Web Appendix 1 – Estimation of Trend in Maternal Mortality in Malawi from 1977 to 2012

The best-fitting line representing the observed national level MMR data for Malawi was calculated by applying multi-term fractional polynomial transformations to a linear regression of MMR by year using the **fracpoly** command in Stata 13.0 for Mac:

fracpoly, degree(3) compare: regress mmr year

The **fracpoly** command transforms the independent variable **year** many times using the powers -2, -1, -.5, 0, 1, 2, 3 in combination. The number of terms used is specified by the **degree()** option. Here we used **3** as that was determined to produce a better fitting model (as assessed by the deviance statistic of the maximum likelihood estimator) than a model with 2 terms and a not statistically significantly different (at $p<0.05$) fit to a model with 4 terms. The three terms were transformations to the powers -1, 2 and 3 (each with added constants) as this combination was found to produce the best-fitting model.

The subsequent command:

predict mmrfit

produces the MMR trend predicted by this best-fitting fractional polynomial model, which was plotted as the gold line in Figure 1 of the paper.

The above calculation of the trend line was based on using the same estimate for each of the years represented by each of the 6 analyses of the 4 nationally representative surveys used (all of the data plotted as larger black dots on Figure 1). We believe this to be more representative than only assuming the survey estimates apply to the mid-points of the period they cover (e.g. for the DHS 2010, which spans 2004-2010, assuming the estimate of 675 only applies to 2007 rather than each of the years 2004 to 2010). Using only the mid-points to calculate the best-fitting fractional polynomial trend-line as a sensitivity analysis results in a fractional polynomial model with two terms with the powers 3 and 3 (each with added constants) and estimates of MMR that show a comparatively flatter trend over the 1990 to 2010 time-period (Web Table 1). We prefer the model using the data applied to all years covered by the survey as this uses more of the information provided by the survey.

Web Table 1: Results of sensitivity analysis of MMR trend estimate

1990	1995	2000	2005	2010	Source
748	916	970	846	484	Estimates applied to all years covered by survey
824	941	933	801	545	Estimates applied to mid-points of survey periods only

Web Appendix 2 – Estimation of Maternal Mortality due to HIV in Malawi

We used the relative-risk of pregnancy-related mortality in HIV positive compared to HIV negative women estimated by Calvert and Ronsmans via systematic review and meta-analysis to be 7.74 [1], to estimate the proportion of the MMR that is due to HIV depending on the HIV prevalence. We did this using the formula provided by Calvert and Ronsmans [1]:

PAF = hiv*(RR-1)/((hiv*(RR-1))+1

Where: PAF, the Population Attributable Fraction is the proportion of the MMR (Maternal Mortality Ratio) due to HIV; hiv is the HIV prevalence; and RR is the relative-risk of 7.74. The MMR due to HIV is then obtained by multiplying the MMR by the PAF.

We adjusted the proportion of MMR due to HIV downwards from 2003 to 2010 to account for the increasing impact of the antiretroviral therapy (ART) programme in Malawi [2 3]. The effect of the ART programme on MMR due to HIV was estimated as follows. Using the estimate of 35% of HIV positive pregnant women being on ART provided in section 3.2.2 of the Malawi Ministry of Health ART programme report for the second quarter of 2010 [4] and the reported numbers of people on ART in each of the years from 2002 to 2007 provided by Mwagomba et al [2] as an estimate of the exponential expansion path of the ART programme we calculated a percentage of pregnant women on ART for each of the years from 2002 to 2010 (Web Table 2). To fill in the years 2008, 2009 and 2010 we used the **fracpoly** command in Stata 13.0 for Mac (see Web Appendix 1) to estimate the expected number of people on ART given the Mwagomba *et al* data and applied the 2010 figure (27153) as equalling the 35% of pregnant women on ART in 2010 (Web Table 2).

We then estimated the effectiveness of the ART programme using the 'current practice' data from Fasawe *et al* (2013) which accounts for drug stockouts, adherence and drug effectiveness and estimates 18267 pregnant women out of the 59850 initially reached by ART (90% of the estimated 66500 HIV positive pregnant women) would be alive after 10 years. Assuming a proportionally equal year on year decline this translates to 52465 being alive after 1 year (the approximate length of the maternal period of pregnancy and post-partum), i.e. an effectiveness of the ART programme of 87.6%. This could increase to an estimated 96.2% with Option B+ which is currently being rolled-out across Malawi [3].

Finally we applied the estimate of 87.6% effectiveness to the estimates of ART programme coverage for each of the years to arrive at the estimate of the effect of the ART programme on MMR due to HIV (Web Table 2). We then multiplied the MMR due to HIV by 1 minus the effect of the ART programme for the given year to reducing it in line with the effect of the ART programme.

Web Table 2: Estimation of effect of ART programme on MMR due to HIV

Year	Number ever started on ART[a]	% of HIV+ pregnant women on ART, assuming 27153 people in 2010 represents 35% [b]	Estimate of ART programme effect (% reduction) on MMR due to HIV assuming 87.6% effectiveness
2002	0	0%	0.0%
2003	421	0.5%	0.5%
2004	1550	2.0%	1.8%
2005	3145	4.1%	3.6%
2006	6216	8.0%	7.0%
2007	10215	13.2%	11.5%
2008	14877	19.2%	16.8%
2009	20554	26.5%	23.2%
2010	27153	35.0%	30.7%

[a] 2002 to 2007 numbers taken from the final column of Table 1 of Mwagomba et al [2]. 2008 to 2010 figures estimated using best-fitting trend line determined by fracpoly command in Stata 13.0

[b] The Malawi government report 35% of HIV positive pregnant women were on antiretroviral therapy [4]

References for Web Appendices 1 and 2

1. Calvert C, Ronsmans C. The contribution of HIV to pregnancy-related mortality: a systematic review and meta-analysis. AIDS 2013;**27**:Feb 25 [Epub ahead of print]
2. Mwagomba B, Zachariah R, Massaquoi M, et al. Mortality Reduction Associated with HIV/AIDS Care and Antiretroviral Treatment in Rural Malawi: Evidence from Registers, Coffin Sales and Funerals. PLoS One 2010;**5**(5):e10452
3. Fasawe O, Avila C, Shaffer N, et al. Cost-Effectiveness Analysis of Option B+ for HIV Prevention and Treatment of Mothers and Children in Malawi. PLoS One 2013;**8**(3):e57778
4. Government of Malawi Ministry of Health. Quarterly HIV Programme Report: April - June 2010. Available at: http://www.hivunitmohmw.org/uploads/Main/Quarterly HIV Programme Report 2010 Q2.pdf (accessed 13/08/2013), 2010.