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Prediction of outcome from adult bacterial meningitis in a high HIV seroprevalence, resource-poor setting using the Malawi Adult Meningitis Score (MAMS)

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Summary: The MAMS meningitis prediction tool accurately estimates risk of clinical outcome from bacterial meningitis in sub-Saharan Africa. Clinical trial analysis by risk stratification reveals more severe outcomes in low risk groups receiving adjunctive glycerol compared to placebo.

Abstract

Acute bacterial meningitis (ABM) in adults residing in resource-poor countries is associated with mortality rates in excess of 50%. To improve outcome, interventional trials and standardised clinical algorithms are urgently required. To optimise these processes we developed and validated an outcome prediction tool to identify ABM patients at greatest risk of death.

Methods: We derived a nomogram using mortality predictors derived from a logistic regression model of a discovery database of adult Malawian ABM patients (n=523, 65% CSF culture positive). We validated the nomogram internally using a bootstrapped procedure and subsequently used the nomogram scores to further interpret the effects of adjunctive dexamethasone and glycerol using clinical trial data from Malawi.

Results: ABM mortality at six week follow-up was 54%. Five of fifteen variables tested were strongly associated with poor outcome (CSF culture positivity, CSF WCC, haemoglobin, GCS and pulse rate), and were used in the derivation of the Malawi Adult Meningitis Score (MAMS) nomogram. The C-index (area under the curve) was 0.76 (95% CI 0.71 : 0.80) and calibration was good (Hosmer-Lemeshow c-statistic, =5.48, df=8, p=0.705). Harmful effects of adjunctive glycerol were observed in groups with relatively low predicted risk of poor outcome (25-50% risk): CFR 21% in the placebo group, 52% in the glycerol group p<0.001. This effect was not seen with adjunctive dexamethasone.

Conclusion: MAMS provides a novel tool for predicting prognosis and improving interpretation of ABM clinical trials by risk stratification in resource-poor settings. Whether MAMS can be applied to non-HIV endemic countries requires further evaluation.

Keywords: bacterial meningitis, adults, Africa, HIV, outcome, risk factors, severity score, decision support

Introduction

Acute bacterial meningitis (ABM) in sub-Saharan Africa (SSA) is common and associated with high rates of death and co-morbidity in both adults and children [1, 2]. Throughout the African continent, bacterial meningitis is predominately caused by *Streptococcus pneumoniae* [3-5], with the exception

of the ‘meningitis belt’ Sahel region, where seasonal epidemic meningococcal meningitis also occurs [6]. In Malawi, the incidence of ABM in adults is 12/100 000, and the associated mortality is 54% compared to 20-30% in Europe and the United States [1, 2, 7, 8]. Despite intensive efforts, high mortality remains unchanged region-wide, adjunctive treatments such as corticosteroids and glycerol are ineffective and possibly harmful [9-12].

To improve ABM outcome, interventional trials testing new treatment approaches and resource-appropriate standardised clinical algorithms are urgently required. A robust outcome prediction tool would help optimise these processes and provide a basis to examine why previous adjunctive interventions have been unsuccessful [13].

Well validated scores used for risk stratification in life-threatening infection include CURB-65 for pneumonia, APACHE II and SOFA for sepsis [14-17]. Two good quality scores have been reported for ABM in developed settings [18, 19]. A meningitis score has been developed in the African sub-continent [20] but was developed specifically for outcome prediction during meningococcal outbreaks.

We have previously identified clinical predictors of death from adult ABM in Malawi [1]. In the present study, we grouped these outcome predictors to generate and validate a severity score nomogram for use in resource-poor settings. We used the validated score to analyse data from large placebo-controlled trials of adjunctive dexamethasone and glycerol in Malawi, to better understand why these treatments were ineffective.

Patients and Methods

Patient selection

Clinical data from the Malawi meningitis database (MMD) [1], and patient data from a recent clinical trial of goal directed therapy (ISRCTN96218197) were used (Figure 1). All patients had been enrolled into clinical studies of adult ABM in Queen Elizabeth Central Hospital (QECH) in Blantyre, Malawi between 2000-2013 (Figure 1). The inclusion criteria for the MMD were: aged >14 years with proven cerebrospinal fluid (CSF) infection on culture, PCR or Gram’s stain of bacteria known to cause meningitis (proven meningitis), or appropriate clinical history <5 days with a CSF white cell count

(WCC) >50 cells/mm^3 and >50% neutrophils (probable meningitis). In HIV co-infected individuals, the CSF WCC threshold for probable meningitis was lowered to >5 cells/ mm^3, (100% neutrophils), to include HIV co-infected individuals with low CD4 counts who mount a weak CSF inflammatory response in ABM [1, 4].

Cases were excluded if there was CSF evidence of *Cryptococcus neoformans* or *Mycobacterium tuberculosis*, CSF WCC >50% lymphocytes with no documented pre-hospital antibiotics, or on trial-specific exclusion criteria such as diabetes for the glycerol trial [9, 10]. Diagnostic testing for viral meningitis was not available and is an uncommon cause of neurological infection in our centre [21]. MMD patients randomised to receive glycerol were excluded from the nomogram development, as glycerol receipt was an independent predictor of poor outcome [10].

Ascertainment of Clinical Characteristics and Outcomes

All prospective clinical trial data were utilised with permission from the principal investigator. Individual study protocols were examined; only identical variables across the studies were collected (data collected in the same units, at similar time points, using the same normal ranges). All studies were undertaken in the same hospital, used the same laboratories and similar case record forms. Physiological data are from the first recording to minimise both heterogeneity and biases associated with delays to antibiotic therapy, and increase applicability for clinical use in the region. Outcome was measured as death or survival at day 40 post admission to account for additional acute post discharge mortality, which has been reported to occur due from late complications in 5-10% of initial survivors of ABM. [9, 22]. Data on in-hospital delays and morbidity, (principally deafness) were collected variably across the studies and were not included to minimise heterogeneity.

Ethical approvals

All contributing clinical studies were granted ethical approval by the College of Medicine Research and Ethics Committee, University of Malawi and the Liverpool School of Tropical Medicine Research Ethics Committee and conformed to institutional guidelines. All trial participants or named patient guardians gave written informed consent.

Selection of predictor variables

A literature search was performed to determine predictor variables for adults with bacterial meningitis [1]. Individual predictors of mortality from the published analysis of the MMD (coma, seizures, anaemia and tachycardia) [1] and variables associated in other studies with poor outcome (age, gender, HIV status, CSF white cell count and CSF culture) were finally used [7, 19, 23, 24].

Statistical methods, derivation of the nomogram and validation methods

Data were summarised as follows: Continuous normally distributed data using means and standard deviations, skewed data using medians and interquartile range and categorical data using percentages. Analyses using a univariate logistic regression model were performed on all relevant covariates and factors to assess any association with day 40 outcome. The unadjusted estimates were reported using odds ratios and 95% confidence intervals. Multivariable analyses followed on the discovery cohort using a logistic regression model to assess factors and covariates independently associated with the day 40 outcome. This model included all variables with statistical significance on univariate analysis. Variables with high proportions (>50%) of missing data were excluded to reduce risks of over fitting. All analyses were performed using IBM SPSS software package, version 20.0 (IBM statistics, USA) and Stata software version 13.0 (StataCorp, College Station, Texas®). Statistical significance was set at a p value of <0.05.

All variables with significance in the multivariable model were used to model the predictive tool, using *R* software version R i386 3.0.3 (www.r-project.org) using *rms* package, the *lrm* and *nomogram* commands.

The developed model was validated to estimate the potential model performance. Since external data for validation has not yet been identified, an internal validation procedure was performed using bootstrapping (5000 samples), based on calibration, and discrimination [25, 26]. This procedure was selected to optimise the number of cases available while minimising risks of overfitting.

A logistic regression model was used to obtain the predicted deaths. The Hosmer-Lemeshow C-Statistic was used to assess calibration, low insignificant H-L C-Statistic indicated good fit [27]. The calibration assessment was supplemented by the use of a Brier score, (range 0 and 1), a value less than alpha of 0.05 (5% significance level) was used to determine model fit. [28, 29]. A receiver

operating characteristic (ROC) curve was plotted and used to calculate the validated concordance index. The ROC curve was obtained with the C-Index (AUC) and associated 95% confidence intervals. The sensitivity and specificity of the model is based on a cut off of 50% risk score. Individual Malawi Adult Meningitis Scores (MAMS) were calculated for patients using IBM SPSS version 20.0.

Analysis of clinical trial data using MAMS

MAMS scores were calculated for all patients that had been recruited to clinical trials testing adjunctive dexamethasone and glycerol. Cases were risk stratified by quartile risk of poor outcome, and separated by placebo or intervention. Case fatality ratios (CFRs) were calculated within each quartile group and compared to the predicted risk of poor outcome; statistical significance was determined using Chi squared tests. Data were analysed using both original complete case and bootstrapped data.

Results

Clinical characteristics of the patients

Data on patients meeting the inclusion criteria were available for 607 ABM cases, and were used for univariate analyses, of which 593 had CSF results available,384/593,(64%) were CSF culture positive (supplementary Table 1). Complete case data were available for 523 cases of bacterial meningitis, which were used for the multivariable analyses and development of the nomogram. Mean age was 32.5 years (standard deviation 10.8), 50.7% (308/607) were female, 86% (506/584) were HIV co-infected and 31% (171/551) had an acute seizure within the first six hours of admission. Presenting characteristics by outcome group are detailed in Table 1.

The case fatality rate (CFR) was 44% (267/607) at day 10, and 54% (320/593) at day 40.

The following associations with death at day 40 were observed univariately in the discovery cohort (Table 1): Age, temperature, low GCS (low oxygen saturations, high pulse rate, low CSF WCC, and low haemoglobin (Table 1). Other included variables showed no association with outcome on

univariate analysis: gender, HIV sero-status, mean arterial blood pressure, respiratory rate, CSF culture, seizures and blood glucose (Table 1).

All variables tested were included in the multivariable analysis model, with the exception of oxygen saturations, temperature and respiratory rate (>50% missing data) (Table 1). All variables with univariate significance, with the exception of age, also had an association with outcome on multivariable analysis (ORs per unit of measure change): GCS OR 0.77 (0.72 : 0.83) p<0.001, Pulse rate OR 1.01 (1.00 : 1.03) p=0.01, Log_{10} CSF WCC OR 0.66 (0.53 : 0.80) p<0.001, and Hb OR 0.84 (0.78 : 0.90) p<0.001.

Although CSF pneumococcal culture had no significant association with outcome on univariate analysis, the multivariable model demonstrated a significant association with survival (OR 0.36 (95% CI 0.23 – 0.57 p<0.001). Outcome data by organism (supplementary Table 1) showed that increased mortality was observed in patients with non-pneumococcal meningitis. Although numbers were small, increased mortality in the non-pneumococcal groups (CFR 56.5% compared to 51.5% for *S.pneumoniae*), were correlated with lower GCS, and hence associated with poor outcome in the multivariable model. The lack of significant association with mortality on univariate analysis for the remainder of the variables, including HIV status, was retained on multivariable analysis.

Results of the nomogram

Five variables strongly associated with day 40 mortality were used to develop the nomogram: GCS, pulse, CSF WCC, pneumococcal culture and haemoglobin (Figure 2). To calibrate the nomogram, the continuous variables were categorised either by quartile around the median, or by standard normal clinical ranges. To optimise the nomogram, calibration data derived from the categorical data were compared with continuous data [30]. Categorical data led to over fitting and poorer performance; therefore the nomogram using continuous data is reported (Figure 2).

The database was subject to 5000 bootstraps, and then the entire derivation process was repeated using the bootstrapped data. The log (OR) and associated Bootstrapped Confidence Intervals are reported (supplementary Table 2). The data shows shrinkage factor (bias) used to adjust the estimated regression coefficients in the final model for overfitting. Supplementary Table 2 details the bootstrapped confidence intervals for estimated coefficients.

The Corresponding Receiver Operating Characteristic (ROC) curve for the final nomogram is shown in Figure 3. The AUC was 0.76 (95% CI 0.71 – 0.80). The sensitivity of this model using a cut-off of 50% risk score is 71.7% (95% CI 66.0 - 76.9) with a specificity of 63.1%, (95% CI 56.7 -69.2).

Calibration

Goodness-of-fit analysis was assessed to calibrate the nomogram. Hosmer–Lemeshow *C*-statistic was χ^2 =5.48, df=8, p=0.705. Calibration was good across individual centiles of estimated mortality probability (Table 2). The Brier Score was 0.2 (95% Bootstrap CI 0.185 - 0.215). Both the *C*-Statistic and Brier score indicate good calibration. Discrimination was primarily determined by the Concordance Index (AUC). The observed C-index was 0.755 from the original sample, optimism corrected or adjusted C-Index (mean over 5000 bootstraps) was 0.760, (95% Bootstrapped CI 0.71 - 0.79).

MAMS, the European Meningitis Score (EMS) and an older outcome score developed in the US were all derived using similar methods. Therefore when the C-Index (*CI*) of MAMS was compared directly to the published *CI* of these scores [18, 19, 31], MAMS was equivalent. When tested using Malawi data, the EMS *CI* was 0.68 (0.63 – 0.73), compared to MAMS *CI* of 0.76 (95% CI 0.71 - 0.80), suggesting MAMS may be better score than EMS in this setting.

Mortality effects of glycerol and dexamethasone

Case fatality ratios (CFR) were compared by quartile of predicted risk in two clinical trials of dexamethasone and glycerol [9, 10]. In the dexamethasone study, an increased CFR was seen in the lowest risk quartile but no differences were observed in other risk quartiles (Table 3a). In contrast, glycerol was associated with increased risk of death across all but the highest risk quartile in that study, (Table 3b). The same trends were observed when non-bootstrapped data were used, but were not statistically significant (data not shown).

Discussion

This analysis shows that estimation of mortality risk from bacterial meningitis in adults in sub-Saharan Africa (SSA) is possible using simple clinical parameters. MAMS is derived from community acquired

meningitis data, from an African region with a high HIV prevalence and burden of adult bacterial meningitis. This score is therefore likely to be relevant to similar settings but not regions where epidemics of both *N. meningitidis* and *S. pneumoniae* occur seasonally [2, 6, 32]. We demonstrate the utility of MAMS in the assessment of clinical trials, showing that compared to placebo, adjunctive glycerol is associated with the greatest increased risk of death in those patients predicted to have a lower risk of poor outcome. The only other score published from Africa was derived in the Sahel region and therefore while applicable to settings with epidemic of meningococcal meningitis [20], is of limited utility elsewhere.

We used similar data processes to develop MAMS as used in the European Meningitis Score (EMS) and a score developed in the USA [18, 19]. The EMS was developed on a discovery cohort of 691 patients [7] and underwent validation on 301 separate patients from the European Dexamethasone study [33]. Patients receiving either dexamethasone or placebo were included, and interestingly, the authors comment EMS performed better in those in receipt of dexamethasone who had better outcomes, compared to placebo [18, 33]. In the development of our score, we included patients who received dexamethasone, but excluded those receiving glycerol to minimise biases; glycerol was independently associated with mortality in Malawi [1, 9, 10]. The Concordance-Index (CI) of MAMS falls within the 95% confidence interval for the CI of both the EMS and the US based score, and therefore can be considered of equal strength as the other scores in their validation settings.

The EMS performed less well in an external validation exercise, utilising data from dexamethasone clinical trials from Vietnam and Malawi [9, 31, 34]. This may simply be due to differing methodology, including the use of categorised data in the EMS nomogram and the selection of categorical cut-offs may have been less appropriate for these younger African patients, [18]. However, we believe that the poorer performance of the EMS in those settings highlights critical differences between developed and developing country ABM populations including longer time to presentation, a higher prevalence of HIV and anaemia, greater frequency of complications and lower resources available for clinical management [35, 36].

The original trial of adjunctive glycerol in Malawi was stopped early due to unexpected increase in mortality in the glycerol arm [10]. Why this effect was predominately in those with lower predicted risk of death as determined by MAMS is uncertain. However, we hypothesise that in less severely ill

patients, glycerol induced vasodilatation of pial micro-arterioles and osmotic effects may decompensate fragile but balanced fluid compartments in the brain and the systemic circulation with adverse effects on brain swelling and perfusion [37, 38]. By comparison, in severely ill patients, breakdown of the blood brain barrier is advanced, hence glycerol has no additive adverse effect.

A major limitation in the development both of EMS and MAMS was missing data, managed using bootstrapping for both scores to reduce the risk of over-fitting [18]. The developed model was validated to estimate the potential for overfitting and optimism in model performance using an internal validation procedure. This methodology is advised in the absence of external validation data, instead of use of split samples or cross-validation without replication [25, 26]. The nomogram was optimised using standard validation exercises to reduce overlap, high levels of agreement were observed. Cohort assembly was done using data from multiple studies in the same hospital, biases from inter-observer disagreement were minimised by only selecting variables that were collected uniformly across all studies. All data were collected prospectively in the same units, by research staff trained in the same institution, using the same equipment to minimise potential biases associated with post-hoc cohort assembly. We used data from the first recording after admission to hospital in all studies to minimise the effect of in-hospital delays on alterations on physiological variables that may otherwise affect the prognostic power of the score. Other limitations include use of data from only one country, relative infrequency of HIV-uninfected patients, lack of inclusion data on morbidity endpoints and processes of care including antibiotic delays, and relatively few patients with meningococcal compared to pneumococcal meningitis [6]. The MAMS nomogram requires external prospective validation in other populations, including specific validation in countries at risk of epidemic meningococcal disease.

It is clear that in the development of a severity score, other factors beyond those measured in the score may be important in determining outcome of adults with bacterial meningitis in sub-Saharan Africa. Although HIV co-infection was not associated with mortality and not included in the nomogram, it is possible that low CSF WCC and low Hb may both correlate with advanced immunosuppression, CD4 data are currently lacking in this setting.

In conclusion, the MAMS risk stratification tool has a good predictive power for use in ABM in adults in sub-Saharan Africa outside the epidemic meningitis belt. MAMS can be used in the analysis of prospective clinical trial data, testing efficacy of interventions in different risk groups. The differences between MAMS and EMS scores highlight important differences between ABM patients in these contrasting environments. Further work is required to explore these differences, to test MAMS prospectively, and design optimal interventions to reduce the unacceptable mortality from meningitis in Africa.

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NOTES:

Conflict of interest statements

All authors have no conflicts of interest to declare

Role of the funding source

The funding body had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Ethics committee approval

All contributing clinical studies were granted ethical approval by the College of Medicine Research and Ethics Committee, University of Malawi and the Liverpool School of Tropical Medicine Research and Ethics Committee and conformed to institutional guidelines. All trial participants or named patient guardians gave written informed consent.

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Legends for Tables and Figures

1. **Table 1:** Results of the univariate analysis and predictors of outcome from the complete case data
2. **Table 2:** Summary of the agreement of the nomogram per risk centile
3. **Table 3:** Day 40 mortality outcomes from dexamethasone and glycerol compared to placebo by MAMS risk centile (bootstrapped data).
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Table 1 Results of the univariate analysis and predictors of outcome from the complete case data

Parameter		Day 40		Univariate (unadjusted)		Multivariable (adjusted)*	
		Alive	Dead	Odds ratio (95% CI)	p	Odds ratio (95% CI)	p
Sample size n=607		273 (%)	320				
Age	mean (sd)	31.5 (10.9)	32 (10.6)	1.01 (1.00 : 1.03)	**0.01**	1.00 (0.95 : 1.06)	0.84
	> 40 years	42 (14.6)	53 (16.6)	1.30 (0.67 : 2.5)	0.42		
Gender	male	136 (47)	163 (50.9)	1.17 (0.85 : 1.62)	0.32		
HIV status	positive	226 (78)	280 (87)	0.79 (0.32 : 1.95)	0.61		
	not known	10 (3.5)	13 (4.1)				
Admission out of hours		122 (42.5)	139 (43.9)	1.20 (0.68 : 1.28)	0.40		
	not known	30 (10.5)	29 (9.1)				
GCS	mean (sd)	12 (2.8)	9.9 (3.5)	0.82 (0.78 : 0.86)	**<0.001**	0.77 (0.72 : 0.83)	**<0.001**
1 or more acute	One seizure	45 (16)	70 (22)	0.61 (0.30 : 1.23)	0.16		
seizure episodes	Two seizures	18 (6.3)	37 (11.6)	0.75 (0.33 : 1.70)	0.49		
Temperature (°C)	mean (sd)	38.2 (1.1)	38.4 (1.3)	1.17 (1.02 : 1.34) ‡	**0.02**	†	
SpO_2 (%)	mean (sd)	95.5 (2.5)	96 (6.5)	0.90 (0.82 : 1.00) ‡	0.07	†	
Pulse rate (beats/min)	mean (sd)	98.6 (19)	104.8 (19.8)	1.01 (1.00 : 1.02) ‡	**<0.001**	1.01 (1.00 : 1.03)	**0.01**
MAP (mmHg)	mean (sd)	89.9 (15.1)	90.5 (16.7)	1.00 (0.99 : 1.01)	0.81		
Respiratory rate (breaths/min)	mean (sd)	24.7 (6.6)	26.9 (7.9)	1.04 (0.99 : 1.09) ‡	0.11	†	
CSF White cell count (cells/mm^3)**	Median (IQR)	356 (64–1280)	215 (35 – 630)	0.49 (0.37 : 0.64) ‡	**<0.001**	0.66 (0.53 : 0.80)	**<0.001**
CSF culture positive for *S. pneumoniae*		160 (55)	165 (51.6)	1.06 (0.66 : 17.1) ‡	0.96	0.36 (0.23 : 0.57)	**<0.001**
Plasma glucose (mmol/L)	mean (sd)	7.5 (2.7)	7.6 (3.8)	1.00 (0.95 : 1.05)	0.87	†	
Haemoglobin (g/dL)	mean (sd)	11.2 (2.6)	10.1 (2.6)	0.86 (0.80 : 0.91) ‡	**<0.001**	0.84 (0.78 : 0.90)	**<0.001**

† : proportion of missing data >50% so variable excluded from multivariable analysis ‡ : odds ratio for a unit change in predictor variable *performed on complete case data only, n=523

** OR calculated on log10 data. 15 patients were CSF culture negative with CSF WCC >50 cells/mm^3, a further six were HIV co-infected with cell counts >5 cells/mm^3.

Table 2 Summary of the agreement of the nomogram per risk centile

Group	Probability centile of death	Observed deaths (%)	Predicted deaths (%)	Total
1	0.234	6 (11.3)	9 (17.0)	53
2	0.326	14 (26.9)	15 (28.8)	52
3	0.389	23 (44.2)	19 (36.5)	52
4	0.460	24 (45.3)	22 (41.5)	53
5	0.540	25 (48.1)	26 (50.0)	52
6	0.604	30 (57.7)	30 (57.7)	52
7	0.677	30 (56.6)	34 (64.2)	53
8	0.763	40 (76.9)	37 (71.2)	52
9	0.836	42 (80.8)	42 (80.8)	52
10	0.962	45 (86.5)	46 (88.5)	52
Total		279	279	523

Hosmer-Lemeshow C-Statistic, χ^2 =5.48, df=8, p=0.705

Table 3a

MAMS risk probability of death at day 40	Placebo N=1293		Dexamethasone N=1268		(CFR%) (p value)
	Alive	**Dead** n (CFR%)	**Alive**	**Dead** n (CFR%)	
<25%	61	0 (0%)	48	6 (11%)	P=0·010
25-50%	232	106 (31%)	236	126 (35%)	P=0·330
50-75%	252	311 (55%)	173	264 (60%)	P=0·100
>75%	66	265 (80%)	99	316 (78%)	P=0·210
Total	**611**	**682 (53%)**	**556**	**712 (56%)**	**P=0·120**

CFR Case fatality rate.

Table 3b

MAMS risk probability of death at day 40	Placebo N=549		Glycerol N=592		CFR% Significance of CFR intervention v placebo
	Alive	**Dead** N (CFR %)	**Alive** **n**	**Dead** N (CFR (%)	

<25%	51	6 (10%)	49	14 (22%)	P=0·080
25-50%	112	31 (21%)	85	92 (52%)	P<0·001
50-75%	119	124 (51%)	69	167 (70%)	P<0·001
>75%	18	88 (83%)	29	87 (75%)	P=0·140
Total	**300**	**249 (45%)**	**232**	**360 (61%)**	**P=0·001**

CFR case fatality rate.

Figure 1: CONSORT figure of selection of studies for the Malawi Adult Meningitis Score Development

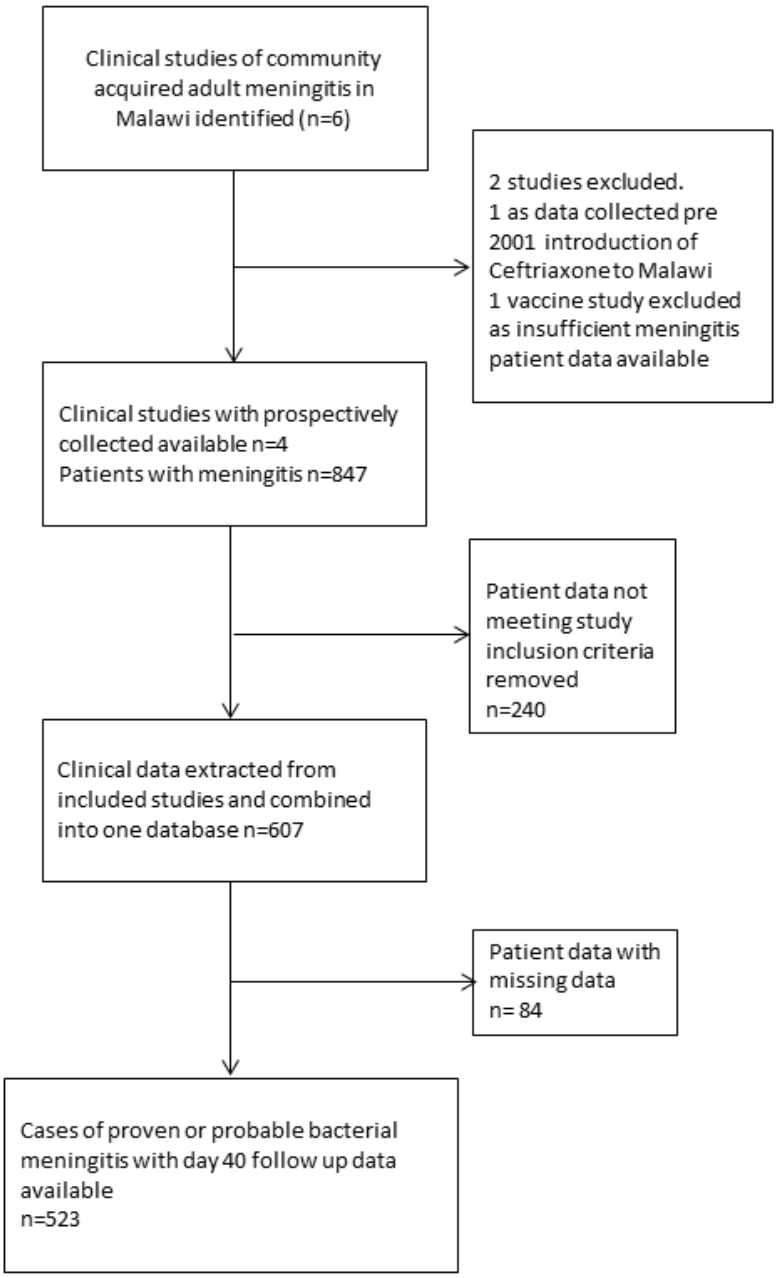

Figure 2. MAMS nomogram

Guide for use: A variable is measured and then its value is matched to corresponding point on the first row of the nomogram. The points are then added for all the five variables for each patient. The total points for the patient are matched to the corresponding risk score % at the bottom i.e. match up two last rows of the nomogram

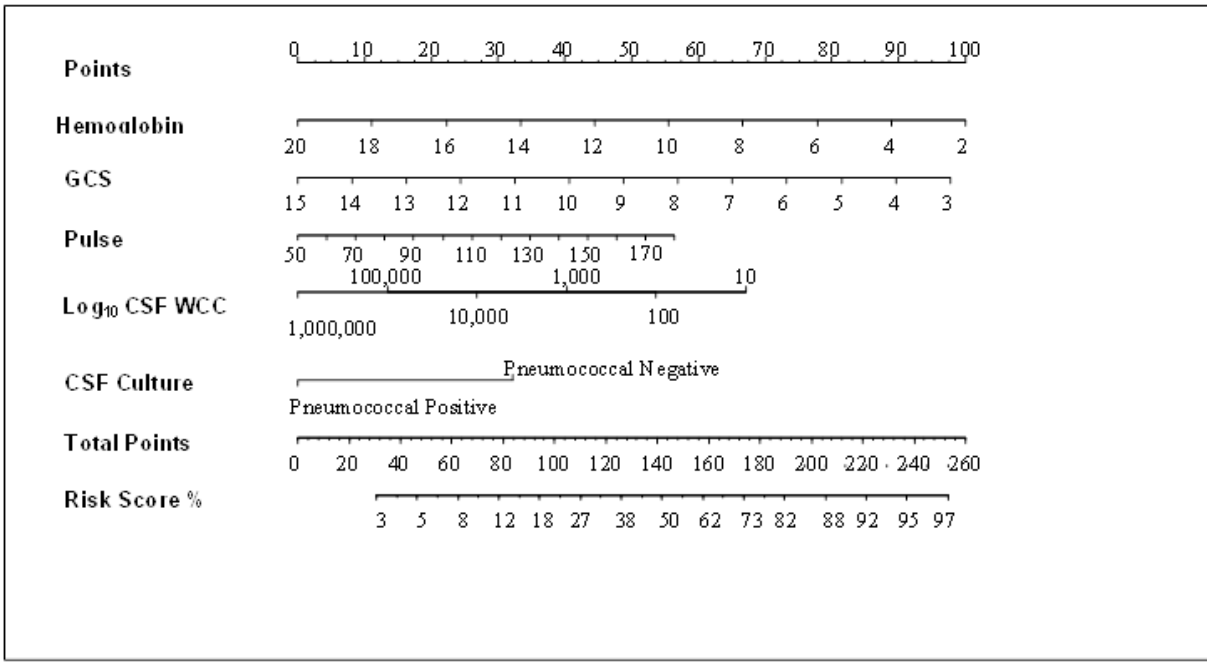

Figure 3: **ROC curve showing MAMS Receiver Operated Curve for the Malawi Adult Meningitis Score sensitivity**