Articles

Women's risk of death beyond 42 days post partum: a pooled analysis of longitudinal Health and Demographic Surveillance System data in sub-Saharan Africa

Ursula Gazeley, Georges Reniers, Hallie Eilerts-Spinelli, Julio Romero Prieto, Momodou Jasseh, Sammy Khagayi, Veronique Filippi

Summary

Background WHO's standard definitions of pregnancy-related and maternal deaths only include deaths that occur within 42 days of delivery, termination, or abortion, with major implications for post-partum care and maternal mortality surveillance. We therefore estimated post-partum survival from childbirth up to 1 year post partum to evaluate the empirical justification for the 42-day post-partum threshold.

Methods We used prospective, longitudinal Health and Demographic Surveillance System (HDSS) data from 30 sites across 12 sub-Saharan African countries to estimate women's risk of death from childbirth until 1 year post partum from all causes. Observations were included if the childbirth occurred from 1991 onwards in the HDSS site and maternal age was 10–54 years. We calculated person-years as the time between childbirth and next birth, outmigration, death, or the end of the first year post partum, whichever occurred first. For six post-partum risk intervals (0–1 days, 2–6 days, 7–13 days, 14–41 days, 42–122 days, and 4–11 months), we calculated the adjusted rate ratios of death relative to a baseline risk of 12–17 months post partum.

Findings Between Jan 1, 1991, and Feb 24, 2020, 647104 births occurred in the HDSS sites, contributing to 602170 person-years of exposure time and 1967 deaths within 1 year of delivery. After adjustment for confounding, mortality was $38 \cdot 82$ (95% CI $33 \cdot 21-45 \cdot 29$) times higher than baseline on days 0–1 after childbirth, $4 \cdot 97$ ($3 \cdot 94-6 \cdot 21$) times higher for days 2–6, $3 \cdot 35$ ($2 \cdot 64-4 \cdot 20$) times higher for days 7–13, and $2 \cdot 06$ ($1 \cdot 74-2 \cdot 44$) times higher for days 14–41. From 42 days to 4 months post partum, mortality was still $1 \cdot 20$ ($1 \cdot 03-1 \cdot 39$) times higher (ie, a 20% higher risk), but deaths in this interval would be excluded from measurement of pregnancy-related mortality. Extending the WHO 42-day post-partum threshold up to 4 months would increase the post-partum pregnancy-related mortality ratio by 40%.

Interpretation This multicountry study has implications for measurement and clinical practice. It makes the case for WHO to extend the 42-day post-partum threshold to capture the full duration of risk of pregnancy-related deaths. There is a need for a new indicator to track late pregnancy-related deaths that occur beyond 42 days, which are otherwise excluded from global maternal health surveillance efforts. Our results also emphasise the need for international agencies to disaggregate estimates by antepartum, intrapartum, postpartum, and extended post-partum periods. Additionally, the schedule and content of postnatal care packages should reflect the extended duration of post-partum risk.

Funding The UK Economic and Social Research Council.

Copyright © 2022 The Author(s). Published by Elsevier Ltd. This is an Open Access article under the CC BY 4.0 license.

Introduction

Improving survival in the post-partum period—defined as the first 42 days following birth, termination of pregnancy, or miscarriage—as well as in the extended post-partum period up to 1 year is crucial. Data from high-income countries, where maternal mortality is low, indicate that the majority of maternal deaths occur post partum.¹ In sub-Saharan Africa, which accounts for two-thirds of maternal deaths wordwide,² 2013 data indicate that 48% of maternal deaths occurred between 24 h and 42 days post partum, and a further 13% occurred between 43 days and 1 year (authors' own calculation).³ More evidence is needed, although there are indications that improvements in post-partum survival have not kept pace with the rapid decline in antepartum and intrapartum mortality in recent decades.^{3,4} Consistent with the epidemiological transition, deaths in the extended post-partum period will continue to increase in relative importance in sub-Saharan Africa.³

The primary indicator used to monitor maternal survival up to 42 days post partum is the maternal mortality ratio (MMR)—the number of maternal deaths per 100 000 livebirths. The MMR is the key indicator reported by international agencies and is used to track progress towards Sustainable Development Goal 3.1.1. Identifying maternal deaths, however, requires information on both the cause and time of death. A maternal death must occur within 42 days of the end of pregnancy, from any direct





Lancet Glob Health 2022; 10: e1582–89

Department of Infectious Disease Epidemiology (U Gazelev MSc. Prof V Filippi PhD) and **Department of Population** Health (G Reniers PhD, H Eilerts-Spinelli PhD J R Prieto PhD), London School of Hygiene & Tropical Medicine, London, UK: Medical Research Council Unit The Gambia at London School of Hygiene & Tropical Medicine, Fajara, The Gambia (M Jasseh PhD); Kenya Medical Research Institute-Center for Global Health Research, Kisumu, Kenva (S Khagayi PhD)

Correspondence to: Ms Ursula Gazeley, Department of Infectious Disease Epidemiology, London School of Hygiene & Tropical Medicine, London WC1E 7HT, UK ursula.gazeley@lshtm.ac.uk

Research in context

Evidence before this study

We searched MEDLINE and Embase for studies that analysed the risk of death (maternal or pregnancy-related) in the extended post-partum period. We used the following search terms: ("pregnancy-related" or "maternal" or "postpartum" or "postnatal" or "late maternal") and ("mortality" or "death" or "risk") and ("over time" or "time since delivery" or "time since birth" or "six weeks" or "42 days") and (MEDLINE expert search for all low-income and middle-income countries) for articles published from inception up to May 26, 2022, without language or date restrictions. We noted 141 publications, only four of which were relevant upon screening of title and abstract. These four studies showed that women's risk of death could remain elevated until 3–6 months post partum, casting doubt on the empirical basis for the 42-day post-partum threshold.

Added value of this study

This existing research is now outdated, mostly from observation periods before the millennium. Most studies were also based on

(obstetric) or indirect (non-obstetric) cause related to or aggravated by the pregnancy.⁵ Deaths that occur from direct or indirect causes beyond 42 days but within 1 year are classified as late maternal deaths. Maternal and late maternal deaths are jointly termed "comprehensive maternal deaths" in the International Classification of Diseases 11th revision (ICD-11).

In the absence of cause of death (COD) information, however, the number of pregnancy-related deaths and estimates of the pregnancy-related mortality ratio (PRMR) are used. Pregnancy-related deaths occur within 42 days of pregnancy, irrespective of the cause, and include causes incidental to the pregnancy.⁵ Surveillance of pregnancy-related mortality is particularly crucial in sub-Saharan Africa, where medical certification of the cause of death (COD) is rare⁶ and measurement of maternal mortality is often not possible.⁷ Without COD information, the Demographic and Health Surveys,⁵ Multiple Indicator Cluster Surveys,⁵ and population censuses⁸ estimate pregnancy-related mortality, and are key inputs into WHO global maternal mortality modelling.

Whichever definition is applicable, depending on the presence or absence of COD information, the definitions of maternal, late maternal, and pregnancyrelated deaths are all contingent on the 42-day postpartum threshold. Explanations for this cut-off often invoke the timing of physiological changes that occur post partum, such as the return of the uterus to its new post-pregnancy size and the resumption of menstruation for non-lactating women.⁹ However, for women who are partially or exclusively breastfeeding, lactational amenorrhoea can last much longer.¹⁰ The ability of the body to recuperate from the trauma of relatively small cohorts, and only one article was based on a population in sub-Saharan Africa. In our study, we provide a long-overdue update on the evidence of women's risk of death following delivery, on the basis of an unparalleled sample size, from multiple countries in sub-Saharan Africa where the burden of maternal mortality remains the highest.

Implications of all the available evidence

Our finding that women's risk of death remains 20% elevated until 4 months post partum questions the empirical justification of the 42-day postpartum threshold, integral to WHO's standard definitions of maternal, late maternal, and pregnancy-related death. Based on post-partum pregnancy-related mortality, this study reaffirms calls for the 42-day post-partum threshold to be revised to better capture the full duration of elevated mortality risk. It also implies that the schedule and content of postnatal care visits should be reconsidered. Finally, in contexts where the availability of cause-of-death data are poor, the definition and measurement of late pregnancy-related mortality beyond 42 days postpartum is crucial.

pregnancy and childbirth by 42 days might also be hindered by direct obstetric complications, and infectious or non-communicable comorbidities.^{3,11}

In an era where indicators govern global health priorities, the 42-day post-partum threshold has implications for mortality surveillance, maternal health interventions, and post-partum care policy and practice.

Surveillance of maternal survival beyond the 42-day post-partum threshold is often poor when COD information is available,4 and virtually non-existent when it is not. WHO recommends countries monitor late maternal mortality, but deaths are not coded uniformly according to ICD (code JB61 in ICD-11, previously O96 in ICD-1012), resulting in measures that are often not comparable between countries.4 There exists no official definition of what could be called late pregnancy-related deaths-ie, those that occur beyond 42 days but within 1 year post partum. Where COD is not available, these deaths will not be counted. A reliance on the MMR and PRMR to track progress might therefore lead to an overestimation of improvement in maternal survival if mortality reduction is more rapid for antepartum, intrapartum, and early postpartum periods than beyond 42 days.^{3,13}

The 42-day post-partum threshold might itself also directly affect estimates of the distribution of direct, indirect, or incidental causes of death within 1 year post partum. Whether a woman's death occurred within 42 days of delivery, termination, or miscarriage is a question in the WHO 2022 verbal autopsy instrument.¹⁴ This timing field is used as an input for both physician coding and automated coding of verbal autopsy data to assign the likely COD where medical certification of COD is lacking. Accurate estimates of the disease burden are a vital component of public health policy and programme prioritisation. $^{\mbox{\tiny 15}}$

Finally, the 42-day post-partum threshold is also integral to post-partum care policy and practice, an often-neglected aspect of quality maternal care.¹⁶ Current WHO guidelines recommend postnatal contacts within the first 24 h, and follow-up contacts on day 3, between 7 days and 14 days, and 6 weeks after birth.¹⁷ There are no guidelines for visits scheduled beyond the 6-weeks' postpartum period, despite WHO's acknowledgement that some physiological or psychological changes could take longer than 6 weeks to manifest.¹⁶ Accurate estimates of the duration of the elevated risk following pregnancy and delivery are necessary to inform post-partum care practices and ensure the effective transfer between maternity services and primary or secondary health care for women who need longer term management.^{18,19}

Research that analyses the risk of death over an extended post-partum period in low-income and middleincome countries (LMICs) is scarce. The few studies that do exist suggest that mortality risk might remain elevated far beyond 42 days.^{11,20-22} All but one of these studies are based on cohorts with small sample sizes,^{11,20} and one study is a case review with no exposure sample.²¹ Only one study is based on a population in sub-Saharan Africa.¹¹ The three cohort studies are also extremely outdated,^{11,20,21} with the last observation period ending in 2001.²¹ Given maternal survival has improved substantially since then,⁵ the duration of post-partum risk must be revisited.

We aimed to estimate the duration of post-partum risk after the end of pregnancy. Based on an analysis of the risk of post-partum (late) pregnancy-related mortality up to 1 year, we assess the validity of the WHO's 42-day post-partum threshold.

Methods

Data and sample

We used prospective, longitudinal data from 30 Health and Demographic Surveillance System (HDSS) sites, across 12 sub-Saharan African countries (Tanzania, Ethiopia, Kenya, Malawi, Mozambique, South Africa, Nigeria, The Gambia, Burkina Faso, Cote d'Ivoire, Senegal, and Ghana). Data from 28 of these sites are open access from the INDEPTH Network's iShare database.23 whereas access to the data from two additional sites (Basse in The Gambia and Siaya in Kenya) was arranged through datasharing agreements with the principal investigators of these sites. HDSSs collect data on births, deaths, and migrations that occur within a small geographical area. Households and individuals residing within the radius of the site are visited between quarterly and annually, depending on the site, and all vital events that occurred since the last visit are recorded.23 Further detail about HDSS data is documented elsewhere.24,25

All individuals in the HDSS sites are assigned a unique identification code, which facilitates data linkage

across HDSS datasets to estimate post-partum survival. Childbirths were identified using the HDSS delivery file (at the level of the female, the event of a pregnancy ending after 28 weeks' gestation, including livebirths and stillbirths, although stillbirths are likely to be underreported).²⁶ The birth outcome (livebirth or stillbirth), records of pregnancies ending before 28 weeks' gestation (miscarriage or abortion), and obstetric history before residency in the site, are not recorded universally across sites and therefore not included in the consolidated HDSS data.

Childbirths before 1991, before most sites were fully operational, were excluded (n=13 274). Return migrants or new in-migrants were included in the sample if site entry preceded the end of pregnancy. Observations were included as long as the woman gave birth in the site and their age at childbirth was between 10 and 54 years, inclusive. Based on the calendar year the childbirth occurred, observations were grouped into 5-year childbirth cohorts. The London School of Hygiene and Tropical Medicine ethics committee approved the study. Each HDSS site had their own consent procedure (either written or verbal), but in most sites informed consent was at the household level.²⁴

Statistical analysis

For each childbirth, exposure time (person-years) was calculated as the time between a delivery (n) and start date of the next pregnancy (n+1 delivery date minus 281 days), outmigration from the HDSS, death, or the end of the first year post partum, whichever occurred first. In the case of multiple births (eg, twins), exposure was counted only once. The distribution of deaths by days since childbirth was adjusted to correct for the overestimation of days until death when calculated using calendar days (eg, a woman who survived less than 24 h but who died on the next calendar day would be misattributed to day 1), splitting deaths between the calendar day of occurrence and the day before.

To estimate the risk of death, we moved from individual-level data to an aggregate model of maternal survival, approximated using a Piecewise Constant Hazard Model (PCHM). The standard 42-day postpartum period was split into risk intervals (0-1 day, 2-6 days, 7-13 days, and 14-42 days). In the PCHM, the risk of death is assumed to be constant for the duration of each interval, and so intervals were closely spaced where the risk of death declines rapidly, and more widely spaced as the risk of death changes more slowly (appendix p 4). Beyond 42 days, we incrementally estimated the point at which women's risk of death remains elevated at 95% significance. We estimated this to be up to 122 days, and hence the remainder of the first year post partum was split accordingly (42-122 days and 4-11 months). Within each risk interval, counts of deaths and person-years were aggregated. The period 12-17 months was used as the baseline risk of death, to

See Online for appendix

	Alive or censored by the end of the 1-year post- partum follow-up (n=645 137 births)*	Died within the 1-year post-partum follow-up (n=1967 births)
Childbirth cohort		
1991 to 1995	20203 (3·1%)	81 (4.1%)
1996 to 2000	47339 (7·3%)	204 (10·4%)
2001 to 2005	81419 (12.6%)	382 (19·4%)
2006 to 2010	182158 (28.2%)	575 (29·2%)
2011 to 2015	270 817 (42.0%)	641 (32.6%)
2016 to 2020	43201 (6.7%)	84 (4.3%)
Country		
Burkina Faso	65 817 (10.2%)	97 (4·9%)
Côte d'Ivoire	10460 (1.6%)	17 (0.9%)
Ethiopia	67 287 (10.4%)	169 (8.6%)
The Gambia	105 382 (16.4%)	286 (14.5%)
Ghana	82126 (12.7%)	200 (10·2%)
Kenya	67716 (10.5%)	194 (9·95)
Malawi	100 (<0.1%)	0 (0)
Mozambique	13331 (2.1%)	46 (2.3%)
Nigeria	22 836 (3·5%)	53 (2.7%)
Senegal	48 578 (7·5%)	176 (8.9%)
South Africa	73 810 (11.4%)	364 (18.5%)
Tanzania	87695 (13.6%)	365 (18.6%)
Parity in HDSS†		
1	375 498 (58.2%)	1214 (61.7%)
2-3	212 279 (32.9%)	586 (29.8%)
4-5	50559 (7.9%)	150 (7.6%)
6+	6801 (1·1%)	22 (1.1%)
Maternal age at tim	e of childbirth‡	
<15 years	3285 (0.5%)	11 (0.6%)
15–24 years	269 459 (41·8%)	639 (32.5%)
25-34 years	271648 (42.1%)	897 (45.6%)
35+ years	100745 (15.6%)	425 (21.6%)

Data are n (%). HDSS=Health and Demographic Surveillance System. *Some women gave birth multiple times within the HDSS site. Multiparous women might contribute to multiple categories. †Parity is likely to be poorly recorded in the HDSSs, as often only births to women resident in the site are recorded, rather than full obstetric histories. ‡Observations where maternal age at the end of pregnancy was <10 years or >54 years were excluded (n=1108, 0·17% of the sample), in line with the Global Burden of Disease protocol.²⁴ These observations will be mostly, though not exclusively, caused by HDSS sites erroneously recording the maternal date of birth or the date of childbirth.

Table 1: Frequency distribution for births within the HDSS

represent women's unexposed state." Following Høj and colleagues, " we chose this interval as it occurs after the cut-off for late maternal death after the first year post partum, and is long enough to provide stable statistical estimates." For subsequent births (n+1) that occurred before the end of 17 months post partum, we adjusted the person-years as half of the exposure time between birth n and n+1.

As we were working with aggregated counts of deaths and person-years, we estimated the PCHM using negative binomial regression, which also corrects for overdispersion in the data by adjusting the standard

	Death distribution*	Person-years	Crude death rate per 1000 person- years
0 to 1 day	306	3541	86.6
2 to 6 days	118	8841	13.4
7 to 13 days	101	12354	8.2
14 to 41 days	223	49145	4·5
42 to 122 days	363	139387	2.6
4 to 11 months	856	388 903	2.2
12 to 18 months	574	263592	2.2

*Adjusted death distribution to correct for misattribution of deaths to the next calendar day (eg, women who survive less than 24 h but die on the next calendar day would be misattributed to day 1). Half of deaths are assumed to occur on the calendar day, and half on the day before. A comparison of adjusted and unadjusted distributions can be found in the appendix (p 3).

Table 2: Crude death rates by interval up to 1.5 years post partum

error. We accounted for the effect of potential confounders that were available in the HDSS data (maternal age at childbirth, parity in the HDSS, and delivery cohort). The final multivariable model was specified as follows: the dependent variable was the death count; the independent variable was the time interval from childbirth; and the additional predictors were maternal age at the time of birth, parity in the HDSS, and childbirth cohort. Personyears was the offset variable to weight the death counts by the exposure. We also included HDSS site dummies to estimate aggregate-level fixed effects to control for unobserved heterogeneity between sites.

Finally, in the absence of COD information, and with exposure beginning from the date of childbirth onwards, we estimated the postpartum pregnancy-related mortality ratio (life table analysis available in the appendix p 5).

Role of the funding source

The funders of this study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Between Jan 1, 1991, and Feb 24, 2020, 647104 births occurred in the HDSS sites, contributing 602170 total person-years-at-risk, among 386318 women (multiparous women contributed more than one post-partum exposure period). The sample characteristics for women who delivered in the HDSS sites are described in table 1. There were 1967 deaths within 1 year post partum, of which 748 deaths occurred within 42 days of childbirth, and 363 between 42 days and 4 months. Deaths, person-years, and crude deaths rates for each interval are summarised in table 2.

After adjustment for confounding, mortality was $38 \cdot 82$ (95% CI $33 \cdot 21-45 \cdot 29$) times higher than baseline on days 0–1 after childbirth, $4 \cdot 97$ ($3 \cdot 94-6 \cdot 21$) times higher for days 2–6, $3 \cdot 35$ ($2 \cdot 64-4 \cdot 20$) times higher for days 7–13, $2 \cdot 06$ ($1 \cdot 74-2 \cdot 44$) times higher for days 14–41, and

p value

<0.0001

<0.0001

<0.0001

<0.0001

0.016

Multivariable analysis (negative

binomial)

Rate ratio (95% CI)

38.82 (33.21-45.29)

4.97 (3.94-6.21)

3.35 (2.64-4.20)

2.06 (1.74-2.44)

1.20 (1.03-1.39)

1.20 (1.03–1.39) times higher from 42 days to 4 months post partum (table 3, figure).

Women who gave birth for the first time in the HDSS face 1.30 (95% CI 1.17 to 1.44) times the risk of death relative to second or third birth in the HDSS (table 3). Women aged 15-24 years had lower mortality (0.63 [0.57 to 0.70] times that of women aged 25-34 years), whereas women aged 35 years and older had higher mortality (1.32 [1.18 to 1.48] times that of women aged 25-34 years). Relative to births in the HDSS between 1996 and 2000, from 2006 to 2010 onwards successive cohorts have a lower risk of pregnancy-related death, indicating improving mortality conditions. Further analysis of the decline in post-partum pregnancy-related mortality from 1991–95 to 2016–20 versus sample heterogeneity can be found in the appendix (p 2).

The Wald test of joint significance confirms that aggregate-level fixed effects for HDSS site are significant. Relative to the site in Basse, five sites in South Africa, Tanzania, Kenya, and Senegal had a higher risk of death; nine sites in Tanzania, Senegal, Kenya, Ghana, Ethiopia, Cote d'Ivoire, and Burkina Faso had a lower risk of death; and there was no significant effect in 15 sites in South Africa, Tanzania, Senegal, Nigeria, Mozambique, Malawi, Kenya, The Gambia, Ghana, and Ethiopia. The full results for HDSS site heterogeneity are available in the appendix (p 6).

For deaths within 42 days, the approximate postpartum PRMR was 117 per 100 000 births for the period 1991–2020. Extending the limit to 4 months post partum results in an estimate of 174 per 100 000 births, a 40% increase (ln [174/116]). This illustrates the sensitivity of the PRMR to the choice of the threshold, and hence the implications of WHO's standard definition of maternal mortality to mortality surveillance.

Given the lack of consistency between studies in the choice of the risk period beyond 42 days, we tested the sensitivity of the effect size to the choice of the interval. The shorter the risk period after 42 days, the higher the mortality risk. This strengthens the case that the risk of death is not constant at prepregnancy levels by 42 days. We also tested the sensitivity of the results to the choice of the post-partum period used as the baseline (12-17 months), using the periods 12-23 months and 12-35 months instead. Our main result is robust to the choice of the baseline, with the risk of death from 42-122 days being 1.17 (95% CI 1.01-1.33) and 1.15 (1.01-1.30) when a 12-23 month or 12-35 month baseline period was used, respectively. The full set of results from sensitivity analyses is available in the appendix (pp 4-6).

Discussion

To our knowledge, this study is the first to estimate the duration of an elevated risk of all-cause mortality during the extended post-partum period in a large dataset compiled of sub-Saharan African HDSSs.

,	()		(,			
4–11 months	1.01 (0.91–1.12)	0.83	1.02 (0.90–1.15)	0.76		
12-18 months‡	1.0		1.0			
Parity (within HDSS)†						
1	1.18 (1.08–1.29)	<0.0002	1.30 (1.17–1.44)	<0.0001		
2–3‡	1.0		1.0			
4–6	1.02 (0.87–1.20)	0.79	0.86 (0.71-1.03)	0.095		
7+	1.19 (0.83–1.71)	0.35	0.74 (0.48–1.10)	0.15		
Maternal age at childbirth						
<15 years	1.05 (0.62–1.77)	0.87	0.86 (0.48–1.41)	0.58		
15–24 years	0.73 (0.67–0.80)	<0.0001	0.63 (0.57–0.70)	<0.0001		
25–34 years‡	1.0		1.0			
≥35 years	1.28 (1.16–1.42)	<0.0001	1.32 (1.18–1.48)	<0.0001		
Childbirth cohort						
1991 to 1995	0.91 (0.73–1.14)	0.40	0.95 (0.74–1.22)	0.71		
1996 to 2000‡	1.0		1.0			
2001 to 2005	1.07 (0.92–1.24)	0.38	0.99 (0.83–1.17)	0.88		
2006 to 2010	0.73 (0.64–0.84)	<0.0001	0.81 (0.69–0.96)	0.015		
2011 to 2015	0.57 (0.50-0.66)	<0.0001	0.69 (0.58–0.82)	<0.0001		
2016 to 2020	0.58 (0.46-0.72)	<0.0001	0.64 (0.48–0.87)	0.0027		
HDSS=Health and Demographic Surveillance System *HDSS site aggregate level fixed-effects results available in the						

p value

<0.0001

<0.0001

<0.0001

<0.0001

0.0078

Univariable analysis

Rate ratio (95% CI)

39.78 (34.63-45.70)

6.16 (5.06-7.51)

3.78 (3.06-4.66)

2.09 (1.79-2.44)

1.20 (1.05-1.36)

Interval

0-1 day

2-6 days

7–13 days

14-41 days

42-122 days

HDSS=Health and Demographic Surveillance System. *HDSS site aggregate level fixed-effects results available in the appendix (p 6). †No adjustment for correlated data is made. Although exposure for women who survive can be clustered, the outcome (death) is an absorbing state, and hence cannot be clustered by woman. ‡Reference category.

Table 3: Univariable and multivariable results: risk of death by time since childbirth, with predictors and HDSS site fixed effects*†

With an exposure size of almost 650000 births and 1967 deaths within 1 year of childbirth, we find that women remain at 20% higher risk of death from day 42 until 4 months post partum. This result is robust to the choice of the post-partum reference period (ie, 12–17 months, 12–23 months, or 12–35 months post partum) and is substantial, with the increased risk of the post-partum period exceeding any general increase in mortality with age. We also estimate that including deaths up to 4 months post partum would increase the post-partum PRMR by 40%. These results strengthen the evidence that the 42-day post-partum threshold does not to capture the full duration of post partum risk of death.

These results of the duration of an increased risk of post-partum pregnancy-related mortality are consistent with previous research on maternal mortality (where COD was ascertained), although the magnitude of the risk is lower than in other studies. In Guinea-Bissau, the risk of maternal death remained elevated until 91 days relative to 12–17 months post partum (risk ratio 2.8,

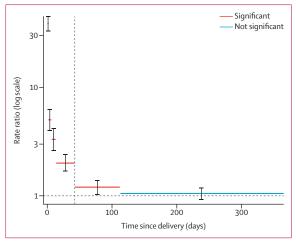


Figure: Rate ratios of death by time interval since childbirth for the estimated Piecewise Constant Hazard Model

95% CI 1.4-5.4);¹¹ in Bangladesh, the risk remained elevated until 180 days (adjusted risk ratio 1.5, 95% CI 1.3-2.1),²¹ relative to the third and fourth year post partum. Conversely, our estimate of the effect of an upward revision of the 42-day threshold on the postpartum PRMR is higher than an estimate of the effect on the MMR: in Guinea-Bissau, extending the measurement of maternal death up to 3 months would increase the MMR by 10–15%.¹¹ However, differences in methodology mean these estimates are not directly comparable: the post-partum threshold differs and as deaths during pregnancy are not included in this HDSS data, the relative contribution of an extension in the post-partum threshold will be greater.

Deaths during the first year post partum can either be direct maternal, indirect maternal, or coincidental. Without COD information to exclude coincidental causes, our results question the justification of the 42-day threshold for pregnancy-related deaths. The contribution of coincidental causes to the pregnancy-related deaths might be substantial, estimated as 46% in one study in sub-Saharan Africa.7 But since maternal deaths are more likely to be misclassified as non-maternal in the later post-partum period,3 this is likely an overestimate. The causes that are coincidental or accidental are likely to be constant over the pregnancy and post-partum period because they are not aggravated or caused by pregnancy. Yet, since we see an increased risk of death between 42 days and 4 months, this is most plausibly explained by causes that are aggravated or caused by pregnancy. The increased risk is more likely related to conditions that could manifest later than 42 days post partum (eg, direct late maternal deaths from suicide¹ or cardiomyopathy⁴), or unresolved chronic conditions and infectious disease (eg, indirect late maternal deaths). Evidence on the causes of late maternal deaths in sub-Saharan Africa is sparse. However, studies up to 42 days post partum suggest that indirect causes (from HIV,27,28 tuberculosis,29 malaria,⁷ pneumonia,⁷ and cardiovascular disease⁷) might be substantial in the extended post-partum period.

Our results emphasise a need to revisit the schedule and content of post-partum care. The proportion of women who receive routine post-partum care up to 42 days in sub-Saharan Africa is not as high as it should be.²⁹ But the provision of care for women who experience chronic morbidity in the extended post-partum period must also be prioritised to improve maternal health. Patient transfer from maternity services to higher level care beyond 42 days in sub-Saharan Africa requires further research.

The implications of our findings for tracking progress in maternal survival are four-fold. First, our results reaffirm calls for a review of the 42-day post-partum threshold to better capture the full duration of increased risk of death after birth.^{11,22} Although an upward revision of the 42-day post-partum threshold would complicate comparisons of the MMR and PRMR over time, a change to the standard definition could, in turn, help to improve awareness of the duration of the post-partum risk women face.

Second, our results also expose the need to define and count what could be called late pregnancy-related deaths over an extended post-partum period, particularly in sub-Saharan Africa, where medical certification of COD remains uncommon.6 Until medical certification of COD is routine in sub-Saharan Africa, an internationally agreed indicator to monitor the burden of late pregnancyrelated mortality is essential. Without an indicator, these deaths will continue to fall through the cracks of global efforts to monitor maternal health outcomes-captured neither in statistics on pregnancy-related mortality, nor in estimates of late maternal death. In a world where indicators continue to govern global health prioritisation, late pregnancy-related deaths must be officially defined and counted. As a start, the availability of data would be greatly improved if the Demographic and Health Surveys extended the sisterhood method from 8 weeks to 1 year post partum.

Third, in contexts where COD information is available, our results suggest that monitoring of late maternal deaths requires renewed dedication and institutionalisation.^{4,29} To plan interventions and prevent late maternal deaths, we urgently need to know the reasons for maternal mortality beyond 42 days in LMICs. Data from the UK Confidential Enquiries suggest the majority of late maternal deaths fall into one of four causes: cardiovascular, cancer, suicide, or thromboembolism,³⁰ but audits of the causes of late maternal deaths in LMICs are lacking.4 The relative contribution of causes is likely to differ in LMICs due to differences in the disease burden affecting populations, as well as the capacity of health systems to identify underlying conditions during antenatal care and unresolved conditions during the post-partum period. Even in the rare instances that the cause of late maternal deaths are reported, egregious inconsistencies, particularly in LMICs, around the ad-hoc coding of deaths from suicide as an indirect cause of maternal death or incidental to the pregnancy mean that data are often not comparable.³⁴ Improved surveillance of late maternal deaths will therefore require better compliance with ICD-11, which might require increased WHO support. It might also require improved linkage of childbirth and other health records to better identify women's post-childbirth status in health information systems. Ultimately, the dearth of data on the causes of late maternal deaths in LMICs leads to missed opportunities to address causes and reduce preventable mortality.

Fourth, incentivising and institutionalising international reporting on late maternal and late pregnancy-related deaths in the extended post-partum period beyond 42 days will only be achieved once international agencies disaggregate their reports of maternal and pregnancyrelated deaths by time—the antepartum, intrapartum, post-partum, and extended post-partum (up to 1 year) periods.

There are several important limitations to this analysis. First, because we consolidated HDSS data that do not include pregnancy status reports, this study only considered post-partum risk from the date of the childbirth. The exclusion of antepartum and some intrapartum deaths is likely to substantially underestimate maternal risk (eg, deaths from unsafe abortion, ectopic pregnancy, and eclampsia before childbirth).7 The underestimation of mortality, however, does not invalidate this study's main conclusion that mortality remains elevated beyond WHO's 42-day post-partum threshold. Second, there might be additional confounders that could affect women's post-partum survival not available in HDSS data that we were unable to adjust for. Third, analysis of date heaping suggests that date imputation is standard practice in many HDSS sites (examples can be found in the appendix pp 10-11). Bias from imputation error is a concern, but these results are still valuable when the alternative is an absence of evidence. Fourth, HDSSs cover small, geographically concentrated, and often rural populations. Whether findings from HDSSs are generalisable to broader or national populations is unclear.25

In summary, our results suggest that the global community and sub-Saharan African countries are underestimating the number of deaths associated with pregnancy. It is likely, therefore, that women who should receive routine and specialist care are not receiving the support they need. We call for revisions to the definitions of maternal and pregnancy related deaths and for research on the implications of a longer duration of increased risk of death following childbirth for postnatal care.

Contributors

UG, VF, and GR conceived the idea and developed the study design. UG and HE-S analysed the data. HE-S and JRP provided methodological support. UG reviewed the literature and wrote the initial draft of the manuscript. MJ and SK were responsible for data acquisition. All authors were involved in commenting on subsequent revisions. All authors are the guarantors. All authors had full access to all relevant data in the study and had final responsibility for the decision to submit for publication.

Declaration of interests

We declare no competing interests.

Data sharing

Data for 28 of the HDSS sites included in this analysis are open access via <u>the INDEPTH Network</u> and the microdata are available upon application on the website.

Acknowledgments

This study was funded by the UK Economic and Social Research Council (PhD grant reference ES/P000592/1).

References

- Knight M, Bunch K, Tuffnell D, et al. Saving lives, improving mothers' care—lessons learned to inform maternity care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2017–19. Oxford: National Perinatal Epidemiology Unit, 2021.
- 2 WHO. Maternal mortality 2019. https://www.who.int/news-room/ fact-sheets/detail/maternal-mortality (accessed May 16, 2022).
- 3 Kassebaum NJ, Bertozzi-Villa A, Coggeshall MS, et al. Global, regional, and national levels and causes of maternal mortality during 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2014; 384: 980–1004.
- 4 Sliwa K, Anthony J. Late maternal deaths: a neglected responsibility. Lancet 2016; 387: 2072–73.
- 5 WHO. Trends in Maternal Mortality 2000–2017: estimates by WHO, UNICEF, UNFPA. Geneva: World Bank Group and the United Nations Population Division, 2019.
- 6 Sankoh O, Dickson KE, Faniran S, et al. Births and deaths must be registered in Africa. *Lancet Glob Health* 2020; 8: e33–34.
- 7 Streatfield PK, Alam N, Compaoré Y, et al. Pregnancy-related mortality in Africa and Asia: evidence from INDEPTH Health and Demographic Surveillance System sites. *Glob Health Action* 2014; 7: 25368.
- 8 Hill K, Johnson P, Singh K, Amuzu-Pharin A, Kharki Y. Using census data to measure maternal mortality: a review of recent experience. *Demogr Res* 2018; **39**: 337–64.
- 9 Romano M, Cacciatore A, Giordano R, La Rosa B. Postpartum period: three distinct but continuous phases. J Prenat Med 2010; 4: 22–25.
- 10 Chowdhury R, Sinha B, Sankar MJ, et al. Breastfeeding and maternal health outcomes: a systematic review and meta-analysis. *Acta Paediatr* 2015; **104**: 96–113.
- 1 Høj L, da Silva D, Hedegaard K, Sandström A, Aaby P. Maternal mortality: only 42 days? *BJOG* 2003; **110**: 995–1000.
- 12 WHO. The WHO application of ICD-10 to deaths during pregnancy, childbirth and the puerperium: ICD-MM. Geneva: World Health Organization, 2012.
- 13 Storeng KT, Drabo S, Ganaba R, Sundby J, Calvert C, Filippi V. Mortality after near-miss obstetric complications in Burkina Faso: medical, social and health-care factors. *Bull World Health Organ* 2012; 90: 418–25B.
- 4 WHO. Verbal autopsy standards: ascertaining and attributing causes of death tool. 2022. Available from: https://www.who.int/ standards/classifications/other-classifications/verbal-autopsystandards-ascertaining-and-attributing-causes-of-death-tool (accessed May 18, 2022).
- 15 Shiffman J, Smith S. Generation of political priority for global health initiatives: a framework and case study of maternal mortality. *Lancet* 2007; 370: 1370–79.
- 16 WHO. WHO technical consultation on postpartum and postnatal care. 2010. https://apps.who.int/iris/handle/10665/70432 (accessed July 5, 2021).
- 17 WHO. WHO recommendations on maternal and newborn care for a positive postnatal experience. 2022. https://www.who.int/ publications/i/item/9789240045989 (accessed Sept 14, 2022).
- 18 National Institute for Health and Care Excellence. Postnatal care. 2021. https://www.nice.org.uk/guidance/ng194/chapter/ Recommendations#organisation-and-delivery-of-postnatal-care (accessed May 26, 2022).

For the INDEPTH Network see www.indepth-network.org

- 19 Firoz T, McCaw-Binns A, Filippi V, et al. A framework for healthcare interventions to address maternal morbidity. Int J Gynaecol Obstet 2018; 141 (suppl 1): 61–68.
- 20 Pradhan EK, West KP Jr, Katz J, et al. Risk of death following pregnancy in rural Nepal. Bull World Health Organ 2002; 80: 887–91.
- 21 Hurt LS, Alam N, Dieltiens G, Aktar N, Ronsmans C. Duration and magnitude of mortality after pregnancy in rural Bangladesh. Int J Epidemiol 2008; 37: 397–404.
- 22 Lamadrid-Figueroa H, Montoya A, Fritz J, Olvera M, Torres LM, Lozano R. Towards an inclusive and evidence-based definition of the maternal mortality ratio: an analysis of the distribution of time after delivery of maternal deaths in Mexico, 2010–2013. *PLoS One* 2016; 11: e0157495.
- 23 INDEPTH Network. Burkina Faso, Côte d'Ivoire, Ghana, The Gambia, Nigeria, Senegal, Ethiopia, Kenya, Malawi, Mozambique, Tanzania, Uganda, South Africa—consolidated HDSS data from 29 sub-Saharan African sites, 1990–2018. https://www. indepth-ishare.org/index.php/catalog/181 (accessed Jan 10, 2022).
- 24 Hinga AN, Molyneux S, Marsh V. Towards an appropriate ethics framework for Health and Demographic Surveillance Systems (HDSS): learning from issues faced in diverse HDSS in sub-Saharan Africa. *BMJ Glob Health* 2021; 6: e004008.

- 25 Bocquier P, Sankoh O, Byass P. Are health and demographic surveillance system estimates sufficiently generalisable? *Glob Health Action* 2017; **10**: 1356621.
- 26 Bocquier P, Ginsburg C. Manual of event history data management using HDSS data. https://static-content.springer.com/esm/art%3A1 0.1186%2Fs13104-017-2541-9/MediaObjects/13104_2017_2541_ MOESM1_ESM.pdf (accessed May 18, 2022).
- 27 Kassebaum NJ, Barber RM, Bhutta ZA, et al. Global, regional, and national levels of maternal mortality, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet* 2016; 388: 1775–812.
- 28 Zaba B, Calvert C, Marston M, et al. Effect of HIV infection on pregnancy-related mortality in sub-Saharan Africa: secondary analyses of pooled community-based data from the network for Analysing Longitudinal Population-based HIV/AIDS data on Africa (ALPHA). *Lancet* 2013; 381: 1763–71.
- 29 Zumla A, Bates M, Mwaba P. The neglected global burden of tuberculosis in pregnancy. *Lancet Glob Health* 2014; 2: e675–76.
- 30 Knight M. The findings of the MBRRACE-UK confidential enquiry into maternal deaths and morbidity. Obstetrics, Gynaecol Reprod Med 2019; 29: 21–23.