Appendix

Title: Prevalence of all epilepsies in urban informal settlements in Nairobi, Kenya: A two-stage population-based study

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Statistical models

Prevalence estimation

Let $Z_i, i=1,2,\ldots,N$ be a random variable where $P(Z_i=1)$ indicates the probability of an individual being diagnosed with epilepsy by a neurologist and $P(Z_i=0)$ be the probability that an individual is confirmed as being negative for epilepsy. Then, the total number T of individuals diagnosed as positive for epilepsy is given by

$$T=\sum_{i=1}^{n} z_i$$

and crude measure of the parameter of interest (prevalence of epilepsy (expressed per 1000 people in the population)) denoted by θ is given by

$$\theta=\frac{T}{N}\times 1000$$

This is the ideal scenario where all individuals screened positive in the first stage are available for assessment by the neurologist in the second stage. In the presence of attrition, T, will be less as not all individuals were assessed by the neurologist.

Now, N is the population size at stage I, let m be the number of individuals screened probable cases in stage I. If l is defined as the number not assessed at stage II, then the response rate (r ; ¿ in the stage II will be given by

$$r=\frac{m-l}{m}\times 100$$

and attrition (a ; %) will be given as $a=100-r$

This therefore means that the final diagnosis will be missing for $a\%$ of the possible cases.

Complete case analysis which means analysing the cases with complete data and excluding those with missing data may underestimate θ because T will be less, especially in a census (population-based study). The most common and recommended approach used to account for attrition is multiple imputation (MI) proposed by Rubin.[1-3] It has been found to result to reasonably unbiased estimates.[4]

Multiple imputation model

MI assumes that the data are missing at random (MAR), which means that other observable variables in the dataset can explain the missing data. Other missing data mechanisms include missing completely at random (MCAR) and missing not at random (MNAR). MCAR assumption occurs when the probability of missingness is independent of observed and unobserved components of the dataset. MNAR assumption occurs when the probability of a value being missing depends on unobservable characteristics.

Given the basic specification of the MI approach, and the type of the variable to be imputed, the relevant statistical model is used in the imputation model. For a dichotomous response, like in our present study, the logistic regression model is applied with relevant covariates included in the model.[5] The resultant dataset will be complete with the missing diagnosis filled with the imputed values from the posterior distribution of the missing data given the observed data.

Let V be the number of imputed datasets. For each dataset, we estimate $\hat{\theta}_v$ (the parameter of interest for each imputed dataset). The final estimate under the MAR assumption $\hat{\theta}_{MAR}$ is estimated as;

$$\hat{\theta}_{MAR} = \frac{1}{V} \sum_{v=1}^{V} \hat{\theta}_v$$

Multiple frameworks exist for the multiple imputation model including multivariate imputation by chained equations (MICE) also known as fully conditional specification or sequential regression multiple imputation, joint modeling imputation framework (JM) and multi-level MI in JM framework. Detailed description of these frameworks is available elsewhere.[6]

For this study, we make a plausible assumption of MAR because the reasons for missingness are not associated with the disease. Multiple imputation involves two sequential steps.[2,7] First, using Bayesian framework, draw independent random samples from the posterior predictive distribution of the missing values given the observed data and repeat this process many times (often between 10-50 times), resulting in many datasets with replaced missing information. Second, the many imputed datasets are analysed, and estimates from each imputed dataset are combined using standard combining rules.[2,8]

Let vector $Y = Y_i, i = 1,2,\ldots,N$ be random variable where $P(Y ¿¿ i = 1)¿$ is the probability that diagnosis ($Z_i ¿$ is observed for the i^{th} individual ($Y_{obs} ¿$ and $P(Y ¿¿ i = 0)¿$ is the probability that diagnosis is missing due to attrition between the first and the second stage ($Y_{miss} ¿$. With a well assumed prior-distribution of missing data, the posterior distribution of θ given the observed data, is given by

$$P(\theta \vee Y_{obs}) = \int P(\theta \vee Y_{obs}, Y_{miss}) P(Y_{miss} \vee Y_{obs}) d Y_{miss}$$

which can be understood as marginal means over a series of imputations serving as the posterior predictive distribution of missing data given the observed data.

Given the basic specification of the MI approach, and the type of variable to be imputed, the relevant statistical model is used in the imputation model. For a dichotomous response, like in our present study, the logistic regression model is applied with relevant covariates included in the model.[5] The resultant dataset will be complete with the missing diagnosis filled with the imputed values from the posterior distribution of the missing data given the observed data.

Diagnostic tests after multiple-imputation

Conducting imputation diagnostics is one of the most critical tests for post-imputation analysis. This includes assessment of the imputation variance, relative increase in variance (RVI), fraction of missing information (FMI) and relative efficiency (RE). Imputation variance is assessed using the variance between (Vb) and variance within (Vw). Vb measures variability in the parameter estimates obtained from the v imputed datasets. Vw is the arithmetic mean of the sampling variances from each of the v imputed datasets. Total variance is the sum of all the sources of variance. The larger the number of imputations, the more precise the estimate will be and the smaller the variance. RVI is the proportional increase in total sampling variance due to missing information. Variables with large amount of missing information tend to have high RVI. FMI is the proportion of total sampling variance due to the missing data. A high FMI indicates presence of a problematic variable in the imputation model. Conventionally, the number of imputations (at least) should be equal the highest FMI percentage. RE measures how well the true population parameter was estimated. Having many imputations (>5) is recommended to get reasonable variance estimates.

Additionally, it is recommended that the Monte Carlo error estimate be included in the diagnostic test to assess adequacy of the number of imputations used.[9] A significant p-value implies that the number of imputations used was adequate.

Another important analysis post-imputation is the sensitivity analysis. The underlying concept for the sensitivity analysis is that, MAR assumption for MI cannot be confirmed from the observed data alone. It is necessary to conduct sensitivity analysis for the MAR assumption and recommended to assess robustness of the estimates post-imputation. This is done under three general frameworks: selection models, shared parameter models and pattern-mixture models.[10] While it is an important post-imputation process, sensitivity analysis for MI is rarely reported in practice because of its computation complexity.[11,12] Additionally, statistical analysis software's sensitivity analysis methods are underdeveloped.[10] For this study, we adopted a selection model approach where we specified a model for the missing status for epilepsy diagnosis given the observed data using a logistic regression model with an off-set parameter δ governing how this depends on unobserved data.[9]

Multiple imputation for the present study

Overall attrition rate was 22% and this was higher in Viwandani (28%) when compared to Korogocho (10%). Multiple imputation model was used to account for this attrition by imputing the values of outcome variable (final diagnosis of epilepsy in the second stage) based on the logistic regression with age, sex, education level, employment status, marital status and participant’s response on the history of convulsion or epilepsy attacks as the covariates. None of these covariates had missing data because they were all derived from the first stage of the screening. We generated 10 imputed datasets under the MAR assumption. The imputation diagnostics are presented in Table S3. RVI was 0·009 and FMI was 0·009, which shows that the imputation model was reasonably robust. Monte carlo error estimate had a p-value of <0·001, indicating that the number of imputations were adequate.

Table S1: Multiple imputation diagnostics for the outcome variable

Complete	Incomplete	Imputed	RVI	FMI	DF
56172	253	253	0·009	0·009	56424

We acknowledge that one of the limitations of MI is that the assumption of MAR cannot be tested using empirical data, which necessitates further studies on how best accuracy of MI can be evaluated. For the sensitivity analyses, all covariates were fully observed with data missing only for the outcome. The reasons for the attrition, as captured during the facility-level screening, were outmigration, declining consent and being engaged at work.

Assessment of heterogeneity in prevalence

For a binary response variable, logistic regression is most commonly used to examine the association between the response variable and a set of covariates. It is a generalised linear model (GLM) with a log link, which is symmetric at about 0·5 such that θ approaches 0 at the same rate as it approaches 1. For an imbalanced dataset however (asymmetric outcome), where the distribution is skewed towards one of the classes (0 or 1), logistic regression is known to result to biased estimates since the resulting model tends to be biased towards the majority class.[13,14]

Complementary log-log (cloglog) is an alternative model for estimating risk or prevalence ratios and the most preferred when the probability of the outcome is very small or very large.[15-17] It is a GLM with a log link that is asymmetric such that θ approaches 0 fairly slowly but approaches 1 quite sharply and vice-versa. The link function of the cloglog model is specified below.

Let $X = x_1, x_2, x_3, \dots x_k$ denote a vector of k covariates, θ be as previously defined, and the linear predictor of θ given by

$$q = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 + \dots + \beta_k x_k$$

then, the link function $g(\theta)$ is given by

$$g(\theta) = \log(-\log(1-\theta)) = q$$

Sensitivity of the screening tool

The sensitivity of the screening instrument was conducted by matching 40 controls (those with no epilepsy) with 120 cases (confirmed epilepsy cases) using propensity score matching (ratio 1:3). A neurologist assessed all of these cases. They were matched by age, sex, marital status, education, employment and site. The computation of the sensitivity and specificity is as previously defined.[8]

Table S2: Sensitivity analysis

		Neurologist (Gold standard)		
		Positive	Negative	**Total**
Screening questionnaire	Positive	72 (TP)	48 (FP)	**120**
	Negative	2 (FN)	38 (TN)	**40**
	Total	**74**	**86**	**160**

TP=True positive, FP=False positive, FN=False negative, TN=True negative

Prevalence distribution by socio-demographic characteristics

Table S3: Prevalence of epilepsy by socio-demographic characteristics stratified by site (Korogocho and Viwandani)

	Korogocho			**Viwandani**		
	Prevalence per 1000 people	**Prevalence Ratio**	**p-value**	**Prevalence per 1000 people**	**Prevalence Ratio**	**p-value**
Sex						
Male	13·6 (11·3-15·8)	1·0 (Ref)		10·4 (9·0-11·9)	1·0 (Ref)	
Female	12·3 (10·1-14·3)	0·9 (0·7-1·1)	0·37	12·4 (10·6-14·1)	1·2 (0·9-1·4)	0·18
Age (Years)						
0-5	7·3 (4·5-10·9)	1·0 (Ref)		6·2 (3·9-8·6)	1·0 (Ref)	
6-12	12·4 (8·6-16·2)	1·6 (1·0-2·7)	0·072	12·9 (9·4-16·4)	2·1 (1·3-3·3)	0·0020
13-18	13·5 (9·2-17·8)	1·8 (1·0-3·0)	0·036	16·8 (12·1-21·6)	2·7 (1·7-4·3)	<0·0001
19-28	14·8 (11·2-18·4)	1·9 (1·2-3·1)	0·0080	12·3 (10·0-14·6)	1·9 (1·3-2·9)	0·0020
29-49	14·3 (11·1-17·4)	1·9 (1·2-3·0)	0·010	11·5 (9·6-13·5)	1·9 (1·3-2·8)	0·002
50 or older	12·6 (7·6-17·4)	1·6 (0·9-2·9)	0·10	5·8 (2·5-9·0)	0·9 (0·5-1·9)	0·88
Marital status						
Married/living with a partner	10·0 (7·6-12·5)	1·0 (Ref)		9·4 (7·8-10·9)	1·0 (Ref)	
Never married	20·5 (16·1-24·9)	2·3 (1·5-3·5)	<0·0001	12·9 (10·0-15·7)	1·2 (0·9-1·7)	0·19
Separated/Divorced	17·0 (11·3-22·6)	1·7 (1·1-2·7)	0·015	24·0 (17·0-31·0)	2·7 (1.9-3·8)	<0·0001
Employment						
Full/part time	12·6 (3·9-18·7)	1·0 (Ref)		5·5 (3·8-7·1)	1·0 (Ref)	
Not employed	20·7 (16·4-25·2)	1·9 (0·9-3·8)	0·079	17·4 (14·1-20·8)	3·3 (2·2-4·9)	<0·0001
Self-employed	11·9 (7·5-16·3)	1·0 (0·9-2·0)	0·94	11·5 (8·6-14·6)	2·2 (1·5-3·3)	<0·0001
Informal	10·9 (8·1-13·8)	0·9 (0·4-1·7)	0·70	13·5 (10·2-16·7)	2·4 (1·7-3·6)	<0·0001
Education						
Secondary	5·1 (3·2-6·9)	1·0 (Ref)		6·2 (4·9-7·4)	1·0 (Ref)	
Post-secondary	14·0 (2·8-25·3)	2·8 (1·1-7·4)	0·041	9·0 (4·6-13·4)	1·2 (0·7-2·1)	0·52
Primary	15·3 (12·4-18·1)	3·5 (2·0-6·4)	<0·0001	13·4 (11·1-15·6)	2·3 (1·7-3·0)	<0·0001
< Primary or no education	16·6 (13·6-19·4)	5·1 (2·8-9·3)	<0·0001	20·8 (17·3-24·3)	6·2 (4·3-8·7)	<0·0001

Distribution of prevalence by village in Korogocho and Viwandani

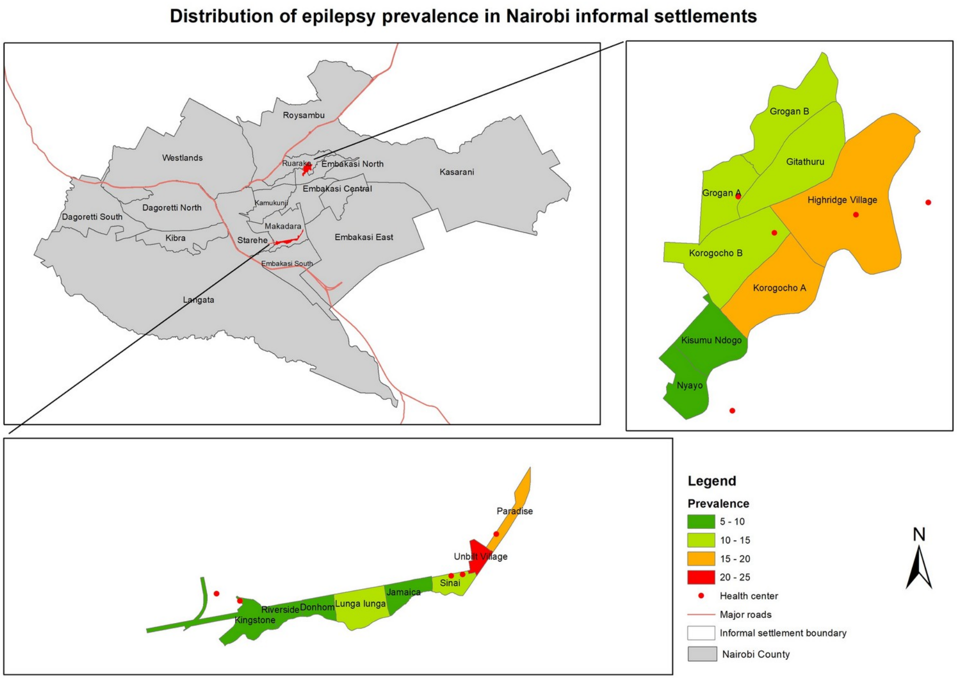

Figure S1: Spatial distribution showing heterogeneity of epilepsy prevalence (p<0·0001) in two Nairobi informal settlements

Screening tool

Table S4: Screening questionnaire for epilepsy at household level with Swahili translations

3.0 Epilepsy screening	
PART 1a: History of convulsive seizure Next I am going to ask you questions about any history of seizures among the members of your household Kwa kifupi, ningependa tudajili mambo machahe kuhusu wewe binafsi na wale unoaishi nao kwenye nyumba hii. Mwanzo kabisa ni kuhusu tatizo la "seizure" au "Kufitika" kwa lugha ya kimombo. Mara nyingi tatizo hili humfamya mtu kutememeka mwilini kiasi cha kushishindwa kuithibiti	
3.1(a) Has (NAME) ever had attacks of shaking of legs or arms which could not be controlled? **Je (JINA) amewahi kupatwa na kutetemeka kwa mikono au miguu ambayo haukuweza kuthibiti**	1. Yes 2. No
(b) Has someone ever told you that (NAME) had attacks of shaking of legs or arms which could not be controlled? **Je, umewahielezwa na mtu yeyote kwamba (JINA) amewahi kupatwa na kutetemeka kwa mikono au miguu ambayo haukuweza kuthibiti?**	1. Yes 2. No

PART 1b: History of non-convulsive seizure	
Next I am going to ask you questions about any history of non-convulsive seizures among the members of your household Kwa kifupi, ningependa tudajili mambo machahe kuhusu wewe binafsi na wale unoaishi nao kwenye nyumba hii.. Mwanzo kabisa ni kuhusu tatizo la "non-convulsive seizure" au "Kufitika kisichoambatana na kutememeka mwilini kwa ghafla kiasi cha kushindwa kuditbiti.	
Focal seizures without impaired awareness or simple partial seizures 3.4a) Has (Name) have experiences such as hallucinations or strange feelings e.g. epigastric rising and smells that are non-existent, and sudden emotional changes, such as unexplained fear, anxiety, or even déjà vu? Je (Jina) amewahi kumbwa na shida kama vile kusikia sauti za kiajabu mara kwa mara au kupatwa na hisia za kiajabu kama vile kunusia harufu zisizokuweko au kuhisi kama vile gesi/asidi/kiungulia kupanda toka tumboni hadi kinywani , au hisia zako kubadilika kwa na kushikwa na uwoga, wasi wasi na kupoteza imani ? 1. Yes 2. No	
Focal seizures with impaired awareness or complex partial seizures 3.4b) Has (Name) ever experienced a blank stare, unfamiliarity with surrounding and fumbling and chewing movements, and have/has no recollection of anything that happened at that time? Je, (Jina) amewahi julishwa kuhusu wakati alipokuwa katika hali ya kutojua kinachoendelea kama vile kutosikia au kujibu kile anachoulizwa, au kwa ghafla kutazama bila kuona chochote , au kukatiz a shughuli ulizo kuwa ukiendeleza kwa sekunde chache, wakati mwingine ikiwa ameyainua macho juu au kuyazungusha? 1. Yes 2. No	
Absence seizures or absences 3.5a) Has (Name) ever had reports of being unresponsive, or had an abrupt blank stare or interruption of ongoing activities for few seconds, sometimes with upward eye deviation/rolling Je wewe au (Jina) amewahi julishwa kuhusu wakati alipokuwa katika hali ya kutojua kinachoendelea kama vile kutosikia au kujibu kile anachoulizwa, au kwa ghafla kutazama bila kuona chochote , au kukatiz a shughuli ulizo kuwa ukiendeleza kwa sekunde chache, wakati mwingine ikiwa ameyainua macho juu au kuyazungusha? 1. Yes 2. No	
Drop attacks 3.5b) Do you or your child abruptly fall on your or their head/face/buttocks/back, sometimes sustaining injuries, and waking up soon thereafter? Je, (Jina) huanguka kwa ghafla kwa kichwa/uso/makalio/ mgongo, wakati mwingine hata uki pata majeraha na kuumia, na kuamka muda mfupi baadaye? 1. Yes 2. No	

PART 2: Nature of the history of convulsive seizure	
FW: If "no" Q 3.1 (a) and Q 3.2 (b) Skip to 4.0	
3.6 Pop up the NAMES and IDs of household members who enter answer yes in Q 3.1 (a) **or** Q 3.1 (b) **Next I am going to ask you questions about NAME. (list all the names in 3.6)** (**Maswali yafuatayo nitakuuliza ni kuhusu (JINA la aliyemtaja**) *FW: fill this section for each household member mentioned in* Q 3.1 (a) and Q 3.2 (b)	
3.7(b) Has the person NAME ever had attacks in which he/she fall and become pale? **Je, JINA amewahi kuanguka na rangi ya ngozi yake kubadilika?**	1. Yes 2. No
3.8 (b) Has NAME ever lost consciousness	1. Yes

Je, JINA amewahi kupoteza fahamu?	2. No
3.9 (b) Has NAME ever had attacks in which he/she fall with loss of consciousness? **Je, JINA amewahi kuanguka na kupoteza fahamu?**	1. Yes 2. No
3.10 (b) Has NAME ever had attacks in which he/she fall and bite your tongue? **Je, JINA amewahi kanguka na kuuma ulimi?**	1. Yes 2. No
3.11 (b) Has NAME ever had attacks in which he/she fall and lose control of your bladder? **Je, JINA amewahi kuanguka na kupoteza udhibiti wa mpira wake wa mkojo?**	1. Yes 2. No
3.12 (b) Has NAME ever had brief attacks of shaking or trembling in one arm or leg or in the face? **Je, JINA amewahi kupatwa na kutetemeka kwa mda mfupi kwenye mkono, mguu au uso?**	1. Yes 2. No
3.13 (b) Has NAME ever had attacks in which he/she lose contact with the surroundings and experience abnormal smells? **Je, JINA amewahi kupata shida mwilini na kisha kupoteza ufahamu wa mazingira yake na kupata harufu isiyo ya kawaida?**	1. Yes 2. No
3.13 (a) Have you ever had attacks in which you lose contact with the surroundings and experience abnormal smells? **Je, JINA amewahi kupata shida mwilini na kisha kuipoteza ufahamu wa mazingira yako na kupata harufu isiyo ya kawaida?**	1. Yes 2. No
3.15 (a) Have you ever fallen to the ground without reason and experienced twitching **Je, JINA amewahi kuanguka bila sababu na kutetemeka ghafla kwa mikono au miguu ambayo haukuweza kudhibiti.**	1.Yes 2. No
3.16 (a) Did some seizures occur with a febrile illness or fever? **Je, kufitika ilitokea pamoja na ugonjwa au homa?**	1.Yes 2. No
3.17 (a) When did the seizures start? **Je! Shida ya kufitika ilianza lini**	DD MM YY
3.18 (a) When was the last seizure? **Kufitika kwako mara ya mwisho ilikua lini?**	DD MM YY
3.19 (a) Did the seizures involve one body part? **Je! Shida ya kufitika ilihusisha sehemu moja ya** mwili?	1.Yes 2. No
3.20 (a) Did the seizures involve all body parts? **Je! kufitika ilihusisha sehemu zote za mwili?**	1.Yes 2. No
3.21 (a) How long did the seizures last **Je! kufitika kulidumu baada ya muda gani**	☐☐☐☐ HRS. MIN.
3.22 (a) Did the seizures last ≥30 minutes **Je! kufitika kulidumu kwa dakika ≥30**	1.Yes 2. No
3.23 (a) Did the seizures last longer than boiling a pot of maize **Je! kibitkas multichoke mudra refund kulich Kachemak Masindi?**	1.Yes 2. No
3.24 (a) Did the seizures last longer than a sermon in church or mosque **Je! kufitika kulichukua muda mrefu kuliko mahubiri ya kanisani au msikitini**	1.Yes 2. No

3.25 (a) Have you ever visited a traditional healer for treatment of seizures? **Je! Umewahi kumtembelea mganga wa kienyeji kwa matibabu ya kufitika**	1.Yes 2. No
3.26 (a) Were the seizures and/or the febrile illness treated at a hospital? **Je! Kufitika uliyemkumba aliyetajwa umewahi kutibiwa hospitalini**	1.Yes 2. No
3.27 (a) Have you ever been told that you have or had epilepsy or epileptic fits? Je! Umewahi kuambiwa kuwa una kifafa au kwamba shida ya kuanguka kulitokana na ugonjwa wa kifafa?	1. Yes 2. No
3.28 (a) Have you ever been told by a doctor that you have epileptic fits? Je! Umewahi kuambiwa na daktari kuwa una kifafa?	1. Yes 2. No
3.29 Household screening **FW/Software Programmer: ALGORITHM** *Any question between (**3.7a|b TO 3.15a|b**) OR **(3.27a|b TO 3.28a|b) OR (3.4a TO 3.5b)** if affirmative renders the respondent positive and hence a possible case*	 1.Negative 2. Positive

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