a) **Full title:** Responsiveness of Emergency Obstetric Care Systems in Low- and Middle-Income Countries: a Critical Review of the "Third Delay"

b) **Running headline (max 49 characters):** Responsiveness of EmOC in developing countries

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ABSTRACT

We reviewed the evidence on the duration, causes and effects of delays in providing emergency obstetric care to women attending health facilities (the third delay) in low- and middle-income countries. We performed a critical literature review using terms related to obstetric care, birth outcome, delays and developing countries. A manual search of key articles' reference lists was also performed. 69 studies met the inclusion criteria. Most studies reported long delays to providing care, and the mean waiting time for women admitted with complications was as much as 24 hours before treatment. The three most cited barriers to providing timely care were shortage of treatment materials, surgery facilities and qualified staff. Existing evidence is insufficient to estimate the effect of delays on birth outcomes. Delays to providing emergency obstetric care seem common in resource-constrained settings, but further research is necessary to determine the effect of the third delay on birth outcomes.

KEYWORDS AND ABBREVIATIONS

Keywords: third delay; emergency obstetric care; low- and middle-income countries; responsiveness; health services research

Abbreviations:

EmOC	Emergency obstetric care
LMIC	Low- and middle-income countries
WHO	World Health Organisation

KEY MESSAGE

Better understanding of the magnitude of effect of delays in providing emergency obstetric care in low- and middle-income countries has the potential to improve maternal and perinatal survival. Standardised approaches to measure their frequency, duration and effects should be developed.

Introduction

Each year, an estimated 287,000 women die as a result of pregnancy or childbirth, and 2 million intrapartum-related stillbirths and neonatal deaths occur (1, 2). Over 99% of these deaths occur in low- and middle-income countries (LMICs), and most are concentrated in sub-Saharan Africa and south Asia (3-5). The majority of maternal and neonatal deaths take place during or immediately after delivery: globally, up to 45% of maternal and neonatal deaths occur within 24 hours of birth (4, 6).

Obstetric complications require prompt intervention to avert death or severe morbidity, as illustrated by the short average time from onset to death (7). Emergency obstetric care (EmOC) services, as defined by the WHO EmOC signal functions (8), therefore need to be rapidly accessible to women in order to prevent maternal and perinatal deaths.

Thaddeus and Maine's landmark paper (9) laid out the conceptual framework for analysing barriers to receiving appropriate care after the onset of obstetric complications, including delays in deciding to seek care (first delay), in reaching a facility (second delay), and in receiving care after reaching the health facility (third delay). The "three delays" framework has been used to systematically analyse maternal (10-12) and perinatal (13) deaths in developing countries. Three reviews (14-16) have summarised factors affecting access to maternal health services; yet there has been no review of the third delay in receiving care within health facilities.

While it seems intuitive that longer time to treatment for emergencies would result in poorer outcomes, what is unknown is how long women have to wait in low-resource settings before being provided with life-saving care once they reach a health facility, and the magnitude of the effect of that third delay on birth outcomes. This in turn is important in order to determine the burden of maternal and perinatal deaths attributable to delays in these settings. The aim of this critical literature review is to examine how the third delay has been defined, and synthesise the evidence-base to date relating to the duration of delays, the reasons for delays to EmOC and their association with maternal and perinatal outcomes in low- and middle-income countries.

Material and methods

We carried out a literature search in July 2011 in four electronic databases (Medline, Global Health, Popline and Africa-Wide Information). Keyword search terms relating to (1) emergency obstetric care, (2) maternal and perinatal outcomes (including morbidity and mortality), (3) delays and (4) low- and middle-income countries were combined. A manual search of the reference lists of the most relevant articles and websites (WHO Reproductive Library and Population Council) was further performed to identify grey literature publications and any missed articles.

Only publications written in English or French were included in this review, and no restrictions were placed on date of publication. Quantitative evidence exclusively was considered when reviewing the duration of delays and its effect on birth outcomes; qualitative evidence was additionally taken into account when reviewing definitions of the third delay and its causes. Only studies conducted in LMICs were included, and all facility levels were taken into account, irrespective of their ability to provide EmOC. Articles were included if they proposed a conceptual or operationalised definition of the "third delay", measured the duration of delays, explored the causes of delays, or presented evidence on the effect of delays on maternal and perinatal health outcomes.

The identified publications were first screened on the basis of abstract and title. As a second step, articles were assessed on the basis of full text. Those meeting the inclusion criteria were assessed for relevance to the topic and quality of evidence (see criteria presented in figure 1).

A systematic review was not attempted for this topic due to the lack of established index terms, methodological differences between studies, and because the effect on birth outcomes is likely to be context-specific (that is, dependent on other factors such as delays in reaching the facility and quality of services). Similarly, a formal ranking system was not used to assess the quality of evidence, in light of the diversity of study designs and objectives addressed in this review.

Conceptual framework

We expanded the third delay framework in order to critically analyse its components, by integrating two frameworks developed by Edson et al. and Gabrysch & Campbell (Figure 2) (16, 17). This framework distinguishes between women who arrive at the facility with complications, after potentially experiencing delays in deciding to seek care and in transport, and those who develop complications during planned hospital deliveries (and therefore do not experience the first or second delay). Delays to care after reaching the hospital are broken down according to the

five “critical events” on the pathway to care conceptualised by Edson (admission, professional evaluation, diagnosis, decision to treat and treatment administration) (17).

Three additions are made to these models: we expanded the framework by incorporating care events identified in the reviewed articles but not included in the Edson or Gabrysch models. Firstly, referrals are incorporated under the third delay (see Okonufua et al. (18)) rather than the second delay, because the decision to refer and availability of ambulances directly depend on health system performance. Secondly, delays were reported between prescription and purchase of drugs or blood for transfusion (19), and between call and arrival of the ambulance (20-24): two additional steps were incorporated for “obtaining treatment” and “securing transport” on the treatment and referral pathways, respectively (these are shown in the shaded boxes in figure 2).

Results

Findings of literature search

The literature search identified 714 unique articles. In the first step, 520 articles were excluded on the basis of title or abstract, leaving 194 articles to be reviewed. A manual search of reference lists identified 14 additional publications. Of these 208 remaining articles, the full text was retrieved for 199 publications, but could not be obtained for 9 publications. In the second step, 130 articles were excluded based on full text, because they reported anecdotal findings on the duration of delays or their effect on outcomes in a non-random sample of patients, studied other aspects of maternity care, or were not original reports of the study findings. Figure 3 summarises the findings of the literature search.

A total of 69 publications were finally selected (Table 1). The majority were case reviews of adverse outcomes (n=38), including audits, verbal autopsies, retrospective chart-based reviews, and qualitative interviews with women or their families. Ten studies were prospective observational studies, seven were cross-sectional studies of obstetric emergencies or emergency caesareans, and five were case-control studies of maternal deaths or intrapartum stillbirths. One study was a randomised controlled trial of intrapartum monitoring of fetal heart rate, and seven were pre-post evaluations of complex, hospital-level interventions not related exclusively to shortening delays to care (including audits, training, and facility renovation).

Fewer than half of the studies included in this review (n=26) stated as their primary purpose investigating delays to care within health facilities. Other studies aimed to identify risk factors for adverse birth outcomes (n=27) or investigate substandard care (n=15), and assess the effect of

therapeutic interventions (n=1). The great majority of studies (n=53) were conducted in sub-Saharan Africa, while seven were conducted in South America and five each in South-East Asia and Eastern Mediterranean regions. Only two studies were based in primary-level health centres, five in secondary facilities (district hospitals), and 40 in referral hospitals (including regional, national and teaching hospitals); 22 studies looked at multiple facility levels.

Defining the third delay

Only six publications addressed the issue of how to define the third delay. Edson et al. define delays as an interval lasting longer than a threshold beyond which patients are at risk of adverse outcomes (17). In the absence of evidence-based guidelines for defining delay thresholds, they instead use expert panel reviews to determine which cases experienced delays to care after reaching a facility, similarly to another study in Egypt (25). Among all publications, over 40 different definitions of the third delay were recorded.

Four other studies provide a quantitative definition of delay to care within health facilities. One study in Argentina and Uruguay defined timely caesarean as within 30 minutes (26), in line with guidelines in the UK and USA (27, 28). Holme et al. define delayed response to obstructed labour as spending more than half a day in labour at a health facility (29), while Wagaarachchi et al. adopt a less conservative definition by stating that foetuses should be delivered within 2 hours of the diagnosis of obstructed labour (30). In Tanzania, Urassa et al. define referral delay as a decision-to-transfer interval of over one hour (31). There is a clear lack of established time measures used to define the third delay.

Measuring the third delay

Sixty-six articles included in this review presented a measure of delays to care or to referral for women who had already presented to a health facility. Overall, the proportion of cases experiencing delays was found to be 4-97% among women who died (n=11 studies), around 50% among perinatal deaths and intrapartum stillbirths (n=2), but lower among women with complications (3-28%, n=3) and a random sample of deliveries (9%, n=1). Referral delays were identified in 11-43% of transfers (n=4), and a delayed decision to refer was found in 66% of cases of uterine rupture in one study (24).

In the absence of accepted guidelines defining what constitutes a delay to care within a facility, a number of studies report the duration of intervals between care events as indicators of delay. Table 2 presents the range of mean intervals reported across studies and across different groups

within the same study (n=31 studies). Mean intervals from admission with complications to treatment ranged from 1.2-24hrs (n=8), and 0.75-6hrs for emergency surgery (n=3). Most studies focused on decision-to-treatment intervals, which ranged 1-11hrs for surgery (n=5), 1-8.5hrs for emergency caesareans (n=7) and 3.5-48hrs for blood transfusion (n=2). Six studies reported a time interval for referrals. Among these, the range for ambulance request-to-arrival (0.75-48hrs, n=3) was longer than for actual transportation (0.6-5hrs, n=2).

In addition to mean waiting time, nineteen studies reported on the distribution of delays among cases, using a range of different time thresholds to define the third delay. It appears that more women who survive complications are treated within 24 hours of admission than women who die (32). Extensive intervals before care are common in many settings: for instance, 10% of maternal deaths in Mexico waited more than 4 hours to be examined (33), 55% of fistula patients spent more than one day in labour before an intervention was attempted (29), and 12% of women requiring emergency caesareans had to wait longer than 12 hours after the clinical decision was made in Nigeria (34). These findings suggest that the third delay can sometimes be substantial.

Causes of delays to EmOC

Thirty-seven studies presented findings on the causes of the third delay: the occurrence of different barriers is presented in Figure 4, grouped into three categories (resource, staff and institutional factors). The most frequently mentioned barriers to timely provision of treatment within health facilities were shortage of medical supplies (65% of studies), surgery facilities (49%) and staff (46%). Lack of EmOC skills, including errors in management and shortage of trained personnel, were mentioned in 38% of articles, and were reported more frequently than the organisation of care or providers' poor attitudes. Institutional factors, including administrative processes and lack of protocols for treating obstetric complications, were reported less frequently (4-30%) but they were often specific to a sub-region. Five articles explicitly stated that lack of staff or resources was not thought to have been factors in delays.

The most commonly mentioned institutional cause of delays (reported in 11 studies) was linked to the purchase of treatment materials prior to surgery, including gathering money and travelling to pharmacies outside the hospital in West Africa and South America (17, 35, 36), and assembling the surgical kit before emergency caesareans in Côte d'Ivoire (37). The cost of blood for transfusion, surgical supplies, and surgery fees is prohibitive in many of these settings (38), leading to delays while families try to assemble the required amount. In Kinshasa, one woman's death was described by her mother-in-law:

> *She suffered from a major hemorrhage […]. The doctor told us she needed a caesarean section. Her husband left to look for money. As the bleeding continued, she died before a caesarean section was performed* (32).

Malfunction of the blood supply for transfusions was mentioned as a factor in 19 studies, and several articles reported patients' families having to travel long distances or donate their own blood, due to blood shortages in the hospital (32, 36, 39).

Effect of the third delay on birth outcomes

Very few studies have linked the duration of time-to-care after reaching a health facility with obstetric outcomes (Table 3). Three articles reported the effect of referral interval length on maternal and/or paerinatal outcomes in LMICs. Two case-control studies in India and Nigeria found strong evidence of longer referral intervals among maternal deaths than survivors of complications (p<0.01), and intrapartum stillbirths than live births (p<0.0001) (19, 40). A prospective cohort study in Nigeria found maternal deaths spent more days in a primary facility before referral than women who were alive, though no p-value is reported (41) .

Three studies look at the effect of long time-to-care after reaching a health facility for all treatments in Eritrea, Nigeria and Cameroon (18, 35, 42). All three find evidence of longer intervals before treatment among cases of maternal death than women who survive.

Six studies address the effect of pre-surgery interval length on maternal and/or perinatal outcomes in LMICs. Findings from cross-sectional studies suggest rising rates of maternal mortality and hysterectomy with longer decision-to-delivery intervals for emergency caesareans (34, 43), though no statistical results are reported. Evidence linking decision-to-delivery intervals and perinatal outcomes is ambiguous: in both cohort and cross-sectional studies, studies in Nigeria and Pakistan suggest no evidence of increased risk of mortality, low Apgar score or intensive care admission (44, 45), while three others suggest increased perinatal mortality with longer decision-to-delivery intervals in Nigeria (34, 43, 46).

Discussion

The evidence-base relating to the third delay attests of poor responsiveness of EmOC systems in LMICs. Substantial time-to-care delays were identified particularly before surgery, blood transfusions and referrals to higher-level facilities. Only one of six articles found a mean decision-delivery interval for emergency cesareans of under 75min (47), a threshold associated with

adverse birth outcomes in England (48). In contrast, most studies in high-income countries achieve at least 60% of decision-to-delivery intervals within 30min (49-51).

Furthermore, there are indications that EmOC referral systems, considered cornerstones in health systems' responsiveness to obstetric emergencies (52), are widely dysfunctional. Onwudiegwu et al. point to poor management in primary-level facilities as an important source of delays before referrals (41). Recorded time from requesting an ambulance to arrival at the referring facility ranged from 45min to 48hrs (21-23), emphasising that the lack of ambulances stationed at lower-level facilities are a significant component of referral delays. In South Africa, ambulance response time did not vary by priority of call (21), suggesting that patients in critical condition were not successfully prioritised for transport.

Lack of medical supplies, drugs and blood for transfusion emerged as the most common causes of the third delay, followed by staff availability. Lack of EmOC skills was also responsible for significant delays in diagnosis, decision to treat and referral. Results from the Global Voices for Maternal Health survey similarly emphasised lack of training as a key concern among maternal health providers in LMICs (53).

Payment of user fees before treatment was identified as a major barrier to timely care within facilities, and constituted the main component of delays before surgery in Côte d'Ivoire (37). Langer found that better educated women were more likely to be referred in Mexico (33), suggesting that they are more proactive in decision-making, or receive differential treatment from staff. Longer delays to care were also found for patients with abortion complications in Gabon, compared to women experiencing postpartum hemorrhage or eclampsia (54). While this may be the result of stigma from care providers (as the authors suggest), it is also plausible that in countries where abortion is illegal, providers do not get trained in post-abortion care (55) and consequently delay clinical decisions. These observations raise concerns about equity in access to care within health institutions, and emphasise that even after reaching a facility, socio-economic inequalities in access may persist.

The evidence base to date is inadequate to quantify the effect of delays on birth outcomes, despite the plausibility of delays as a risk factor for poor obstetric outcomes. The evidence-base in high-income countries shows a 50% increase in odds of maternal special care and 70% increase in odds of Apgar score below 7 after 75 minutes of the decision to perform a caesarean (48). The fact that most decision-to-delivery intervals reported in LMICs are longer than 75 minutes suggests that delays could be responsible for large proportion of maternal and perinatal deaths in these settings. Identifying a potential threshold beyond which the risk of adverse outcomes is higher is essential to develop guidelines for managing obstetric emergencies in

LMICs. Health workers' ability to provide treatment within a recommended time interval will nevertheless be limited by their capacity to diagnose and monitor complications.

Overall, the evidence base regarding the third delay in LMICs is of poor quality. Most studies are low-grade observational studies, with poorly defined study populations. Issues of measurement error and bias relating to imprecise definitions of delays were seldom addressed. Of studies reporting a summary duration of intervals, most report a mean duration, which is likely to be inflated by a few patients with very long intervals. Because of the skewness of the data, medians are more appropriate summary measures.

Divergent definitions of the third delay are illustrated by the over 40 different measures of delays identified, raising questions about the robustness and comparability of results. This is partly due to the lack of evidence on the effect of delays on birth outcomes, and the resulting absence of established guidelines for timely management of obstetric complications. As a result of differences in methodology, study design and population, it was not possible to calculate summary measures of delay (such as mean duration of decision-to-delivery interval across studies).

Reported causes of delays could be affected by observer bias, which may have led to an overreporting of resource shortages, and an underreporting of institutional factors such as organisation of care. Only half of the studies reporting on the association with birth outcomes report a test statistic or p-value, and none of the articles report controlling for confounders (such as the severity of complication, identified as an important confounder in the high-income country literature) (56), potentially leading to an underestimate of the strength of association with adverse birth outcomes.

Recommendations for future research

Three main research recommendations arise from the findings of this review. First, there is a need to adopt a standardised methodology to defining the third delay and ensure findings are comparable across studies: the conceptual framework (Figure 2) represents a possible approach to systematically analyse delays to care in future research.

Second, tools should be developed for monitoring the performance of facilities regarding the duration and causes of delays, including for basic EmOC. The third delay should be monitored as an indicator of EmOC availability: the WHO framework considers a signal function to be "available" in a facility if it was performed within the last three months (8), but it may still not be

accessible to patients. Particular attention should be paid to investigating implications for equity in access to EmOC.

Third, scarce evidence on the effect of delays on birth outcomes is problematic insofar as there are no established guidelines for timely management of obstetric complications. Randomised controlled trials are poorly suited to develop this evidence-base, due to ethical concerns and the impracticality of preventing contamination between trial arms. Well-conducted observational studies of obstetric emergencies should therefore be replicated in LMICs, controlling for type and severity of condition.

Conclusion

The available evidence suggests that women who need emergency obstetric care experience extremely long delays after reaching a health facility in low- and middle-income countries. Therefore, problems in accessing appropriate care persist after reaching a health facility. In light of the time-sensitivity of obstetric emergencies, delays to EmOC could potentially be responsible for a large burden of maternal and perinatal mortality worldwide. There is an urgent need for high quality studies on the third delay and its effect on birth outcomes.

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Conflicts of interest

No conflicts of interest are declared.

3. References

1. WHO, UNICEF, UNFPA, Bank World. Trends in maternal mortality: 1990 to 2010. Geneva: World Health Organisation, 2012.

2. Lawn J. E., Lee A. C., Kinney M., Sibley L., Carlo W. A., Paul V. K., et al. Two million intrapartum-related stillbirths and neonatal deaths: where, why, and what can be done? Int J Gynaecol Obstet. 2009;107 Suppl 1:S5-18, S9.

3. Lawn Joy E., Blencowe Hannah, Pattinson Robert, Cousens Simon, Kumar Rajesh, Ibiebele Ibinabo, et al. Stillbirths: Where? When? Why? How to make the data count? Lancet. 2011;377(9775):1448-63.

4. Lawn J. E., Cousens S., Zupan J. 4 million neonatal deaths: when? Where? Why? Lancet. 2005;365(9462):891-900.

5. Ronsmans Carine, Graham Wendy J., Lancet Maternal Survival Series steering group. Maternal mortality: who, when, where, and why. Lancet. 2006;368(9542):1189-200.

6. Li X. F., Fortney J. A., Kotelchuck M., Glover L. H. The postpartum period: The key to maternal mortality. Int J Gynecol Obstet. 1996;54(1):1-10.

7. WHO. Studying maternal mortality in developing countries. A guidebook: rates and causes. Geneva, Switzerland: World Health Organisation, 1987.

8. WHO, UNFPA, UNICEF, AMDD. Monitoring emergency obstetric care: a handbook. Geneva, Switzerland: World Health Organisation. 2009.

9. Thaddeus S., Maine D. Too far to walk: maternal mortality in context. Social Science & Medicine. 1994;38(8):1091-110.

10. Barnes-Josiah D., Myntti C., Augustin A. The "three delays" as a framework for examining maternal mortality in Haiti. Social Science & Medicine. 1998;46(8):981-93.

11. Cham M., Sundby J., Vangen S. Maternal mortality in the rural Gambia, a qualitative study on access to emergency obstetric care. Reproductive Health. 2005;2(1):3.

12. Ramos Silvina, Karolinski Ariel, Romero Mariana, Mercer Raul, Maternal Mortality in Argentina Study Group. A comprehensive assessment of maternal deaths in Argentina: translating multicentre collaborative research into action. Bulletin of the World Health Organization. 2007;85(8):615-22.

13. Kidanto Hussein L., Mogren Ingrid, van Roosmalen Jos, Thomas Angela N., Massawe Siriel N., Nystrom Lennarth, et al. Introduction of a qualitative perinatal audit at Muhimbili National Hospital, Dar es Salaam, Tanzania. BMC Pregnancy & Childbirth. 2009;9:45.

14. McNamee P., Ternent L., Hussein J. Barriers in accessing maternal healthcare: evidence from low-and middle-income countries. Expert Review of Pharmacoeconomics & Outcomes Research. 2009;9(1):41-8.

15. Say L., Raine R. A systematic review of inequalities in the use of maternal health care in developing countries: examining the scale of the problem and the importance of context. Bulletin of the World Health Organization. 2007;85(10):812-9.

16. Gabrysch S., Campbell O. M. Still too far to walk: literature review of the determinants of delivery service use. BMC Pregnancy Childbirth. 2009;9:34.

17. Edson W, Burkhalter B, Harvey S, Boucar M, Djibrina S. Safe motherhood studies -- timeliness of in-hospital care for treating obstetric emergencies: results from Benin, Ecuador, Jamaica, and Rwanda. *Operations Research Results.* Washington, D.C.: Quality Assurance Project, United States Agency for International Development, 2006.

18. Okonofua F. E., Abejide A., Makanjuola R. A. Maternal mortality in Ile-Ife, Nigeria: a study of risk factors. Studies in Family Planning. 1992;23(5):319-24.

19. Chigbu Chibuike O., Okezie Obioma A., Odugu Boniface U. Intrapartum stillbirth in a Nigerian tertiary hospital setting. International Journal of Gynaecology & Obstetrics. 2009;104(1):18-21.

20. Hofman J. J., Dzimadzi C., Lungu K., Ratsma E. Y., Hussein J. Motorcycle ambulances for referral of obstetric emergencies in rural Malawi: do they reduce delay and what do they cost? Int J Gynecol Obstet. 2008;102(2):191-7.

21. Marcus J. K., Clow S. E. Response times of ambulances to calls from midwife obstetric units of the Peninsula Maternal and Neonatal Service (PMNS) in Cape Town. Curationis. 2009;32(1):59-66.

22. Sabitu K., Alti-Mu'azu M., Musa A. A., Ifenne D. I., Essien E. S., Golji N. G., et al. The effect of improving maternity services in a secondary facility, Zaria, Nigeria. The Zaria PMM Team. International Journal of Gynaecology & Obstetrics. 1997;59 Suppl 2:S99-106.

23. Samai O., Sengeh P. Facilitating emergency obstetric care through transportation and communication, Bo, Sierra Leone. The Bo PMM Team. Int J Gynecol Obstet. 1997;59 Suppl 2:S157-64.

24. van den Akker Thomas, Mwagomba Beatrice, Irlam James, van Roosmalen Jos. Using audits to reduce the incidence of uterine rupture in a Malawian district hospital. International Journal of Gynaecology & Obstetrics. 2009;107(3):289-94.

25. Nada K. H., Barakat A. A., Gipson R. Quality of care for obstetric emergencies in 4 general hospitals in Egypt: an observational study of delays in receiving care and blood bank services. Eastern Mediterranean Health Journal. 2011;17(1):19-25.

26. Karolinski Ariel, Mazzoni Agustina, Belizan Jose M., Althabe Fernando, Bergel Eduardo, Buekens Pierre. Lost opportunities for effective management of obstetric conditions to reduce maternal mortality and severe maternal morbidity in Argentina and Uruguay. International Journal of Gynaecology & Obstetrics. 2010;110(2):175-80.

27. ACOG. ACOG committee opinion No. 433: optimal goals for anesthesia care in obstetrics. Obstetrics & Gynecology. 2009;113(5):1197-9.

28. NICE. Caesarean section. NICE Clinical Guideline 132. Available: http://www.nice.org.uk/cg132. London: National Institute for Health and Clinical Excellence; 2011.

29. Holme A., Breen M., MacArthur C. Obstetric fistulae: a study of women managed at the Monze Mission Hospital, Zambia. BJOG : an international journal of obstetrics and gynaecology. 2007;114(8):1010-7.

30. Wagaarachchi P. T., Graham W. J., Penney G. C., McCaw-Binns A., Yeboah Antwi K., Hall M. H. Holding up a mirror: changing obstetric practice through criterion-based clinical audit in developing countries. Int J Gynecol Obstet. 2001;74(2):119-30; discussion 31.

31. Urassa E., Massawe S., Lindmark G., Nystrom L. Operational factors affecting maternal mortality in Tanzania. Health Policy & Planning. 1997;12(1):50-7.

32. Kabali E., Gourbin C., Brouwere V. de. Complications of childbirth and maternal deaths in Kinshasa hospitals: testimonies from women and their families. BMC Pregnancy and Childbirth. 2011;11(29).

33. Langer A. , Hernández B., García-Barrios C., Saldaña-Uranga G., National Safe Motherhood Committee of Mexico. Identifying Interventions to Prevent Maternal Mortality in Mexico: A Verbal Autopsy Study. In: Berer M, Ravindran TKS, editors. Safe Motherhood Initiatives: Critical Issues. London: Reproductive Health Matters; 2000.

34. Orji E. O., Ojofeitimi E. O., Esimai A. O., Adejuyigbe E., Adeyemi A. B., Owolabi O. O. Assessment of delays in receiving delivery care at a tertiary healthcare delivery centre in Nigeria. Journal of obstetrics and gynaecology : the journal of the Institute of Obstetrics and Gynaecology. 2006;26(7):643-4.

35. Mbassi S. M., Mbu R., Bouvier-Colle M. H. Délai de prise en charge des complications obstétricales: étude dans 7 maternités au Cameroun. [Time-to-care for management of obstetric complications: study in 7 maternity units in Cameroon.] (in French). Medecine Tropicale. 2009;69(5):480-4.

36. Saizonou J., Brouwere V. de, Vangeenderhuysen C., Dramaix-Wilmet M., Buekens P., Dujardin B. Audit de la qualité de prise en charge des « échappées belle » (near miss) dans les maternités de référence du Sud Bénin [Audit of the quality of treatment of "near miss" patients in referral maternities in Southern Benin] (in French). Cahiers d'Etudes et de Recherches Francophones/Sante. 2006;16(1):33-42.

37. Gohou V., Ronsmans C., Kacou L., Yao K., Bohoussou K. M., Houphouet B., et al. Responsiveness to life-threatening obstetric emergencies in two hospitals in Abidjan, Cote d'Ivoire. Tropical Medicine & International Health : TM&IH. 2004;9(3):406-15.

38. Sepou A., Yanza M. C., Nguembi E., Ngbale R., Kouriah G., Kouabosso A., et al. Les ruptures utérines à la maternité de l'hopital communautaire de Bangui (Centrafrique). [Uterine rupture in the maternity ward of the Bangui Community Hospital in Central African Republic.] (in French). Medecine Tropicale. 2002;62(5):517-20.

39. Onah H. E., Okaro J. M., Umeh U., Chigbu C. O. Maternal mortality in health institutions with emergency obstetric care facilities in Enugu State, Nigeria. Journal of Obstetrics & Gynaecology. 2005;25(6):569-74.

40. Ganatra B. R., Coyaji K. J., Rao V. N. Too far, too little, too late: a community-based case-control study of maternal mortality in rural west Maharashtra, India. Bulletin of the World Health Organization. 1998;76(6):591-8.

41. Onwudiegwu U., Ezechi O. C. Emergency obstetric admissions: late referrals, misdiagnoses and consequences. Journal of Obstetrics and Gynaecology. 2001;21(6):570-5.

42. Ghebrehiwet B. Delay in seeking and receiving emergency obstetric care in Eritrea. Journal of the Eritrean Medical Association. 2007;2(1):8-13.

43. Orji E. O., Fasubaa O. B., Onwudiegwu U., Dare F. O., Ogunniyi S. O. Decision-intervention interval in ruptured uteri in Ile-Ife, Nigeria. East African Medical Journal. 2002;79(9):496-8.

44. Khan Rozilla S., Naru Tahira, Nizami Faryal. Umbilical cord prolapse--a review of diagnosis to delivery interval on perinatal and maternal outcome. JPMA J Pak Med Assoc. 2007;57(10):487-91.

45. Onah H. E., Ibeziako N., Umezulike A. C., Effetie E. R., Ogbuokiri C. M. Decision - delivery interval and perinatal outcome in emergency caesarean sections. Journal of Obstetrics & Gynaecology. 2005;25(4):342-6.

46. Onwudiegwu U., Makinde O. N., Ezechi O. C., Adeyemi A. Decision-caesarean delivery interval in a Nigerian university hospital: implications for maternal morbidity and mortality. Journal of Obstetrics and Gynaecology. 1999;19(1):30-3.

47. Mbaruku Godfrey, van Roosmalen Jos, Kimondo Iluminata, Bilango Filigona, Bergstrom Staffan. Perinatal audit using the 3-delays model in western Tanzania. International Journal of Gynaecology & Obstetrics. 2009;106(1):85-8.

48. Thomas J., Paranjothy S., James D. National cross sectional survey to determine whether the decision to delivery interval is critical in emergency caesarean section. Brit Med J. 2004;328(7441):665-8.

49. Chauhan S. P., Magann E. F., Scott J. R., Scardo J. A., Hendrix N. W., Martin J. N., Jr. Emergency cesarean delivery for nonreassuring fetal heart rate tracings. Compliance with ACOG guidelines. Journal of Reproductive Medicine. 2003;48(12):975-81.

50. Helmy W. H., Jolaoso A. S., Ifaturoti O. O., Afify S. A., Jones M. H. The decision-to-delivery interval for emergency caesarean section: is 30 minutes a realistic target? Bjog-Int J Obstet Gy. 2002;109(5):505-8.

51. Hillemanns P., Strauss A., Hasbargen U., Schulze A., Genzel-Boroviczeny O., Weninger E., et al. Crash emergency cesarean section: decision-to-delivery interval under 30 min and its effect on Apgar and umbilical artery pH. Archives of Gynecology and Obstetrics. 2005;273(3):161-5.

52. Campbell O. M., Graham W. J. Strategies for reducing maternal mortality: getting on with what works. Lancet. 2006;368(9543):1284-99.

53. Knight H. Views from the frontline of maternal healthcare: Over 2000 practitioners worldwide make their voices heard! http://maternalhealthtaskforce.org/component/wpmu/2011/01/27/views-from-the-frontline-of-maternal-healthcare-over-2000-practitioners-worldwide-make-their-voices-heard/. . Published online: 27th Jan 2011 [2nd April 2012].

54. Mayi-Tsonga Sosthene, Oksana Litochenko, Ndombi Isabelle, Diallo Thierno, de Sousa Maria Helena, Faundes Anibal. Delay in the provision of adequate care to women who died from abortion-related complications in the principal maternity hospital of Gabon. Reproductive Health Matters. 2009;17(34):65-70.

55. Brookman-Amissah E., Moyo J. B. Abortion law reform in sub-Saharan Africa: no turning back. Reproductive Health Matters. 2004;12(24 Suppl):227-34.

56. Huissoud C., Dupont C., Canoui-Poitrine F., Touzet S., Dubernard G., Rudigoz R. C. Decision-to-delivery interval for emergency caesareans in the Aurore perinatal network. Eur J Obstet Gyn R B. 2010;149(2):159-64.

57. Ahmed Y., Shehu C. E., Nwobodo E. I., Ekele B. A. Reducing maternal mortality from ruptured uterus--the Sokoto initiative. African Journal of Medicine & Medical Sciences. 2004;33(2):135-8.

58. Amaral Eliana, Souza Joao Paulo, Surita Fernanda, Luz Adriana G., Sousa Maria Helena, Cecatti Jose Guilherme, et al. A population-based surveillance study on severe acute maternal morbidity (near-miss) and adverse perinatal outcomes in Campinas, Brazil: the Vigimoma Project. BMC Pregnancy & Childbirth. 2011;11:9.

59. Bako B., Chama C., Audu B. M. Emergency obstetrics care in a Nigerian tertiary hospital: a 20 year review of umblical cord prolapse. Nigerian Journal of Clinical Practice. 2009;12(3):232-6.

60. Cham M., Vangen S., Sundby J. Maternal deaths in rural Gambia. Global Public Health. 2007;2(4):359-72.

61. Cham Mamady, Sundby Johanne, Vangen Siri. Availability and quality of emergency obstetric care in Gambia's main referral hospital: women-users' testimonies. Reproductive health. 2009;6:5.

62. De Muylder X. Maternal mortality audit in a Zimbabwean province. Archives of Gynecology & Obstetrics. 1990;247(3):131-8.

63. Fawcus S., Mbizvo M., Lindmark G., Nystrom L. A community-based investigation of avoidable factors for maternal mortality in Zimbabwe. Studies in Family Planning. 1996;27(6):319-27.

64. Khanam R. A., Khatun M. Ruptured uterus: an ongoing tragedy of motherhood. Bangladesh Med Res Counc Bull. 2001;27(2):43-7.

65. Kongnyuy Eugene J., Mlava Grace, van den Broek Nynke. Facility-based maternal death review in three districts in the central region of Malawi: an analysis of causes and characteristics of maternal deaths. Womens Health Issues. 2009;19(1):14-20.

66. Lema V. M., Changole J., Kanyighe C., Malunga E. V. Maternal mortality at the Queen Elizabeth Central Teaching Hospital, Blantyre, Malawi. East African Medical Journal. 2005;82(1):3-9.

67. Lori Jody R., Starke Amy E. A critical analysis of maternal morbidity and mortality in Liberia, West Africa. Midwifery. 2012;28(1):67-72.

68. Mbaruku G. Enhancing survival of mothers and their newborns in Tanzania: Karolinska Institutet, Stockholm, Sweden; 2005.

69. Moodley J., Pattinson R. C., Bennun M., Cronje H. S., Dichabe M., Kambaran S. R., et al. A review of maternal deaths in South Africa during 1998. SAJOG South African Journal of Obstetrics and Gynaecology. 2000;6(2):16-23.

70. Moodley J. Maternal deaths associated with eclampsia in South Africa: lessons to learn from the confidential enquiries into maternal deaths, 2005-2007. SAMJ South African Medical Journal. 2010;100(11):717-9.

71. Omo-Aghoja I. O., Aisien A. O., Akuse J. T., Bergstrom S., Okonofua F. Maternal mortality and emergency obstetric care in Benin City, South-south Nigeria. Journal of Clinical Medicine and Research. 2010;2(4):55-60.

72. Onah H. E., Umeh U. A. Maternal mortality at the University of Nigeria Teaching Hospital, Enugu, 1999-2003. Global Journal of Medical Sciences. 2006;5(1):13-6.

73. Shah Nusrat, Khan Nusrat H. Third delay of Maternal Mortality in a tertiary hospital. Rawal Medical Journal. 2007;32(2):163-7.

74. Shah Nusrat, Hossain Nazli, Shoaib Rizwana, Hussain Ayesha, Gillani Rehma, Khan Nusrat H. Socio-demographic characteristics and the three delays of maternal mortality. Jcpsp, Journal of the College of Physicians & Surgeons - Pakistan. 2009;19(2):95-8.

75. Spies C. A., Bam R. H., Cronje H. S., Schoon M. G., Wiid M., Niemand I. Maternal deaths in Bloemfontein, South Africa--1986-1992. Samj, S. 1995;85(8):753-5.

76. Supratikto Gunawan, Wirth Meg E., Achadi Endang, Cohen Surekha, Ronsmans Carine. A district-based audit of the causes and circumstances of maternal deaths in South Kalimantan, Indonesia. Bulletin of the World Health Organization. 2002;80(3):228-34.

77. Tank Parikshit D., Chauhan Anahita R., Bhattacharya Moudhulika S., Warke Himangi S., Raut Vanita S. Neurological complications in eclampsia: a case series. International Journal of Fertility & Womens Medicine. 2004;49(2):61-9.

78. Weeks Andrew, Lavender Tina, Nazziwa Enid, Mirembe Florence. Personal accounts of 'near-miss' maternal mortalities in Kampala, Uganda. BJOG: An International Journal of Obstetrics & Gynaecology. 2005;112(9):1302-7.

79. Dellagi R. T., Belgacem I., Hamrouni M., Zouari B. [Evaluation of the maternal mortality surveillance system in public facilities in Tunisia (1999-2004)]. Eastern Mediterranean Health Journal. 2008;14(6):1380-90.

80. Jahn A., Dar Iang M., Shah U., Diesfeld H. J. Maternity care in rural Nepal: a health service analysis. Tropical Medicine & International Health: TM&IH. 2000;5(9):657-65.

81. Ayaya S. O., Esamai F. O., Rotich J., Liechty E. Perinatal mortality in the Special Care Nursery of Moi Teaching and Referral Hospital, Eldoret, Kenya. East African Medical Journal. 2004;81(11):555-61.

82. Cisse C. T., Faye E. O., Bernis L. de, Diadhiou F. Uterine rupture in Senegal: epidemiology and quality of management. [French]. Medecine Tropicale. 2002;62(6):619-22.

83. Mayi-Tsonga Sosthene, Meye Jean-Francois, Tagne Alain, Ndombi Isabelle, Diallo Thierno, Oksana Litovchenko, et al. [Audit of the severe obstetrical morbidity (near miss) in Gabon]. Sante. 2007;17(2):111-5.

84. Ouedraogo C., Zoungrana T., Dao B., Dujardin B., Ouedraogo A., Thieba B., et al. Quality of caesareans at the Yalgado Ouedragogo Hospital Centre, Ouagadougou, Burkina Faso. Analysis of quality determinants with reference to 478 cases in the Department of Gynaecology and Obstetrics. [French]. Medecine d'Afrique Noire. 2001;48(11):443-51.

85. PMM. Situation analyses of emergency obstetric care: examples from eleven operations research projects in west Africa. The Prevention of Maternal Mortality Network. Social Science & Medicine. 1995;40(5):657-67.

86. Ifenne D., Essien E., Golji N., Sabitu K., Alti-Mu'azu M., Musa A., et al. Improving the quality of obstetric care at the teaching hospital, Zaria, Nigeria. International Journal of Gynaecology & Obstetrics. 1997;59 Suppl 2:S37-46.

87. Okaro J. M., Umezulike A. C., Onah H. E., Chukwuali L. I., Ezugwu O. F., Nweke P. C. Maternal mortality at the University of Nigeria Teaching Hospital, Enugu, before and after Kenya. African Journal of Reproductive Health. 2001;5(2):90-7.

88. Sorensen Bjarke Lund, Rasch Vibeke, Massawe Siriel, Nyakina Juma, Elsass Peter, Nielsen Birgitte Bruun. Impact of ALSO training on the management of prolonged labor and neonatal care at Kagera Regional Hospital, Tanzania. International Journal of Gynaecology & Obstetrics. 2010;111(1):8-12.

89. Strand R. T., de Campos P. A., Paulsson G., de Oliveira J., Bergstrom S. Audit of referral of obstetric emergencies in Angola: a tool for assessing quality of care. African Journal of Reproductive Health. 2009;13(2):75-85.

90. Mahomed K., Nyoni R., Mulambo T., Kasule J., Jacobus E. Randomised controlled trial of intrapartum fetal heart rate monitoring. Brit Med J. 1994;308(6927):497-500.

4. Legends of Figures and Tables

Figure 1: Criteria used to assess the quality of studies included

Figure 2: Conceptual framework of third delay (adapted from Gabrysch & Campbell (16) and Edson et al. (17))

The right-hand column shows the pathway to care for obstetric emergencies arising during home deliveries: women have to make the decision to seek care (first delay), and reach a health facility (second delay), before being admitted. Planned facility deliveries are represented on the left-hand column, where the decision to seek care is made in advance, and women are at the facility when complications develop. In all cases, the patient has to be examined before a diagnosis can be made, leading to either a decision to treat or to refer the woman to an appropriate EmOC facility. Treatment materials and vehicles must be obtained before treatment or referrals can be carried out (these added components are represented in the shaded boxes).

Figure 3: Identification of studies

Figure 4: Reported frequency of causes of the third delay (N=37 studies)*

*Some studies mention multiple barriers

Table 1: Articles included in the review

Table 2: Mean duration of intervals between critical care events (range reported in 31 studies)

Table 3: Summary of evidence on effect of delays to care on birth outcomes (N=12 studies)

5. Tables

Table 1: Articles included in the review

Study / setting	Study design and sample size	Primary aim of study	Definition of delay used	Duration of delay reported	Reasons for delay reported	Evidence of effect on birth outcomes
Review of adverse events (including audit, verbal autopsy and qualitative interviews)						
Ahmed, 2004 (57); university hospital, Sokoto, Nigeria	Review of 18 cases of ruptured uterus	Assess the success of loan scheme for emergency surgery	Admission-to-surgery interval	Mean admission-surgery interval = 3.5hrs	None	None
Amaral, 2011 (58); 9 hospitals in Campinas city, Brazil	Audit of 159 adverse perinatal events (maternal and perinatal deaths, maternal near-miss)	Determine the rate of adverse perinatal outcomes and the prevalence of three delays	Delay in receiving care	Third delay in 20% of adverse perinatal outcome	None	None
Bako, 2009 (59); university hospital, Borno state, Nigeria	Retrospective study of 66 cases of umbilical cord prolapse	Determine the incidence of umbilical cord prolapse, predisposing factors and fœtal outcome	Decision-to-delivery interval for emergency caesarean	Mean decision-delivery interval = 77.1min	None	None
Barnes-Josiah, 1998 (10); multiple facilities, rural Haiti	Verbal autopsy of 12 maternal deaths	Investigate the medical and social circumstances of maternal deaths	Delay in receiving adequate and appropriate care once the facility is reached	Third delay in 7 of 12 maternal deaths	None	None
Cham, 2005 (11); multiple facilities, rural Gambia	Verbal autopsy of 32 maternal deaths (qualitative study)	Describe socio-cultural and health service factors associated with maternal deaths	Delay in receiving prompt and adequate care after reaching the hospital	Third delay in 31 of 32 maternal deaths	Lack of blood transfusion and basic medical supplies; delay in intervention by medical team; poor management of staff availability (particularly doctors)	None

Cham, 2007 (60); multiple facilities, rural Gambia	Audit and verbal autopsy of 42 maternal deaths	Gain a comprehensive picture of medical causes and contributing factors	Delay in receiving care at the facility, including delayed operative delivery and delay in examination	Third delay in 25% maternal deaths	Periodic electricity supply; lack of trained personnel; malfunction of the blood transfusion service (blood subject to corruption and illegal charging)	None
Cham, 2009 (61); national teaching and referral hospital, Gambia	In-depth interviews with 30 women treated for acute obstetric conditions	Assess availability and quality of EmOC in Gambia's main referral hospital	Delay before being attended; delay receiving blood; delay obtaining caesarean; delay receiving medicines	Average delay initiating blood transfusion = 48hrs	Lack of blood for transfusion; shortage of doctors for caesareans; shortage and high cost of drugs (magnesium sulphate)	None
De Muylder, 1990 (62); multiple health facilities, Midlands province, Zimbabwe	Audit of 70 maternal deaths	Identify common avoidable factors associated with maternal deaths	Delayed patient arrival in theatre; delay before correct diagnosis and effective action	Delayed arrival in theatre (2 cases); delayed diagnosis (1 case of ruptured uterus); delayed intervention (2 cases)	None	None
Fawcus, 1996 (63); multiple facilities, Zimbabwe	Community-based investigation of preventable factors associated with 166 maternal deaths	Assess the preventability of maternal deaths	Delay in decision to refer; delay in diagnosis; delay in treatment	Delay in referral: 43% women (rural) and 11% (Harare); delayed diagnosis: 17% (rural) and 18% (Harare); delayed treatment: 10% (rural) and 31% (Harare)	Failure to appreciate severity of patient's condition (post-abortion complications and sepsis); poor supervision; lack of clear protocols; lack of surgical facilities; poor organisation of obstetric team	None
Gohou, 2004 (37); one teaching and one regional hospital in Abidjan, Côte d'Ivoire	Audit of 23 severe maternal morbidity cases requiring life-saving surgery	Document the frequency of severe obstetric morbidity, intervals between admission/decision to surgery and factors contributing to delays	Admission-to-surgery interval; decision-to-surgery interval	Median admission-surgery interval = 5.7hrs (teaching hospital), 1.5hrs (regional); median decision-surgery interval = 4.8hrs (teaching), 0.9hrs (regional)	Patients needing to obtain and assemble surgical kit; operating theatre occupied (7 cases); poor staff communication (1); lack of blood (2); errors in diagnosis / failure to recognise severity of complications (4); lack of staff (1)	None
Holme, 2007 (29); fistula repair referral hospital, Zambia	Cross-sectional study of 259 fistula repair patients	Describe and compare characteristics of women with fistulae	Proportion of fistula patients spending more than one day in labour at a facility	55% of women spent >1day in labour at clinic; 18% experienced delay in care at hospital	Lack of transportation for referral (47%); staff stating woman would deliver normally (19%)	None

Karolinski, 2010 (26); 24 hospitals in Argentina and Uruguay	Cross-sectional study of 26 maternal deaths and 80 cases of severe morbidity	Review the use of evidence-based guidelines in cases of maternal mortality and severe morbidity	Admission / diagnosis-to-caesarean interval (timely caesarean defined as <30min)	Timely caesarean in 75% of patients (95% CI: 51-91)	None	None
Khan, 2007 (44); university hospital, Karachi, Pakistan	Cross-sectional study of 44 cases of umbilical cord prolapse	Determine the effect of diagnosis-to-delivery interval on perinatal outcomes in cases of umbilical cord prolapse	Diagnosis-to-delivery interval for umbilical cord prolapse	Mean diagnosis-delivery interval = 18min; 64% of women delivered within 20min	None	No statistical difference in Apgar score at 5min (p=0.159); perinatal death (p=0.614); NICU admission (p=0.314); maternal complications (p=1.00)
Khanam, 2001 (64); university hospital, Dhaka, Bangladesh	Retrospective review of 424 cases of ruptured uterus	Determine the frequency of ruptured uterus, possible risk factors and foeto-maternal outcome	Admission-to-surgery interval	Range of admission-surgery interval = 45min-2hrs	Arrangement for blood transfusion; scarcity of operating theatre facilities	None
Kidanto, 2009 (13); national hospital, Dar-Es-Salaam, Tanzania	Qualitative audit of 133 perinatal deaths	Identify suboptimal factors and classify them into to the three levels of delay	Delayed clinical decisions; delayed implementation of actions; delayed referrals	Delay to care in 46.6-64.6% deaths; delayed operation in 11.3-16.5%; delayed referral in 13.3-23.3%	Referral delay: lack of 24h EmOC and emergency transport; delayed decision: poor fœtal heart rate monitoring, partogram not filled; implementation delay: shortage of surgery space	None
Kongnyuy, 2009 (65); 9 hospitals in Central Malawi	Review of 43 maternal deaths	Identify causes and avoidable factors in maternal deaths	Delay in starting treatment; delay in decision to refer	Delayed treatment: 47% deaths; delayed decision to refer: 21%; prolonged abnormal observation without treatment: 33%	None	None
Langer, 2000 (33); multiple facilities in three regions, Mexico	Verbal autopsy of 164 maternal deaths	Identify factors associated with maternal deaths	Interval between care provision at first and last facility; waiting time for care provision	First-last care provision: 23% within <1hr, 17% in 1-4hrs, 23% in 5-12hrs, 37% in >12hrs; waiting time: 58% immediately, 12% within <1hr, 20% in 1-4hrs, 10% in >4hrs	None	None
Lema, 2005 (66); teaching hospital, Blantyre, Malawi	Retrospective descriptive study of 204 maternal deaths	Identify maternal characteristics, immediate causes and operational factors in maternal deaths	Delay in being offered appropriate EmOC	Delayed offer of EmOC in 24.5% maternal deaths	None	None

Lori, 2012 (67); multiple facilities, rural county in Liberia	Secondary analysis of audits of 28 maternal deaths and 120 cases of near-miss	Explore the causes and circumstances surrounding maternal deaths and near-miss	Delays to care	Delays to care in 3% near-miss and 4% maternal deaths	None	None
Mayi-Tsonga, 2009 (54); referral hospital in Libreville, Gabon	Review of 76 maternal deaths	Compare delay in initiating care by characteristics of the woman	Mean interval between admission and treatment	Mean admission-treatment interval = 1.2hrs (PPH / eclampsia), 23.7hrs (abortion complications)	Stigma against abortion; lack of equipment does not play a role	None
Mbaruku, 2005 (68); regional hospital in Kigoma, Tanzania	Cross-sectional study and audit of 200 perinatal deaths	Identify main phases of delay	Interval from calling doctor to arrival	Mean call-to-arrival interval = 60min (range: 30min-4hrs)	Late/wrong diagnosis (18%), wrong procedure (9%), delayed intervention (11%), absent equipment (1.5%), low skills (15%), staff attitude (7%), no doctor (1%), undetermined (2%)	None
Mbaruku, 2009 (47); regional hospital, western Tanzania	Audit of 385 perinatal deaths	Assess intrapartum stillbirth and early neonatal death and identify contributing delays	Call-to-arrival interval for doctors; decision-caesarean interval	Mean doctor call-to-arrival = 1hr (range: 0.5-4.0hrs); decision-caesarean interval = 1hr (range: 0.25-2.5hrs)	None	None
Moodley, 2000 (69); multiple facilities, South Africa	Analysis of 585 maternal deaths reports	Document causes and prevalence of maternal mortality and identify avoidable factors	Delay in referral (decision and transport); treatment delay	Delayed transport between institutions: 14% deaths; delayed admission (2%); delayed decision to refer (9%); delayed treatment (5%)	None	None
Moodley, 2010 (70); all facilities, South Africa	Review of all 622 maternal deaths associated with eclampsia	Identify number and avoidable factors related to maternal deaths from eclampsia	Delay in transport between institutions; delay in referring patients	Referral delay: 18% of women w/ third delay; delayed transport: 11% of all women	None	None
Omo-Aghoja, 2010 (71); university hospital, Benin City, Nigeria	Review of 84 maternal deaths	Estimate MMR and identify contribution of third delay	Delay after arrival in hospital	Third delay in 62% maternal deaths	Delayed referral from private hospitals (92%); lack of blood (3.5%); lack of oxygen (1.8%); lack of back-up equipment (1.8%); limited operating theatre space; poor communication/teamwork	None

Onah, 2006 (72); teaching hospital, Enugu, Nigeria	Retrospective analysis of 88 maternal deaths	Assess maternal mortality ratio and risk factors	Delays in receiving care at health facilities (including referral delay)	Third delay in 33% maternal deaths	Referral delay in 45% of women w/ third delay, delay in obtaining blood (25%), inability of patient to provide drugs (10%), lack of linen in theatre (5%), inability to pay hospital fees (5%), referral delay due to relations apathy (5%), delay in anaesthetic review (5%)	None
Onah, 2005 (39); CEmOC hospitals in Enugu State, Nigeria	Retrospective analysis of 141 maternal deaths	Establish maternal mortality ratio and risk factors	Delay in management; referral delay; delay in getting blood for transfusion	Third delay in 53% of deaths	Referral delay (46% of cases w/ delay), delay obtaining blood (29%), inability to obtain drugs (7%), lack of linen in theatre (4%), lack of oxygen (4%), inability to pay hospital fees (4%), delay in anaesthetic review (4%),	None (anecdotal)
Orji, 2002 (43); teaching hospital, Ile-Ife, Nigeria	Cross-sectional study of 102 cases of ruptured uterus	Determine decision-intervention interval	Decision-intervention interval for surgery	Mean decision-intervention interval = 2.8hrs (range: 0.5-4.5hrs); 74% patients not operated on within 1hr	Lack of compatible blood (88%); lack of electricity (5%); unsterile instruments (4%); delayed arrival of obstetrician (3%), anaesthetist (2%), and neonatologist (2%)	Maternal / perinatal mortality and risk of total hysterectomy rise with decision-intervention interval (no statistical tests reported)
Ramos, 2007 (12); multiple facilities in Argentina	Verbal autopsy of 25 maternal deaths	Describe causes of death, identify risk factors in health care delivery and social determinants	Delays in receiving timely care, delays in referral	None	Errors in diagnosis and clinical decision-making; lack of medical supplies (blood) and staff proficiency; bad condition of roads for referrals	None
Sepou, 2002 (38); national referral hospital, Bangui, Central African Republic	Cross-sectional study of 35 cases of uterine ruptures	Determine incidence of uterine rupture, identify predisposing factors and evaluate prognosis	Decision-delivery interval for emergency caesarean	Decision-delivery interval >60min in 71% (uterine rupture), 31% (all caesareans, $p<0.001$)	Lack of financial means (45% of women w/ delays); lack of operating field (22%); theatre in use (18%); instruments being sterilised (9%); lack of oxygen (7%)	None
Shah, 2007 (73); Civil Hospital, Karachi, Pakistan	Retrospective cross-sectional study of 152 maternal deaths	Assess the magnitude, causes and substandard care factors responsible for the third delay	Delay in receiving quality care at the facility; delay in arranging blood and delay in surgical intervention	Delay in treatment in 73% maternal deaths	Delay replacing blood / surgery: 26% all cases; failure/delay performing laparotomy: 20% (sepsis, abortion, uterine rupture, ectopic pregnancy)	None

Shah, 2009 (74); tertiary teaching hospital, Karachi, Pakistan	Cross-sectional study of 104 maternal deaths	Describe socio-demographic characteristics and three delays of maternal mortality	Delay in receiving adequate care at the facility	Third delay in 48% of maternal deaths	Delay obtaining blood (49% of women w/ third delay); delay in surgery (45%) due to delayed diagnosis, anaesthetist response and operating room busy	None
Spies, 1995 (75); tertiary referral hospital, South Africa	Review of 91 maternal deaths	Determine MMR and main causes of maternal deaths	Delay in diagnosis, treatment, surgery, referral	Delayed treatment in 21 deaths, delayed diagnosis (14), late referral (30), delayed surgery (11)	None	None
Supratikto, 2002 (76); multiple facilities, three provinces in Indonesia	Audit of 130 maternal deaths	Assess substandard care and recommend improvements in access and quality of care	Delay in seeing health provider	Delay in seeing health provider in 37% (of 30 deaths with information)	None	None
Tank, 2004 (77); referral centre, Mumbai, India	Retrospective review of 19 cases of eclampsia	Analyse the epidemiology and outcome of eclamptic patients	Admission-to-delivery interval for patients admitted with eclampsia	Mean admission-delivery interval = 10.38hrs (range: 2.2-14.5hrs)	None	None
Urassa, 1997 (31); multiple facilities, Ilala District, Tanzania	Audit of 117 maternal deaths	Identify operational factors in maternal deaths	Decision-to-transfer interval; delay in adequate care	85% women transferred <30min, 15% in 1-3hrs; delayed referral in 10% of women; adequate care delayed in 12%	None	None
Van den Akker, 2009 (24); district hospital, Malawi	Audit of 35 cases of uterine ruptures	Assess cases for delays in diagnosis, treatment and referral	Delay in recognising prolonged labour; delay in providing adequate treatment after diagnosis; delay in decision to refer; delay in ambulance arrival at referring facility	Delayed recognition of prolonged labour (4 of 4 cases); delayed care (2 of 4); delayed decision to refer (2 of 3); delayed ambulance arrival (2 of 3); average decision-to-surgery interval of 96min	None	None (anecdotal)
Weeks, 2005 (78); teaching hospital in Kampala, Uganda	Semi-structured interviews of 30 women with near-miss	Explore the socio-economic determinants of maternal mortality through cases of near-miss	Delays in obtaining care or referrals	None (anecdotal)	Delay obtaining referral letter; high case load; lack of qualified staff for caesareans; lower priority for subacute complications (e.g. pelvic abscesses)	None
Cross-sectional studies						

Dellagi, 2008 (79); 11 referral hospital in Tunis, Tunisia	Analysis of 18 process and outcome indicators in 85 maternal deaths	Assess the performance of the maternal death reporting system	Delay in treatment	Delayed treatment in 18 of 85 cases of maternal deaths	None	None
Edson, 2006 (17); multiple facilities in Benin, Ecuador, Jamaica, Rwanda	Retrospective review of 328 patients presenting with obstetric emergencies	Define and measure third delay	Delay in evaluation, diagnosis and definitive treatment (outlines pathway to care)	Third delay in 31% patients; delayed evaluation: 12%; delayed diagnosis: 14%; delayed treatment: 28%; mean evaluation interval = 30min; diagnosis-treatment interval = 175min	Evaluation: lack of staff; diagnosis: missed diagnosis/symptoms, poor patient monitoring, provider skill; treatment: pharmacy closed, patient unable to pay for materials, unavailability of operating theatre, poor availability of clinical team	None
Hofman, 2008 (20); 3 health centres and 1 district hospital, Malawi	Descriptive study of 112 obstetric referrals	Compare duration of referral delay by motorcycle ambulance and other transport means	Referral delay (including time to contact vehicle, to vehicle arrival, and transportation time)	Mean duration of transport from health centre to hospital = 1.5-5hrs (motorcycle ambulance)	Lack of communication means with drivers; obtaining family consent; lack of emergency transportation at referring health centres; poor state of roads	None
Jahn, 2000 (80); one referral hospital and 43 first-level facilities, Nepal	Health services indicators analysis of 44 facilities in district	Assess the performance of maternity care in district	Decision-delivery interval for emergency caesarean	Mean decision-delivery interval = 4.5hrs (range: 40min-11hrs)	None	None
Marcus, 2009 (21); five midwife obstetric units in Cape Town, South Africa	Descriptive study of ambulance response times in 48 obstetric and neonatal transfers	Establish ambulance response times and compare them across units and severity of complication	Interval between request and arrival at referring facility	Mean response time: 107min (range: 10-330min); 35.5% within 60min	None	None
Mbassi, 2009 (35); 7 third-level maternity units in Cameroon	Retrospective chart review of 2847 cases of obstetric complications	Determine MMR associated with obstetric complications and relate them to staff competency and time-to-care	Time-to-care after admission with complication	44.6% women were managed within 30min; 31.7% in 30-60min; 23.7% in >60min	None	Risk of death increases with time-to-care ($p<0.05$)

Orji, 2006 (34); University Teaching Hospital, Ile-Ife, Nigeria	Descriptive cross-sectional study of 96 women admitted in labour or with obstetric emergencies at labour wards	Assess the delays in the management of pregnant women admitted with complications	Delays in care after the patient arrives at the hospital; decision-delivery interval for emergency caesarean	Mean decision-delivery interval of 4.48h; 6% <30min; 16% <1h; 88% ceasareans were started <6h after decision; none 6-12h; 12% >12h after decision	Theatre-related factors in 44% of women w/ third delay (poor electricity supply, theatre unavailable), awaiting doctors review: 26% (unavailability of anaeasthetist/ paediatrician), lack of blood: 22%, delay obtaining consent: 4%, delay opening case notes: 4%	Higher maternal and perinatal mortality with longer decision-delivery interval (10% perinatal mortality <6h, 44% in >12h – no statistical test reported; only case of maternal mortality occurred with decision-delivery interval >12hrs (p<0.001))
Prospective observational studies						
Ayaya, 2004 (81); teaching hospital, Eldoret, Kenya	Prospective cross-sectional study of 335 infants admitted to Special Care Nursery	Determine the mortality rate and causes of death in all infants admitted to Special Care Nursery	Interval from presentation at labour ward to examination by obstetrician; decision-delivery interval for caesarean	Mean presentation-examination interval = 1.95hrs; mean decision-delivery = 5.34hrs; 27% examined immediately; 11% in >5hrs; 8.7% decision-delivery <1hr	Delayed caesarean: physician unavailability (38%), unavailability operating theatre (20%), delays in obstetrical consultations (12.5%), lack of theatre supplies (5%), delays in obtaining consent (2.5%), other (24%)	No association between decision-delivery interval and neonatal mortality (authors attribute to small numbers, no p-value reported)
Cisse, 2002 (82); all surgical maternity units in Senegal	Prospective longitudinal study of 50 cases of uterine rupture	Analyse risk factors and quality of care in cases of uterine rupture	Decision-to-operation interval	Mean decision-operation interval =11hrs	Lack of surgical kit (46%); lack of blood (30%); unavailability of anaesthetist (6%); cost of supplies to patient	None
Mayi-Tsonga, 2007 (83); referral hospital in Libreville, Gabon	Prospective observational study of 137 near-miss cases	Identify main weak points in caring for obstetric complications	Admission-to-examination by qualified personnel; surgical delay; delay in performing blood transfusion	61% patients seen by qualified personnel in <45min; mean surgical delay = 5.25h (range: 0.5-24hrs); mean delay in blood transfusion = 3h40 (range: 0.5-72hrs)	Surgical delay: unavailability of theatre (53%); on-call surgeon busy with another intervention (53%); lack of sterile materials (61%); lack of anaesthetic products (33%)	None

Nada, 2011 (25); 4 general hospitals in Egypt	Observational study of 102 women with complications	Assess the quality of care in emergency obstetric services	Delays in admission, assessment, ordering blood for transfusion; delayed administration of blood	Mean arrival-registration interval = 20min; registration-examination = 26min; diagnosis- intervention = 3hrs; examination-blood order = 1h20; blood order-arrival = 50min; blood arrival-administration = 39min immediate availability of anaesthesia: 45%; immediate order of blood: 63%	None	None
Onah, 2005 (45); one national and one teaching hospital, Nigeria	Prospective study of 224 emergency caesarean sections	Determine the decision-delivery interval for emergency caesareans, impact on perinatal outcome and reasons for delays	Decision-delivery interval for emergency ceasarean section	Mean decision-delivery interval = 8.5hr (teaching hospital), 3.4hrs (national hospital)	Anaesthetic delay (66% of delays); delay obtaining materials and blood; delayed patient transfer to theatre (13-24%); delayed preparation for surgery (17-20%); delayed surgeon arrival (13-15%); delay patient preparation on ward (7-20%); poor supervision; lack of theatre space (13-15%); lack of staff	No association between decision-delivery interval and Apgar score (p>0.05) or risk of death (p=0.31); no difference in mean decision-delivery interval by survival status (p=0.78)
Onwudiegwu, 1999 (46); university hospital, Ile-Ife, Nigeria	Prospective study of 134 emergency caesareans over 5mths	Determine the decision-delivery interval for emergency caesareans, factors responsible for delays and maternal-fœtal outcome	Decision-delivery interval for emergency caesareans	Mean decision-delivery interval = 4.4hrs (range: 0.5-26hrs)	Preparing patient for surgery due to staff/resource shortages (32%); unavailability of paediatrician (20%) and anaesthetist (14%); unreadiness of operating theatre (12%); seeking second opinion (6%); delayed consent (6%); resuscitation time (4%); lack of blood (2%); electricity failure (2%); others (4%)	Mean decision-delivery interval higher among 5 stillborn infants (5.7hrs) (not significant, no p-value reported)
Onwudiegwu, 2001 (41); university hospital, Ile-Ife, Nigeria	Prospective study of 144 emergency obstetric admissions	Examine the nature of obstetric emergencies, delays in referral and misdiagnoses, and their contribution to outcomes	Delay in referral to teaching hospital	25% of patients referred within 1 day; 16% in 1-2 days; 18% in 2-3days; 15% in 3-4 days; 8% in 4-5; 18% in 5-28 days	Incorrect diagnoses at referring hospital	Mean delay longer for maternal deaths (5.2 days) than mothers alive (4.3 days) (not significant)

Ouedraogo, 2001 (84); national referral hospital, Burkina Faso	Prospective study of 478 caesareans over 6mths	Analyse determinants of the quality of caesarean sections	Admission-to-delivery interval for emergency caesarean among referred patients	27% caesareans conducted <1hr of admission	Delayed caesarean: surgical factor in 52% (unavailability of surgeon, incomplete team, incomplete kit, technical problems); delayed decision in 14% (non-utilisation of partograph, lack of standard protocols, technical difficulties)	None
PMM, 1995 (85); 11 facilities in Ghana, Nigeria, and Sierra Leone	Situation analyses of use and functioning of 11 EmOC facilities	Identify resource needs and management problems in EmOC facilities	Admission-to-treatment interval	Mean admission-treatment interval = 2.6-15.5hrs (across sites)	Lack of drugs and essential supplies, leading patients to purchase at pharmacies; lack of surgical facilities	None
Saizonou, 2006 (36); 2 teaching, 2 regional and 3 district hospitals in Benin	Prospective audit of 557 women admitted with near-miss complications	Examine the availability and timeliness of EmOC	Interval between admission and provision of EmOC (including surgery, blood transfusion, anticonvulsants and antibiotics)	EmOC provision <30min in 61% patients; 36-58% surgeries <60min (depending on condition); blood transfusion started within 60min for 10-47% patients; 50% anticonvulsants <60min; 53% antibiotics <60min	None	None
Case-control study						
Chigbu, 2009 (19); teaching hospital, Enugu, Nigeria	Case-control study of 316 intrapartum stillbirths and 316 controls	Examine the non-medical factors contributing to intrapartum stillbirths	Decision-to-intervention interval; call-to-arrival interval for senior obstetricians/anaesthetists; drug prescription-to-purchase interval	Third delay in 84 cases and 11 controls; delay in transfer in 55 cases and 4 controls; delay in receiving care in 144 cases and 29 controls	Delay purchasing drugs (53 cases); delay obtaining blood (41); lack of electricity (29); lack of sterile materials (21); delayed arrival of aneasthetist (19) and obstetrician (11); no apparent reason (17); lack of water (9); delayed consent for surgery (2)	Higher prevalence of third delay among stillbirths than controls (p<0.0001); higher prevalence of delay in transfer (p<0.0001); higher prevalence in delay receiving care (p<0.0001)
Ganatra, 1998 (40); multiple facilities, rural Maharashtra, India	Population-based case-control study of 121 maternal deaths and matched controls (2+ per case)	Compare interval from decision to seek care to reaching appropriate facilities between maternal deaths and survivors	Interval between first health services contact and reaching appropriate health facility	Interval first-to-appropriate health facility = 4.9hrs (controls) and 12hrs (cases)	None	Longer interval between reaching first and appropriate health facility among maternal deaths (p<0.01)

Ghebrehiwet, 2007 (42); multiple facilities, Eritrea	Population-based case-control study of 58 maternal deaths and 53 matched survivors of near-miss	Identify avoidable factors associated with maternal deaths and near-miss	Delay or failure in receiving care at health facilities; delay in referral	33% cases and 40% controls referred <3hrs of reaching referring facility; 33% cases and 27% of controls in 4-12hrs	None	Varying proportion of cases and controls referred within certain time limits (no emerging trend, no statistical test reported)
Kabali, 2011 (32); 12 referral hospitals in Kinshasa, DR Congo	Case-control study of 110 maternal deaths and 208 cases of near-miss (semi-structured interviews)	Compare the circumstances of survivors and non-survivors of severe obstetric complications	Interval from arrival to appropriate intervention	Appropriate intervention <2hrs in 19% maternal deaths and 40% survivors; proportion <24hrs = 44% maternal deaths and 85% survivors	Shortages of blood, medicines and equipment; unavailability of operating theatre; poor organisation of care; staff attitudes and perceived competences; cost of interventions	None (anecdotal)
Okonufua, 1992 (18); university hospital, Nigeria	Case-control study of 35 maternal deaths and 35 controls	Determine risk factors for maternal mortality	Delay in receiving adequate care at the facility (including referral delay)	Third delay in 40% maternal deaths and 17% controls	Incorrect treatment (4 cases), lack of facilities (4), poor staff attitude (4), delayed referral from health centre (2 cases and 6 controls)	OR=6.6 and RR=2.7 (p<0.01)
Pre-post evaluation of intervention						
Ifenne, 1997 (86); teaching hospital, Zaria, Nigeria	Pre-post evaluation of EmOC improvement	Assess the impact of EmOC improvement on delays to treatment and case fatality rates	Admission-to-treatment interval; proportion of women treated <30min	Mean admission-to-treatment interval = 3.7hr (1990), 1.6hr (1995); proportion treated <30min = 39% (1993), 97% (1995)	None	Decline in CFR from 14% to 11%; but 61% decrease in admissions and 80% decrease in major obstetric complications over same period
Okaro, 2001 (87); teaching hospital in Enugu, Nigeria	Comparative retrospective analysis of 309 maternal deaths in two periods	Evaluate the effect of the Safe Motherhood Initiative on maternal mortality	Decision-intervention interval in cases of obstructed labour	Mean decision-intervention interval = 1.5hrs (period 1), 5.8hrs (period 2)	Patients required to pay for materials prior to intervention (second period)	None (anecdotal)
Sabitu, 1997 (22); health centre, Zaria, Nigeria	Pre-post evaluation of training and facility renovation (n=289 cases of complication)	Assess the impact of EmOC improvement on delays to treatment and case fatality rates	Admission-to-treatment interval; recommendation-to-departure time for referrals	Mean admission-to-treatment interval = 9.5h (1990), 1.5h (95); recommendation-departure interval = 48h (1990), 0.75 (95)	Reduction of delays attributed to intervention (reinstatement of ambulance, institution of community loan, staff training, facility renovation, revolving drug fund)	None
Samai, 1997 (23); district hospital in Sierra Leone	Pre-post evaluation of improved referral system (n=56 obstetric referrals)	Assess the impact of improvements in referral system on management and outcomes	Mean time from ambulance call to arrival at referral hospital	Mean interval call-arrival at hospital = 3h7min (range: 1h30-6h06)	None	None

Sorensen, 2010 (88); Kagera regional hospital, Tanzania	Pre-post evaluation of Advanced Life Support in Obstetrics training (n=1132 deliveries)	Evaluate the impact of ALSO training on management of prolonged labour and neonatal care	Delay in action after crossing action line in partograph	Mean delay in action after crossing action line = 180min (pre and post, no difference)	None	None
Strand, 2009 (89); network of primary facilities and two referral facilities, Luanda, Angola	Audit of 157 cases of emergency obstetric referrals, and pre-post study of intervention	Assess the effectiveness of a EmOC referral network	Interval from admission to evaluation by doctor	Mean admission-evaluation interval = 13.7hrs (first period) and 71min (second); mean transport time to hospital = 36min (range: 15-225min, second period)	None	Lower maternal case fatality rate in second period (0) than in first (18%), but intervention addressed partograph use and other training in addition to minimising delays
Wagaarachchi, 2001 (30); two district hospitals in Ghana and two in Jamaica	Pre-post evaluation of criterion-based audit (n=889 life-threatening complications)	Assess feasibility and effectiveness of criterion-based audits to measure and improve EmOC	Delivery of fœtus for obstructed labour (timely defined as within 2hrs)	100% fœtus delivered within 2hrs (2 at baseline and 3 after implementation)	None	None
Randomised controlled trial						
Mahomed, 1994 (90); maternal referral hospital, Harare, Zimbabwe	Randomised controlled trial of intrapartum fœtal heart monitoring (n=1255 women)	Compare effectiveness of different methods of intrapartum fœtal heart rate monitoring	Delayed decision to perform caesarean; delay in operation	Delayed decision in 2-3% patients; delays in operation in 1-8% (across methods)	Delayed decision: lack of doctor on wards; delayed caesarean: unavailability of theatre	Anecdotal (based on case review)
Review article						
Thaddeus, 1994 (9); developing countries	Review of factors affecting interval between onset of complication and treatment	Review the factors delaying decision to seek care, arrival at hospital and provision of adequate care	Third delay: delay in receiving adequate care at the facility (original framework)	None	None	None

Table 2: Mean duration of intervals between critical care events (range reported in 31 studies)

Interval measured in study	*Case population in which interval measured*	*Mean interval duration reported in studies (hrs)*[1]	*Publication references*
In-facility treatment			
Admission-to-treatment	Maternal deaths following PPH/eclampsia	1.2	Mayi-Tsonga (54)
	Maternal deaths following post-abortion complications	23.7	Mayi-Tsonga (54)
	Maternal deaths	1.6-3.7	Ifenne (86)
	Eclampsia	10.38	Tank (77)
	Obstetric complications	1.5-15.5	PMM (85), Sabitu (22)
Admission-to-surgery	Ruptured uterus	0.75-3.5	Ahmed (57), Khanam (64)
	Severe maternal morbidity	1.5-5.7 [2]	Gohou (37)
Admission-to-evaluation	Obstetric complications	0.5-13.7	Edson (17), Nada (25), Strand (89)
	Infants admitted to intensive care	1.95	Ayaya (81)
Arrival-to-administration of blood transfusion	Obstetric complications	0.67	Nada (25)
Doctor call-to-arrival	Perinatal deaths	1	Mbaruku (47, 68)
Examination-order blood transfusion	Obstetric complications	1.3	Nada (25)
Diagnosis-to-treatment	Obstetric emergencies	2.9-3	Edson (17), Nada (25)
	Prolonged labour (diagnosed with partogramme)	3	Sorensen (88)
Diagnosis-delivery	Umbilical cord prolapse	0.3	Khan (44)
Decision-delivery for emergency caesarean	All emergency caesareans	3.4-8.5	Jahn (80), Onah (45), Onwudiegwu (46), Orji (34)
	Perinatal deaths	1	Mbaruku (47)
	Umbilical cord prolapse	1.3	Bako (59)
	Infants admitted to intensive care	5.3	Ayaya (81)
Decision-intervention interval	Maternal deaths following obstructed labour	1.5-5.8	Okaro (87)
Surgery delay	Maternal near-miss	5.25	Mayi-Tsonga (83)
Decision-surgery interval	Severe maternal morbidity	0.9-4.8 [2]	Gohou (37)
	Ruptured uterus	1.6-11	Cisse (82), Orji (43), Van den Akker (24)
Order-to-arrival of blood	Obstetric complications	0.83	Nada (25)
Order-to-blood transfusion	Obstetric emergencies	48	Cham (61)
	Maternal near-miss	3.7	Mayi-Tsonga (83)
Referrals between facilities			
Ambulance request-to-arrival	Obstetric referrals	0.75-48	Marcus (21), Sabitu (22), Samai (23)
Transportation to referral hospital	Obstetric referrals	0.6-5	Hofman (20), Strand (89)
Interval first-last health facility	Maternal deaths	12	Ganatra (40)
	Maternal near-miss	5	Ganatra (40)

[1] The figures presented in this column refer to the means reported across different studies, or across different groups within the same study (e.g. different health facilities) where no single mean was reported.
[2] Median interval duration

Table 3: Summary of evidence on effect of delays to care on birth outcomes (N=12 studies)

Author/population	Study design	Sample size	Exposure measure	Outcome measure	Results
Referral delay					
Chigbu (19); hospital-based	Case-control	316 stillbirths, 316 controls	Delay in transfer from referring hospital (clinician-determined based on record review)	Intrapartum stillbirth	OR=16.43 of transfer delay comparing cases to controls (p<0.0001)
Ganatra (40); population-based	Case-control	121 cases, 2+ matched controls per case	Time interval from first contact with health system to reaching appropriate facility (median interval length)	Maternal death	Median interval length: 4.9hrs (cases) and 12hrs (controls) (p<0.01)
Onwudiegwu (41); women referred from health centres	Prospective cohort	142	Referral delay to teaching hospital (mean number of days before referral)	Maternal death	Mean number of days before referral: 5.2 days (maternal deaths) and 4.3 days (women who were alive) (no p-value reported)
Delay to treatment (all treatments)					
Ghebrehiwet (42); population-based	Case-control	58 deaths, 53 matched controls	Delays to care	Maternal death	Higher prevalence of delays to care among dead women than controls (no p-value reported)
Mbassi (35); women with complications	Cross-sectional	2,847	Time-to-care (admission to treatment)	Maternal death	p<0.05
Okonufua (18); hospital-based	Case-control	35 deaths, 35 controls	Delays to care	Maternal death	OR=6.6, RR=2.7, p<0.01
Delay to emergency obstetric surgery					
Ayaya (81); neonates admitted to Special Care Nursery	Cross-sectional	192	Decision-to-delivery interval	Neonatal death	No association (attributed to small sample, no p-value reported)
Khan (44); women with umbilical cord prolapse	Cross-sectional	44 (of which 39 caesareans)	Diagnosis-to-delivery interval (delay threshold: 20min)	Apgar score ≤7 at 5min	No association (p=0.159; OR=0.36)
				Perinatal death	No association (p=0.614; OR=0.54)
				Admission to NICU	No association (p=0.314; OR=2.4)
				Maternal complications	No association (p=1.00; OR=1.2)
Onah (45); emergency caesareans	Prospective cohort	224	Decision-to-delivery interval (mean interval length)	Apgar score at 1min and 5min (continuous)	No association (p>0.05 with one-way ANOVA; effect estimate not reported)
			Decision-to-delivery interval (distribution of delays between <2hrs, 2-4hrs, 4-6hrs, 6-8hrs, 8-10hrs, >10hrs)	Perinatal death	No association (p=0.31 with chi-square test for trend; effect estimate not reported)
Onwudiegwu (46); emergency caesareans	Prospective cohort	134	Decision-to-delivery interval (mean interval length)	Stillbirths	Mean interval: 5.7hrs (stillborn) and 4.4hrs (average); (no p-value or effect estimate reported)

Orji (43); women with ruptured uterus	Cross-sectional	102	Diagnosis-to-surgery interval (distribution of delays between <0.5hrs, 0.5-1hrs, 1-2hrs, >2hrs)	Maternal death; total hysterectomy; perinatal death	Rising prevalence of three outcomes with interval length (no p-value or effect estimate reported)
Orji (34); women admitted in labour or with complications receiving a caesarean	Cross-sectional	50	Decision-to-delivery interval (distribution of delays between <6hrs, 6-12hrs and >12hrs)	Maternal death	Rising prevalence with interval length (p<0.001; no effect estimate reported)
				Perinatal death	Rising prevalence with interval length (no p-value or effect estimate reported)