

Progress and inequities in maternal mortality in Afghanistan (RAMOS-II): a retrospective observational study



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Summary

Background The risk of maternal death in Afghanistan is among the highest in the world; however, the risks within the country are poorly understood. Subnational maternal mortality estimates are needed along with a broader understanding of determinants to guide future maternal health programmes. Here we aimed to study maternal mortality risk and causes, care-seeking patterns, and costs within the country.

Methods We did a household survey (RAMOS-II) in the urban area of Kabul city and the rural area of Ragh, Badakshan. Questionnaires were administered to senior female household members and data were collected by a team of female interviewers with secondary school education. Information was collected about all deaths, livebirths, stillbirths, health-care access and costs, household income, and assets. Births were documented using a pregnancy history. We investigated all deaths in women of reproductive age (12–49 years) since January, 2008, using verbal autopsy. Community members; service providers; and district, provincial, and national officials in each district were interviewed to elicit perceptions of changes in maternal mortality risk and health service provision, along with programme and policy documentation of maternal care coverage.

Findings Data were collected between March 2, 2011, and Oct 16, 2011, from 130 688 participants: 63 329 in Kabul and 67 359 in Ragh. The maternal mortality ratio in Ragh was quadruple that in Kabul (713 per 100 000 livebirths, 95% CI 553–873 in Ragh vs 166, 63–270 in Kabul). We recorded similar patterns for all other maternal death indicators, including the maternal mortality rate (1.7 per 1000 women of reproductive age, 95% CI 1.3–2.1 in Ragh vs 0.2, 0.1–0.3 in Kabul). Infant mortality also differed significantly between the two areas (115.5 per 1000 livebirths, 95% CI 108.6–122.3 in Ragh vs 24.8, 20.5–29.0 in Kabul). In Kabul, 5594 (82%) of 6789 women reported a skilled attendant during recent deliveries compared with 381 (3%) of 11366 women in Ragh. An estimated 85% of women in Kabul and 47% in Ragh incurred delivery costs (mean US\$66.20, IQR \$61.30 in Kabul and \$9.89, \$11.87 in Ragh). Maternal complications were the third leading cause of death in women of reproductive age in Kabul, and the leading cause in Ragh, and were mainly due to hypertensive diseases of pregnancy. The maternal mortality rate decreased significantly between 2002 and 2011 in both Kabul (by 71%) and Ragh (by 84%), plus all other maternal mortality indicators in Ragh.

Interpretation Remarkable maternal and other mortality reductions have occurred in Afghanistan, but the disparity between urban and rural sites is alarming, with all maternal mortality indicators significantly higher in Ragh than in Kabul. Customised service delivery is needed to ensure parity for different geographic and security settings.

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Introduction

Worldwide, maternal mortality decreased by more than 40% between 1990 and 2015 (from 532 000 to 303 000 deaths per year).¹ However, disparities exist both between and within countries, with Afghanistan being among the highest burden countries.^{1,2} When the present study was implemented, only one nationally representative maternal mortality study existed: the 2010 Afghanistan Mortality Survey (AMS), which reported a national maternal mortality ratio of 327 per 100 000 livebirths (95% CI 260–394).³ However, the findings were considered to underestimate true mortality levels.⁴ National estimates of maternal mortality are needed to assess trends and inform international public

health policy; however, data for subnational estimates are essential for understanding inequities that need to be addressed in order to achieve progress towards the Sustainable Development Goals (SDGs).

In 2011, a reproductive age mortality survey (RAMOS-II) was commissioned to assess changes in the magnitude and causes of maternal death in four districts of Afghanistan, previously studied in a 2002 study known as RAMOS-I.⁵ In RAMOS-I, researchers reported that all indicators of mortality risk were among the highest recorded globally and increased substantially with remoteness: the maternal mortality ratio ranged from 418 deaths per 100 000 livebirths (95% CI 235–602) in the most urban district of Kabul city to 6507 deaths per 100 000 livebirths (5026–7988) in the most

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Research in context

Evidence before the study

We reviewed all publicly available data for maternal mortality in Afghanistan from 2000 to 2016, including the UN Maternal Mortality Estimation Inter-agency Group (MMEIG) and Institute for Health Metrics and Evaluation estimates, and peer-reviewed studies of the maternal and newborn health and health services. We searched PubMed with the search terms “maternal mortality” and “Afghanistan”; or “maternal” and “Afghanistan”, or “health services” and “Afghanistan” for reports published in English. In addition, internet searches for reports and other grey literature were implemented; and Afghan co-authors and colleagues provided relevant documents and data in the grey literature area. No study up to now has measured trends in maternal mortality at subnational levels, or documented significant disparities between urban and rural remote districts over time.

Added value of the study

This study is the third in a series of three large maternal mortality studies implemented among Afghan women; the first was done in Pakistan in Afghan refugees in 2000, and the

second in Afghanistan in 2002. It includes data for maternal mortality magnitude and causes, risk factors, and care-seeking, including cost of care. It is the only large-scale study to document changes in maternal mortality status at a subnational level and examine potential contributions to maternal mortality decline. We also provide recommendations for future focus.

Implications of all available evidence

Documenting maternal mortality status at a subnational level is important for understanding and addressing inequities in access to and impact of health services. Lessons learned from Afghanistan can also inform programme implementation in other low-resource and crisis-affected settings. All available evidence, including findings from this study, point to the need for context-specific programme strategies and reliable ongoing maternal mortality measurement methods to reduce preventable maternal mortality in different geographic, cultural, and security conditions.

Panel: Study setting

Kabul, Afghanistan’s capital, faced sustained conflict after Soviet occupation ended in 1989. From 1996 to 2001, Taliban control restricted women’s mobility, education, and employment, which affected health-care availability and access.^{8,13} In 2002, less than 50% of women nationally delivered with a skilled attendant.¹⁴ Comprehensive emergency obstetric care was limited to two hospitals. Limited availability and quality of medical education and medical supplies hindered quality of care.¹⁴ By 2011, health services expanded to include 47 public facilities, including seven hospitals, employing more than 900 female doctors and midwives. In 2012, nearly 80% of pregnant women received antenatal care and delivered at facilities.¹² However, gaps in availability and quality of services persist and are exacerbated by continued restrictions on female mobility, low literacy, and poverty.^{11,15}

Ragh, Badakshan, is located more than 320 km northeast of Kabul in the Hindu-Kush mountains. In 2002, the region was sparsely populated, snowbound for half of the year, and food insecure, with most residents subsistence farming and raising livestock. Provincial data suggest that 12% of females older than 15 years had basic literacy, and only 0.4% were able to read and write.¹⁴ There was only one health centre in Ragh, with the nearest facility providing comprehensive emergency obstetric care located 120 km away (10 days’ walk) in the provincial capital. By 2011, health infrastructure expanded to three health centres, staffed by seven midwives and three female doctors, including one facility with comprehensive emergency obstetric care capacity. Mobile phone service flourished, and a road was built, reducing travel to the closest referral facility to 6–8 h drive in summer. Provincial indicators show that nearly 50% of pregnant women received antenatal care and 10% delivered in a health facility.¹²

remote district Ragh, Badakshan.⁵ Maternal deaths exceeded all other causes in women of reproductive age outside of Kabul.⁵ The resulting national maternal mortality ratio estimate of 1600 deaths per 100 000 livebirths (excluding Ragh as an outlier) was consistent with several estimates that used modelling methods independent of the RAMOS study data.⁶

In 2002, less than 40% of the population had access to any health services within several hours travel time, weather conditions permitting. Nationally, 17% of health facilities provided basic reproductive health services, and in 2003 fewer than 10% of births were attended by a skilled birth attendant.^{7,8} Since 2002, the Ministry of Public Health has prioritised maternal mortality reduction as a key component of public health strategies.⁹ Investments resulted in remarkable progress in health systems development, including increases in human resources and availability of obstetric care.^{10–12}

Here we report on the findings of the RAMOS-II study, which include maternal mortality risk and causes, care-seeking patterns, and costs measured in 2011. We also assess change in key indicators over time by comparing key results with the 2002 RAMOS-I study findings.

Methods

We replicated the RAMOS-I methods for RAMOS-II, using a similar study design and procedures to estimate maternal mortality from Jan 1, 2008, to Oct 16, 2011 (mid-point February, 2010), and additional qualitative methods to assess factors contributing to changes recorded over time.

Study setting

RAMOS-I included four districts selected to reflect an urban to rural or remote continuum measured by population density and distance to emergency obstetric care services: Kabul city, Kabul province (urban); Alisheng, Laghman province (semi-rural); Maiwand, Kandahar province (rural); and Ragh, Badakshan province (rural remote).⁵ In 2011, the Ministry of Public Health advised

against conducting the survey in Maiwand because of insecurity; consequently this area was not included in sample size calculations. Escalating conflict necessitated withdrawing the survey from Laghman; thus, data collection was completed in two of four RAMOS-I districts—Kabul and Ragh—representing extremes on the urban to rural or remote continuum (panel). Qualitative data collected in all four districts are reported separately.¹⁶

Data collection

We conducted a survey in all households in the randomly selected villages and neighbourhoods to collect information about all deaths, livebirths, and stillbirths in every neighbourhood or village; as well as data for health-care access and costs (inflation adjusted using 2015 World Bank consumer-price indices in US\$¹⁷), household income, and assets. Births were documented using a pregnancy history. We investigated all deaths in women of reproductive age since January, 2008, using the RAMOS-I verbal autopsy method with minor updates from the 2007 WHO Verbal Autopsy Standards.¹⁸ In a few cases, drugs taken by the women who had died were in the homes, and relevant information about illnesses associated with the prescribed drugs was recorded. Causes of death were classified by three Afghan medical doctors trained in International Classification of Diseases-10 (ICD-10) coding, originally for the aforementioned AMS; the Ministry of Public Health provided refresher training.

Data were collected between March 2 and October 16, 2011, by a team of female interviewers with secondary school education. Interviewers in Kabul worked in pairs; in Badakshan, they were accompanied by male relatives. Questionnaires were administered to senior female household members. Male field supervisors reviewed forms daily and district supervisors periodically. To assess potential bias or error, an independent data quality-control team observed at least two interviews per day and re-interviewed minimally 3% of all household survey participants. When discrepancies were identified, the quality control team's data were used. Completed forms were reviewed by Kabul-based study team members before double-entry into a central database. Intermittent data quality checks were run to check for entry errors. Completed forms were stored securely by the study team until transfer to Ministry of Public Health guardianship in 2013.

Sampling

We designed RAMOS-II to detect a 25% reduction in the combined maternal mortality ratio for the three original study districts from 1370 to 1020 deaths per 100 000 livebirths. We estimated that 20 000 births (6667 per year for 3-year retrospective data collection) were required to detect this difference (0·78). Assuming a general fertility rate of 173·5 births per 1000 women based on Ramos-I data⁵ and the number of women of

| | Kabul city, Kabul | Ragh, Badakshan |
|--|-------------------|-----------------|
| Sampled population | 3 289 000 | 87 400 |
| Number of villages selected for data collection/ total villages in district | 10/not available* | 259/325† |
| Study households | 8963 | 8845 |
| Study population | 63 329 | 67 359 |
| Number of women of reproductive age | 18 850 | 16 838 |
| Total livebirths | 6011 | 10 658 |
| Total deaths | 865 | 2534 |
| Deaths in women of reproductive age | 71 | 180 |
| Maternal deaths | 10 | 76 |

*100% of the villages selected for inclusion in 2002 were visited and contained within the sample. †Estimates of the total population and villages were not available. Therefore, RAMOS team members estimated the total number of villages in collaboration with local authorities and District Health Officials.

Table 1: Population and sample characteristics for 3-year data collection preceding survey in Kabul city, Kabul, and Ragh, Badakshan, 2002 and 2011

reproductive age per average household in all provinces (1·53),¹⁹ a sample of 38 316 women in 25 043 households was required; 8348 households per district when divided evenly between Alisheng, Kabul, and Ragh districts. The number of households and people per household per district exceeded expectation and the sample size was subsequently increased to 26 295 households. Excluding the incomplete sample from Alisheng resulted in 17 808 households with 35 688 women of reproductive age, sufficient to detect a more than 25% reduction in the two districts. In Kabul, all ten neighbourhoods from 2002 were included in the 2011 survey; because Kabul's population tripled, the target sample size was achieved without surveying any additional neighbourhoods. In Ragh, 27 of 32 villages sampled in 2002 were located, and an additional 258 were randomly selected. Snow and insecurity limited access to 26 villages, resulting in a final sample of 259 villages (table 1). This study was approved by the Afghanistan Ministry of Public Health and Johns Hopkins University Institutional Review Boards. Oral consent was sought due to varying literacy rates in the country.

Statistical analysis

Analyses were done with Stata (versions 11 and 13). All vital events occurring from Jan 1, 2008, to Oct 16, 2011, (date of the last interview) were analysed. Person-time was accrued beginning on Jan 1, 2008, at birth, or when a person joined the household, and stopped accruing at the day of interview, death, or if a person left the household. Non-response was minimal (1%). Because a census of each randomly selected village was done with equal probability of selection, there were no sampling weights to incorporate into calculations.

Data quality checks included population composition, sex ratios at birth, and age ratios, none of which deviated significantly from expected.

The RAMOS-II dataset is available online.

For the RAMOS-II dataset see <https://zenodo.org/record/438680#.WNutOhQjEa0>

| | Kabul city, Kabul | Ragh, Badakshan |
|--|-------------------|---------------------|
| Crude death rate per 1000 population* | 4.9 (4.4–5.5) | 13.1 (12.6–13.6) |
| Maternal mortality ratio per 100 000 livebirths | 166 (63–270) | 713 (553–873) |
| Maternal mortality rate per 1000 women of reproductive age | 0.2 (0.1–0.3) | 1.7 (1.3–2.1) |
| Lifetime risk of maternal death† | 1 in 135 (51–218) | 1 in 16 (12–19) |
| Proportion of deaths in women of reproductive age due to maternal causes | 14% (6–22) | 42% (35–49) |
| Crude birth rate per 1000 population‡ | 28.9 (27.6–30.3) | 47.7 (46.1–49.4) |
| General fertility rate per 1000 women of reproductive age§ | 97 (92–101) | 190 (183–197) |
| Natural rate of population increase | 2.9 (2.8–3.0) | 4.2 (3.8–4.7) |
| Infant mortality rate per 1000 livebirths¶ | 24.8 (20.5–29.0) | 115.5 (108.6–122.3) |
| Perinatal mortality rate per 1000 livebirths | 29 (25–34) | 57 (53–62) |
| Neonatal mortality rate per 1000 livebirths** | 13.6 (10.5–16.7) | 50.7 (46.1–55.4) |
| Under-5 mortality rate per 1000 livebirths¶¶ | 36.7 (30.9–42.4) | 176.7 (168.3–185.0) |

Data are n (95% CI) or % (95% CI). *Crude death rates were calculated as the total number of deaths in months 0–11 before the survey interview divided by the midpoint population during that year (to obtain the midpoint population, starting with the total population in sampled households at the interview date, 1/2 of deaths during months 0–11 prior to interview were added back and 1/2 of births were subtracted). †Lifetime risk of maternal death was calculated as / (38*[maternal death rate]). We used the age range of 12–49 years (38 year span) rather than the typical 15–49 years (35 year span) due to early marriage and childbearing. ‡Crude birth rates were calculated as the total number of births in months 0–11 before the survey interview divided by the midpoint population during that year (multiplied by 1000). §The general fertility rate was calculated as the total number of births in months 0–11 before the interview over the number of women of reproductive age (ages 15–50 years, 50 included due to age heaping) who completed interviews (multiplied by 1000). ¶Under-5 and infant mortality rates were calculated by transforming direct estimates into probabilities of death per 1000 livebirths using standard life table formulas. ||Perinatal mortality was calculated as the number of stillbirths and early neonatal deaths (≤7 days age) over the total number of births (includes stillbirths and livebirths). **Neonatal mortality rates were calculated as the number of deaths within 28 days of life.

Table 2: Demographic indicators in Kabul city, Kabul and Ragh, Badakshan, 2008–11

Role of the funding source

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

Results

Data were collected between March 2, 2011, and Oct 16, 2011, from 130 688 participants: 63 329 in Kabul city, Kabul, and 67 359 in Ragh, Badakshan. An estimated 35 688 (27%) of the study population were women of reproductive age and nearly 20% were children younger than 5 years. In Kabul, the number of children under-5 was less than the number aged 5–9 years, which might reflect a decline in fertility or age misreporting. As expected, age heaping (where age is rounded to the nearest 5 or 10 years and is reflective of a largely innumerate population),^{3,20} was especially pronounced in older ages (≥50 years); this therefore did not affect maternal mortality estimates. Livebirth sex ratios did not significantly deviate from the expected ratio of approximately 1.05, suggesting minimal sex-selective under-reporting of births. Population pyramids for both districts reflect the expected demographic profile of each region (appendix p 1). In Ragh, the wide pyramid base indicates a young, high fertility population with high mortality overall, and high under-5 mortality.

See Online for appendix

| | Kabul city, Kabul (N=10) | Ragh, Badakshan (N=76) |
|--|--------------------------|------------------------|
| Demographic indicators | | |
| Age (years) | 27.2 (2.1) | 32.2 (0.9) |
| Literate | 4 (40%) | 6 (8%) |
| Husband literate | 8 (80%) | 21 (28%) |
| Socioeconomic status | | |
| Household assets | | |
| Own radio | 7 (70%) | 44 (58%) |
| Number living in household | 7.9 (1.0) | 9.5 (0.6) |
| Sufficient food | 4 (40%) | 37 (49%) |
| Obstetric history | | |
| Number of livebirths | 3.0 (0.8) | 5.6 (0.4) |
| Number of living children | 2.0 (0.7) | 3.4 (0.3) |
| History of stillbirth | 4 (40%) | 26 (35%) |
| Health-care access during last pregnancy before death | | |
| One or more antenatal care visit | 8 (80%) | 18 (24%) |
| Took antenatal vitamins during pregnancy | 5 (50%) | 13 (17%) |
| Given clean delivery kit | 0 | 4 (5%) |
| Skilled birth attendant at birth immediately preceding death | 9 (90%) | 16 (21%) |
| Ever used contraceptive | 3 (30%) | 5 (7%) |
| Outcome of last pregnancy before death | | |
| Livebirth | 2 (20%) | 50 (66%) |
| Child survived | 1/2 (50%) | 12/50 (24%) |
| Stillbirth | 3 (30%) | 8 (11%) |
| Undelivered, in labour | 0 | 9 (12%) |
| Pregnant, before onset of labour | 5 (50%) | 9 (12%) |

Data are mean (SD) or n (%).

Table 3: Characteristics of women who died of maternal causes in Kabul city, Kabul and Ragh, Badakshan, 2008–11

Of 16 669 women of reproductive age with livebirths during the recall period, 251 deaths were reported, including 86 maternal deaths (ten in Kabul, 76 in Ragh; table 1). All measures of mortality and fertility were significantly higher in Ragh than in Kabul (table 2). The maternal mortality ratio in Ragh (713 per 100 000 livebirths; 95% CI 553–873) was four times higher than in Kabul (166 per 100 000 livebirths; 63–270). We recorded similar patterns in lifetime risk of maternal death, maternal mortality rate, and proportion of deaths of women of reproductive age due to maternal causes, as well as crude and child mortality indicators (table 2). The maternal mortality rate calculated for Ragh was 8.5 times higher than for Kabul. We estimate that if Ragh had the same maternal mortality rate as Kabul, 83% fewer deaths, or only 13 would occur versus the 76 deaths reported. The general fertility rate in Ragh (190 per 1000 women of reproductive age; 95% CI 183–197) was 50% higher than in Kabul (97; 92–101), a pattern also reflected in the

number of livebirths reported among the deceased (table 3). Infant mortality and under-5 mortality were also higher in Ragh than in Kabul (infant mortality rate 116 per 1000 livebirths in Ragh vs 25 per 1000 livebirths in Kabul, under-5 mortality 177 per 1000 livebirths in Ragh vs 37 per 1000 livebirths in Kabul).

In Ragh, the proportion of maternal deaths (76 [42%] of 180) exceeded all other causes of death in women of reproductive age (figure 1). Of the 72 maternal deaths, 55 (72%) were attributed to direct causes: 27 (36%) to pregnancy-induced hypertensive diseases, 20 (26%) to haemorrhage, five (7%) to sepsis, and three (4%) to obstructed labour; ten (13%) were due to indirect causes; and the remaining eight had an unclear cause. In Kabul, ten (14%) of 71 deaths in women of reproductive age were maternal and attributed to pregnancy-induced hypertensive diseases (four [40%]), sepsis (two [20%]), haemorrhage (one [10%]), and indirect causes (one [10%]). In both sites, indirect deaths were from tuberculosis, malaria, obstetric tetanus, and circulatory diseases.

We noted differences in care-seeking between women in Kabul and Ragh: 80–90% of survivors in Kabul reported receiving both antenatal care and intrapartum care (ie, skilled birth attendance), whereas in Ragh only 3231 (28%) of 11437 women reported receiving antenatal care and 381 (3%) of 11352 reported having a skilled birth attendant (figure 2). Care-seeking of survivors and deceased did not differ substantially in Kabul. In Ragh, skilled birth attendance was higher in women who subsequently died (16 [21%] of 76) than in surviving women (381 [3%] of 11352), suggesting that women experiencing complications actively seek care, a finding supported by qualitative data published elsewhere¹³ (tables 3 and 4).

Women who died in Ragh were older, less likely to be literate, and fewer owned radios (which is indicative of household assets) than their counterparts in Kabul (table 3). In both Kabul and Ragh, a surprisingly low proportion of women who died had reported having sufficient food (four [40%] of ten in Kabul and 37 [49%] of 76 in Ragh). Women who died in Ragh had more births and living children. Only 50 (66%) of 76 women in Ragh had a livebirth before dying, and of these, only 12 (24%) survived.

To understand the context in which maternal death occurred, we studied care-seeking in all women (table 4) as well as out-of-pocket costs incurred for intrapartum and post-partum care (table 5). In Kabul, of the almost 90% (6036 of 6780) of women who accessed any antenatal care, 50% (3398) reported more than four visits, the recommended number at the time. Whereas in Ragh of the 3231 (28%) women who had any antenatal care, only 662 (6%) reported more than four visits. When asked about reasons for not seeking antenatal care, Ragh women reported transportation barriers (3407 [42%] of 8078) and not thinking it was important or necessary (1565 [19%]); the latter was also the main reason for foregoing antenatal care in Kabul (262 [39%] of 667).

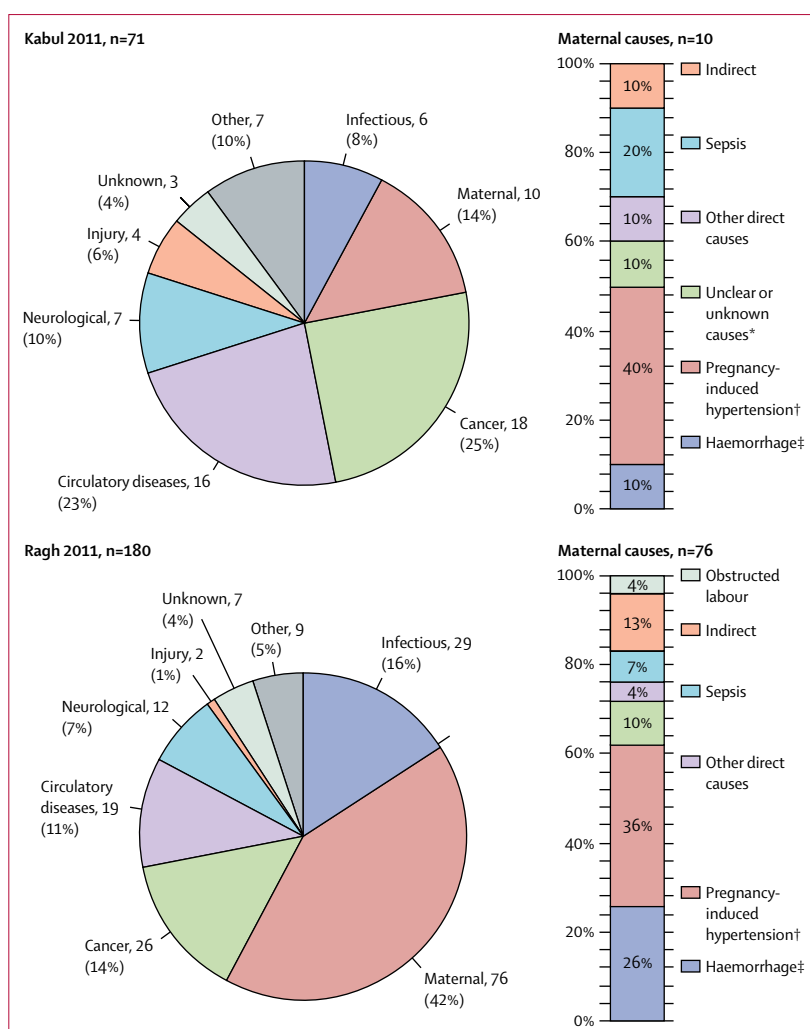


Figure 1: Causes of death in women of reproductive age in Kabul city, Kabul and Ragh, Badakshan, 2008–11

*Verbal autopsy was either done and the cause of death was found to be unclear but related to pregnancy, childbirth, or the post-partum period, or includes cases for which we could not investigate with verbal autopsy to confirm cause of death, but the family indicated that the cause of death was maternal during the death-identification survey. †Including pre-eclampsia and eclampsia and includes cases for which we could not investigate with verbal autopsy to confirm cause of death, but the family indicated that the cause of death was maternal during the death-identification survey. ‡Includes those related to placental abruption and placenta previa.

In Kabul, most births (5470 [81%] of 6789) took place at health facilities (table 4). The most common reason reported for not seeking delivery facility was that facility delivery was not deemed necessary. Conversely, in Ragh, the vast majority (11001 [97%] of 11366) of births occurred at home, and the main reason reported for not seeking facility-based delivery was transportation barriers (4448 [41%] of 10921). 5747 (85%) of 6789 respondents in Kabul and 5350 (47%) of 11366 in Ragh incurred intrapartum care costs (table 5). Among those who incurred costs, the mean cost was \$66.20 (median \$33.62) in Kabul and \$23.54 (\$9.89) in Ragh. Nearly half of all respondents reported paying out-of-pocket for gifts, the mean cost of which was \$18.44 (\$3.96) in Kabul and \$17.48 (\$9.89) in Ragh. Amongst sub-categories of

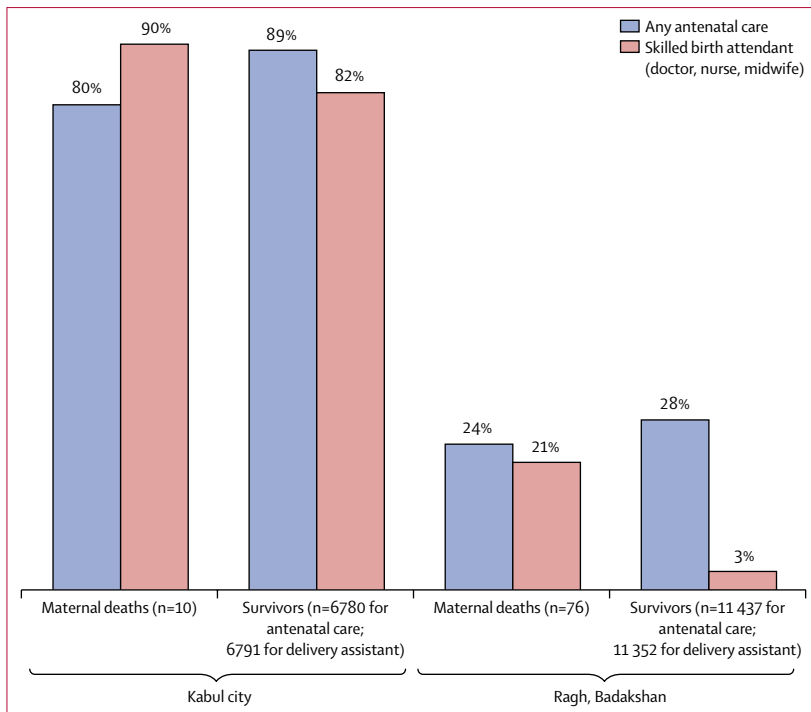


Figure 2: Care-seeking for antenatal care and delivery assistance for most recent pregnancy in deceased and surviving women in Kabul city, Kabul and Ragh, Badakshan, 2008–11

cost, drug costs were reported by 4893 (72%) of 6789 women in Kabul and 964 (8%) of 11366 women in Ragh at a mean cost of \$22·14 and \$4·32, respectively.

Post-partum care-seeking was low in both sites (table 4): 192 (17%) of 1131 women in Kabul and 1116 (10%) of 11310 in Ragh. 802 (71%) of 1131 women in Kabul sought care at a government hospital, whereas 686 (61%) of 1116 women in Ragh sought care at a health-care centre. Mean costs for post-partum care were \$36·95 (\$20·76) in Kabul and \$30·05 (\$12·85) in Ragh. In both sites, drug costs constituted the majority of out-of-pocket payments, followed by transportation and consultation fees (table 5).

Table 6 presents changes in demographic indicators between 2002 and 2011. All maternal mortality measures significantly decreased in Ragh between the two RAMOS studies. Although maternal mortality also decreased in Kabul, only the maternal mortality rate showed a significant decrease, possibly because of the small number of deaths found (n=10). Decreases in infant mortality rate and under-5 mortality were also found in both Kabul and Ragh. The appendix (p 2) presents differences in the two study populations. The total study population in 2011 was twice that of 2002, providing a sample size large enough to detect a 25% decrease in maternal mortality ratio. The percentage difference of women of reproductive age was 10% larger than the study population (62% more vs 53%) and might reflect improved female survival. We do not account for other population changes, such as migration.

Discussion

Our data suggest that remarkable improvements in maternal mortality can be achieved in a relatively short time, but also underscore persistent disparities between urban and rural areas. Marked inequity remains between rural Ragh, Badakshan, and Kabul city, as shown by the statistically higher measures of maternal mortality, including the maternal mortality ratio and rate in Ragh. The maternal mortality ratio of 713 per 100 000 livebirths in Ragh fits WHO's high maternal mortality strata (500–999 deaths per 100 000 livebirths), whereas that of Kabul (166 per 100 000 livebirths) matches WHO's moderate classification (100–299 deaths per 100 000 livebirths).¹ Patterns in care-seeking reflect these inequities: in Kabul, almost 80% of all women surveyed gave birth at a health facility compared with only 3% in Ragh. Other sources confirm significantly lower antenatal care and skilled birth attendance in women in lower wealth quintiles, as well as lower coverage of services in the northeast region (includes Badakshan) compared with Kabul.²¹ If similar mortality risk as in Ragh exists for the 75% of the population who live in rural areas,²² 83% of deaths could possibly be prevented by reaching the risk level in Kabul.

We recorded a substantial reduction in maternal mortality between the 2002 and 2011 RAMOS studies, including significant decreases in the maternal mortality rate in both Kabul and Ragh, as well as in the maternal mortality ratio and the lifetime risk of maternal deaths in Ragh.⁷ Although the proportion of deaths of women of reproductive age due to maternal causes decreased in Kabul and in Ragh,⁷ the relative burden remained the same; maternal deaths remained the leading cause of death in women of reproductive age in Ragh, and the third leading cause among women of reproductive age in Kabul. We noted significant decreases in nearly all other mortality indicators in both sites, including infant mortality rate and under-5 mortality. While changes in crude birth rate and general fertility rate between 2002 and 2011 were also significant, these decreased in Kabul but increased in Badakshan, as did the natural rate of population increase. This pattern is also reflected in the increase in number of livebirths and living children among women who died in Badakshan.

Additional maternal mortality ratio estimates present a complex picture. In addition to RAMOS-II, three major surveys have been done since 2010: a Socio Demographic and Economic Survey (SDES) implemented by the Central Statistics Office and United Nations Population Fund (UNFPA) in nine of 34 provinces between 2011 and 2016; the 2010 AMS; and the 2015 Demographic and Health Survey;²³ the latter two calculated national maternal mortality ratio estimates. The SDES sampled half of each province's populations: maternal mortality ratios ranged from 293 in Kabul to 1882 in Ghor.²⁴ If the newly released DHS maternal mortality ratio estimate of 1291 per 100 000 livebirths (95% CI 1071–1512) is an overestimate as

| | Kabul City, Kabul | Ragh, Badakshan |
|--|-------------------|-----------------|
| Care-seeking during pregnancy | 6780 | 11 437 |
| Any antenatal care | 6036 (89%) | 3231 (28%) |
| Antenatal care 4+ | 3398 (50%) | 662 (5.8%) |
| Source of antenatal care | | |
| Private hospital | 525 (9%) | 1 (0%) |
| Government hospital | 4652 (77%) | 598 (19%) |
| Health centre | 727 (12%) | 2445 (76%) |
| Health facility subtotal | 5936 (98%) | 3044 (94%) |
| Residence | 46 (1%) | 153 (5%) |
| Other | 85 (1%) | 34 (1%) |
| Reasons for not obtaining antenatal care | 667 | 8078 |
| Financial problems | 121 (18%) | 734 (9%) |
| Transportation | 66 (10%) | 3407 (42%) |
| Lack of quality care | 50 (8%) | 1057 (13%) |
| Lack of female provider | 8 (1%) | 46 (0.6%) |
| Discrimination | 137 (21%) | 1223 (13%) |
| Not necessary or not important | 262 (39%) | 1565 (19%) |
| Other | 23 (3%) | 46 (1%) |
| Care-seeking for delivery | 6789 | 11 366 |
| Delivery location | | |
| Private hospital | 3431 (51%) | 1 (0%) |
| Government hospital | 1763 (26%) | 134 (1%) |
| Health centre | 276 (4%) | 212 (2%) |
| Health facility sub-total: | 5470 (81%) | 347 (3%) |
| Residence | 1271 (19%) | 11 001 (97%) |
| Other or don't know | 48 (1%) | 18 (0%) |
| Delivery assistant | 6791 | 11 352 |
| Skilled birth attendant (doctor, nurse, midwife) | 5594 (82%) | 381 (3%) |
| Family member | 965 (14%) | 7254 (64%) |
| Daya or traditional birth attendant | 96 (1%) | 3002 (26%) |
| Community health worker | 136 (2%) | 715 (6%) |

(Table 4 continues in next column)

| | Kabul City, Kabul | Ragh, Badakshan |
|--|-------------------|-----------------|
| (Continued from previous column) | | |
| Reasons for not obtaining delivery care at a health facility | 1083 | 10 921 |
| Financial problems | 201 (19%) | 873 (8%) |
| Transportation | 234 (22%) | 4448 (41%) |
| Lack of quality care | 104 (10%) | 1662 (15%) |
| Lack of female provider | 27 (3%) | 94 (1%) |
| Security problems | 4 (0%) | 2 (0%) |
| Discrimination | 143 (13%) | 1356 (12%) |
| Not necessary or not important | 292 (27%) | 2376 (22%) |
| Other | 78 (7%) | 110 (1%) |
| Post-partum care-seeking | 6705 | 11 310 |
| Any post-partum care | 1131 (17%) | 1116 (10%) |
| Source of post-partum care | | |
| Private hospital | 195 (17%) | 1 (0%) |
| Government hospital | 802 (71%) | 245 (22%) |
| Health centre | 71 (6%) | 686 (61%) |
| Health facility subtotal | 1077 (94%) | 932 (83%) |
| Residence | 30 (3%) | 174 (16%) |
| Other | 33 (3%) | 10 (1%) |

The number of pregnancies is higher than the reported number of livebirths in table 1 as here we include all pregnancies regardless of birth outcome.

Table 4: Pregnancy, delivery, and post-partum care-seeking patterns in women in Kabul city, Kabul and Ragh, Badakshan, 2008–11

suggested in the report, and the AMS an underestimate at 327 per 100 000 livebirths (260–394), trend assessment is difficult. However, the magnitude of difference between the two studies suggests that maternal mortality has increased since 2010. The UN Maternal Mortality Estimation Group's maternal mortality ratio estimates suggest that mortality declined by 67% in Afghanistan from 1100 deaths per 100 000 livebirths (95% CI 745–1570) in 2000 to 396 (95% CI 253–620) in 2015,¹ but the 2010 onwards estimates drew from the 2010 AMS. Independent maternal mortality ratio estimates modelled by the Institute of Health Metrics and Evaluation, which did not use AMS data in their estimation, suggest that no change has occurred since 1990 (maternal mortality ratio 732 per 100 000 livebirths, 95% CI 451–1131), and that the maternal mortality ratio in 2015 was 789 per 100 000 livebirths, 464–1219).² Confidence intervals for RAMOS-I and RAMOS-II estimates, which show a decrease in maternal

mortality, do not overlap; neither do confidence intervals for the 2010 AMS and 2015 DHS national estimates, which conversely show an increase. Qualitative research done as part of RAMOS-II also points to a decrease in national maternal mortality between 2000 and 2010. We postulate that the reported increase in maternal mortality from the DHS occurred amidst increasing insecurity since 2010, but additional multi-disciplinary research may help shed light on the matter.

While maternal mortality is a complex, multi-faceted problem, decreases recorded between RAMOS-I and RAMOS-II might be explained by several factors including prevention of mistimed and higher risk pregnancies; general improvements in women's health, nutrition, and wellbeing;^{13,25} and fewer maternal deaths due to increased availability and quality of care.¹³ The Ministry of Public Health's focus on maternal and child health led to well documented improvements across all levels of the health system including the establishment of a midwifery workforce, increased availability of primary health care, and improved family planning coverage, antenatal care, skilled birth attendance, immunisation, and nutrition.^{9,11,13,26} Socioeconomic and intersectoral developments must also be recognised as contributors to improved maternal health.²⁵ Increases in female literacy observed in our sample population mirror national trends, which suggest that from 2001 to 2011 the number of children attending school increased from 1 million to 7.2 million.¹¹ Since 2002, completion of national and regional highways impacted mobility and livelihood

| | Kabul city, Kabul | | Ragh, Badakshan | |
|---|-------------------|----------------------------|-------------------|------------------------------|
| | Incurred any cost | Cost (US\$)* | Incurred any cost | Cost (US\$)* |
| Care-seeking for delivery | 6789 | .. | 11366 | .. |
| Total cost | 5747 (85%) | \$66.20/\$33.62 (\$61.30) | 5350 (47%) | \$23.54/ \$9.89 (\$11.87) |
| Delivery gifts | 3234 (48%) | \$18.44/\$3.96 (\$13.84) | 4771 (42%) | \$17.48 /\$9.89 (\$13.84) |
| Transportation | 4173 (61%) | \$6.41/\$5.93 (\$8.90) | 134 (1%) | \$1.43/\$0.00 (\$0.00) |
| Drugs | 4893 (72%) | \$22.14/\$9.89 (\$14.83) | 964 (8%) | \$4.32/\$0.00 (\$0.00) |
| Consultation fees | 1406 (21%) | \$14.33/\$0.00 (\$0.00) | 203 (2%) | \$0.27/\$0.00 (\$0.00) |
| Bed fees | 483 (7%) | \$4.87/\$0.00 (\$0.00) | 21 (0%) | \$0.04/\$0.00 (\$0.00) |
| Other: blood, laboratory, surgical fees | 1544 (23%) | \$12.38/\$0.00 (\$3.96) | 468 (4%) | \$2.01/\$0.00 (\$0.00) |
| Costs by source | | | | |
| Residence | 768 (60%) | \$25.29/\$9.89 (\$23.73) | 5065 (46%) | \$20.72/\$9.89 (\$12.85) |
| Health centre | 248 (90%) | \$40.47/\$25.71 (\$33.12) | 55 (74%) | \$41.12/\$19.78 (\$39.55) |
| Government hospital | 1498 (85%) | \$125.74/\$92.94 (\$87.01) | 119 (89%) | \$119.99/\$59.33 (\$169.87) |
| Private hospital | 3000 (93%) | \$50.18/\$29.66 (\$33.62) | 1 (100%) | \$63.28/\$63.28 (\$63.28) |
| Other | 33 (69%) | \$61.45/\$53.39 (\$65.26) | 8 (44%) | \$22.49/\$9.89 (\$14.83) |
| Post-partum care-seeking | 1131 | .. | 1116 | .. |
| Total cost | 1028 (91%) | \$36.95/\$20.76 (\$26.70) | 897 (80%) | \$30.05/\$12.85 (\$17.80) |
| Transportation | 764 (68%) | \$4.93/\$3.96 (\$5.93) | 147 (13%) | \$5.48/\$0.00 (\$0.00) |
| Drugs | 913 (81%) | \$21.84/\$11.87 (\$13.84) | 858 (77%) | \$20.81/\$9.89 (\$13.85) |
| Consultation fees | 676 (60%) | \$4.66/\$2.97 (\$3.96) | 194 (17%) | \$1.17/\$0.00 (\$0.00) |
| Bed fees | 19 (2%) | \$0.84/\$0.00 (\$0.00) | 6 (1%) | \$0.40/\$0.00 (\$0.00) |
| Other: laboratory, blood | 91 (8%) | \$10.70/\$0.00 (\$0.00) | 77 (7%) | \$2.20/\$0.00 (\$0.00) |
| Costs by source | | | | |
| Residence | 26 (87%) | \$38.29/\$19.78 (\$54.38) | 146 (84%) | \$28.30/ \$10.58 (\$12.06) |
| Health centre | 63 (89%) | \$27.66/ \$15.82 (\$23.73) | 530 (77%) | \$21.93/ \$11.87 (\$11.87) |
| Government hospital | 742 (93%) | \$39.47/ \$22.74 (\$26.70) | 212 (87%) | \$50.53/ \$19.78 (\$40.54) |
| Private hospital | 174 (90%) | \$28.61/ \$17.80 (\$20.76) | 1 (100%) | \$316.41/\$316.41 (\$316.41) |
| Other | 23 (70%) | \$42.71/ \$27.69 (\$32.23) | 8 (80%) | \$22.00/ \$15.82 (\$29.66) |

Data are n, n (%), or mean/median (IQR). *The denominator includes only those women who incurred a cost. Costs calculated using the 2015 exchange rate.

Table 5: Out-of-pocket costs incurred by households for care-seeking during delivery and post-partum in 2016 USD in Kabul City, Kabul and Ragh, Badakshan, 2008–11

opportunities. The average income per person increased from US\$120 in 2001 to \$622 in 2011, along with increased government revenues from \$200 million to \$1.65 billion in 2011.²⁷ However, wide disparities persist and population-based studies also report significant variation in the availability and provision of care.¹⁰

Appraising each district in more detail, the country's capital and largest city Kabul benefited from investments in health facilities, staffing, and resources; health service availability increased substantially between the two RAMOS studies, and antenatal care, skilled attendance, and contraceptive use climbed. Ministry of Public Health statistics show the caesarean rate in Kabul province was 8% in 2011 (Sayed Ataullah Sayedzai, Ministry of Public Health, personal communication). History has shown that rapid decreases reducing maternal mortality ratios to less than 200 can happen when quality emergency obstetric care is scaled up.²⁸ Maternal mortality reductions recorded in Kabul are similar to those reported in other low-income and middle-income countries in the late 20th century, including Thailand, Sri Lanka, and

Bangladesh, which were attributed to significant improvement in skilled attendance coverage, primarily from midwives using aseptic techniques with referral systems for complicated deliveries. Enhanced efforts in the 1940s (Sri Lanka) occurred to ensure free village-level care as well as confidential maternal death reviews to further improve quality care.²⁹

Factors underpinning the significant decrease in rural Ragh are more complex. The higher number of births providing a larger denominator in Ragh explains some of the lower maternal mortality ratio estimate. But in 2002, there was minimal basic emergency obstetric care in the district and no roads to access the comprehensive emergency obstetric care hospital in the provincial capital; by 2011, there were three clinics in Ragh, one with comprehensive and two with basic emergency obstetric care capacity, and paved roads to facilitate referrals to the provincial hospital. Women facing complications were more likely to seek care (21% of deceased women accessed skilled delivery vs 3% of surviving), which might partly explain this low overall skilled attendance concurrent with

| | Kabul city, Kabul | | | Ragh, Badakshan | | |
|---|-------------------|-------------------|----------------|------------------|----------------------|----------------|
| | 2002 | 2011 | Overall change | 2002 | 2011 | Overall change |
| Crude death rate per 1000 population* | 5.7 (5.2–6.1) | 4.9 (4.4–5.5)† | –14% | 27 (25–29) | 13.1 (12.6–13.6)† | –51% |
| Maternal mortality ratio per 100 000 livebirths | 418 (235–602) | 166 (63–270) | –60% | 6507 (5026–7988) | 713 (553–873)† | –89% |
| Maternal mortality rate per 1000 women of reproductive age | 0.7 (0.4–1.0) | 0.2 (0.1–0.3)† | –71% | 10.5 (8.2–12.9) | 1.7 (1.3–2.1)† | –84% |
| Lifetime risk of maternal death | 1 in 42 (29–74) | 1 in 135 (51–218) | .. | 1 in 3 (3–4) | 1 in 16 (12–19)† | .. |
| Proportion of deaths among women of reproductive age due to maternal causes | 16% | 14% (6–22) | –13% | 65% | 42% (35–49) | –35% |
| Crude birth rate per 1000 population* | 36 (35–37) | 29 (28–30)† | –19% | 36 (34–38) | 48 (46–49)† | 33% |
| General fertility rate per 1000 women of reproductive age* | 166 (160–171) | 97 (92–101)† | –42% | 162 (151–173) | 190 (183–197)† | 17% |
| Natural rate of population increase | 3.1 (3.0–3.2) | 2.9 (2.8–3.0) | .. | 0.9 (0.7–1.2) | 4.2 (3.8–4.7)† | .. |
| Infant mortality rate | 78 (64–91) | 24.8 (20.5–29.0)† | –68% | 217 (178–257) | 115.5 (108.6–122.3)† | –47% |
| Perinatal death rate | 29 (24–34) | 29 (25–34) | 0% | 106 (87–127) | 57 (53–62)† | –46% |
| Neonatal death rate | NA | 13.6 (10.5–16.7) | .. | NA | 50.7 (46.1–55.4) | .. |
| Under-5 death rate | 109 (87–130) | 36.7 (30.9–42.4)† | –66% | 323 (266–378) | 176.7 (168.3–185.0)† | –45% |

Data are n (95% CI) or %. NA=not available. *In 2002 the crude birth rate, crude death rate, and general fertility rate were calculated with person-years denominators and a 3-year time period. Because the sample sizes were much larger in the 2011 survey, we chose to use the more standard 0–11 month period before the survey for tabulating births and deaths and the midpoint population of that period for the denominator. Unless there were major fluctuations in the rates in the 3 years before each survey, the rates from the two methods should be quite comparable. †Signifies significant difference measured by calculating 95% CIs around each estimate and compared to the 95% CIs if available from the 2002 published report. Rates calculated as in table 2.

Table 6: Overall change in demographic indicators in Kabul city, Kabul and Ragh, Badakshan, 2002 and 2011*

the significant decrease in maternal mortality. We were unable to identify data for earlier caesarean rates, but local sources assert that timely access to Faizabad for a caesarean was very rare—an assertion supported by the RAMOS-I finding that none of the deceased women delivered with a skilled attendant. Health Management Information System (HMIS) reports indicate that the caesarean rate in Badakshan province was 2.5% in 2011 (Sayed Ataullah Sayedzai, Ministry of Public Health, personal communication). This pattern was also documented in Nepal—a country challenged with similar mountainous terrain, seasonal weather, and dispersed population to Afghanistan. Yet Nepal's maternal mortality ratio halved from 539 in 1996 to 221 in 2006. Factors contributing to this decline are uncertain as skilled attendant coverage and facility use were very low, and quality of care improvements unlikely, although caesarean section deliveries tripled over the decade to nearly 3% in rural areas.³⁰

Supporting development of the health system and related sectors should be the goal in all settings. However, public health programming to reduce maternal deaths should be tailored for different contexts. The obstetric transition framework can guide priority strategies.^{31,32} In rural settings like Ragh, improved health facility infrastructure and skilled attendance, as well as efforts to address the barriers to timely decisions to seek and the ability to access care, are important, yet more fully realised primary prevention efforts can save lives. More than 26 000 community health workers, half female, were deployed nationally since 2002; however, monitoring is difficult and this platform is not fully used.³³ Continuing to strengthen this platform to provide evidence-based interventions is essential to ensure

complete coverage of community-distributed pre-conception, antenatal care, and postnatal interventions including contraceptives, iron-folate supplementation, antimalarial bednets (where malaria is endemic), clean delivery kits, and further scale up of the existing community-based misoprostol distribution programme. Increasing district-level emergency obstetric care availability beyond the WHO guideline of one comprehensive emergency obstetric care per 100 000 population is recommended. Outreach, and task shifting from doctors to midwives and midwives to community health workers, has proven effective in similar settings.³⁴ Community mobilisation, including women-led community health committees, home visitation, addressing financial barriers with demand and supply financial schemes, and maternity waiting homes can aid referral.³⁵ The challenging context merits innovation: promising interventions include walking blood banks and diagnostic and referral methods for community health workers to identify newborn and maternal sepsis.³⁶ As mobile phone technology has flourished, exploring mHealth applications to promote care-seeking and facilitate referrals is merited.³⁷ Addressing the snow-bound winters in Ragh merits exploration of simple transport methods used in other countries with severe winter conditions, for example, snowshoes and dog-sleds for transporting ill women.

In Kabul, the situation is quite different. In settings with high levels of skilled birth attendance, programmes should emphasise quality, respect, and specialised care, and avoid over-medicalisation.³² Quality care is a concern and efforts must be sustained in this area.^{38,39} Koblinsky and colleagues note that “Adherence to high-quality

clinical practice guidelines, combined with simulation-based training, can improve providers' knowledge, clinical skills, attitudes, and women-centred approaches.³² Maternal death reviews can improve quality of care: the "Maternal Death Surveillance and Response" programme is implemented in Afghanistan, but is not fully implemented.⁴⁰ The needs of the peri-urban poor with less health-care access need addressing.

In both districts, the cost of delivery care was concerning (especially in government hospitals), as were informal gifts to providers and the cost of drugs. Analyses of trends suggest that from 2008 to 2012, total health expenditures in Afghanistan increased by 24%, corresponding to per capital spending of US\$56 in 2012.⁴¹ Of these expenditures, 16% addressed reproductive, maternal, and newborn health, of which 74% was attributed to out-of-pocket spending borne by the household.⁴¹ While the Ministry of Public Health policy mandates that "the following... will be provided free of charge to any citizen of Afghanistan: immunisation, maternal delivery, antenatal care, family planning...",⁴² in practice this is not occurring and underscores the need to promote better accountability and equitable access to essential, quality services.

Pregnancy-induced hypertension was the leading cause of maternal death in both districts. In 2002, RAMOS-I found haemorrhage to be the leading cause of maternal death in Kabul and obstructed labour to be the most frequent cause in Ragh.⁷ Although not the leading cause, the WHO and Institute for Health Metrics and Evaluation (IHME) estimates support the finding that maternal deaths associated with pregnancy-induced hypertensive diseases increased nationally. A 2010 national survey of comprehensive emergency obstetric and newborn care facilities reported adequate magnesium sulphate supplies.¹⁰ Greater understanding of the increase in pregnancy-induced hypertensive disease deaths, including assessment of the quality of facility-based care available for prevention and management of complications, is needed. Community-based interventions to prevent and manage pregnancy-induced hypertensive diseases that merit exploration include calcium supplementation, prophylactic low-dose aspirin, and early detection or referral.⁴³

There are several limitations associated with this study. An objective of the study was to measure differences in maternal mortality from 2002 to 2011. We were unable to use the raw data from 2002, which limited opportunities for temporal analyses: we present overall trends in mortality drawing from the published 2002 report.⁵ In 2002, no hospital or death records existed, forcing reliance on the household survey alone. In 2011, continued gaps in record-keeping also limited death identification to a household survey. Insecure and more remote areas are less accessible for data collection and might have worse outcomes than accessible areas, potentially biasing results towards indicating a greater mortality risk reduction (fewer maternal deaths found). The small number of maternal deaths in Kabul indicate that sub-analyses

should be interpreted with caution. The validity of verbal autopsy for maternal death identification is established, but additional verbal autopsy studies might benefit from one of the electronic diagnostic methods available.^{44,45}

Improvements in maternal health services achieved in the decade between RAMOS-I in 2002 and RAMOS-II in 2011 are admirable, especially during a challenging decade as the country strove to emerge from more than 30 years of conflict. Evidence that significant reductions in maternal mortality can be achieved in a relatively short time provides motivation for continuing efforts in Afghanistan and other low-resource settings. Dedicated programme efforts continue today;⁴⁶ however, our data highlight an alarming inequity in health outcomes between urban and rural or remote areas. The recent evidence from the 2015 DHS of a potential increase since 2010 is also concerning. Both contextualised programmatic action and reliable maternal mortality measurement sources to document change are needed. Population-based maternal/newborn surveillance systems or sample vital registration with verbal autopsy should be considered. In 2002, the massive response to maternal health in the country necessitated a centralised top-down strategy. Now is the time to change to a locally led, decentralised bottom-up mode of strategic planning to address differing implementation needs in different geographic, cultural, and security conditions and provide quality maternity services for all women and their families.

Contributors

LB was the Principal Investigator. LB, AL, and SAS designed the data collection instruments. LB, AL, AJR, ST, WZ, and SAS coordinated data collection and management. HT, PW, and LZ led the qualitative component of the study. MK provided critical expertise on determining health-system changes. SB, LZ, and AL did the statistical analyses. LB and AL wrote the first draft of the paper with inputs from all other authors.

Declaration of interests

We declare no competing interests.

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