Report of a WHO Technical Consultation on Birth Spacing

Geneva, Switzerland
13–15 June 2005

World Health Organization

Department of Making Pregnancy Safer (MPS)
Department of Reproductive Health and Research (RHR)

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1. EXECUTIVE SUMMARY

Recommendations for birth spacing made by international organizations are based on information that was available several years ago. While publications by the World Health Organization (WHO) and other international organizations recommend waiting at least 2–3 years between pregnancies to reduce infant and child mortality, and also to benefit maternal health, recent studies supported by the United States Agency for International Development (USAID) have suggested that longer birth spacing, 3–5 years, might be more advantageous. Country and regional programmes have requested that WHO clarify the significance of the USAID-supported studies.

With support from USAID, WHO undertook a review of the evidence. From 13 to 15 June 2005, 37 international experts, including the authors of the background papers and WHO and United Nations Children's Fund (UNICEF) staff, participated in a WHO technical consultation held at WHO Headquarters in Geneva. The objective of the meeting was to review evidence on the relationship between different birth-spacing intervals and maternal, infant and child health outcomes and to provide advice about a recommended interval.

Six background papers were considered, along with one supplementary paper. Prior to the meeting, the six main papers were sent to experts for review. Thirty reviews were received: 10 from staff in international organizations and 20 from experts from 13 countries. The reviews were compiled and circulated to all meeting participants. At the meeting, the authors of the background papers presented their work, and selected discussants presented the consolidated set of comments, including their own observations. Together, the draft papers and the various commentaries formed the basis for the discussions of the evidence and for the recommendations made by the group at the meeting for spacing after a live birth and after an abortion.

The background papers contained evidence from studies that used a variety of research designs and analytical techniques. All the papers submitted were drafts, subject to revision based on the discussions. One study used longitudinal data from Matlab, Bangladesh (DaVanzo et al., draft, no date); one contained an analysis of cross-sectional Demographic and Health Surveys (DHS) data from 17 countries (Rutstein, draft, no date). Three of the main background papers were reviews: two provided data from systematic reviews and meta-analysis (Conde-Agudelo, draft 2004; Rutstein et al., draft 2004), and one reviewed literature pertaining specifically to maternal and child nutrition (Dewey and Cohen, draft 2004). The supplementary paper reviewed three studies that used birth records from Michigan and Utah, USA (Zhu, draft 2004). One other background paper specifically looked at post-abortion (miscarriage and induced abortion) inter-pregnancy intervals in Latin America, using hospital records (Conde-Agudelo et al., draft 2004). A list of the papers discussed, the meeting agenda, and the list of participants is given in Annexes 1–3. Together, the set of papers provided an extensive collection of information on the relationship between birth-spacing intervals and maternal, infant and child health outcomes.

The meeting participants noted that the length of intervals analysed and terminology used in the studies varied, making it difficult to compare results. It was therefore agreed that birth-to-pregnancy interval would be used as standard for presenting recommendations. This measure refers to the interval between the date of a live birth and the start of the subsequent pregnancy.

The group discussed the strengths and limitations of the studies presented and of the results. Additional analyses and issues to be addressed in the research reviewed were identified, as were gaps in the body of research. The authors are currently undertaking additional analyses to respond to questions raised at the meeting. These analyses and the final papers will be reviewed when they are available. A supplementary report will be issued at that time.

1.1 Recommendations

The background papers, the expert reviews, and the discussions at the meeting comprised a timely analysis of the latest available evidence on the effects of birth spacing on maternal and child health. The group came to separate conclusions for the different outcomes considered, which were encompassed in two overall recommendations; one on birth spacing after a live birth and one on spacing after an abortion. The particulars of the recommendations and the necessary caveats are noted in detail in the body of the report. The group emphasized that the recommendations must be read in conjunction with the preamble below.

Preamble

Individuals and couples should consider health risks and benefits along with other circumstances such as their age, fecundity, fertility aspirations, access to health services, child-rearing support, social and economic circumstances, and personal preferences in making choices for the timing of the next pregnancy.

Recommendation for spacing after a live birth

After a live birth, the recommended interval before attempting the next pregnancy is at least 24 months in order to reduce the risk of adverse maternal, perinatal and infant outcomes. [1]

Rationale for the recommendation

The studies presented at the meeting considered various maternal, infant and child health outcomes. For each outcome, different birth-to-pregnancy intervals were associated with highest and lowest risks. To summarize, birth-to-pregnancy intervals of six months or shorter are associated with elevated risk of maternal mortality. Birth-to-pregnancy intervals of around 18 months or shorter are associated with elevated risk of infant, neonatal and perinatal mortality, low birth weight, small size for gestational age, and pre-term delivery. Some "residual" elevated risk might be associated with the interval 18–27 months, but interpretation of the degree of this risk depended on the specific analytical techniques used in a meta-analysis. Otherwise, the evidence to discriminate within the interval of 18–27 months was limited. Further analysis was requested to clarify this point. As mentioned, this additional work is being completed and will be considered at a future date.

Evidence about relationships between birth spacing and child mortality was presented but the participants did not reach agreement on its interpretation.

On the basis of the evidence available at the time, the participants fell into two groups: those who considered that the evidence indicated that the most suitable recommended interval was 18 months, and those who considered that the evidence supported a recommended interval of 27 months. Participants were, however, unanimous in agreeing that birth-to-pregnancy intervals shorter than 18 months should be avoided.

At the meeting, a compromise was reached between the two groups, who agreed that the recommendation for the minimum interval between a live birth and attempting next pregnancy should be 24 months.

The basis for the recommendation is that waiting 24 months before trying to become pregnant after a live birth will help avoid the range of birth-to-pregnancy intervals associated with the highest risk of poor maternal, perinatal, neonatal, and infant health outcomes. In addition, this recommended interval was considered consistent with the WHO/UNICEF recommendation of breastfeeding for at

[1] Some participants felt that it was important to note in the report that, in the case of birth-to-pregnancy intervals of five years or more, there is evidence of an increased risk of pre-eclampsia, and of some adverse perinatal outcomes, namely pre-term birth, low birth weight and small infant size for gestational age.

least two years, and was also considered easy to use in programmes: "two years" may be clearer than "18 months" or "27 months".

Recommendation for spacing after an abortion
After a miscarriage or induced abortion, the recommended minimum interval to next pregnancy is at least six months in order to reduce risks of adverse maternal and perinatal outcomes.

Caveat
This recommendation for post-abortion pregnancy intervals is based on one study in Latin America, using hospital records for 258,108 women delivering singleton infants whose previous pregnancy ended in abortion. Because this study was the only one available on this scale, it was considered important to use these data, with some qualifications. Abortion events in the study included a mixture of three types – safe abortion, unsafe abortion and spontaneous pregnancy loss (miscarriage), and the relative proportions of each of these types were unknown. The sample was from public hospitals in Latin America only, with much of the data coming from two countries (Argentina and Uruguay). Thus, the results may be neither generalizable within the region nor to other regions, which have different legal and service contexts and conditions. Additional research is recommended to clarify these findings.

1.2 Suggested areas for future research

- Development of coherent theoretical frameworks explaining and analysing the possible causal mechanisms of birth spacing on outcomes, particularly child mortality, was identified as important for future research.

- Analyses of relationships between birth spacing and maternal morbidity would be useful to add to the few existing studies. For instance, examination of the effects of multiple short birth-to-pregnancy intervals would be useful, as would be more detailed data on the effects of very long intervals. Further analysis of the relationship between birth spacing and maternal mortality would help confirm or refute existing findings, although it is acknowledged that this may often be unfeasible as it may require a very large number of cases.

- There is a need to investigate the relationship between birth spacing and outcomes other than mortality, for instance, maternal and child nutrition outcomes, or impact on child psychological development. Also, it would be helpful to have information on possible benefits, as well as possible risks, of particular spacing intervals.

- More studies on the effects of post-abortion pregnancy intervals are needed in different regions. A distinction between induced and spontaneous abortion, and between safe and unsafe induced abortion, would be particularly helpful in future studies.

- Good-quality longitudinal studies that take more potential confounding factors into account are needed to:

  1. clarify the observed associations between birth-to-pregnancy intervals and maternal, infant and child outcomes;

  2. estimate the potential level of bias in the use of different measures of intervals (birth-to-birth vs. inter-pregnancy interval, for instance);

  3. clarify the potentially confounding effect of short intervals following a child death, both because of shortened breastfeeding and because parents may seek to replace the dead child.

- Finally, there is a need to develop an evidence base for effective interventions to put birth-spacing recommendations into practice.

2. INTRODUCTION

Recommendations for birth spacing made by international organizations are based on information that was available several years ago. While publications by the World Health Organization (WHO) and other international organizations recommend waiting at least 2–3 years between pregnancies to reduce infant and child mortality, and also to benefit maternal health, recent studies supported by the United States Agency for International Development (USAID) have suggested that longer birth spacing, 3–5 years, might be more advantageous. Country and regional programmes have requested that WHO clarify the significance of the USAID-supported studies.

With support from USAID, WHO undertook a review of the evidence. From 13 to 15 June 2005, 30 international experts, including the authors of the background papers and WHO and United Nations Children's Fund (UNICEF) staff, participated in a WHO technical consultation held at WHO Headquarters in Geneva. The objective of the meeting was to review evidence on the relationship between different birth-spacing intervals and maternal, infant and child health outcomes and to provide advice about a recommended interval.

Six background papers were considered, along with one supplementary paper. All the papers submitted were drafts, subject to revision based on the discussions. (See Annex 1 for a list of the papers reviewed at the meeting.)

Prior to the meeting, the six main papers were sent to experts for review. Thirty reviews were received: 10 from staff in international organizations and 20 from experts from 13 countries. The reviews were compiled and circulated to all meeting participants. At the meeting, the authors of the background papers presented their work, and selected discussants presented the consolidated set of comments, including their own observations. Together, the draft papers and the various commentaries formed the basis for the discussions of the evidence and for the recommendations made by the group at the meeting for spacing after a live birth and after an abortion.

The background papers contained evidence from studies that used a variety of research designs and analytical techniques. One study used cohort data from Matlab, Bangladesh (3) one contained an analysis of cross-sectional Demographic and Health Surveys (DHS) data from 17 countries (5). Three of the main background papers were reviews: two provided data from systematic reviews and meta-analysis (1, 6), and one reviewed literature pertaining specifically to maternal and child nutrition (4). The supplementary paper reviewed three studies that used birth records from Michigan and Utah, USA (7). One other background paper specifically looked at post-abortion (miscarriage and induced abortion) inter-pregnancy intervals in Latin America, using hospital records (2). Together, the set of papers provided an extensive collection of information on the relationship between birth-spacing intervals and maternal, infant and child health outcomes.

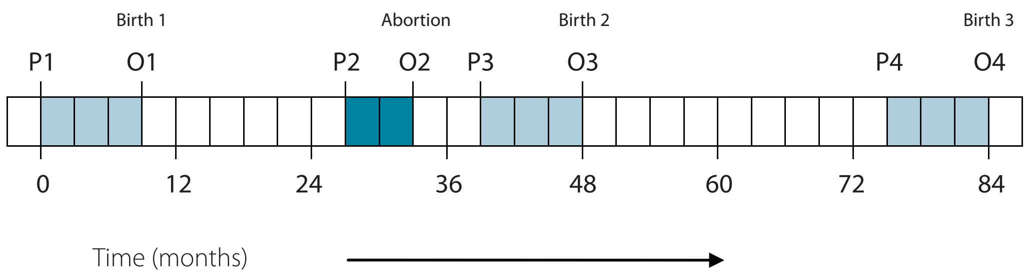
This report provides a summary of the technical consultation meeting. The meeting agenda and the list of participants are given in Annexes 2 and 3.

The working groups presented their conclusions in a final plenary session, at which the overall recommendations were agreed. The final conclusions are presented at the end of this report, along with gaps in research identified at the meeting. During the meeting, additional analyses and clarifications were requested from the authors of the papers. The authors are currently undertaking these analyses, responding to the questions raised at the meeting and drafting final versions of the papers. The additional analyses and the final papers will be reviewed when they are available. A supplementary report will be issued at that time.

2.1 Spacing terminology [2]

One of the tasks at the meeting was to address the fact that the length of intervals analysed and terminology in the studies varied, making it difficult to compare results. A summary of these measures is given in Table 1. There was a discussion of how to reconcile these different measures in a way that would allow comparison between studies. As a starting point to define terms, the following timeline was presented as an example (See Figure 1. below).
Each square on the timeline represents three months. Each pregnancy has an initiation date (P) and an outcome date

Figure 1.



(O), at which the pregnancy ends with either a birth (O1, O3 and O4 in the figure) or other termination (miscarriage or induced abortion: O2 in the figure). The duration of time from P to O is the gestation period. In practice, reported date of last menstrual period is usually measured, not the initiation of pregnancy itself.

To ease comparison of findings across studies, given the wide range of different interval measures used, and in line with the agreed terminology for the recommendations, the main text of this report only uses birth-to-pregnancy (BTP) intervals. Other types of intervals are converted as far as possible to approximate this standard interval. BTP intervals measure the time period between the start of the index pregnancy and the preceding live birth (as opposed to other pregnancy outcomes).

The studies principally used four measures of intervals preceding the index pregnancy (see "interval types" column of Table 1). Using Figure 1. above, and taking P3 to O3 to represent the index pregnancy for the purposes of this illustration, these can be described as follows: 1. Birth-to-birth intervals: time between the index live birth (O3 in the figure) and the preceding live birth (O1) – note that this measure does not take into consideration the pregnancy P2 to O2 because it ends in a non-live birth; 2. Inter-outcome intervals: time between the outcome of the index pregnancy (O3) and the outcome of the previous pregnancy (O2) – note that the starting point (as in this case) and/or the end point with this measure can be a non-live birth; 3. Birth-to-conception intervals: time between the conception of the index pregnancy (P3) and the previous live birth (O1) – note that this measure also omits pregnancy P2 to O2 from consideration; 4. Inter-pregnancy intervals: time spent not pregnant prior to the index pregnancy (O2 to P3 in the figure) – again, these intervals can begin with non-live births. Few studies used true inter-pregnancy intervals, although this term was sometimes used as a synonym for birth-to-pregnancy intervals. Studies occasionally examined subsequent birth intervals (e.g. subsequent birth-to-birth interval would be time elapsed from the index birth to the subsequent birth – O3 to O4 in the figure) but these were less common and were not discussed in any detail at the meeting.

[2] This discussion was based on the description in DaVanzo et al., draft, no date.

The four principle measures were converted to birth-to-pregnancy intervals as follows:

1. Birth-to-birth intervals minus nine months = birth-to-pregnancy interval
2. Inter-outcome interval minus nine months = birth-to-pregnancy interval
3. Birth-to-conception interval = birth-to-pregnancy interval
4. Inter-pregnancy interval = birth-to-pregnancy interval

For estimates 1. and 2., in the absence of further information, the conversion assumes full gestation, hence nine months are subtracted to account for the approximate time elapsed from the start of the pregnancy to the end. Measures 3. and 4. already give the interval without the gestation period added, so do not need to be adjusted in this way. For measures 1. and 3. all measured intervals begin with live births.

To illustrate the potential variation in estimates obtained using different measures, consider the index outcome O3 in the figure. In this case, the birth-to-birth interval (O1 to O3) in Figure 1. would be converted to a birth-to-pregnancy interval of 39 minus nine months = 30 months. The inter-outcome interval for the same birth (O2 to O3) on the other hand would give a birth-to-pregnancy interval of 15 minus nine = six months. Similarly, from the beginning of the index pregnancy, P3, the birth-to-conception interval (O1 to P3) would be converted directly into birth-to-pregnancy interval but so would inter-pregnancy interval (O2 to P3), giving a birth-to-pregnancy interval of 30 months in the former case, and six months in the latter case, even though the index pregnancy is the same. Where the preceding pregnancy is a live birth, this discrepancy does not arise. On average, however, for the reasons described, measures 1. and 3. will tend to yield somewhat longer birth-to-pregnancy intervals than measures 2. and 4. The degree of difference in the measures will depend on the population in question and the accuracy of the data.

Because non-live births are often not recorded, researchers may have limited choices about which intervals they examine.

Throughout this report, the intervals quoted refer to birth-to-pregnancy (BTP) intervals. Precise conversions from other measures to BTP intervals are not possible, for the reasons given above, and the quoted figures therefore give an approximate value only.

2.2 Outcomes measured

The major groups of outcomes measured by the studies reviewed at the meeting were divided into maternal, perinatal, neonatal, post-neonatal, child, and post-abortion outcomes. The different maternal outcome measures are listed in Table 2, along with their definitions, as provided in the separate papers. The equivalent information for perinatal and neonatal outcomes is shown in Table 3, and for post-neonatal and child outcomes in Table 4. Definitions of the outcome measures were not always given in the papers and, where given, definitions were not always consistent between studies. Of the 39 different outcomes measured in the six papers, 18 were included in more than one.

3. MAIN FINDINGS FOR EACH GROUP OF OUTCOMES

Working groups examined the evidence pertaining to a specific set of outcomes. Their findings are presented below, along with information about the evidence examined and the discussions arising from the evidence. Table 5 shows a simplified summary of the main evidence for maternal, perinatal, infant and child outcomes.

3.1 Maternal outcomes

3.1.1 Summary

On the basis of the evidence available, the working group concluded that intervals of less than six months between birth and subsequent pregnancy are associated with maternal morbidity and possibly also maternal mortality. Women with BTP intervals over 59 months have an elevated risk of morbidities including pre-eclampsia.

3.1.2 Evidence: maternal mortality

There was some evidence that short BTP spacing (<12 months) might increase risk of maternal mortality (1), and although the Matlab data did not reach statistical significance, results were in the same direction (3). Matlab data also showed an increase in mortality when BTP intervals were very long (>75 months) (3).

3.1.3 Evidence: maternal morbidity

For maternal morbidity, very long intervals were associated with more adverse effects than very short intervals, although there was no clear cut-off point at which long intervals became risky. For instance, some studies included in the systematic review showed an association between long BTP intervals (of varying lengths, but all were over approximately 60 months) and pre-eclampsia (1). One study also showed an association with intrapartum fever (1). Very short intervals (<six months BTP), on the other hand, were associated with premature rupturing of membranes (1), and in single studies only, with anaemia (4) and puerperal endometritis (1). The systematic literature review reported studies suggesting that among women with previous low-transverse caesarean section who had undergone a trial of labour, there was also increased risk of uterine rupture with short BTP intervals (<16 months) (1). Data from Matlab showed elevated risk of pre-eclampsia and high blood pressure with very short (<six months) and long (>75 months) BTP intervals, although there was no effect on premature rupturing of membranes, anaemia or bleeding (3).

There was no consistent evidence about the relationship between maternal anthropometric status and birth spacing (4).

3.1.4 Discussion points raised

- In Matlab, risk of induced abortion was higher after short BTP intervals (3). In countries where access to induced abortion is highly restricted and unsafe abortion is prevalent, induced abortion is associated with maternal mortality and morbidity. It was noted that potentially important links between induced abortion, birth spacing and maternal outcomes were not fully addressed in the studies reviewed.

- The group noted that there is relatively little evidence available about the relationship between maternal mortality and birth-spacing intervals and this should be borne in mind for future research.

3.2 Perinatal outcomes

3.2.1 Summary

The working group concluded that risk of prematurity, fetal death, low birth weight and small size for gestational age are highest for BTP intervals shorter than 18 months. Intervals of over 59 months are also associated with these adverse outcomes.

3.2.2 Evidence: miscarriage, induced abortion, stillbirth

In the DaVanzo et al. study, very short BTP intervals (<six months) were associated with higher risk of stillbirths and miscarriages. There were reduced odds of stillbirth if the preceding pregnancy ended in miscarriage, suggesting that women with non-live births may have been taking precautions to prevent it happening again (3). The odds of having an induced abortion were 10 times that of having a live birth if the BTP interval was very short (<six months) (3), presumably reflecting the higher proportion of unintended pregnancies occurring at shorter compared with longer intervals. Some but not all studies included in the systematic review showed increased risk of fetal death with short intervals (<15 months), and there was some evidence that long intervals (various but all >35 months BTP) were also associated with some elevation in risk (1). In the meta-analysis, the lowest risk was among the group with 18–36 months BTP intervals, and the highest risk was with very short (<six months), and very long (>71 months) intervals (1).

3.2.3 Evidence: pre-term live birth, small size for gestational age, low birth weight, low Apgar scores at five minutes

Several, but not all studies included in the systematic literature review showed an increased risk of pre-term live birth, small size for gestational age and low birth weight when BTP intervals were shorter than 18 months (1). Some also showed increased risk with long intervals (various but >47 months) (1). In the meta-analysis, the lowest risk was associated with BTP intervals of 18–23 months, with the highest risk for intervals under 18 and over 59 months (1). Data from the USA showed elevated risk of these three outcomes with BTP intervals of <18 months and of >60 months (7). The Matlab data showed that very short (<six months) BTP intervals were associated with shorter gestation times (3). Risk of pre-term live birth was also elevated with short (<six months) post-abortion pregnancy intervals.

No association was found between spacing and low Apgar scores at five minutes (1; 2).

3.2.4 Discussion points raised

- Definitions of terms and measurement of intervals was not consistent across studies, making comparisons difficult.

3.3 Neonatal mortality (deaths under age 28 days [3])

3.3.1 Summary

Most of the data indicated that risk of neonatal mortality was highest for BTP intervals of under approximately 18 months, but some also suggested elevated risk at longer intervals (see Table 5 and below). The group concluded that the lowest risk was for BTP intervals of at least 27 months. The group noted certain limitations of the evidence (see 3.3.3 on the following page).

3.3.2 Evidence: neonatal mortality

The Matlab data showed a higher risk of neonatal death with very short BTP intervals (<nine months) compared with longer intervals (27–50 months), with risk remaining somewhat elevated for intervals 15–27 months long (3). Some studies included in the Rutstein et al. systematic literature review (6) also indicated that short BTP intervals (<18 months) were associated with higher risk. DHS data from 17 developing countries also showed increased risks of neonatal mortality with intervals shorter than around 21 months; risks increased as intervals decreased until relative odds of mortality reached a level over twice as high at under nine months compared with the lowest risk category, 27–38 months BTP intervals (5). The Rutstein et al. meta-analysis (6) found that, compared with the reference category of BTP intervals of 28 or more months, odds ratios of neonatal mortality were: OR=2.3 (1.9–2.9) for <nine months and OR=1.2 (1.1–1.4) for 9–27 months. The meta-regression analysis by the same authors showed similar

[3] NB the Rutstein et al. meta-analysis and the Rutstein DHS analysis define this measure as "death in the first month of life" and "death in the first 30 days of life", respectively (see Table 4).

results (6). In the Conde-Agudelo meta-analysis, however, excess risk of early neonatal mortality (deaths in the first week of life) was found with BTP intervals of under 18 months, and not with greater intervals. Conde-Agudelo's meta-regression analysis showed similar results to the meta-analysis he reported in the same paper (1).

The Conde-Agudelo review noted some evidence of detrimental effects of long (> approximately 59 months) BTP intervals on early neonatal mortality (1), but such effects were not found in the Matlab study (3) or in the DHS data (5).

3.3.3 Discussion points raised

The group noted the following concerns:

- Interpretation of the data for this outcome was subject to the specific analytical techniques in one meta-regression analysis. Otherwise the evidence to discriminate within the interval 18–27 months was limited. Further checks were requested from the authors to ensure the conclusions from the meta-regression are robust (see final discussion point in this section). The outcome of this additional work will be considered at a future date.

- The Rutstein et al (draft, 2004) (6) meta-analysis evidence was largely influenced by two studies: DaVanzo et al. (draft, no date) (3) and Rutstein (draft 2004) (5), both of which were also considered separately.

- Many social factors are likely to be important but data for these were not available, e.g. violence, economic factors, access to medical care. For example, higher income might be associated with ability to achieve longer spacing through greater access to contraception services and also with the ability to afford better nutrition and healthcare, both of which would independently affect the survival of the neonate.

Further discussion of the evidence for this outcome included the following observations:

- Two analyses found the risk of neonatal death was highest for intervals shorter than 27 months: DaVanzo et al. (draft, no date) (3) and Rutstein et al. meta-analysis (draft 2004) (6). In the DaVanzo et al. analysis, however, the more risky category was 15–27 months, and in Rutstein et al. it was 9–27 months. Neither study therefore was able to distinguish between intervals longer and shorter than 18 months. Thus, it was unclear whether or not the findings simply reflected the excess risk associated with intervals under 18 months found in other studies, rather than indicating excess risk for the entire range of intervals included up to 27 months. Further analysis was requested to clarify this point.

- It was noted that the data from cross-sectional surveys (5) showed a higher level of risk than data from the prospective Matlab study (3) (see Table 6). This was surprising because the cross-sectional data could take more potential confounding factors into account, which would be expected to reduce the measured risk, not increase it. Cross-sectional data are more vulnerable to recall bias than prospective data, particularly when women are asked to recall dates of births and deaths from a long time before the survey, as in this case, where all births and deaths included occurred at least five years before the survey. The figures in Table 6 may differ because the cross-sectional data refer to the entire country while the prospective data only apply to Matlab. Nevertheless, the figures are very different and some participants were concerned that this difference indicated the presence of an important study-design effect. Some participants were therefore reluctant to rely only on cross-sectional data in reaching conclusions and making recommendations.

- In the Rutstein DHS analysis (draft 2004) (5), confidence intervals were not adjusted to account for the clustered survey design, and confidence intervals were not provided in tables for each category of birth spacing. The author was asked to adjust the figures, provide the missing confidence intervals, and provide data on whether or not there were more missing data for dead than for surviving infants and children. Censored cases were omitted in the analysis and the author was asked to examine whether the observed relationships would hold if censored cases were included using Cox regression. It was also noted that because the analysis included 17 developing countries, and did not use the most recently available data, it would be useful to know if the relationships applied in more recent surveys and in countries with comparatively low mortality.

- The meetings' discussions relied heavily on the findings from meta-regression curves. Some of these meta-regression analyses appeared to double-count data, and some low-quality studies appeared to have been included. There was high heterogeneity reported, and three key limitations were identified: variation in data quality; variation in population type examined (some studies were hospital-based, some population-based); variation in confounding variables included in the different studies. Over and above the limitations of the available data, it was also not clear to what extent the results of the meta-regression analyses were sensitive to the specific techniques used to plot them. For instance, figures obtained from cross-sectional studies and those from prospective studies were combined, which might not be appropriate, and relevant information about study design was not given. The analyses were heavily weighted towards the large studies included, two of which were already being reviewed separately (3; 5). The researchers also elected to use the mid-point of the intervals in their analyses and used an arbitrary multiplier for the open-ended intervals. These decisions are likely to have affected the overall results but no information was given about the estimated size of these effects or why these techniques were chosen for this dataset. Researchers were asked to conduct further analyses to ensure the findings from the meta-analyses were robust.

3.4 Post-neonatal outcomes

3.4.1 Summary

Based on available data, the working group concluded that post-neonatal survival increases if the BTP interval is at least 15 months. Survival may be improved with BTP intervals of 27 months or greater.

3.4.2 Evidence: post-neonatal mortality (deaths from 28 days up to one year)

In Matlab, there was an increased risk of post-neonatal mortality where BTP intervals were shorter than 15 months. The highest risk of post-neonatal mortality was associated with <six month intervals (relative risk compared with 27–50 months intervals was around 1.8) (3). Some studies in the systematic review showed increased risk with BTP intervals of under 15 months, and some showed the reverse: risk of mortality declined with short (<19 months) intervals (6). The meta-analysis, which used data from four studies plus the Rutstein (draft, no date) (5) and DaVanzo et al. (draft, no date) (3) studies included in this review, found that compared with the reference category of 28 or more months from birth-to-pregnancy, 9–27 months intervals were associated with higher risk OR=1.6 (1.4–1.9), as were <nine months BTP intervals: OR=2.3 (1.9–2.9) (6).

3.4.3 Evidence: infant mortality (deaths in first year of life)

Findings for infant mortality were similar to, but less consistent than, those of post-neonatal mortality. For instance, in the systematic literature review, some but not all studies showed increased risk of infant mortality at intervals under approximately 15 months (6). The meta-analysis indicated that the increased risk occurred with BTP intervals under 27 months, and the meta-regression suggested increased risk with intervals under 29 months (6). The Matlab data show excess risk associated with BTP intervals shorter than nine months but not with longer intervals (3).

3.4.4 Discussion points raised

- As in the case of the research on neonatal mortality mentioned above, there was a discussion about whether or not intervals longer than 15 months could be considered risky. The studies were often unable to distinguish effects of different intervals between 15 and 27 months long. Thus, while an effect might be present, it was not clear from the studies where the cut-off for excess risk fell within this range.

- The same discussion points about aspects of the meta-analyses and the other studies arose as for neonatal mortality findings (see above), and the point was made again here that reliance on cross-sectional data might unduly influence the findings (see above and Table 6). As mentioned above, clarification of these points was requested from the researchers.

3.5 Childhood outcomes

3.5.1 Summary

The studies indicated that longer BTP intervals were associated with lower mortality, even at very long intervals. Nevertheless, some participants pointed out that the evidence concerning birth-spacing interval length and childhood deaths (between ages one and five years) was less clear than for infant deaths because of the smaller number of studies, and the fact that the meta-analysis in the Rutstein et al. (draft 2004) (6) paper was dominated by cross-sectional data. Furthermore, the possible causal mechanisms are poorly understood. The anthropometric evidence is inconclusive (4), and the results from Rutstein's DHS (5) analysis reveal considerable variability between countries and modest averaged effects of short preceding interval length on stunting and underweight. Meeting participants did not come to a consensus about interpretation of the evidence for this outcome.

3.5.2 Evidence: child nutrition

The review showed there are inconsistent findings for the relationship between child nutrition outcomes and birth spacing. Some studies showed positive associations, some negative, and some showed no effect at all (4). In the DHS analysis, no significant results were found for wasting (5), although short BTP intervals (exact length not specified) were, in a minority of countries, associated with underweight (two countries) or stunting (two countries) or both (four countries) (5).

3.5.3 Evidence: child mortality (deaths in age group 1 to 4 years)

The Matlab study indicated that there was increased child mortality with BTP intervals of under 26 months. Having little household space and no education, however, had larger effects than did short intervals.

Female children were at higher risk of child mortality than male, despite male children having higher risk of first-week mortality (3). Some studies included in the systematic literature review found increased risk of child mortality with BTP intervals of around <24 months, although three other studies recorded a decrease in mortality risk with shorter intervals (6). The meta-analysis, which included three studies, plus the Rutstein and DaVanzo studies reported here, found that, compared with the reference group of 28 or more months BTP intervals, there was increased risk of child mortality associated with BTP intervals of 9–25 months: OR=1.5 (1.3–1.7), and with intervals of <nine months: OR=1.9 (1.2–2.9) (6).

3.5.4 Evidence: under-5 mortality (all deaths under age 5)

The Rutstein (5) and Rutstein et al. (6) studies examined this outcome, and the findings were very similar to those for child mortality, which this measure encompasses. The systematic literature review indicated some risk was associated with BTP intervals of under 15 months, and the meta-analysis showed that, compared with the reference category of 28 or more month intervals, 9–27 month intervals were associated with increased risk: OR=1.4 (1.2–1.7), as were intervals of <nine months: compared with a reference category of 27 or more months: OR=2.1 (1.5–3.1); the meta-regression analysis showed declining risks associated with increasing intervals for intervals shorter than 40 months (6).

In the DHS analysis, compared with the reference category of 27–32 months BTP intervals, longer intervals were associated with lower mortality (e.g. 51 or more months: OR=0.8). Shorter BTP intervals were associated with increased under-five mortality (e.g. 15–20 months: OR=1.6; <nine months: OR=3.0) (5) (confidence intervals not provided).

3.5.5 Discussion points raised

- The effects of birth spacing on child mortality are uncertain because possible causal mechanisms are unclear. It would be expected that any biological effect of spacing would occur near to the time of pregnancy or birth, the reverse of what is observed here. This suggests that child outcomes are more susceptible to environmental factors, some of which might be related to spacing (perhaps via sibling competition) or possibly to long-lasting effects carried through from pregnancy or birth. Alternatively, other unmeasured environmental factors might be confounding the relationship.

- The limitations of cross-sectional data were of particular concern with this outcome, especially in terms of the imputation of missing dates. Researchers were asked to give more information about the procedures used for imputation, level of imputation and the likely impact on the results observed.

- Participants also asked for more information about the distribution of causes of death, whether having an older sibling increased risks, and whether this varied by sex.

3.6 Post-abortion spacing

3.6.1 Summary

Based on the evidence available, the working group concluded that after a miscarriage or induced abortion, intervals of less than six months before the subsequent pregnancy are associated with increased risk of adverse maternal and perinatal outcomes.

3.6.2 Evidence: post-abortion spacing

One study (2) examined the effects of post-abortion spacing, analysing data from hospital records for women who delivered singleton infants in public hospitals. Data came from 18 Latin American countries but two countries (Argentina and Uruguay) accounted for around 40% of all cases analysed. Intervals of shorter than six months between abortion and subsequent pregnancy were associated with elevated risks of premature rupturing of membranes, anaemia and bleeding, pre-term and very pre-term births, and low birth weight, compared with longer intervals. There was no significant effect of post-abortion spacing on pre-eclampsia or on eclampsia, gestational diabetes, third trimester bleeding, post-partum haemorrhage, puerperal endometritis, small size for gestational age, non-live birth, or early neonatal mortality.

3.6.3 Discussion points raised

Participants were concerned that there was only one study which provided evidence for post-abortion spacing outcomes. Nevertheless, they recognized that this study provides valuable guidance for post-abortion pregnancy-spacing interval recommendations, being the only large-scale study available. Participants indicated that any recommendation must be considered in the context of the following limitations:

- It was not possible to distinguish between spontaneous and induced abortions. Given that the study was in Latin America, where induced abortions are legally restricted and frequently unsafe, this distinction would have been useful in assessing generalizability of the findings.

- All data came from public hospitals and from one region. The data may therefore not be wholly applicable within the region or generalizable to other regions.

- While the study was able to control for many confounding factors, it was not possible to take the following into account: history of previous pre-term delivery, gestational age at time of abortion, number of previous abortions, wantedness of pregnancy, sexual violence.

4. CONCLUSIONS AND RECOMMENDATIONS

The conclusions from the separate working groups set out above were presented in a final plenary session, where the strengths and limitations of the available evidence were discussed. Final recommendations were then agreed.

4.1 Strengths and limitations of the evidence

The background papers, the expert reviews, and the discussions at the meeting comprised a timely analysis of the latest available evidence on the effects of birth spacing on maternal and child health.

Many world regions were covered by the studies reviewed, although not all outcomes were examined for all regions.

Participants mentioned the following limitations of the evidence available in addition to the technical points mentioned above.

Causal mechanisms that might explain the associations between birth spacing and the outcomes examined are not known. Hypotheses point to the possible importance of malnutrition, anaemia, reproductive tract infections, sub-fecundity and maternal depletion. Two possible links with infant and child mortality are competition for parental attention/household resources or cross-infection, although neither explanation can muster decisive empirical support.[4] When causal mechanisms are unknown, "over-controlling" might be a problem. For instance, short spacing might lead to low birth weight which might in turn increase mortality risk. If low birth weight is included as a confounding factor in the analysis, some of the association between spacing and mortality will be masked.

[4] E.g. see Setty-Venugopal V, Upadhyay UD. *Birth spacing: three to five saves lives. Population Reports, Series L* 2002:pp7-8.

The variety of the types and lengths of spacing used in the studies made them difficult to compare, and estimates of gestational age using self-report of last menstrual period can be inaccurate: few studies use estimates derived from ultrasonography or physical and neurological assessment of the newborn (1). Underreporting of non-live births may have led to inaccurate assessments of spacing.

Generalizability of the study findings was discussed. For instance, it may be necessary to distinguish between well-nourished and malnourished mothers in any explanations of maternal and perinatal outcomes. Some women may benefit more than others from longer spacing between births. To what extent is the maternal depletion hypothesis relevant in the context of rising obesity, for example? Do interval lengths have different effects at different maternal ages? Does a good nutritional status ameliorate adverse consequences of short birth intervals?

Taking into account these strengths and limitations, the group was split in terms of the recommended optimal interval after a live birth with some favouring 18 months and others 27 months. However, it was noted that WHO and UNICEF recommend that breastfeeding continue for up to two years or more and this observation helped the group reach an agreement. Evidence pertaining to the two-year breastfeeding recommendation, however, was not reviewed during the meeting and related factors such as recuperation periods for the woman and the effect of pregnancy on breastfeeding were not assessed.

4.2 Recommendations

The particulars of the recommendations and the necessary caveats are noted in detail above. The group stressed that recommendations must be considered in conjunction with the preamble on the following page.

Preamble

Individuals and couples should consider health risks and benefits along with other circumstances such as their age, fecundity, fertility aspirations, access to health services, child-rearing support, social and economic circumstances, and personal preferences in making choices for the timing of the next pregnancy.

Recommendation for spacing after a live birth

After a live birth, the recommended interval before attempting the next pregnancy is at least 24 months in order to reduce the risk of adverse maternal, perinatal and infant outcomes. [5]

Rationale for the recommendation

The studies presented at the meeting considered various maternal, infant and child health outcomes. For each outcome, different BTP intervals were associated with highest and lowest risks. To summarize, BTP intervals of six months or shorter are associated with elevated risk of maternal mortality. BTP intervals of around 18 months or shorter are associated with elevated risk of infant, neonatal and perinatal mortality, low birth weight, small size for gestational age, and pre-term delivery. Some "residual" elevated risk might be associated with the interval 18–27 months, but interpretation of the degree of this risk depended on the specific analytical techniques used in a meta-analysis. Otherwise, the evidence to discriminate within the interval of 18–27 months was limited. Further analysis was requested to clarify this point. This additional work will be considered at a future date.

Evidence about relationships between birth spacing and child mortality was presented but the participants did not reach agreement on its interpretation.

On the basis of the evidence available at the time, the participants fell into two groups: those who considered that this evidence indicated that the most suitable recommended interval was 18 months, and those who considered that the evidence supported a recommended interval of 27 months. Participants were, however, unanimous in agreeing that BTP intervals shorter than 18 months should be avoided.

At the meeting, a compromise was reached between the two groups, who agreed that the recommendation for the minimum interval between a live birth and attempting next pregnancy should be 24 months.

The basis for the recommendation is that waiting 24 months before trying to become pregnant after a live birth will help avoid the range of BTP intervals associated with the highest risk of poor maternal, perinatal, neonatal, and infant health outcomes. In addition, this recommended interval was considered consistent with the WHO/UNICEF recommendation of breastfeeding for at least two years, and was also considered easy to use in programmes: "two years" may be clearer than "18 months" or "27 months".

Recommendation for spacing after an abortion

After a miscarriage or induced abortion, the recommended minimum interval to next pregnancy is at least six months in order to reduce risks of adverse maternal and perinatal outcomes.

Caveat

This recommendation for post-abortion pregnancy intervals is based on one study in Latin America, using hospital records for 258,108 women delivering singleton infants whose previous pregnancy ended in abortion. Because this study was the only one available on this scale, it was considered important

[5] Some participants felt that it was important to note in the report that, in the case of birth-to-pregnancy intervals of five years or more, there is evidence of an increased risk of pre-eclampsia, and of some adverse perinatal outcomes, namely pre-term birth, low birth weight and small infant size for gestational age.

to use these data, with some qualifications. Abortion events in the study included a mixture of three types – safe abortion, unsafe abortion and spontaneous pregnancy loss (miscarriage), and the relative proportions of each of these types were unknown. The sample was from public hospitals in Latin America only, with much of the data coming from two countries (Argentina and Uruguay). Thus, the results may not be generalizable within the region nor to other regions, which have different legal and service contexts and conditions. Additional research is recommended to clarify these findings.

4.3 Suggested areas for future research

- Development of coherent theoretical frameworks explaining the possible causal mechanisms of birth spacing on outcomes, particularly child mortality, was identified as important for future research.

- Analyses of relationships between birth spacing and maternal morbidity would be useful to add to the few existing studies. For instance, examination of the effects of multiple short BTP intervals would be useful, as would be more detailed data on the effects of very long intervals. Further analysis of the relationship between birth spacing and maternal mortality would help confirm or refute existing findings, although it is acknowledged that this may often be unfeasible as it may require a very large number of cases.

- There is a need to investigate the relationship between birth spacing and outcomes other than mortality, for instance, maternal and child nutrition outcomes, or impact on child psychological development. Also, it would be helpful to have information on possible benefits, as well as possible risks, of particular spacing intervals.

- More studies on the effects of post-abortion pregnancy intervals are needed in different regions. A distinction between induced and spontaneous abortion, and between safe and unsafe induced abortion, would be particularly helpful in future studies.

- Good-quality longitudinal studies that take more potential confounding factors into account are needed to:

  1. clarify the observed associations between birth-to-pregnancy intervals and maternal, infant and child outcomes;

  2. estimate the potential level of bias in the use of different measures of intervals (birth-to-birth vs. inter-pregnancy interval, for instance);

  3. clarify the potentially confounding effect of short intervals following a child death, both because of shortened breastfeeding and because parents may seek to replace the dead child.

- Finally, there is a need to develop an evidence base for effective interventions to put birth-spacing recommendations into practice.

Table 1. Study design, interval types, interval lengths and control variables pertaining to the studies considered in the review

Paper/Author(s)	Study design	Interval types	Interval lengths	Control variables
Conde-Agudelo (draft, 2004)	Systematic review including 77 studies: 57 cohort or cross-sectional and 20 case-control studies. 26 studies in USA, remaining 51 studies in Latin America (22 countries), Asia (20 countries), Africa (14 countries), Europe (seven countries), North America (two countries), Australia. META-ANALYSIS of three outcomes using studies that used inter-pregnancy interval (IPI), provided data for four or more IPI strata, provided enough data to construct a 2x2 table and calculate unadjusted OR and 95%CI. Outcomes analysed: pre-term birth (eight studies); low birth weight (four studies); small size for gestational age (seven studies). META-REGRESSION ANALYSIS also included: examining pre-term birth (15 studies); low birth weight (10 studies); small size for gestational age (13 studies); fetal death (seven studies); early neonatal death (four studies)	Birth-to-conception interval, birth-to-birth interval, or both. Meta-analysis used inter-pregnancy interval	Various. In meta-analysis they use <6, 6–11, 12–17, 18–23, 24–59, 60 or more months	Various. Studies had to have controlled for at least maternal age and socioeconomic status (the socioeconomic status variables were variable, but included occupation, work status, education level, income, housing "or other variables")
Conde-Agudelo et al. (post-abortion) (draft, 2004)	Cohort study, retrospective, women delivering singleton infants in public hospitals and whose previous pregnancy was aborted	Post-abortion inter-pregnancy interval	0–2, 3–5, 6–11, 12–17, 18–23, 24–59, ≥60 months	Maternal age, parity, mother's education, marital status, cigarette smoking, pre-pregnancy body mass index (BMI), weight gain during pregnancy, history of low birth weight (LBW), perinatal death, chronic hypertension, gestational age at first attendance for antenatal care, number of antenatal visits, geographic area, hospital type, year of delivery. Two outcome measures: early neonatal death and low Apgar score, were also adjusted for birth weight and gestational age
DaVanzo et al. (draft, no date)	Longitudinal, Demographic Surveillance System (DSS) Matlab, Bangladesh	Inter-outcome and inter-birth intervals	Inter-outcome intervals of <15, 15–17, 18–23, 24–35, 36–59, 60–83, 84 or more months	Various, depending on analysis. CHILD AND PERINATAL: maternal age, parity, month of birth, wantedness of pregnancy, residence in treatment area, maternal education, paternal education, religion, household space, outcome of preceding pregnancy, interactions between shortest interval and outcome of preceding pregnancy, calendar year, subsequent pregnancy and birth. Also breastfeeding and immunization for the women in the treatment area. MATERNAL MORTALITY: age, gravidity, prior experiences of child death and pregnancy loss, education, household space, and four time periods (1982–2002). MATERNAL MORBIDITY: as for mortality, but not time periods, and including religion. NB the morbidity section only includes women who attend antenatal care in the treatment area

Table 1. continued

Paper/Author(s)	Study design	Interval types	Interval lengths	Control variables
Dewey & Cohen (draft, 2004)	Review of 27 papers representing 33 studies: five prospective cohort studies, 27 cross-sectional studies, three case-control studies (two contained both cohort and case-control studies)	Inter-pregnancy interval (two studies), inter-birth interval, recuperative interval (duration of the non-pregnant, non-lactating interval)	Various in the different studies	Various and not consistent but including child age, sex, maternal age, parity, maternal education. Only six controlled for breastfeeding, three for maternal height
Rutstein (DHS) (draft, no date)	Cross-sectional Demographic and Health Surveys, nationally representative, 17 countries: Bangladesh, Bolivia, Cote d'Ivoire, Egypt, Ghana, Guatemala, India, Indonesia, Kenya, Morocco, Nepal, Nigeria, Peru, Philippines, Tanzania, Uganda, Zambia	Birth-to-birth intervals	<18, 18–23, 24–29, 30–35, 36–41, 42–47, 48–53, 54–59, 60 or more months	UNDER-FIVE MORTALITY: Sex of child, birth order, multiplicity of birth, mother's age at birth, survival of preceding child by date of conception, prenatal care provider, timing of first ANC visit (if any), number of prenatal tetanus toxoid vaccinations, delivery attendant, urban-rural residence, mother's education, index of household wealth. NEONATAL AND INFANT MORTALITY: As for under-five plus wantedness of child, whether birth result of contraceptive failure. STUNTING and UNDERWEIGHT: As for under-five but not multiplicity of birth, and adding type of infant feeding, drinking water supply, type of toilet, whether household has refrigerator
Rutstein et al. (draft, 2004)	Systematic review and meta-analysis of 65 studies. The review focused on cohort, cross-sectional, or case-control studies. Includes 29 studies from Asia (nine of which were from Matlab, Bangladesh), 15 from sub-Saharan Africa, 11 from Latin America and the Caribbean, two from middle East, three from Europe (two of which were historical cohorts), five multi-regional. Includes META-ANALYSIS of five mortality outcomes: neonatal (six studies), post-neonatal (six studies), infant (five studies), child (three studies) and under-five (three studies) mortality. Also, META-REGRESSION ANALYSIS of same outcomes, using 28 studies (number of studies per outcome not specified)	50 used preceding birth interval, nine preceding inter-pregnancy interval, eight succeeding birth interval, three succeeding birth-to-conception interval, three whether or not there was succeeding conception in the mortality range (numbers exceed total number of studies. The reason for this is not stated in the text, but it is possible that multiple measures may have been used in individual studies)	Various. In meta-analysis they use 18 months and 37 months as the cut-off between the three categories: <18 months, 18–36 months, and ≥ 37 months birth-to-birth intervals	Various. Studies had to have controlled for at least maternal age and socioeconomic status (one study used birth order rather than maternal age and the socioeconomic status variables were diverse)

Table 1. continued

Paper/Author(s)	Study design	Interval types	Interval lengths	Control variables
Zhu (draft, 2004)	Two cross-sectional studies (CS) in Utah and Michigan, one retrospective cohort (RC) study in Michigan, all using birth records	Inter-pregnancy interval	0–5, 6–11, 12–17, 18–23, 24–59, 60–119, 120 or more months (Michigan CS study used 60–95, 96–136 months for the upper intervals)	UTAH CS: maternal age at delivery, outcome of most recent recognized pregnancy, number previous live-born infants still alive, number previous live-born infants who had died, number previous spontaneous or induced abortions, height, pre-pregnancy weight, weight gain during pregnancy, trimester at which prenatal care started, number of prenatal care visits, marital status, education, race/ethnic group, residence (rural/urban), tobacco use during pregnancy, alcohol use during pregnancy MICHIGAN CS: (NB population divided into white and African-American groups) age at delivery, marital status, education, adequacy of prenatal care, outcome of preceding pregnancy (i.e. live birth or stillbirth), total number of previous pregnancies, tobacco use during pregnancy, alcohol use during pregnancy MICHIGAN RC: preceding infant's birth weight, paternal acknowledgment on birth certificate, mother's age at delivery, race, education, adequacy of prenatal care utilization, outcome of preceding pregnancy (live birth, stillbirth), tobacco and alcohol use during pregnancy

Table 2. Definitions of maternal outcomes used in the studies (blank cell indicates outcome not considered by study)

	Maternal outcomes										
Paper/Author(s)	Maternal anthropo-metric status	Pre-eclampsia	High blood pressure	Premature rupturing of membranes	Protein-uria	Edema	Anaemia	Eclampsia	Postpartum haemor-rhage	Uterine rupture	Placenta accreta
Conde-Agudelo (draft, 2004)		no definition		no definition			no definition	no definition	no definition	uterine rupture in women with previ-ous low-transverse C-section who had undergone a trial of labour	no definition
Conde-Agudelo et al. (post-abortion) (draft, 2004)		ICD-10 code 014		ICD-10 code 042			ICD-10 code 099.0	ICD-10 code 015	ICD-10 code 072		
DaVanzo et al. (draft, no date)		any two of the conditions of edema, proteinuria, or high blood pressure	diastolic 90mmHg or greater	clinical	clinical	clinical	clinical				
Dewey & Cohen (draft, 2004)	definitions varied						one study: haemoglobin <110g/L at any time during preg-nancy; others measured different times				
Rutstein (DHS) (draft, no date)											
Rutstein et al. (draft, 2004)											
Zhu (draft, 2004)											

Table 2. continued

	Maternal outcomes (continued)					
Paper/Author(s)	Maternal infection	Puerperal endometritis	Gestational diabetes	Bleeding during preg-nancy	Intrapartum fever	Maternal mortality
Conde-Agudelo (draft, 2004)	no definition	no definition	no definition	third trimes-ter bleeding	no definition	no definition
Conde-Agudelo et al. (post-abortion) (draft, 2004)		ICD-10 code 085	ICD-10 code 024.4	ICD-10 codes 044.1 and 045		
DaVanzo et al. (draft, no date)				no definition		death during pregnancy or in the 42 days fol-lowing pregnancy from pregnancy-related or birth-related causes
Dewey & Cohen (draft, 2004)						
Rutstein (DHS) (draft, no date)						
Rutstein et al. (draft, 2004)						
Zhu (draft, 2004)						

Table 3. Definitions of perinatal and neonatal outcomes used in the studies (blank cell indicates outcome not considered by study)

	Perinatal outcomes											
Paper/ Author(s)	Abortion	Non-live birth	Miscarriage	Stillbirth	Pre-term live birth	Small for gestational age	Low birth weight	Low Apgar scores at five min	Early neonatal mortality	Late neonatal mortality	Neonatal mortality	Perinatal death
Conde-Agudelo (draft, 2004)		"fetal death" (no definition)			no definition	no definition	no definition	score of under seven	no definition			no definition
Conde-Agudelo et al. (post-abortion) (draft, 2004)		delivery of dead baby at or before 20-week gestation			delivery at <37 weeks gestation; 32 weeks for "very pre-term"	<10th percentile for gestational age and gender using Williams et al. reference curve	live baby <2500g at birth	score of under seven	deaths in first seven days of life			
DaVanzo et al. (draft, no date)	induced abortion			no definition	no definition				deaths in first week of life	deaths in weeks 2–4 of life of those surviving first week		
Dewey & Cohen (draft, 2004)												
Rutstein (DHS) (draft, no date)											deaths in first 30 days of life	
Rutstein et al. (draft, 2004)									deaths in days 0–6		deaths in first month of life	
Zhu (draft, 2004)					gestational age <37 weeks	<10th percentile in Utah (Utah CS study) or in USA (Michigan CS study)	<2500g					

Table 4 . Definitions of post-neonatal and child outcomes used in the studies (blank cell indicates outcome not considered by study)

	Post-neonatal /child outcomes									
Paper/ Author(s)	Post-neonatal mortality	Infant mortality	Toddler mortality	Under-2 mortality	Child nutrition	Wasting	Underweight/ stunting	Child mortality	Under-5 mortality	Mortality at non-standard ages
Conde-Agudelo (draft, 2004)										
Conde-Agudelo et al. (post-abor-tion) (draft, 2004)										
DaVanzo et al. (draft, no date)	deaths in 5th–52nd week of life							deaths among 1–4 year olds of those sur-viving to age one		
Dewey & Cohen (draft, 2004)					includes stunting, underweight					
Rutstein (DHS) (draft, no date)		deaths at age 0–11 months				z-score less than −2 S.D. for weight-for-height	stunting: height-for-age z-score <2 S.D. below the mean; underweight: z-score < −2 S.D. for weight-for-age		deaths to any children age under 5	
Rutstein et al. (draft, 2004	deaths at age 1–11 months	Conflicting definition: deaths under 12 months vs. deaths at 0–12 months	Conflicting definitions: deaths at age 13–23 months vs. 12–23 months	deaths before 24 months				Conflicting definitions: deaths at age 13–59 months vs.12–59 months	Deaths at age <60 months	various
Zhu (draft, 2004)										

Table 5. Simplified summary of the data presented at the June 2005 meeting, by author and by outcome. The numbers given are the upper and lower cut-offs (in months) for birth-to-pregnancy intervals (estimated from the intervals used in the separate studies) at which adverse outcomes were measured in each study. Where studies reported more than one finding, the most conservative estimates have been presented, i.e. the highest figures for the lower cut-off points, and the lowest figures for the upper cut-off points.

	Conde-Agudelo	DaVanzo et al.	Rutstein DHS	Rutstein et al. review	Zhu
Maternal mortality	SLR <6	>75	-	-	-
Pre-eclampsia*	SLR <4, >48	<6, >75	-	-	-
Miscarriage	-	<6	-	-	-
Fetal death	SLR <15, >x Rgrsn <20, >66	-	-	-	-
Stillbirth	-	<6	-	-	-
Pre-term birth	SLR <15, >x Meta <18, >59 Rgrsn <15, >60	-	-	-	<12, >120
Small size for gestational age	SLR <18, >59 Rgrsn <15, >47	-	-	-	<12, >24
Low birth weight	SLR <12, >59 Rgrsn <20, >55	-	-	-	<12, >59
Perinatal death	SLR <23, >x	-	-	-	-
Overall neonatal mortality	-	<9	<21	SLR <18, Meta <27** Rgrsn <28, >62	-
Early neonatal mortality	SLR <24, >59 Meta <17, >71 Rgrsn <18, >56	<17	-	-	-
Late neonatal mortality	-	<27**	-	-	-
Post-neonatal mortality	-	<15	-	SLR <15, Meta <27** Rgrsn <33, >75	-
Infant mortality	-	<9	<27	SLR <15, Meta <27** Rgrsn <29	-
Child mortality	-	<51 or <14 (2 different graphs)	-	SLR <15 Meta <27** Rgrsn <47	-
Under-five mortality	-	-	<60	SLR <15 Meta <27** Rgrsn <40	-

SLR = figures from cases included in the systematic literature review, **Meta** = figures from the meta-analysis, **Rgrsn** = figures from the meta-regression analysis (by eye, where line indicates natural log of relative risk is 0.05 above lowest point), **>x** = evidence of risk at longer intervals but hard to summarize; **-** = not included in the study.

*Very little information on maternal morbidities available. Other outcomes examined in single studies only.

** In the Rutstein et al. meta-analysis, the calculation for this figure included all intervals from 9–27 months. In the DaVanzo et al. study, it included all intervals 15–27 months. No analysis was available for more discrete categories.

Table 6. Relationship between birth-to-birth interval length and infant and child mortality, comparing data from Matlab DSS (DaVanzo et al., no date) and Bangladesh DHS (Rutstein, no date). Adjusted odds ratios with 36–41 months as reference group.

Interval length	**Matlab**	**DHS**
<18 months		
Neonatal	2.0	1.9
Infant	2.0	2.6
Under-five	1.8	2.7
18–23 months		
Neonatal	(1.2)	1.5
Infant	(1.2)	1.5
Under-five	1.4	1.8
24–29 months		
Neonatal	(1.0)	1.4
Infant	(1.0)	1.6
Under-five	(1.1)	1.3
30–35 months		
Neonatal	(0.9)	1.0
Infant	(0.9)	1.0
Under-five	(1.0)	1.1

Note: Matlab estimates are derived visually from DaVanzo et al., no date (Appendix Figure 1). Non-significant results are shown in brackets.

ANNEX 1. PAPERS REVIEWED AT THE MEETING

1. Conde-Agudelo A (draft, 2004). Effect of birth spacing on maternal and perinatal health: a systematic review and meta-analysis. Report prepared for The Academy for Educational Development and The CATALYST Consortium.

   An amended and abridged version of this report (not reviewed by the WHO consultation) has now been published as follows:

   Conde-Agudelo A, Rosas-Bermúdez A, Kafury-Goeta AC. Birth spacing and risk of adverse perinatal outcomes: a meta-analysis. *JAMA*, 2006, 295:1809–1823.

2. Conde-Agudelo A, Belizán, JM, Breman R, Brockman SC, Rosas-Bermudez A (draft, 2004). Effect of the interpregnancy interval after an abortion on maternal and perinatal health in Latin America.

   This paper has now been published as follows:

   Conde-Agudelo A, Belizán, JM, Breman R, Brockman SC, Rosas-Bermudez A. Effect of the interpregnancy interval after an abortion on maternal and perinatal health in Latin America. *International Journal of Gynaecology and Obstetrics,* 2005, 89:S34–S40 (supplement).

3. DaVanzo J, Razzaque A, Rahman M, Hale L, Ahmed K, Khan MA, Mustafa AG, Gausia K (draft, no date). The effects of birth spacing on infant and child mortality, pregnancy outcomes and maternal morbidity and mortality in Matlab, Bangladesh.

4. Dewey KG, Cohen RJ (draft, 2004). Birth-spacing literature: maternal and child nutrition outcomes. Report prepared for The Academy for Educational Development and The CATALYST Consortium.

5. Rutstein SO (draft, no date). Effects of preceding birth intervals on neonatal, infant and under-five years mortality and nutritional status in developing countries: evidence from the Demographic and Health Surveys.

   This paper has now been published as follows:

   Rutstein SO. Effects of preceding birth intervals on neonatal, infant and under-five years mortality and nutritional status in developing countries: evidence from the Demographic and Health Surveys. *International Journal of Gynaecology and Obstetrics*, 2005, 89:S7–S24 (supplement).

6. Rutstein SO, Johnson K, Conde-Agudelo A (draft, 2004). Systematic literature review and meta-analysis of the relationship between interpregnancy or interbirth intervals and infant and child mortality. Report prepared for The CATALYST Consortium.

Supplementary paper

7. Zhu BP (draft, 2004). Effect of interpregnancy interval on birth outcomes: findings from three recent US studies.

   This paper has now been published as follows:

   Zhu BP. Effect of interpregnancy interval on birth outcomes: findings from three recent US studies. *International Journal of Gynaecology and Obstetrics,* 2005, 89: S25–S33 (supplement).

ANNEX 2. MEETING AGENDA

Technical Consultation: Review of Scientific Evidence for Birth Spacing
13–15 June 2005, WHO, Geneva
Salle A, Main Building

Monday, 13 June 2005	Agenda item	Presenter
09:00 – 09:30	**Opening**	
	• Welcome remarks	Paul Van Look, Department of Reproductive Health and Research, WHO
	• Presentation of the Chair, Rapporteurs and participants	
	• Background, objectives and expected outcomes of the meeting	Monir Islam, Department of Making Pregnancy Safer, WHO
	• Overview of the agenda	Barbara Hulka, Chair
09:30 –10:00	**The Birth spacing Initiative**	
	• Presentation of the initiative	Jim Shelton, Office of Population and Reproductive Health, USAID
	• Introduction to the research	Agustín Conde-Agudelo, Principal Investigator
10:00 –12:45	**Birth spacing and maternal and perinatal health**	
	• Presentation Zhu BP. *Effect of interpregnancy interval on birth outcomes: findings from three recent US studies*	Bao-Ping Zhu
	• Presentation Conde-Agudelo A et al. *The effect of the interpregnancy interval after an abortion: implications for maternal and perinatal health in Latin America*	Agustín Conde-Agudelo
	• Commentary	Anibal Faundes
	• Questions for clarification	

Monday, 13 June 2005 – continued	Agenda item	Presenter
	Birth spacing and maternal and perinatal health – continued	
	• Presentation DaVanzo J et al. *The effects of birth spacing on infant and child mortality, pregnancy outcomes, and maternal morbidity and mortality in Matlab, Bangladesh*	Julie DaVanzo
	• Commentary	John Cleland
	• Questions for clarification	
	• Presentation Dewey KG and Cohen RJ. *Birth spacing literature review: maternal and child nutrition outcomes*	Katherine Dewey
	• Commentary	Inge Hutter
	• Questions for clarification	
14:00 –15:30	• Presentation Conde-Agudelo A. *Effect of birth spacing on maternal and perinatal health: a systematic review and meta-analysis.*	Agustín Conde-Agudelo
	• Commentary	Jacqui Bell
	• Questions for clarification	
	• Bringing the evidence together	Cicely Marston
16:00 –17:45	• Discussion in Plenary	
	• Group work	

Tuesday, 14 June 2005	Agenda item	Presenter
08:30 –10:00	**Birth spacing and maternal and perinatal health – continued** • Discussion in plenary and recommendations	
10:00 –10:30	**Birth spacing and child health**	
	• Presentation DaVanzo J et al. *The effects of birth spacing on infant and child mortality,pregnancy outcomes, and maternal morbidity and mortality in Matlab, Bangladesh*	Julie DaVanzo
	• Commentary	John Cleland
	• Questions for clarification	
11:00 –12:45	• Presentation Katherine Dewey Dewey KG and Cohen RJ. *Birth spacing literature review: maternal and child nutrition outcomes*	Katherine Dewey
	• Commentary	Inge Hutter
	• Questions for clarification	
	• Presentation Rutstein S and Johnson K with sections written by Conde-Agudelo A. *Systematic review and meta-analysis of the relationship between inter-pregnancy or inter-birth intervals and infant and child mortality* Rutstein S. *Effects of preceding birth intervals on young childhood mortality and nutritional status in developing countries: evidence from the Demographic and Health Surveys*	Shea Rutstein
	• Commentary	Wong Yut-Lin and Zeba Sathar
	• Questions for clarification	

Tuesday, 14 June 2005 – continued	**Agenda item**	**Presenter**
14:00 –18:00	**Birth spacing and child health – continued** • Bringing the evidence together • Discussion in plenary • Group work	 Cicely Marston Chair
Wednesday, 15 June 2005	**Agenda item**	**Presenter**
	Birth spacing and child health – continued	
08:30	• Discussion in plenary	
	Conclusions and recommendations of the meeting	
09:00	• Review of conclusions of working groups • Final statements and recommendations - for birth-spacing intervals - on terminology - on identified gaps in research - on next steps	
15:00	Closure of the meeting	

ANNEX 3. LIST OF PARTICIPANTS

Technical Consultation: Review of Scientific Evidence for Birth Spacing
Salle A, World Health Organization, Geneva, Switzerland, 13 - 15 June 2005

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