                                       | NA                                | NA                  | 3.19 (0.95-10.73) | 0.062              | 2.70 (0.81-9.04)  | 0.107               | 3.57 (1.05-12.13) | 0.041 <sup>a</sup>  |
| Marital status                             |                                   |                     |                   |                    |                   |                     |                   |                     |
| Married or living with someone             | Reference                         |                     | NA                |                    | NA                |                     | NA                |                     |
| Separated/divorced/widowed                 | 1.61 (0.36-7.19)                  | 0.532               | NA                | NA                 | NA                | NA                  | NA                | NA                  |
| Single                                     | 6.33 (0.63-63.27)                 | 0.116               | NA                | NA                 | NA                | NA                  | NA                | NA                  |
| Education                                  |                                   |                     |                   |                    |                   |                     |                   |                     |
| More than primary                          | Reference                         |                     | Reference         |                    | Reference         |                     | Reference         |                     |
| Primary or less                            | 4.72 (1.24-17.95)                 | 0.023 <sup>a</sup>  | 4.15 (1.22-14.12) | 0.023 <sup>a</sup> | 4.70 (1.41-15.66) | 0.012 <sup>a</sup>  | 3.94 (1.22-12.72) | 0.022 <sup>a</sup>  |
| Number of parents deceased                 |                                   |                     |                   |                    |                   |                     |                   |                     |
| None                                       | Reference                         |                     | Reference         |                    | Reference         |                     | Reference         |                     |
| At least one                               | 4.73 (1.27-17.64)                 | 0.021 <sup>a</sup>  | 3.42 (1.07-10.98) | 0.039 <sup>a</sup> | 4.47 (1.43-13.94) | 0.010 <sup>a</sup>  | 5.71 (1.77-18.40) | 0.004 <sup>a</sup>  |
| Overall model evaluation                   |                                   |                     |                   |                    |                   |                     |                   |                     |
|  | $\chi^2$ (df)                     | P value             | $\chi^2$ (df)     | P value            | $\chi^2$ (df)     | P value             | $\chi^2$ (df)     | P value             |
| Likelihood ratio test                      | 26.48 (6)                         | <0.001 <sup>a</sup> | 22.10 (5)         | 0.001 <sup>a</sup> | 23.22 (5)         | <0.001 <sup>a</sup> | 27.18 (5)         | <0.001 <sup>a</sup> |
| Goodness-of-fit test (Hosmer and Lemeshow) | 10.64 (8)                         | 0.223               | 4.34 (8)          | 0.825              | 7.54 (8)          | 0.479               | 6.76 (8)          | 0.563               |

aOR, adjusted odds ratio; CI, confidence interval; df, degrees of freedom; DUP, duration of untreated psychosis; NA, not applicable.

<sup>a</sup> P value <0.05.

believe that they were mentally ill and required medical attention. Thus, it is possible that this kind of perception prolonged DUP to a greater extent in the study area and, hence, in this sample. Furthermore, in other cases where the symptoms of psychosis were correctly interpreted by patients or their relatives, the majority sought first help from a traditional healer. This phenomenon was shown to prolong DUP (Al Fayed, Lappin, Murray, & Boydell, 2017), although the data of this sample showed no evidence to that effect. In spite of that, results of some qualitative study in the same study area attributed help-seeking delays to subjects' perception of mental illness (Chilale, Silungwe, Gondwe, & Masulani-Mwale, 2017). That study found that, in Northern Malawi, the socio-cultural explanation of witchcraft and spirit possession was dominant and determined help-seeking behaviour among psychosis patients and their guardians, with the majority very likely to seek first help from traditional healers for diagnosis, and to know who was responsible for causing the disease. However, that study also observed that the majority of the subjects were able to notice benefits to hospital treatment and, in particular, guardians held the key to the choice of treatment modality. Therefore, that study proposed that guardians could be used to influence timely help-seeking for effective treatment of mental disorders, through strengthening of a bio-psychosocial intervention model in the treatment of mental illness. Accordingly, early interventions to reduce DUP in this population must educate the public about mental disorders and the need for early treatment of psychosis.

In this study, we could not find related studies investigating the effect of bereavement of a parent on DUP. Nonetheless, bereavement of at least one parent may weaken family influence in help seeking

and, hence, may result in longer DUP (Goulding et al., 2008; Morgan et al., 2006; O'Callaghan et al., 2010). However, other factors, such as timing of parent's death as well as whether there was any abnormal grief reaction experienced by the patient, were not taken into account when analysing this variable. Therefore, this result remains a conjecture and needs further investigation incorporating these factors.

As regards age at onset of psychosis, this study found that DUP reduced with a unit increase in age at onset. Similar result was found in some previous studies (Addington et al., 2015; Dominguez et al., 2013; Norman, Malla, Verdi, Hassall, & Fazekas, 2004). Therefore, in this sample, most subjects had their onset of psychosis in younger age and did not get effective treatment until late in their lifetime. Thus, early interventions to reduce DUP in this population must also focus on identifying and managing early psychosis in adolescents (Dominguez et al., 2013; Norman et al., 2004). However, another study found that younger age was associated with shorter DUP but proposed further investigations on this phenomenon (Kelso, Judith, Victoria, Mima, & Katherine, 2008). May be this inconsistency could be explained by differences in the knowledge of people on the onset of psychosis, their health seeking behaviours, and factors associated with these, in different contexts. Thus, more future investigations incorporating the foregoing variables and relevant others are indeed required to understand more the association between age at onset and DUP.

Moreover, in contrast with other studies which found that level of education was not associated with DUP (Chen et al., 2005; Oliveira et al., 2010), this study's high prevalence of long DUP among the lower educated was in support of the proposition that the lower

educated may lack understanding of the illness and may have ignorance toward the available service provisions (Basu, Subramaniam, Abdin, Poon, & Verma, 2015; Chee, Muhammad Dain, Abdul Aziz, & Abdullah, 2010; Lihong et al., 2012). This speculated difference in knowledge gap between the lower educated and the higher educated may implicitly emanate from the hypothesis that the higher educated could be well positioned than the lower educated in having access to information about the disease from various media sources (Tichenor, Donohue, & Olien, 1970). Therefore, special early interventions targeted at the lower educated are warranted to help them understand psychosis symptoms early and seek for immediate treatment.

Also, similar to results from other studies (Compton et al., 2011; Hui et al., 2015; O'Donoghue et al., 2014), this study found that poor insight prolonged DUP. Individuals with poor insight disagree that they have mental illness, unusual experiences, abnormal behaviours, and that they are in need of clinical treatment (Birchwood et al., 1994; Cooke, Peters, Kuipers, & Kumari, 2005). This kind of attitude is likely to make them delay to receive adequate treatment because on their own they may not seek for treatment and it may not be easy to persuade them to seek for help especially when family ties are weaker (Compton, Goulding, Gordon, Weiss, & Kaslow, 2009; Goulding et al., 2008). Thus, understanding the mechanism of poor insight might help to find better early intervention techniques aimed at convincing poor insight patients to seek for treatment as early as possible (Cooke et al., 2007). In this regard, mental health campaigns on the awareness of insight in early symptoms of psychosis would help to identify poor insight patients, which would in turn influence people to seek for effective treatment as soon as possible.

Although some studies found a relationship between premorbid functioning and DUP (Melle et al., 2004), in this study, premorbid functioning (academic and social domains) did not independently determine DUP. This is consistent with the findings of some previous study (Hui et al., 2015). Also, another study found that premorbid functioning and DUP interacted but to a limited degree (Larsen, Moe, Vibe-Hansen, & Johannessen, 2000). Therefore, more investigations are needed in other populations to explain the association between premorbid functioning and DUP.

In conclusion, this study was conducted in a community setting in Northern Malawi after an awareness campaign, and found a longer median DUP than in most previous studies on DUP. Besides, at least 75% of the participants had long DUP, which was associated with same correlates as in some previous studies, such as having lower level of education (primary or less), poor insight, and younger age at onset. In addition, having at least one parent deceased was independently associated with long DUP, but this result did not take into account some factors, such as the timing of parents' death and grief reactions of the patients. Thus, this remains a speculation for further investigation. Nonetheless, these results suggest that early intervention services to reduce DUP are warranted in this study's population, and these must identify and manage early psychosis in younger aged people, and provide awareness campaigns to influence recommended help seeking practices for mental disorders.

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## CONFLICT OF INTEREST

The authors declare that no competing interests exist among them.

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