Pregnancy loss and neonatal mortality in Rwanda: The differential role of inter-pregnancy intervals

Zwangerschapsverlies en zuigelingensterfte in Rwanda:
De effecten van het interval tussen opeenvolgende zwangerschappen
(met een Nederlandse samenvatting)

Proefschrift

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Contents

List of tables

List of figures

Preface

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Ignace Habimana-Kabano/Utrecht, July 2015.

Chapter 1 Introduction

Rwanda has been very successful in bringing down infant mortality to 50 deaths per 1000 births in 2010. After 2005 in particular, reproductive health services have been improved in both accessibility and quality by further developing a community based health system. Antenatal care and family planning services have had positive effects in avoiding unwanted pregnancies and improving the outcomes of intended pregnancies. So far relatively little attention has been devoted to the spacing of births, yet an extra focus on spacing in the health programs could be both beneficial and feasible.

There are clear indications that both short and long birth intervals can lead to adverse outcomes in terms of perinatal mortality and of maternal morbidity. More healthy intervals could contribute to less pregnancy complications and better outcomes for the mother and the new born child. In Rwanda longer intervals are preferred. However, 20% of the pregnancies were conceived within 24 months after the last birth (RDHS 2010). Enabling women to space their pregnancies would help reduce the proportion of short birth intervals.

Yet the evidence base for this type of intervention is still weak. A number of potential uncertainties and flaws can be identified. Much of the research only considers the intervals between consecutive births; pregnancies that do not end in a life birth go unobserved. This does not only lead to an underestimation of short intervals but also ignores the emotional burden of miscarriages and the effects of pregnancy disruption on the subsequent health and reproductive behavior. The evidence on the duration of a healthy interval after a pregnancy disruption is inconclusive. Some studies indicate that short intervals provide better outcomes with the next pregnancy while other show that it might be wise to wait at least 12 months or even longer before becoming pregnant again. Although it has been theorized that maternal morbidity is an important cause of perinatal mortality the effects of shorter pregnancy intervals on maternal morbidity have hardly been investigated empirically. To further complicate the issue, very long intervals (more than 60 months) also turn out to have adverse effects. Birth spacing of more than 5 years occurs among 10% of all pregnancies in Rwanda.

This lack of proper insight creates dilemmas in devising health programs. Contributing to spacing might mean that intervals extend beyond the point where they are still healthy and this might create new adverse effect. Clearly there is a need for a stronger evidence base and the *objective of this research is to strengthen this base by analyzing the effect of short and very long inter-pregnancy intervals on the risks of losing a pregnancy, of perinatal mortality and of (pregnancy related) maternal morbidity*.

1.1. The health care system in Rwanda

Since the year 2000, the Rwandan Vision 2020 development strategy tackles high population growth as a major hindrance to envisaged development targets and efforts have been oriented to the improvement of family planning services. Over the last decade, Rwanda has been successful in promoting the health status of its population in general and the reproductive health of women in particular. It has instituted a decentralized community based health system by training and deploying 45,000 community health workers. Their tasks include amongst others, paying monthly visits to pregnant women and stimulating them to go for antenatal checks at the Local Health Centers, and to deliver with assistance of a skilled attendant.

In terms of health infrastructure, Rwanda had 469 Local Health Centers each serving 20,000-25,000 people, 42 district hospitals with a catchment area of 150,000-250,000 people, 5 referral hospitals and many private clinics in 2013. The 2012 data from the Ministry of Health's Human Resources Database show a ratio of 1 medical doctor per 15,428 inhabitants, 1 midwife per 23,264 inhabitants, and 1 nurse per 1,138 inhabitants. More recently the quality of the supply side in health care improved by introducing a performance based financing scheme (Binagwaho A. et al., 2012).

Access to community health care was eased by introducing a community based insurance system "mutuelles de santé". Today, more than 90% of the population participates in these *Mutuelles de Santé.* The antenatal checks and the costs of a normal delivery assisted by a nurse or midwife are covered by this basic health insurance scheme. In case of a more complicated delivery in a hospital 10 percent of the total costs of the treatment are charged. The percentage of women delivering with the assistance of a trained professional (midwife, nurse) increased substantially from 31 (1996-2000) to 69 percent in the period 2006-2010. According to the 2010 Demographic and Health Survey (DHS), less than two percent of the women did not have any antenatal medical test before the delivery.

The family planning program has been successful since 2005. The contraceptive prevalence rate has quadrupled from 10% in 2005 to 45% in 2010. The total fertility rate decreased from 6.1 in 2005 to 4.6 children per woman in 2010. Subsequent to these improvements, in combination with other health programs, the infant mortality rate has fallen from 86 per 1000 births in 2004 to 50 per 1000 births in 2010, and the under-five mortality rate declined from 152 to 76 per 1000 births. Likewise, the maternal mortality rate decreased from 750 per 100000 live births in 2005 to 476 per 100000 live births in 2010.

Nevertheless, unmet need for family planning remains persistent and closely spaced births continue to be an issue. The recent RDHS-2010 shows that approximately 19% of married women in Rwanda have an unmet need for family planning during their reproductive age. Among them, more than half (9.7%) expressed an unmet need for birth spacing. This might be a result of the family planning policy in Rwanda which has focused mainly on family planning for birth limitation since the 1983's under the

ONAPO (Office National de la Population) slogan TUBYARE ABO DUSHOBOYE KURERA “let’s give birth to children we are able to raise” Tallon F. 1993)).

This study highlights positive implications of reducing the levels of unmet needs for spacing (avoiding short and very long inter-pregnancy intervals) on maternal pregnancy-related morbidity, fetal death and neonatal mortality.

1.2 Theoretical framework

The debate on the (mechanism underlying) effects of inter-pregnancy intervals on pregnancy outcomes is still unresolved. The traditional practice in Rwanda of prolonged breastfeeding, where around 90% of mothers breastfeed children under six months, leads to extended post-partum amenorrhea and a healthy interval after a live birth (MOH, 2006). Yet the risk of short intervals is high as there is no period of abstinence after delivery. Pregnancy and breastfeeding lead to depletion of maternal resources and at short intervals to competition between the last born and the new pregnancy. Several events might lead to a choice for becoming pregnant again soon. Gender preferences could lead to shortening intervals if women want to arrive at the preferred gender balance. The loss of a wanted pregnancy leads to replacing this pregnancy quickly. The loss of an infant will lead to a return of the menses and the wish for replacement.

Figure 1. Pathways underlying the effects of short inter-pregnancy intervals

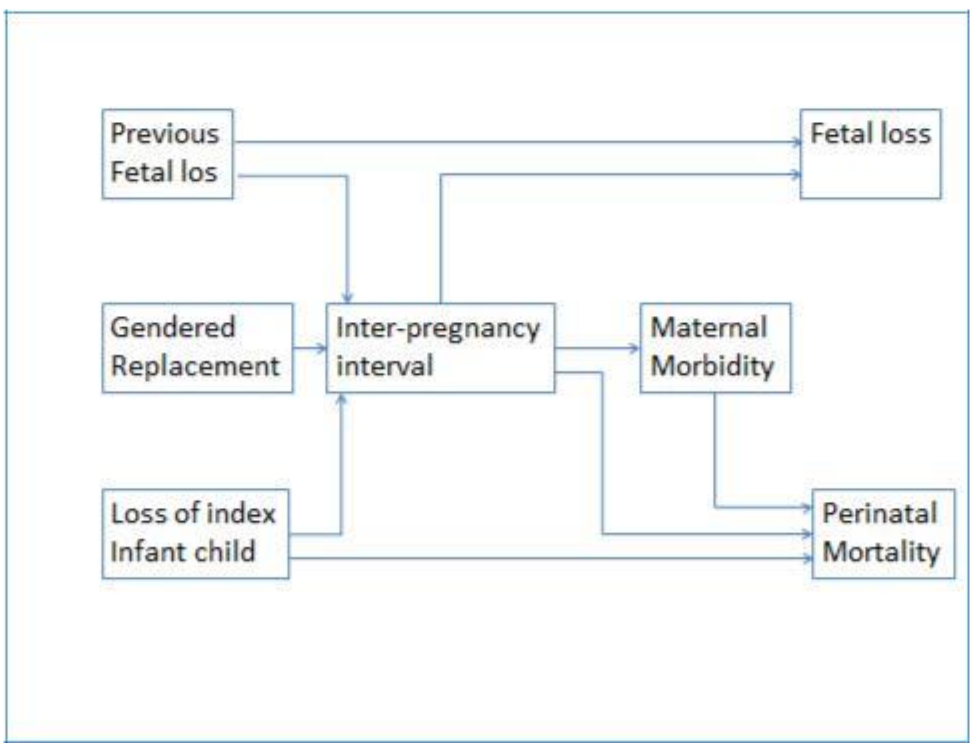

Figure 1 briefly summarizes how one adverse pregnancy might lead to another and how this is related to the length of the interval and the health of the mother. The loss of a child can have various causes and consequences that may also affect the capacity to have another. Some of these causes may be persistent (e.g repeated placental complications) and will also cause the next child to die. This is often referred to as the death trap. Others (e.g. the physiological stress of bearing a child and the mental stress of losing the child) may be more acute and diminish over time. In that case a longer interval will moderate the effects of the previous outcome on the next. The same mechanisms occur with fetal loss, were both persistent and more temporary conditions can define the chances of having another healthy pregnancy. The paradox is that adverse outcomes indicate or create unfavorable conditions for a subsequent pregnancy, while the wish to replace the loss, leads to a shorter interval to the next pregnancy.

The health of the mother is a crucial determinant of a successful pregnancy and again adverse outcomes might have a negative effect on this health (e.g. in the case of pregnancy complications), which in turn might affect the success of the next pregnancy. In this case the relation between subsequent outcomes is mediated by the health of the mother. Again the interval between pregnancies might be decisive as it might take time to recover from the previous event. First, a short interval between pregnancies might leave the mother depleted, stressed and unhealed from scares or in hormonal unbalance. Second, a long interval between pregnancies leads to a gradual loss of the maternal physiological adaptation benefits of a previous birth and the mother returns towards an equivalent state to primigravida (first pregnancy).

1.3 Overview of the thesis

This thesis is subdivided into 5 main chapters. Each of these chapters was elaborated following specific research objectives and methodology.

Chapter one *"Fertility decline in Rwanda: Is gender preference in the way?"* deals with the gender specific replacement strategy and estimates to what extent women with at least three living children, but whose only index son or daughter dies, desire extra births to achieve a more balanced gender composition of their offspring, subsequently reducing the waiting time for the next pregnancy. The analysis was restricted to 12831 women with at least 3 living children at the moment of the interviews from three cross-sectional datasets from the Rwanda Demographic and Health Surveys (DHS held in 2000, 2005 and 2010). SPSS was used to run a binary logistic regression.

The replacement strategy has been observed both after the disruption of the index pregnancy as well as after the death of the index infant. In reference to the maternal depletion syndrome theory, the depletion of the mother will be less after a fetal loss (but in most cases when the loss occurred before the third trimester) relatively to when there has been a full parturition of the pregnancy. However, if the causes of the fetal loss are taken to the next pregnancy a – fetal loss trap – will occur. A lost pregnancy will lead to the next regardless of the interval.

Chapter two *"Effect of interpregnancy interval and previous pregnancy outcome on pregnancy loss in Rwanda (1996-2010)"* highlights the combined effect of IPI and the type of previous pregnancy or infant survival outcomes on fetal loss in Rwanda.

STATA (12) software was used to conduct a binary regression analysis on 21532 last pregnancy outcomes from the 2000, 2005 and 2010 Rwanda Demographic and Health Surveys. The combined effects of the preceding pregnancy outcome and the inter-pregnancy intervals on fetal loss (death) were tested, controlling for age of the mother, pregnancy timing, place of residence, and year of the survey.

As an effect of the death of an index infant, the mother stops breastfeeding and thereafter this causes either a quick return of menses or a quick replacement in a short interval. This reproductive health outcome on the other hand is more likely to lead to a death trap, a situation where the death of child leads to an increased risk of dying for his/her younger sibling. The depletion status further increases when the index pregnancy is preceded by a viable birth and breastfeeding. Lastly, while estimating the effect of IPI on infant mortality, previous studies ignored the fact that fetal death removes the population at risk of infant mortality; a selection effect which may lead to biased results. On the basis of three cross-sectional data from the Rwanda Demographic and Health Survey (2000, 2005 and 2010) and STATA (12) software, Chapter three *"Effect of inter-pregnancy interval on fetal survival and neonatal mortality: A Heckman selection analysis"* uses two-step heckprobit models to control for selection bias by simultaneously estimating the combined effect of IPIs and the type of event that started the interval on both pregnancy survival and neonatal mortality.

There is a lack of sufficient empirical evidence on the effect of IPI on Maternal morbidity in the past or current scientific debates. Few existing studies are based on hospital data for which interpretation and conclusion should be done with utmost attention because of selected group of women that are either referred or manage to come to hospital for pregnancy and delivery care.

Chapter four "*Effect of IPI on maternal morbidity in Rwanda: A retrospective analysis of RDHS (2010) and Kibagabaga district hospital maternity records, 2012-2013"* consists of two analyses. On the basis of RDHS 2010, it first analyzes to what extent short or longer IPI lengths and the previous events are related to maternal pregnancy and delivery-related referrals to district hospitals in Rwanda. Second, it analyses the effect of primi-gravidity status, short or longer IPI on gestational hypertension, third trimester bleeding, premature rupture of membranes and lower limb edema for 2500 women who were referred to Kibagabaga district hospital between 2012 and 2013. Binary logistic regression analyses are conducted for both analyses.

As previous studies have evidenced, the survival of the infant is in relationship with the health of the mother and the gestation period has equal risks of both the mother and her baby. This means that, the observed effects of shorter (and longer) pregnancy intervals on maternal morbidity is more likely to contribute to perinatal mortality.

On the basis of Kibagabaga district hospital's maternity records files for years 2012-2013, and using Andrew F. Hayes' process Method for SPSS which is a useful computational tool for path (mediation) analysis and its integration into conditional process modelling), Chapter five *"Effect of Interpregnancy Interval and Maternal Morbidity on Perinatal Mortality: A Mediation Perspective"* estimates the mediating effect of maternal morbidity on perinatal mortality.

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Chapter 2. Fertility Decline in Rwanda: Is Gender Preference in the Way?

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Co-authored by Annelet Broekhuis and Pieter Hooimeijer

Abstract

In 2007 Rwanda launched a campaign to promote 3 children families and a program of community based health services to improve reproductive health. This paper argues that mixed gender offspring is still an important insurance for old age in Rwanda and that to arrive at the desired gender composition women might have to progress beyond parity 3. The analyses are twofold. The first is the parity progression desire given the gender of living children. The second is gender specific replacement intention following the loss of the last or only son or daughter. Using the Demographic and Health Surveys of 2000, 2005, and 2010, we show that child mortality does not lead to extra parity progression beyond three, while having single gender offspring does and even more so when this is the result of the loss of the last son or daughter.

2.1 Introduction

In 2007, the Government of Rwanda started a discussion about the introduction of legislation that should regulate family size to a maximum of three children. The debate has continued ever since. The government emphasizes that, given Rwanda's very high population density and its agricultural based economy, the poverty reduction strategies are hampered by the current high population growth of nearly 3% per year [1]. While the government is still working on the legislation, policies were already introduced to encourage fertility decline through sensitization campaigns in the media and through dialogues at community level. The latter played a crucial role in implementing the integrated Population Health and Environment Policy. The dialogues on program objectives and community needs took place in traditional forums that have been (re)invoked after the genocide, more specifically during the umuganda (community service), the ubudehe (participatory planning meetings), and the urugwiro (national dialogue sessions) [2]. The policies do not include specific goals with respect to preferences for sons or daughters, but strongly promote gender equity in every life domain, including education and political participation. Gender equality is a constitutional right [3] and is enforced in many laws [4–7]. Besides the sensitizing campaigns, community based health care services, including contraceptive provision, have been implemented to improve the reproductive health status of the population in every part of the country [8].

As a result Rwanda is making a substantial progress in reaching its Millennium Development Goals [9]. The recently released Demographic and Health Survey results (RDHS 2010) [10] show that the aim to reduce the infant mortality rate from 107 in 2000 to 50 in 2020 was already achieved in 2010. This reduction is linked with progress towards another important demographic target, a decline of the total fertility rate (TFR) from 5.8 in the year 2000 to 4.6 children in 2010, which is not far from the previously set target of 4.5 for 2020 [1]. A further decline seems possible because the average ideal family size (IFS) decreased substantially from 4.9 in 2000 to 3.3 children in 2010.

Considering the change in the demographic variables summarized in Table 1, Rwanda is at the beginning of the last phase of the demographic transition. Between 2000 and 2005, the TFR has fluctuated around 6 children per woman, indicating a stalling fertility decline over this period. Even though the TFR dropped after 2005, the current TFR level of 4.6 still remains 1.6 children higher than the government's aspired level of only 3 children and also higher than the average IFS of 3.3 children calculated for 2010. One can wonder if a fast further decline from 4.6 to 3 children is a realistic target with or without a strict legislation, or that the government has to reckon with possible resistance among Rwandan couples. Resistance could be rooted in existing norms or attitudes with respect to the ideal family size, in the ideal gender composition of the offspring, and/or in perceived mortality risks.

In this contribution the link between fertility and gender preference as well as between fertility and mortality will be analyzed. By using three Demographic and Health Survey cross-sectional datasets (DHS-2000 [11], DHS-2005 [12], and DHS-2010 [10]) this paper questions whether gender preference stimulates fertility beyond parity three.

Table 1: Changes in child mortality, fertility, and desired family size in Rwanda

Change Indicators / Year (RDHS)	2000	2005	2010
Infant mortality	107	86	50
Under five mortality	196	152	76
Total Fertility Rate	5.8	6.1	4.6
Ideal family size	4.9	4.3	3.3
Unmet need for contraceptive	36%	38%	24%
Use of modern contraception	4%	10%	45%

Source*: RDHS 2000[11], RDHS 2005[12], RDHS 2010[10] reports*

Studies about replacement or insurance effects on fertility behavior have been published also for African countries, but hardly any study is published about the link between the gender composition of the offspring and fertility intentions [13, 14]. The reason for this omission is obvious: this approach was not yet functional because in general Sub-Sahara Africa was characterized by high levels of fertility that result in families with children of both sexes. When African fertility levels continue to decline gender preferences can become a more distinct issue (see [15] for Bangladesh; and [16] for India), and therefore meaningful in an analysis of fertility attitudes and behavior. Seen its government policy and the rapid fertility decline since 2005, Rwanda is an interesting case to study the possible effects of gender preference on fertility decline.

This paper has the following research objectives:(i) to show the extent to which women with at least three living children, but lacking sons or daughters are more likely to desire extra births to achieve a more balanced gender composition of their offspring;(ii) to highlight the effect of the loss of the only or last son or daughter on women's desire to continue childbearing at parity 3 or over in Rwanda.

The outline of this study is organized as follows. Section 2 presents the theoretical and regional setting and is followed by Section 3 that discusses the data and methods used in the analyses. Section 4 deals with the results followed by a discussion and conclusion in the final section.

2.2 Theoretical and Regional Context

Like elsewhere in the world, people in Rwanda prefer to have both sons and daughters. This is shown in one of the traditional blessing by family and friends to new couples after the wedding ceremony when people say Muzarumbuke, Muzabyare Hungu na Kobwa (translation: “be fruitful, give birth to both sons and daughters”; Sempabwa and Hoemeke 2006 cited in Solo [8]). When the number of children per family is declining, the gender composition can become an important matter of concern if the perceived utility of sons and daughters differs largely, but even more so if people are convinced that it is better to have both. At the current TFR in Rwanda of 4.6 children, statistically only 7.5 percent of the couples have a single gender offspring (given the sex ratio at birth of 102 in Rwanda). At a TFR of 3 children, this percentage will increase to 25%. In case of a strong gender preference or preference for a balanced offspring, these couples will probably opt for a new pregnancy to achieve their desired family composition. Sheps (cited in Park and Cho [18]) has calculated theoretically that if all couples continued childbearing till they have at least two sons, the TFR will end up at 3.88 children. This TFR is closer to four children than to three, the desired family size by the Rwandan Government.

A strong gender preference among parents, in particular son preference, is related to nonexchangeable gender roles in a society which stem from economic, social, cultural, religious, and/or psychological contexts ([13,19–21]). In particular in areas where rigid patrilineal and patrilocal kinship systems regulate inheritance, allocation of productive assets (such as land) and old age support and where a strict labor division exists, sons are preferred above daughters [20]. In the terms used by Arnold and his colleagues it is the higher economic utility of sons compared to that of daughters that causes a strong son preference found in countries in Asia.

The few available studies for Sub-Sahara African countries on gender preference point at a slight son preference (see [22]), but as stated in the introduction the countries in Africa have still relatively high fertility levels and consequently the gender composition of the offspring is not an important issue. What will happen with gender preferences as the three children policy is implemented in Rwanda?

Traditional culture and customs in Rwanda are based on a patrilineal kinship system and lineage-based kinship relations are still important for mutual support [23]. This cultural context points at a possible preference for sons, in particular among fathers. This gender preference was enforced by the resource allocation system, in particular the one regulating access to land. This system changed several times during previous centuries, continually in favor of men by reducing property rights of women who lost their access to land held by the lineage of her father in law and could not enter into formal client relations with land owners in the patronage system [24]. As a result having sons was important for both men and women. Having sons protected a widow against the claims of her brothers in law or patron who demanded the land back that she and her deceased husband cultivated. A good relationship with her son(s) guaranteed a mother access to labor and subsistence security during old age [24].

On the other hand, certain farming and marriage practices illustrate that in Rwanda wives and daughters have an important economic value for their family as well. Like in many Sub-Sahara African countries farming work in Rwanda is performed by both men and women, although the so-called gender specific and gender sequential activities also exist [25]. Women focus more on food crops and men on cash crops such as coffee and tea [26]. Girls, like boys, are also seen as a source of wealth "because their parents are given a bride-price when they get married" [23, page 101]. Clay and Vander Haar [27], on the basis of the 1988 nonfarm Strategies Survey of Rwanda, evidenced that sons are more likely to give support in cash, whereas daughters were more likely to give support in kind, which suggest that Rwandan parents improve their social security by having both sons and daughters.

After 1994, the Government of Rwanda has been formulating and implementing new laws geared to equal rights for men and women. As a consequence, institutional and social systems are in transition. The new Inheritance Law of 1999 does not distinguish anymore between sons and daughters. For the inheritance of land, a scarce production asset in the Rwandan context, this means that land may pass to daughters. However, another law inhibits land fragmentation in parcels below a certain size. It is expected that in that case, fathers will prefer to give their land to sons, following former customary tenure systems (Bledsoe 2003 cited in Lastarria-Cornhiel [28]). After the latest change in tenure regulations, twice as many men got official land titles compared to women [28]. Despite the policy of the Rwandan government geared to gender equity, practices and attitudes rooted in traditional backgrounds do not change overnight. Seen in this light some preference for sons over daughters can be expected in relation to the gender composition of the offspring. This can be tested by analyzing the parity progression, while taking into account the gender composition of the living children. Studies for Korea [29], Bangladesh [30], Vietnam [31], and India [17] that used this approach have shown that in case of a strong son preference, parity progression is higher among women with no or only one son. The results also showed that people prefer to have at least two sons and one daughter. One wonders whether this preference for at least two sons also affects the link between mortality level of children and fertility behavior as part of the insurance strategy.

A more in-depth insight in the gender preferences—fertility behavior linkage will be gained if experiences with child mortality according to gender are added to the analysis. The impact of infant and child mortality on fertility behavior has been studied extensively, also for Africa [32–35]. It is assumed that, based on mortality experiences, parents adopt conscious strategies intending to realize their ultimate family size. Two behavioral responses to mortality of children are distinguished: first the replacement response when one's child dies it is replaced by an additional birth, and second the insurance response that leads to more births than the ideal number of children in order to avoid future risks of losing one or more children. The insurance response is the most "tricky" one of the two responses to study. For individual couples, assessing the mortality risks faced by their children is far from simple. Difficult issues in studying the insurance hypothesis are the measurement of perceptions of mortality levels and trends and the extent to which such perceptions enter into fertility decisions-issues. These matters are hard to derive from available datasets as DHS sets [36, 37]. However, for our objective to study the impact of gender preference on fertility behavior we can include the impact of the loss of either sons or daughters in combination with the gender composition of the surviving children. Both replacement and insurance responses could be valid if we find that parents with at least three living children and with mortality experiences have a higher parity progression ratio compared to parents who did not lose their last son or daughter. We do not intend to check explicitly for replacement or insurance behavior, but as we control for the number of living children, a higher gender-loss specific parity progression will be closer to insurance.

In case of son preference and perceived or experienced risk of infant/child mortality one expects that subsequent births will occur more often after the loss of sons compared to the loss of daughters. For India, Das [38] found that parity progression rates (PPRs) were influenced by mortality experiences and that at parity 2, women with one girl left, had a higher mean PPR than women with one son left. The results of the study of Gyimah and Rajulton [22] for Ghana and Kenya pointed in the same direction: in case the surviving children were all girls the probability of a subsequent birth was higher compared to the situation when all surviving children were boys.

2.3 Study Setting, Data, and Method

2.3.1 Data and Methodology

For the analyses in this study three cross-sectional secondary datasets from the Rwanda Demographic and Health Surveys are used (DHS held in 2000, 2005, and 2010). The DHS dataset is known to be an international reliable database because it follows strict sampling, surveying, and data file procedures and are made by well-trained enumerators and experienced staff. The women's questionnaire is used to collect information on all women in the age 15–49 years and covers a wide range of topics including the background of the respondents, her reproductive history, her knowledge and use of contraceptive methods, the antenatal, child-birth, and postpartum care received, vaccination, and childhood illnesses to mention a few of them.

The dependent variable in our analyses is the desire to have a next child. We used the answers to two questions related to fertility intentions in the questionnaire. Women who were either not pregnant or unsure about their status were asked the question: "Would you like to have another child or would you prefer not to have any more children?" A different question was asked to women who were pregnant at the time of the interview: "After the child you are expecting, would you like to have another child or would you prefer not to have any more children?"

As we wanted to test the impact of the composition of the offspring according to gender on women's desire to have another child and the impact of gender-specific mortality experiences, we restricted our analysis to women with at least three living children at the moment of the interview. In total 12831 women, subdivided in 3745 women for the year 2000, 4219 women for 2005, and 4867 for 2010, fulfilled these selection conditions.

Key independent variables in this study are the gender of living children and the loss of all children of a specific gender prior to the dates of interview. We did not include the parity of the deceased infant(s) in our model, consequently we did not check if (one of) the dead child (ren) was the index child (last born). Women were subdivided into those having both sons and daughters alive, or those having only girls or only boys alive. In reference to prior infant and child mortality experience by gender, women were classified into those with three or more living children of mixed gender with and without any mortality experience. For those who have daughters only, we distinguish the ones that never had a son from those that lost their last or only son. The same distinction was made for those that have sons only. In a bid to highlight the strength covered by gender specific replacement desire, we have included in our model demographic, socio-economic, and socio-cultural control variables.

The first demographic variable is the number of living children. As the chances of arriving at mixed gender increase with parity, controlling for this variable implies that we are not confusing gender imbalance effects with overall desired parity progression. Age over 30 years is used as a continuous variable in the analysis. This demographic variable is important to take into account as it is related to fecundity and fertility experiences and therefore to the capability and wish to have a next child or not. For marital status we divided the women in two categories: those in formal (married) or informal unions (living together) and those without a partner (single, separated, or widowed). Informal unions are accepted and common in Rwanda. Becoming pregnant without an identifiable partner is a strong taboo in Rwanda. These types of pregnancies or births are commonly known as IKINYENDARO, which means a pregnancy/birth coming from a lodge and not from a normal and socially accepted home. We expect that for this reason marital status influences the answers given by women on the main question (dependent variable) about wanting another child. A woman without a partner at the time of the interview could have a wish for a next child, but might not go to further parities given the taboo on children out of wedlock and because of the unfavorable conditions that she has to raise her children without economic and time support of a partner [39]. As an overall indicator of the socioeconomic status of the household of the mother, the living, housing, and hygienic conditions were preferred to the usual wealth index in the Demographic and Health Surveys Reports, for two reasons. Living and hygienic conditions have a direct relationship with the health (morbidity and mortality risks) of family members. Besides, the DHS wealth index does not distinguish between the poorest of the poor from other poor households [40]. For that reason we used an index constructed on various assets mentioned by respondents in the Individual Questionnaire. This questionnaire includes questions concerning the household's ownership of consumer items (telephone, radio); dwelling characteristics such as flooring material; type of drinking water source; toilet facilities, available energy sources, and so forth. We classified the respondents without the listed consumer goods and with poor hygienic (no access to safe drinking water and bad hygienic toilet facilities) and poor housing conditions (uncovered floors) as extreme poor. The category of poor women includes the ones with few possessions, with poor or moderate housing conditions, and with no connection to the water mains. We classified respondents that are living in houses with ceramic tiles, cement or carpet, were in possession of a radio and telephone, and with access to safe drinking water (piped system into their dwelling) as non-poor.

Table 2: The percentage of women with three or more living children who want to have another child

Year / Variable name	2000		2005		2010	
	Yes %	Total #	Yes %	Total #	Yes %	Total #
Gender balance and mortality						
Mixed offspring. no mortality (Ref)	34.7	1479	29.7	1705	16.3	2312
Mixed offspring. lost either sex	23.2	1850	19.7	2006	9.7	1933
Sons only. no loss of daughter(s)	53.6	151	38.7	181	26.0	242
Daughters only. no loss of son(s)	58.1	129	42.7	157	34.1	205
Sons only. lost daughter(s)	36.7	60	34.9	86	23.8	84
Daughters only. lost son(s)	38.2	76	35.7	84	20.9	91
Marital status						
Married or Living together	40.3	2676	31.9	3284	17.8	3954
Widowed/divorced/separated	6.6	1069	5.6	935	3.3	913
Media Exposure						
No Exposure(Ref)	30.3	3009	25.5	3265	15.0	3183
Radio and Newsletter	34.5	357	30.5	609	14.2	402
TV	30.3	379	23.5	345	15.8	1282
Housing and hygienic conditions						
Destitute	28.9	1414	24.0	1414	15.3	1180
Poor	32.1	1494	27.3	1942	15.2	2426
Non-Poor	31.1	837	26.3	863	14.8	1261
Education						
None	25.3	1613	20.8	1493	10.5	1248
Primary	35.2	1772	29.3	2354	17.1	3151
Secondary and higher	32.8	360	26.1	372	13.9	468
Respondent’s Occupation						
No occupation	29.4	520	27.3	718	17.3	446
Agriculture	31.5	2894	26.4	3102	14.6	3863
Bleu collar jobs (Unskilled)	25.8	217	23.1	273	17.1	462
white collar jobs(Managers. clerks..)	23.7	114	16.7	126	14.6	96
Residence						
Urban(Ref)	25.9	691	22.0	829	14.1	623
Rural	31.8	3054	27.0	3390	15.2	4244
Mothers’Religion						
Catholics(Ref)	NA	NA	24.7	1951	12.1	2151
Protestants	NA	NA	27.7	1504	18.8	1860
Adventists	NA	NA	27.1	564	15.8	676
Muslims	NA	NA	17.7	96	5.6	72
No Religion	NA	NA	26.7	75	14.0	100

Total		3745		4219		4867

Sources: *RDHS 2000. RDHS 2005 and RDHS 2010*

The variable women's occupation was divided into four categories, house-wives (those who are not employed), women who are employed in agriculture, women who are employed as unskilled or manual workers (blue collar) and those in managerial, clerical or services positions (white collar). We control for this variable to see if work activities of the mother—a well-known but counterfactual socio-economic determinant of fertility behavior [41] is related to the wish to have another child.

The exposure to media is known to be an important channel for behavioral change in general and in family planning in particular [42]. In this study, media exposure is defined as having heard about family planning on the radio or on television. A number of studies have also shown a positive association between women's years of formal education, use of maternal and child health services, and subsequently a reduced family size [43–45]. Education is therefore included in our model. Urban/rural differentials in fertility are not only related to occupational and educational composition, but also to differences in modernization and in labor market opportunities [46]. We therefore added the urban/rural variable on top of occupation and education.

Religion is another sociocultural factor in shaping fertility preferences and behavior [47]. The RDHS distinguishes Catholics, Protestant, Adventists, and Muslims, the latter being a very small community based mainly in the capital Kigali. Unfortunately this information is not available in the 2000 RDHS and we had to drop this variable in the multivariate model. From the descriptive results in Table 2 it is clear that the percentage of Protestants, that want another child after having three, is slightly higher.

2.3.2 Analytical Model and Tool

A bivariate design was used to check the effect of gender composition and the loss of sons and daughters if the mother expresses the desire to have another child and if she does not have this desire. We used the binary logistic regression from the Statistical Package for Social Sciences (SPSS 20.0 for windows) to estimate the model. Results are presented as adjusted (logged) odds ratios. The results are based on the pooled data set, using year of the interview as one of the explanatory variables. We checked for interaction effects of year of the interview with the other exogenous variables, but none came up as being significant. We also ran the model separately for each year and, apart from the constant, the parameters did not differ substantially.

2.4 Results

Our first results describe the change in gender preferences over the years (Table 3). A striking result is the clear preference for gender balance, shown on the diagonal. Having the same number of boys and girls is preferred by more women than any other combination, and the percentage on the diagonal is larger than any other within each row and each column. This pattern changes in 2010, when the combination of having two sons and one daughter is slightly more popular than having one son and one daughter.

Table 3: Preferred gender combinations in 2000, 2005, and 2010 of women having three or more children

Year	Prefered # of boys	Preferred Number of girls				
		No Preference	1 daughter	2 daughters	3 or more daughters	Total
2000	No Pref.	**471 (12.6%)**	8(0.2%)	9(0.2%)	2(0.1%)	490(13.1%)
	1 son	8(0.2%)	**178(4.8%)**	67(1.8%)	33(0.9%)	286(7.6%)
	2 sons	4(0.1%)	129(3.4%)	**962(25.7%)**	351(9.4%)	1446(38.6%)
	3 and more	5(0.1%)	76(2.0%)	393(10.5%)	**1049(28.0%)**	1523(40.7%)
	Total	488(13.0%)	391(10.4%)	1431(38.2%)	1435(38.3%)	3745(100%)
2005	No Pref.	**645(15.3%)**	4(0.1%)	5(0.1%)	5(0.1%)	659(15.6%)
	1 son	9(0.2%)	**246(5.8%)**	80(1.9%)	23(0.5%)	358(8.5%)
	2 sons	15(0.4%)	188(4.5%)	**1428(33.8%)**	285(6.8%)	1916(45.4%)
	3 and more	10(0.2%)	92(2.2%)	394(9.3%)	**790(18.7%)**	1286(30.5%)
	Total	679(16.1%)	530(12.6%)	1907(45.2%)	1103(26.1%)	4219(100%)
2010	No Pref.	**1137(23.4%)**	3(0.1%)	5(0.1%)	2(0.0%)	1147(23.6%)
	1 son	16(0.3%)	470(9.7%)	256(5.3%)	23(0.5%)	765(15.7%)
	2 sons	10(0.2%)	**555(11.4%)**	**1331(27.3%)**	187(3.8%)	2083(42.8%)
	3 and more	19(0.4%)	75(1.5%)	283(5.8%)	**495(10.5%)**	872(17.9%)
	Total	1182(24.3%)	1103(22.7%)	1875(38.5%)	707(14,5%)	4867(100%)

Sources: *RDHS 2000. RDHS 2005 and RDHS 2010*

In 2000 the modal category is having a combination of three or more of each (28%), directly followed by having two of each (25%). In 2005 the ideal family size dropped and having two sons and two daughters is the most preferred (34%) composition, which is also the case in 2010, but in that year having no preference for either sons or daughters is the second most popular response.

At an uneven number of offspring, boys are clearly preferred to girls. In each year, twice as many women prefer having two sons and one daughter over having two daughters and one son. In later years the (smaller) numbers that want five of more children prefer three sons and two daughters over three daughters and two sons.

At first sight one may therefore conclude that pressure to limit the maximum number of children to three will shift the gender preference balance towards male offspring. Yet the number of women who state not to have any preferences is growing very rapidly and nearly doubled in 10 years of time, and fifteen percent of our population see the combination of one son and one or two daughters as an ideal alternative. Close to fifty percent could probably live with having three children, but half of these want to have at least one son and one daughter.

Table 4: Binary logistic regression of the desire to have another child for women with at least three children (pooled data 2000, 2005, and 2010)

Variable	**N**	**B**	**S.E**	**Odds Ratios**
Gender balance and mortality	**12831**			
Mixed offspring. no mortality (Ref)	5496			
Mixed offspring. lost either sex	5789	-.056	.058	.945
Sons only. no loss of daughter(s)	574	.102	.108	1.108
Daughters only. no loss of son(s)	491	**.365** **	**.114**	**1.441**
Sons only. lost daughter(s)	230	**.371** *	**.171**	**1.449**
Daughters only. lost son(s)	251	**.395** *	**.168**	**1.485**
Year of Interview				
2000 (Ref)	3745			
2005	4219	**-.483** ***	**.060**	**.617**
2010	4867	**-1.452** ***	**.067**	**.234**
Number of Living children (–3)		**-.473** ***	**.024**	**.623**
Current age of the mother (-30)		**-.099** ***	**.005**	**.905**
Marital Status				
In a union (Ref)	9914			
Single/separated/widowed	2917	**-2.094** ***	**.093**	**.123**
Media exposure				
No exposure (Ref)	9457			
Radio and Newsletter	1368	-.027	.080	.974
TV	2006	.023	.082	1.023
Housing and hygienic conditions				
Destitute (Ref)	9457			
Poor	1368	**.125** *	**.059**	**.033**
Non-Poor	2006	.028	.078	.721
Respondents' Education Level				
None	4354			
Primary	7277	.015	.059	1.015
Secondary and Higher	1200	-.025	.111	.975
Respondents' occupation				

None (Ref)	1684			
Agriculture	9859	.054	.077	1.056
Blue collar	952	.034	.116	1.034
White collar	336	**-.417** *	**.185**	**.659**
Place of residence				
Place of residence(Urban)Ref	2143			
Place of residence(Rural)	10688	**.464** ***	**.083**	1590
Constant		.401	.119	1493

Sources: *RDHS 2000. RDHS 2005 and RDHS 2010====Significance: * <0.05 **<0.01 ***0.001*

In our multivariate model (Table 4) we first investigate the impact of the composition of the living offspring according to gender on a couple's wish to stop having children. We expect that in case of a strong preference of any gender (daughters or sons), women with at least three children of the same sex are not satisfied with the gender composition of their offspring and have a higher probability of wanting a next child compared to women with a mixed offspring. Besides we expect that women who have lost a child will more often desire another child compared to women who did not lose one or more children, in particular if the loss of children would mean losing the last or only son or daughter.

As previous studies have hypothesized, women's reproductive behavior (fertility) is influenced by existing mortality patterns in terms of replacement and insurance strategies. But, in many cases, studies have focused on the replacement of the index child who dies before parents reach the desired number of children [48, 49]. Apart from this conscious strategy related to the loss of the index infant, we expect that parents' response on child mortality becomes more accentuated when they have lost a child of a specific gender, in particular when the surviving children have the same gender.

The results in Table 4 show that at parity of 3 living children and above, the desire for an extra child of parents who did not lose any child or who mourned the loss of one or more children does not vary significantly in case the surviving children have a mixed gender composition. The odds ratio (0.945) is close to 1. As we control for the number of living children, replacement might already have occurred, which would indicate that there are no insurance effects of prior child mortality experience.

Insurance effects may be expected if sons or daughters are lacking, in particular in absence of replacement. The third and fourth category of our variable defines the women with sons and daughters only, without having lost children of the opposite gender. Parity progression after three is higher in both cases, but insignificant for those that have sons only. Support in old age seems to be more dependent on the presence of a son than of a daughter.

Both replacement and insurance effects are bound to occur, when people lose their last or only son or daughter. The results of the model show that this is indeed the case. The ones that had at least one daughter but lost all have higher odds to continue childbearing. The effect is also strong among women that had at least one son but lost all the odds ratio is close to 1.5.

The effect of the year of the interview is very prominent, with an odds ratio of 0.234 for 2010 over 2000. The fact that we did not find any interaction effect of this variable with the variable on gender balance and mortality (not shown) indicates that the slight preference for having and replacing sons has not increased significantly over the years. However it also means that losing the last son or daughter has the same strong effect on parity progression in 2010 as in 2000.

For a second check of significant changes over time we ran the model separately for the year 2010. The estimated odds ratios for the gender balance and mortality variable are slightly higher (1.003; 1.162; 1.668; 1.838; 1.686 not shown here), but not significantly different from the odds ratios in the pooled set.

The control variables have the expected sign, with the exception of poverty and education that show limited or no significant relation. The absence of an interaction effect with the year of the interview indicates that the strong campaign to limit childbirth has touched upon each segment of the population in Rwanda, but does not mean that having three children is now favored by everybody. The existing heterogeneity in parity progress remains stable over time, albeit at a lower overall level.

2.5 Conclusion

The lack of a significant difference in the desire to stop at parity 3 between mothers of a mixed offspring with or without a loss of a child indicates that the insurance effect in concern of future mortality is not strong. Mothers do not want at least two children of each gender to be sure that they—seen the experienced risk of child mortality—will be left with a single gender family in the future. Mothers with a single gender family of three children who have lost the only or last child of the opposite sex do have a strong wish to replace that child. In other words, replacement is strongly related to the gender composition of the living children. Still having a mixed gender family does not lead to replacement, but being left with a single gender family does. These results are in keeping with conclusions of others who state that the effect of replacement on mortality is "modest in magnitude" [32, page 61] and that decisions about fertility behavior in relation to child mortality must not be seen in isolation [49]. The determinants of fertility decisions constitute a complex framework in which various components and goals play a role. Health of the mother could be a factor to stop child bearing, costs of children as well according to these researchers, and as our study shows gender composition of the family does also.

Sons and daughters are almost equally important for mothers in Rwanda. We interpreted this as a fertility decline-gender preference trade off, a situation where women find a threat in echoes appealing them to stop childbearing before leveling the gender preference among their living offspring. Even though the total fertility rate has fallen from 6.1 to 4.6 between 2000 and 2010, attitudes towards filling the gender gap for families with 3 single gender living children or replacing dead infants of a specific gender for families who reported having lost all sons or all daughters have not changed over this decade.

The output of this study evidences that, even though the government might focus its effort to reduce the total fertility rate to 3 children through the provision of family planning services or sensitization campaigns, the gender composition of living children remains a corner stone to parity progression for Rwandan women even after reaching the third or higher parities. A gender specific replacement strategy driven by the desire for a mixed family composition was identified to be a strong motivation for parity progression.

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Chapter 3: The effects of inter-pregnancy intervals and previous pregnancy outcome on pregnancy loss in Rwanda (1996-2010)

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Abstract

In 2005, a WHO consultation meeting on pregnancy intervals recommended a minimum interval of 6 months after a pregnancy disruption and an interval of two years after a live birth before attempting another pregnancy. Since then, studies have found contradictory evidence on the effect of shorter intervals after a pregnancy disruption. A binary regression analysis on 21532 last pregnancy outcomes from the 2000, 2005 and 2010 Rwanda Demographic and Health Surveys was done to assess the combined effects of the preceding pregnancy outcome and the inter-pregnancy intervals (IPI) on fetal mortality in Rwanda. Risks of pregnancy loss are higher for primigravida and for mothers who lost the previous pregnancy and conceived again within 24 months. After a life birth, inter-pregnancy intervals less than two years do not increase the risk of a pregnancy loss. This study also confirms higher risks of fetal death when IPIs are beyond 5 years. An IPI of longer than 12 months after a fetal death is recommended in Rwanda. Particular attention needs to be directed to post pregnancy abortion care and family planning programs geared to spacing pregnancies should also include spacing after a fetal death.

3.1 Introduction

An expert consultation organized by the World Health Organization in 2005 made an inventory of available research on births spacing. The experts recommended an inter-pregnancy interval (IPI) of at least 6 months after a miscarriage before attempting a next pregnancy, in order to reduce morbidity and mortality risks for mother, fetus and new born. An IPI of at least 24 months was recommended after a live birth, corresponding to a birth interval of at least 33 months. The consultation team also concluded that future research is needed on the mechanisms underlying the relation between interval length and pregnancy outcomes. More studies using datasets from both rich and poor countries, could contribute to more in-depth knowledge[i]. Contradicting results of research on the effect of short intervals on the risk of adverse pregnancy outcomes[i-iv] conducted after 2005 confirmed the wisdom of these statements. The few studies on the effect of intervals after a previous pregnancy disruption show a large variation by country. Da Vanzo and colleagues[i], emphasized that studies on the effects of inter-pregnancy intervals should to take into account the outcome of the previous pregnancy.

Our study contributes to the debate on pregnancy loss and inter-pregnancy intervals (IPI) in line with these recommendations. We focus on the effect of the duration of the IPI on pregnancy losses by combining the effect of the interval duration and the type of previous pregnancy outcome (pregnancy loss, live births that survived infancy or died in the first year), and controlling for important confounders. In this study the term pregnancy loss includes all pregnancy outcomes (spontaneous and induced abortion, fetal death, and stillbirth) opposite to a live birth.

Fetal loss has got limited attention[ii] compared to other issues, neither in the field of reproductive health, nor in development debates among policy makers, nor in debates among scholars in population studies. This lack of attention is regrettable, because for many women the loss of a pregnancy is an emotional experience which effects their subsequent reproductive health and behavior. The absence of easy accessible and reliable secondary data on pregnancy loss is mentioned as a reason for neglecting the topic of fetal deaths by scientists[iii]. Our contribution will illustrate that the data from Demographic and Health Surveys (DHSs) can be used for this study, although answers on different questions have to be combined to find all fetal deaths in and before the calendar period of the DHSs.

We hope that the results of our study can be useful for reproductive health programs in Rwanda. Reducing adverse pregnancy outcomes contributes to the health of the mother. Contrary to the reduction of maternal morbidity and of infant mortality, reducing pregnancy loss is not a policy objective, but should become so in the future.

3.2 Conflicting evidence

The outcome of our analysis will be discussed in the framework of results of a few[iv] available studies that followed the same approach by including the IPI duration and the previous pregnancy outcome to estimate the risk of a pregnancy loss. The majority of these studies focus on the effect of IPI duration on adverse pregnancy outcomes after a previous spontaneous or induced abortion while only a few have a broader perspective and include also other prior pregnancy outcomes (see Annex). The studies differ on essential points, such as various types of mothers in the sample: nulliparous or multiparous women; various types of adverse pregnancy outcomes: pregnancy loss, preterm births, low birth weight; reference group; categories of IPI; data collection method and geographical region, which could contribute to explain the variety in the findings.

Only two studies, one from the USA the other from Latin America, did not a find significant associations between IPI duration and a fetal or neonatal death after an spontaneous or induced abortion[v vi]. The other studies do find an association between IPI duration and adverse maternal and pregnancy outcomes after a previous fetal loss, but the associations between IPI duration and recurrent pregnancy losses are weak or non-existent for late fetal deaths (stillbirths)[vii viii]. Some results from the USA and Scotland are even the opposite of what is expected on the WHO recommendations after early fetal deaths (miscarriages) [ix x xi]. They find that after a previous early fetal loss, short IPI intervals are associated with a higher likelihood on a live birth compared to longer IPIs.

The studies that focus on the association between IPI duration and the risk of a fetal death (and other adverse pregnancy outcomes) including all types of prior pregnancy outcomes, do not confirm this latter conclusion. Both the meta-analyses by Conde-Agudelo et al.[xii], and the study on Bangladesh by DaVanzo et al.[xiii], conclude that after a fetal loss and a short IPI a higher risk on a subsequent fetal loss exists compared to the risk after a previous life birth and a healthy IPI. The meta-analyses included many countries from all over the world and consequently examples with good and poor health care systems. A study on Sweden[xiv] – a country with an advanced medical health care system - however, stated that risks are only found for long intervals, and that the impact of short intervals may have been overestimated in other studies. From all the three studies we learn that it is important to include the outcome of the previous pregnancy in the analysis and to focus on several previous pregnancy outcomes when analyzing the effect of short IPIs on fetal losses. Therefore we will follow this approach in our analysis.

3.3 Rwanda and regional contexts

Since 2000 Rwanda is experiencing a steady economic growth and since 2005 also a rapid demographic fertility transition. Despite progress made in many fields, it is still a low income country with a Human Development Index of 0.434 in 2012, ranking 167 out of 187 countries[xv] [xvi]. Seen the economic situation and the financial constraints the government has strict priorities for development investments. Next to challenges (see introduction) of poverty reduction and slowing down population growth, Rwanda faces a need to improve its human resource base. This means improving the health and education levels of the population.

The health service infrastructure, which was badly damaged during the civil war and genocide of the ninety-nineties, has been rebuilt to a large extent. At local level, community health centers are established and more than 45,000 community health-care workers, male and female, have been trained to provide basic medical care and drugs and to give information on health matters like insurance, malaria, HIV prevention, and family planning methods. A third of those health care workers were trained in midwifery. The number of qualified medical staff, decimated by the genocide - increased again, yet is still insufficient according to international standards, one medical doctor and one professional midwife per 16,500 and 23,400 inhabitants respectively. More recently the quality of health care improved by introducing a performance based financing scheme[xvii].

The government improved access to community health care by introducing a community based insurance system. Today, more than 90% of the population participates in these *Mutuelles de Santé* which give access to community level health services and, with additional payment, to a package of extra health care at district hospitals. An impressive increase, seen the fact that the percentage was only 7% in 2003.The new system started in 2007 with a flat annual contribution of 1000 Rwandan Francs (less than 2 USA $) per person, an additional payment of RwF 200 per visit to a community health center and a contribution of 10% in the costs of services delivered by district hospitals. In 2011 a revision of the system was necessary to make it financially sustainable. The annual fixed contribution increased substantially according to a three tier premium system based on household wealth.

The prenatal checks and the costs of a normal delivery assisted by a nurse or midwife are covered by the basic health insurance schemes, but exclude the 200 RwF per visit to a health center. In case of a more complicated delivery in a hospital 10 percent of the total costs of the treatment are charged. Despite the costs involved for households, being pregnant and giving birth have become less risky thanks to this health policy. The percentage of women delivering with the assistance of a trained professional (midwife, nurse) increased substantially from 31 (1996-2000) to 69 percent in the period 2006-2010. According to the 2010 Demographic and Health Survey (DHS), less than two percent of the women did not have any antenatal medical test before the delivery. However, the health seeking behavior of pregnant women is still insufficient as only 35 percent of them went for four antenatal checks, as recommended by the WHO. Most pregnant women got their first medical examination in the second trimester of their pregnancy, some even later.

3.4 Methodology

Data from three successive Rwanda Demographic and Health Surveys (RDHS 2000, 2005 and 2010) were merged to analyze the last pregnancy outcome of women within the DHS calendar periods of five years proceeding the moment of interview. Pregnancies and pregnancy outcomes that occurred in the eight months before the month of the interview were not included to be sure that all pregnancies in the analysis had the same probability of ending in a pregnancy termination or a life birth after nine months. In total 21532 women had at least one pregnancy outcome in the three reduced calendar periods before 2000, 2005 and 2010; for 3631 women it was their first pregnancy (primigravida); for the other 17901 women we calculated the date and type of the previous pregnancy outcome. In case of a long inter-pregnancy interval, this previous pregnancy outcome could have occurred before the five year calendar period.

The DHS datasets enable the calculation of the exact date (in terms of month and year) of the events in the reproductive history of women in the sample if one combines answers to various questions in the questionnaire. We constructed Century Month Codes (CMC) – the number of months elapsed since January 1900 - of the pregnancy outcomes (pregnancy loss, infant death, and live birth) reported by the mothers to calculate the IPIs. In case of a life birth as last pregnancy outcome the pregnancy was supposed to start 9 months before the CMC of the birth, as the duration of the pregnancy is not recorded. In case of a fetal loss as last pregnancy outcome the mother did report the duration of the pregnancy. Data from retrospective studies, like the Demographic and Health Surveys, are biased by errors due to memory lapses as the respondents have to report the number and date of the events in the past[xviii]. This is in particular the case when one asks for matters as pregnancy losses and induced abortions. Early pregnancy losses may not be noted or easily forgotten and induced abortions may not be reported as these are illegal in many societies. By focusing on the two last pregnancies of which the last one (and in many cases the previous as well), occurred during the calendar period we reduced the risk of memory errors.

For our analysis we calibrated a binary discrete regression model using the statistical package STATA 12.

The dependent variable is the outcome of the last pregnancy (fetal loss coded as 1, life birth as 0). We checked whether a distinction between early and late losses[xix] gave different results, but this turned out not to be the case. To construct a more powerful model we decided to take all fetal deaths together.

We defined the two main independent variables: length of the inter-pregnancy interval and previous pregnancy outcome as follows. Inter-pregnancy intervals (IPI) were calculated as the time between the outcome of the previous pregnancy that ended either in a pregnancy loss or life birth, and the last conception. Short intervals are defined as shorter than 4 months or 4 up to 12 months after a previous pregnancy loss and shorter than1 year or between 1 and 2 years after a life birth. A healthy interval after a life birth is an interval of at least two years and less than 5 years.

We categorized the life births of the previous pregnancy in two groups: infants that survived the first year of their life or not. We did not exclude multiple gestations, but we considered them as one birth. Subsequently we constructed variables to represent the interaction between those two main independent variables in which we used different classifications for the IPI-duration after the previous pregnancy outcomes.

We tested for several confounding factors, but in the final model included only four control variables that turned out to be of significance. The first is the inevitable bio-demographic control variable age of the mother at conception which is an indicator for her physiological condition at the start of and during her pregnancy. Age refers to her reproductive condition (including fecundity, reproductive health) that contributes to a healthy pregnancy and the birth of a healthy infant. The second control variable is the pregnancy wish: was her pregnancy wanted or not. Response categories included wanted it later, wanted no more and rather not tell. The latter category is used as a proxy for intended pregnancy losses. The third variable is place of residence distinguishing between urban and rural residence. Finally we included the year of the interview to check for changes over time in reproductive health: notably the extent of the possible reduction of fetal mortality. Table 5 gives the descriptive statistics of the research population.

3.5 Results

The results presented in Table 5 illustrate that many Rwandan women still have to deal with pregnancy losses, the death of an infant and unwanted pregnancies: 36 out of 1000 last pregnancies in our sample population ended in a pregnancy loss. Among the women with at least two pregnancies 15 percent mourned a fatal outcome of the previous pregnancy: five percent had a pregnancy loss and nearly ten percent got a child that died in infancy. The results indicate also that the percentages of pregnancies ending in a pregnancy loss are highest after an IPI shorter than 24 months that started after a pregnancy loss. Higher percentages of pregnancy loss than the mean of 3.6 per cent were found after a live born that died in its infancy and an IPI of more than two years, and after a surviving life birth and a very long IPI (> 60 months).

The descriptive statistics in Table 5 show a modest decline of the rate of fetal losses during the period under study. For the three consecutive research periods the rate of pregnancy loss diminished from 41 out of 1000 pregnancies (1996-2000), to 36 (2001-2005) and finally to 33 in the most recent period 2006-2010.

Table 5: Descriptive statistics: last pregnancy outcomes in percentages and in total numbers (pooled data from DHS 2000, 2005 and 2010)

Variable names	Latest pregnancy outcome (N=21532)		
	Pregnancy loss (%)	Live birth (%)	Total number
First pregnancy (primagravida)	3.3	96.7	3631
Previous Pregnancy Outcome * IPI			
Pregnancy loss			
* IPI <=3 months	10.6	89.4	161
* IPI >=4 months & IPI<=12 months	7.9	92.1	381
* IPI >=13 months & IPI<=24 months	8.0	92.0	217
* IPI >=25 months	4.7	95.3	149
Life birth (died in infancy)			
* IPI<=12 months	3.3	96.7	662
* IPI >=13months& IPI >=24 months	2.6	97.4	582
* IPI >=25 months	5.5	94.5	513
Surviving live birth			
* IPI <=12 months	2.3	97.7	1594
* IPI >=13 months& IPI >=24 months	2.7	97.3	5580
* IPI >=60 months	7.6	92.4	1314
* IPI >=24 and IPI <=59 months	3.5	96.5	6740
Age mother at latest conception			
20 years and younger	2.7	97.3	2075
36 years and older	6.8	93.2	4780
21 thru 35 years	2.7	97.3	14677
Pregnancy Timing			
Untimed (later)	1.7	98.3	4116
Unwanted (nomore)	1.4	98.6	2786
Unkown / vague answer	8.7	91.3	5246
Wanted (then)	2.2	97.7	9368
Type of place of Residence			
Urban	4.2	95.8	4125
Rural	3.5	96.5	17407
Year of Interview			
2000	4.1	95.9	6383
2005	3.6	96.4	6816
2010	3.3	96.7	8333
Total	3.6	96.4	21532

Sources: *RDHS 2000. RDHS 2005 and RDHS 2010*

Table 6: Wanted the last pregnancy (in %) according to previous pregnancy outcome and IPI duration

Prev.outc.	IPI	vague	Unwanted	untimed	wanted		tot nbr
primigr.	-	19.6	8.3	13.4	58.8	100.0	3631
Fetal loss	<3	24.8	14.3	14.9	46.0	100.0	161
	4-=<12	20.2	12.9	12.9	54.9	100.0	381
	13-24	37.3	14.2	5.3	43.1	100.0	225
	25+	28.9	14.1	4.0	53.0	100.0	149
Live born	<=12	23.9	9.8	13.7	52.6	100.0	662
Died	13-24	27.0	10.5	9.6	52.9	100.0	582
	>=25	31.6	11.8	6.3	49.7	100.0	513
Surviving	<12	28.4	11.2	39.7	20.7	100.0	1594
live born	13-24	21.1	13.5	31.5	34.0	100.0	5580
	25-59	25.1	15.2	14.0	45.7	100.0	6740
	60+	38.8	16.5	2.2	42.5	100.0	1314
Total		24.4	12.9	19.0	43.5	99.9	21532

Sources: *RDHS 2000. RDHS 2005 and RDHS 2010*

Women who were pregnant for the first time reported the highest percentage wanted pregnancies (nearly 60%, see table 6). Of all last pregnancies by the other women only 40 percent were wanted at that time, while more than a third was unwanted or the mother gave an unclear answer (or answer not known). The cross tabulation presented in table 6 shows that after a pregnancy loss or the loss of an infant a large part of the women want to replace this loss. The percentages wanted pregnancies extend the average of 40 percent. Very low numbers of wanted pregnancies are found among women who became pregnant within 2 years after the birth of the previous child that survived the first year of its life. Those two groups of women had liked to become pregnant later in time (indicated by 40 and 31 % respectively).

A large part of the women became pregnant again before the recommended time (by WHO) for recovery was over. From the women whose previous pregnancy ended with a fetal loss 43 percent was expecting a child again within half a year. For women who had a live born that died afterwards in infancy, 71 percent was pregnant again within two years after the last delivery, which could point at a replacement effect or at a lack of protection against pregnancy. For women whose child survived the first year of its life this percentage was much lower (47%). This group of women is probably temporary sub-fecund due to a longer amenorrhea period caused by lactation.

Table 7: Binary logit coefficients on the risk of pregnancy loss in Rwanda (pooled data 2000, 2005, 2010)

Log likelihood = -3038.95	LR chi2(19) / Prob > chi2 / Pseudo R2			642.2 / 0.000 / 0.096
Variable Names	**N=21532**	**B**	**P>z**	**Exp (B)**
Previous pregnancy outcome and IPI				
Previous live birth*IPI>=25 & IPI <=59 months)(Ref)	6,740			
Pregnancy Termination				
* IPI >=3 months	161	**1.303**	***	**3.680**
* IPI >=4 months and <=12 months	381	**0.974**	**	**2.648**
* IPI >=13 months and <=24 months	225	**0.663**	*	**1.940**
*IPI >=25 months	149	0.102		1.107
Previous Infant Death				
* IPI <=12 months	662	-0.014		0.986
* IPI >=13 months and <=24 months	582	-0.401		0.670
* IPI >=25 months	513	0.257		1.292
Previous surviving live birth				
* IPI <=12 months	1,594	**-0.410**	*	**0.664**
* IPI >=13 months & IPI<=24 months	5,580	-0.083		0.920
* IPI>=60 months	1,314	**0.494**	**	**1.639**
Primigravida	3,631	**0.400**	*	**1.492**
Age of mother at the latest conception				
21 thru 35 years (Ref)	14,677			
20 years and younger	2,075	-0.199		0.819
36 years and older	4,780	**0.843**	***	**2.323**
Pregnancy Timing				
Wanted (ref)	9,368			
Untimed(Later)	4,116	-0.108		0.898
Unwanted (Nomore)	2,786	**-0.751**	***	**0.472**
Unkown / vague answer	5,262	**1.308**	***	**3.698**
Place of Residence				
Rural(Ref)	17,407			
Urban	4,125	**0.217**	*	**1.243**
Year of Interview				
2000(Ref)	6,383			
2005	6,816	-0.117		0.889
2010	8,333	**-0.259**	**	**0.772**
Constant		**-4.004**	***	**0.018**
Significance: * <0.05 **<0.01 ***0.001				

Sources: *RDHS 2000. RDHS 2005 and RDHS 2010*

The constant (Table 7) reflects the risk of a pregnancy loss for the reference category: rural women in 2000, in age category 21-35 years at the time of the last conception, whose last pregnancy was wanted and started after a healthy IPI (25-59 months), and whose previous pregnancy resulted in a child that survived its infancy. The estimate of the risk of experiencing a pregnancy termination for these women is very low (2%). The other variable's Exp(β) give the odds ratios for women in the categories that deviate from the reference category.

Before discussing the relation between pregnancy losses, inter-pregnancy intervals and the outcome of the previous pregnancy, we remark that the likelihood of a pregnancy termination decreased significantly between 2000 and 2010. For 2005 the sign of the coefficient (β) is negative, but the decrease is not significant. In 2010 however, the decrease is significant. Further analyses, not shown here, showed that this decrease pertained to late pregnancy loss only. This may be seen as an indication that improved health-seeking behaviour among pregnant women in particular during the second half of their pregnancy contributed to less pregnancy losses.

Linking the risk of a pregnancy termination with both the outcome of the previous pregnancy and the length of the IPI (interaction variables) shows significant deviations from the risk estimated for the reference group: all except one point at a higher risk. The highest odds are found for women who became pregnant shortly after a previous pregnancy loss. Women who conceived again within 3 months after the previous pregnancy loss are 3.68 times more likely to lose the next pregnancy than the reference group with a healthy interval. The odds ratio is 2.648 for those that waited 4-12 months and even women who waited 12-14 month were almost twice as likely to lose the next pregnancy. Women with a IPI of more than two years after a previous fetal loss had a lower risk compared to the reference group, but the association is not significant.

After a life birth regardless if the new born survived its infancy or not, the likelihood of a pregnancy loss after an IPI considered as unhealthy (< 2 years) is not higher compared to the reference group with a recommended IPI duration. For the mother that became pregnant within one respectively two years after the previous birth the signs of the coefficients are negative, but only significant for women whose infant stayed alive and conceived within one year. Any pregnancy after a live birth seems to prepare for a successful next pregnancy, regardless of the inter-pregnancy interval.

This mechanism vanishes after some years, as an IPI of more than 5 years results in a substantial higher likelihood of a pregnancy loss (1.6 times more likely). The risk on a pregnancy loss for mothers who are pregnant for the first time is of the same magnitude (1.5 times more likely).

According to the literature a higher age at conception leads to lower fecundity and physiological problems of the mother This is reflected in the higher likelihood of a pregnancy loss (2.3 times more likely) for women who were older than 35 years when they became pregnant.

The positive coefficients found for urban women and for women who gave a vague answer or did not answer the question on whether they wanted the last pregnancy, could point at the occurrence of induced pregnancy terminations. As induced abortions are prohibited and a taboo, women who had an illegal abortion will probably answer evasively when asked for their pregnancy timing. The higher risk of pregnancy losses among urban women in our sample fits in with research findings by Basinga and colleagues[xx] who calculated that induced abortions occur more frequently in the capital city of Kigali compared to in other regions of Rwanda.

The finding that women who explicitly declared that the last pregnancy was not wanted, have a significant lower risk to lose the next pregnancy gives food for thought. Maybe these are highly fecund women who become pregnant easily and therefore more often unwanted, and who do not encounter pregnancy problems.

3.6 Discussion and conclusion

The first important result of our analyses is that one needs to take the previous pregnancy outcome into account when estimating the effects of IPIs on the risk of a pregnancy loss. The second main finding is that negative outcomes (in terms of a higher risk on recurrent pregnancy loss) were found for IPIs up to 24 months after a prior pregnancy loss, a period four times as long as the recommended healthy IPI of only 6 months. In contrast, an IPI shorter than 2 years after a life birth does not seem to increase significantly the risk on a pregnancy loss. We are aware that a pregnancy loss is not the only possible adverse pregnancy outcome. Shorter IPIs than two years after a live birth do not give higher risks of a pregnancy loss, but they will affect other pregnancy outcomes such as preterm birth, low birth weight, low Apgar scores and a higher neonatal death.

We found clear indications for negative effects of the replacement mechanism after the loss of a pregnancy[xxi]. The replacement wish after a fetal death leads to shorter IPIs and therefore to a higher risk of another pregnancy loss. Finally, the results of this study confirm the physiological regression hypothesis: a higher risk on a fetal death when IPIs are longer than 5 years and older mothers which are more likely to experience pregnancy losses than younger ones

Our results are partially in line with the ones from Davanzo and colleagues in Bangladesh (2012) based also on a general sample of women with all types of prior pregnancy outcomes. To avoid a higher risk of a next miscarriage or stillbirth also in Bangladesh women should wait longer than the recommended 6 months (up to 15 months) to become pregnant again.

Contrary to our findings the researchers found a significant increased risk on a pregnancy loss after a live birth and an IPI < 6 months. For longer IPI durations up till 74 months after a live birth no significant higher risks on a pregnancy loss were found. After duration of 74 months, the risk was again significantly higher.

Based on the results of this study on Bangladesh and ours on Rwanda one could conclude that in societies without an advanced health care system, the WHO recommendations concerning spacing after a fetal loss still counts. Workers in the health care system should advise women, even if they are eager to become pregnant again, to take actions to prevent a quick new pregnancy and wait even longer than a year to become pregnant again.

The improvements in the Rwandan health care system between 2000 and 2010 and in particular the increased access to this system, contributed to a lower pregnancy loss frequency. Probably the increased ante-natal checks during the last pregnancy period had an impact, as the significant decrease in pregnancy losses between 2000 and 2010 resulted in particular in fewer late fetal losses (after a pregnancy duration of 20 weeks). With a policy that recommends to women an IPI of at least a year till two years after a fetal death and more early pregnancy visits to the community health facility, a decrease in a early fetal death could be achieved as well.

3.7 Limitations of the study

It is difficult to assess if the total number of reported pregnancy losses in the three DHSs used in this study – 36 per 1000 pregnancies is in line with expectations or not. It is a result of measurements over a rather diffuse period of time. The frequency fits within an indication given in medical literature that states that the number of fetal loss in the month after conception is high, but that after a gestation of 8 weeks the loss is about 3 percent[xxii]. This could mean that women in Rwanda did not mention losses that occurred in the first one or two months of a pregnancy, when they were not fully aware of being pregnant. The early pregnancy losses reported in the DHS are probably underestimated as in poor countries the number of stillbirths (after a gestation of 28 weeks) are higher compared to that of rich countries and the stillbirth rate in countries in the central part of Sub-Saharan Africa varies between 25 till 40 or more per 1000 births[xxiii]. With the number of early miscarriages added the final rate must be even higher.

The RDHS-data do not make a distinction between induced and spontaneous pregnancy losses, which is an omission seen the different relations between the two types of abortions at the beginning of the IPI, length of the IPI, and pregnancy outcome found in other research[xxiv]. However, we expect that Rwandan women will not easily indicate that they had an induced abortion as it is illegal, except when the physical health of the mother is in great danger. The study of Basinga and colleagues[xxv] estimated the rate of induced abortion in 2009 between 18 and 31 per 1,000 women in the 15-44 year age-group. Their study also revealed that the induced abortion rate was remarkably higher in the capital city Kigali compared to the situation in the provinces. In most African rural settings, induced abortion remains a taboo and social control in communities watch over virginity as a core value, the reason why in particular rural women support legalization of abortion less compared to urban women[xxvi]. As far as Rwanda is concerned, May et al.[xxvii] stated that in the early nineties induced abortion did not occur traditionally in this country. For that reason we expected that in case this situation changed during the last two decades abortions will be chiefly an urban phenomenon. We tried to control for it by including place of residence (urban versus rural) in the analysis.

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Chapter 4: The Effect of Pregnancy spacing on Fetal Survival and Neonatal Mortality in Rwanda: a Heckman Selection Analysis

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Abstract

Most studies on birth intervals and infant mortality ignore pregnancies that do not result in a live birth. Yet, fetal deaths are important in infant mortality analyses for three reasons. First, ignoring fetal deaths between two live births will lengthen the measured interval between births, implying that short intervals are underestimated. Second, the recommended Inter- Pregnancy Interval (IPI) after a fetal loss is shorter (6 months) than after a live birth (24 months) as the effect of IPI on outcomes might differ according to the previous type of pregnancy outcome. Third, fetal death will selectively reduce the population at risk of neonatal mortality, leading to biased results. This study uses two step Heckman selection models of pregnancy survival and neonatal mortality, to simultaneously estimate the combined effect of IPI duration and the type of pregnancy outcome at the start of the interval. The analysis is based on retrospective data from the Rwanda Demographic Health Surveys of 2000, 2005 and 2010. The results show a significant selection effect. After controlling for the selection bias, short (< 6 months) and long (>60 months) intervals after a fetal death reduce the chances of pregnancy survival, but no longer have an effect on neo-natal mortality. For intervals starting with a life birth, the reverse is true. Short intervals (<24 months) do not affect pregnancy survival but increase the odds of neo-natal mortality. In case the previous child died in infancy the highest odds are found for neonatal death regardless of the IPI duration

Keywords: Pregnancy, fetal, neonatal, Rwanda

4.1 Introduction

Since 2005, the World Health Organization (WHO) has recommended an inter-pregnancy interval (IPI) of at least 24 months after a birth before starting a next pregnancy, in order to reduce the risk of adverse pregnancy outcomes. After a foetal death, an IPI of at least 6 months should be observed for the same reason. A WHO expert meeting called for more studies on the mechanisms behind the effects of birth spacing on maternal and infant health in different regions to discover plausible causal relations (WHO, 2005). Studies following the consultation meeting that refer to a preceding live birth have contributed to a consensus that women should postpone the next pregnancy for at least 24 months (WHO, 2005; Norton, 2005; Conde-Agudelo *et al.,* 2006; Bhalotra & Van Soest, 2007; Da Vanzo *et al.*, 2007; Conde-Agudelo *et al.*, 2012). The rationale is that this interval provides the mother with sufficient time to recover from pregnancy and breastfeeding. Despite this consensus, however, several issues remain.

Firstly, analyses of the effect of IPI on infant mortality (see e.g. meta-studies by Kozuki *et al.*, 2013; Rutstein, 2008) often use the interval between the delivery of the previous infant and the conception of the index child, thus excluding possible foetal deaths (miscarriage, stillbirth) as a preceding event. This issue is pertinent as parents have a desire to quickly compensate for an adverse pregnancy outcome (Spiers *et al.*, 1996; Smits & Essed, 2001; Lindström & Kiros, 2007; Bhalotra & Van Soest, 2007). Even more important is the fact that a prior foetal death removes pregnancies from the 'population at risk' of infant mortality. This selection effect might lead to biased results.

Secondly, studies that did seek to identify the optimum IPI following a foetal death have shown contradictory results on pregnancy outcomes and infant mortality. Studies in high-income countries (Love *et al*., 2010; Smith *et al*., 2003; Stephansson *et al.*, 2003) showed that an IPI of less than six months did not have adverse effects on the next pregnancy. Studies in low-income countries (DaVanzo *et al*., 2007, 2012) did find the expected negative effects and showed that short IPIs after a foetal loss increase the risk that the next pregnancy will be lost. There is clearly a need for more evidence on this relation

This study makes three contributions to the field: it extends the research on the effects of IPI on neonatal mortality in poor countries in sub-Saharan Africa; it applies a model specification that can be applied to data from demographic and health surveys in other countries; and it uses a Heckman selection model to control for selection bias by simultaneously estimating the combined effect of IPI lengths and the type of event that started the interval on both pregnancy survival and neonatal mortality.

4.2 Theoretical framework

The impact of IPI length on the risk of foetal and neonatal mortality is still debated (Conde-Agudelo *et al.*, 2012; Bhalotra & Van Soest, 2007; Stephansson *et al.*, 2003; Den Draak, 2003). The substantive body of research shows conflicting evidence on the association between IPI and pregnancy outcomes. Part of the variation in outcomes is due to the use of birth intervals rather than pregnancy intervals (Miller, 1991). The use of IPI is preferred, because there is evidence that the impact of IPI duration differs according to the type of pregnancy outcome that preceded the index pregnancy (DaVanzo *et al.*, 2007, 2008; Conde-Agudelo *et al*., 2006, 2012). Three preceding pregnancy outcomes – a live birth of a surviving infant, a live born child dying in infancy and a foetal death – are important because the mechanism underlying the effect of intervals on pregnancy outcomes might differ depending on the start of the interval. The theoretical argument is as follows.

After a live birth, an IPI of less than two years is associated with an increased risk of adverse perinatal outcomes and neonatal mortality. In the literature, two causal mechanisms for these adverse effects can be found: maternal depletion and sibling competition. Pregnancies and lactation lead to both nutritional and folate depletion from which the mother will recover only after a longer interval (King, 2003; Allen, 2005). Her weaker health also increases the risk of vertical transmission of infections from mother to child during the pregnancy. Sibling competition occurs as short intervals lead to overlap between the breastfeeding of the older sibling and the next pregnancy, and also increase the risk of horizontal transmission of infections between siblings.

A review of the effects of spacing (Conde-Agudelo *et al*., 2012) shows evidence for some depletion mechanisms. Current evidence does not confirm the 'effects of short IPI on maternal anthropometric status, anaemia and micronutrients to support the maternal nutritional depletion hypothesis' (ibid., p. 97). However, the researchers found strong evidence for the existence of folate depletion during the first three or four months after the delivery and growing evidence for the associations between short IPI, folate depletion and adverse perinatal outcomes. Support was also found for the association between short intervals and higher risks of adverse perinatal outcomes through a vertical transmission of infections or as a result of cervical insufficiency causing a higher risk of a preterm birth (pp. 99–100) (Basso *et al*., 1998). The review also shows evidence for sibling competition. If the previous child stays alive and the mother becomes pregnant while still breastfeeding, some indications were found that this causes suboptimal lactation for the next child, which could increase the risk of adverse neonatal outcomes (Conde-Agudelo *et al*., 2012, p. 101). In addition, in this situation the (underweight) newborn is at a higher risk of further health problems due to infectious diseases spread by the older sibling.

Sibling competition does not occur if the older sibling does not survive infancy (the second possible previous pregnancy outcome). Yet, studies that analysed the effects of a short IPI on increased risk of neonatal mortality or infant mortality according to the survival status of the previous sibling gave conflicting results. Either the risks were lower or higher if the older sibling did not survive, or no significant difference was found (Lindström & Kiros, 2007; Conde-Agudelo *et al*., 2012). Conde-Agudelo *et al.* (2012, p. 102) concluded that the effects of a short IPI seem to be a little stronger if the older sibling has died, which would point to causal mechanisms other than sibling competition or vertical transmission of diseases.

The third preceding event – a foetal death – has received far less attention from researchers studying neonatal and infant mortality. The WHO (2005) recommendation that an IPI should be of at least six months was based on only one study. A number of subsequent studies investigated the risk of a recurrent pregnancy loss. The evidence about the effect of IPI duration on this recurrence, a kind of foetal death trap, is contradictory. Among these studies, Love *et al.* (2010) found that women in Scotland who conceived within six months after an initial early foetal death had the best reproductive outcomes and lowered complication rates in a subsequent pregnancy. For Bangladesh, DaVanzo *et al.* (2007) found that IPIs beginning with a non-live birth (NLB) were generally more likely to end with another NLB, and that short IPIs (<6 months) are associated with higher risks of infant and child mortality. A follow-up study (Da Vanzo *et al.*, 2012) revealed a slightly different pattern by showing that even though shorter IPIs following a miscarriage are more likely to result in a live birth, these shorter IPIs are associated with a higher risk of neonatal mortality for infants born after them. Results presented by Steer (2007) indicate that an IPI of less than six months, even when the last pregnancy ended in a miscarriage, leads to higher risks of infant and child mortality and pregnancy complications. The same observation was made by Smits and Essed (2001), who also found that IPIs shorter than seven months are an independent risk factor for an extremely pre-term birth and neonatal mortality. Other studies, however, did not find statistical evidence showing that after a previous spontaneous or induced abortion, a short IPI duration was associated with increased risks of foetal death and neonatal mortality (Makhlouf *et al.*, 2013; Conde-Agudelo *et al.*, 2005; Stephansson *et al.*, 2003).

Thus, in the case of a surviving newborn infant, the literature shows convincing results on the adverse effects of short IPIs after on the perinatal outcomes of the next pregnancy due to depletion and sibling competition. The fact that short intervals do not have less impact when the previous sibling died in infancy means that there are other probable causes of recurrent neonatal mortality. Depletion and sibling competition are absent if the previous pregnancy ended in a foetal death, yet there is evidence that short intervals could lead to recurrent foetal deaths or higher odds of neonatal mortality in the next pregnancy.

Long intervals also have adverse effects. The association between IPIs of longer than 59 months and higher maternal morbidity (high blood pressure and excess protein in the urine, both of which are symptoms of pre-eclampsia), adverse pregnancy outcomes (low birth weight, complications during the delivery) and perinatal and neonatal mortality is not controversial. Two hypotheses are put forward for those associations: a reduced fecundity at older age of the mother, and physiological regression. The age of the mother is considered to be of paramount importance in pregnancy outcome and infant survival analyses (Anderson *et al.*, 2000; Cleary-Goldman *et al.*, 2005). Older women tend to have fewer reproductive egg-cell stocks and are thus more likely to have longer pregnancy intervals as an effect of sub-fecundity (Ibisomi, 2008; Jolie *et al.*, 2000). The physiological regression hypothesis argues that older mothers gradually lose their childbearing capacity when the length of the IPI exceeds five years. This reduced condition for physiological capacity for pregnancy and delivery also applies to the youngest group of mothers (nulliparous in particular) who are at the start of their childbearing (Zhu *et al*., 1999, 2006; mentioned in Conde-Agudelo *et al.*, 2012). In analysing the effects of intervals, it is therefore important to also distinguish between long and medium intervals and to separate nulliparous women.

Whatever the exact causal pathways from short and long intervals, the fact that there might be overlap between the causes of both foetal and neonatal death creates a theoretical and methodological concern. The theoretical concern is that the foetuses that survive the pregnancy despite either a short or long interval might have unobserved features that give them better chances of surviving the first month. The methodological concern is that this would lead to an underestimation of the effect of short and long intervals on the probability of dying in the first month (Sartori, 2003). This issue of selection bias is dealt with in the section on methodology.

Risks of foetal and neonatal mortality are not only determined by the IPI and the reproductive history of the mother. The health and morbidity of mother and her newborn are also determined by the quality of the local health system and the socioeconomic position of the mother, considering the major causes of worldwide neonatal deaths: infections (sepsis, pneumonia, tetanus, diarrhoea) 35%, preterm births 28% and asphyxia (loss of heartbeat caused by deprivation of oxygen in utero or during delivery) 23% (Lawn *et al.*, 2006). An adequate, accessible and affordable healthcare system might contribute to reducing the antenatal and perinatal mortality risks through regular check-ups of pregnant women by skilled birth attendants (Dewey & Cohen, 2004). This might account for the inconclusiveness of the research on the adverse effects of short intervals after a foetal death, which were found in developing but not developed countries. Post-abortion and antenatal care will reduce these adverse effects and it will be easier to avoid unwanted pregnancies or access safe abortions in developed countries (Barbier J. S. *et al*., 1999; Santelli *et al*., 2003).

The analysis in this article focuses on the impact of IPI duration after three types of previous pregnancy outcomes on neonatal death. Control variables are included (proxies for wealth, health-seeking behaviour of the mother and her attitude towards her last pregnancy) as they are also associated with the survival chances of neonates (McKinnon *et al.*, 2014; Mosley & Chen, 1984; Mutenga, 2004; WHO, 1997; Khanal *et al.*, 2014; Van Geertuyden *et al.*, 2004).

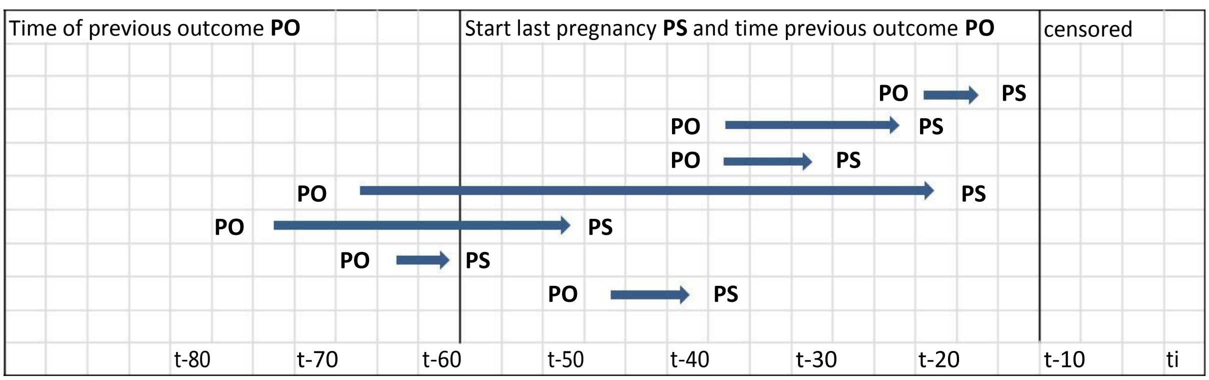
4.3 Data and methods

4.3.1 Data

This study uses merged data from the Rwanda Demographic and Health Surveys (DHSs) 2000, 2005 and 2010. Of the 35,143 women who responded to the surveys, the selection retains 21,045 women who reported having experienced one of the two fundamental events in the analysis (a pregnancy disruption or a viable birth) as their last event and whose last pregnancy started 10–59 months before the interview. To avoid right censoring, all pregnancies that started less than 10 months before the interview are ignored, as these had not been exposed to the risk of neonatal mortality. To identify the moment of the start of the last pregnancy, use is made of the detailed recording in the 'calendar' of the DHS, which gives the pregnancy status for each month over a period of 59 months before the month of the interview. The nature and timing of the previous event is then defined. The exact month of all births, deaths and pregnancy terminations are recorded in the DHS. The duration of the IPI is measured by subtracting the date of the previous pregnancy outcome from the date of the start of the last pregnancy.

Figure 1 illustrates the definition of the intervals. The start of the last pregnancy is recorded when this occurred 10–59 months before the interview. The month of the previous outcome is registered at any time before the start of the last pregnancy. The arrows depict the length of the interval.

Figure 2. Illustration of the measurement of inter-pregnancy intervals



Of the selected women, 3,496 were pregnant for the first time (primigravida) and are analysed separately as they do not have an IPI. In total, 709 women reported a foetal death as the outcome of their last pregnancy; 20,336 delivered a live birth. Of those mothers, 623 lost their newborns in the first month after birth; the infants of 19,713 women survived the neonatal period.

Dependent variables

The dependent variables are foetal survival and neonatal mortality. These two events are interrelated and the occurrence of one reduces the risk of occurrence of the other (selectivity). In medical and demographic terminologies, spontaneous and induced miscarriages and stillbirths are classified as foetal deaths. A neonatal death is defined as a death within 28 days of birth of any live born infant.

Independent variables

The key independent variable IPI is the interval (in months) between the conception of the last pregnancy and the outcome of the previous pregnancy that ended in either a pregnancy disruption or a live birth (see figure 1). Intervals between these pregnancies are classified in accordance with the WHO's recommendation for healthy IPIs. Thus, different IPI categories are used in line with those recommendations for the three outcomes of the previous pregnancy in the construction of interaction variables based on these two most important independent variables in the analysis.

In this study, the environmental and hygienic conditions of the mother are used, rather than the usual wealth index presented in the DHS reports as an overall indicator of living conditions. Characteristics of the mother's dwelling such as availability of sanitation, access to clean water, piped water in the house, material of the floor (uncovered, tiled, cement, etc.) are used, given their direct relationship with the health (morbidity and mortality risks) of family members and especially that of mothers and neonates. An index was constructed using these indicators of living conditions. The index classifies the respondent's living and hygienic conditions as extremely poor, poor or non-poor.

Indicators of health-seeking behaviour include the use of antenatal healthcare and the possession and use of bed-nets for protection against malaria. Answers to the question whether pregnancies were wanted are used to control for pregnancy wantedness. The category of evasive answers, including 'Don't know', is used as a proxy for unintended pregnancy loss. The year of interview is included to capture the decrease in pregnancy losses and neonatal mortality over time. This might reflect the effects of the government health policy and poverty reduction strategies.

4.3.2 Method

Most studies on the effect of IPI on infant mortality ignore pregnancies that do not end in a live birth. However, IPI affects both pregnancies and newborns, and the death of an infant is more likely to originate from complications during pregnancy (Den Draak 2003). Thus, studies that consider only infant mortality run their analyses on a sub-sample of the population, and therefore selectively reduce the population at risk of neonatal mortality, which in turn leads to biased results. In his seminal article, Heckman (1979) identified this bias as a result of unobserved characteristics that define both the odds of being included in the population at risk and the outcomes among those who are included. In his example of the analysis of women's wages, the unobserved characteristic could be a lack of diligence, which would affect both the participation in the workforce and the wages earned. In the present case, the inherent frailty of the foetus/child (or its mother) resulting from genetic or other unknown factors, might go unobserved. It is plausible to assume that the frailest foetuses are unviable and are spontaneously aborted, and thus never appear in the neonatal mortality model. Therefore, unless this is controlled for, neonatal mortality will be estimated using a subset of the less frail individuals. Stated differently, foetuses that survive the pregnancy 'against the odds' will have unobserved features that increase the chances of surviving the first month, as some of the causes of both foetal and neonatal death are the same.

Heckman provided a solution to this problem by estimating two models: a selection model that estimates the probability of being at risk, and an outcome model that estimates the outcome for those at risk. In our case, the selection model estimates the probability that a pregnancy will end in a live birth and the outcome model that the new born will die within a month.

Variables related to both the selection and the outcome variables are included in both models. Age of mother at conception and pregnancy wantedness are included only in the selection equation, given their relationship with foetal survival. Hygienic and living conditions are included only in the outcome equation because these are less related to pregnancy survival but strongly related to neonatal death (WHO, 1997). Antenatal care and the use of a bednet against malaria as indicators of health-seeking behaviour are included in the outcome model and not in the selection model, because the question concerning antenatal care is asked only in relation to the last live birth and not to the (last) pregnancy that ended in a foetal loss. Malaria prevention through possession of bed-nets is measured at household level and not linked to the use by a specific household member. Therefore, this indicator estimates the association with general health-seeking behaviour of the household.

The availability of and access to health facilities in Rwanda increased tremendously after 2005 (NISR *et al*., 2006, 2012). To check for this change, the year of the survey is included in both models.

4.4 Regional context and research population

After the recovery from the devastating effects of the 1994 genocide, the Rwandan government formulated ambitious development objectives in its Vision 2020 strategic policy paper (MINECOFIN 2000) and in successive poverty reduction papers (MINECOFIN 2000, 2007, 2013). Priority was given to reducing population growth by improving reproductive health, and to stimulating economic growth, improving the health and education level of the population, enlarging social protection of the very poor and achieving the Millennium Development Goals.

With substantial assistance from donors, the government succeeded in reconstructing the important infrastructures, including that of health facilities. Since 2006, the nationwide establishment of community-based healthcare facilities and health insurance system has contributed to the rapid adoption and use of healthcare by the population. Rebuilding the infrastructure is not completed, as 51 of the 416 regional departments still have no health centre. In addition, much still has to be done to further improve the equipment and services provided. Electric power, for instance, is still absent from 15% of these health facilities (MINECOFIN, 2013).

Access to health centres is still constrained. In the DHS of 2010, 60% of respondents mentioned at least one obstacle. The most important one (mentioned by 53%) was getting money for treatment; the second (26%) was the distance to the health centre. Despite the health insurance, an additional payment of RWF 200 (US$ 0.35) at each visit is required, except for the very poor. At a district hospital, out-of-pocket costs are 10% of the treatment fee (Lu *et al.*, 2012). According to the latest DHS (2010), 71% of the respondents had health insurance in 2010.

Table 8: Descriptive frequencies for the sample population (period 1995–2009)

Variable names/categories	*Number of pregnancies*	*Number of foetal deaths (%)*	*Number of births*	*Neonatal deaths (%)*
Total	21045	709 (3.4)	20336	623 (3.1)
Previous live birth (reference) * IPI >=24 – <=59 months	7201	231 (3.2)	6970	155 (2.8)
Preceding termination				
* IPI <=6 months	356	37 (10.4)	319	9 (2.8)
* IPI 7–23 months	378	20 (5.3)	358	11 (3.1)
* IPI >=24 months	144	4 (2.8)	140	3 (2.1)
Preceding infant death				
* IPI <=23 months	1170	31 (2.6)	1139	95 (8.3)
* IPI >=24 months	535	28 (5.2)	507	33 (6.5)
Preceding surviving live birth				
* IPI <=23 months	6479	158 (2.4)	6321	165 (2.6)
* IPI >=60 months	1286	91 (7.1)	1195	37 (3.1)
First pregnancy and birth (primigravida)	3496	109 (3.1)	3387	115 (3.4)
Age at conception				
21–35 years (ref cat)	14334	354 (2.5)	13980	366 (2.6)
<21 years	1980	49 (2.5)	1931	64 (3.3)
>35 years	4731	306 (6.5)	4425	193(4.4)
Pregnancy wantedness				
Clear answer (ref)	15789	282 (1.8)	15507	398 (2.6)
Evasive answers	5256	427 (8.1)	4829	225 (4.7)
Antenatal check for pregnancy				
Yes (ref)	15003	266 (1.8)	14737	361 (2.4)
No	6041	443 (7.3)	5598	262 (4.7)
Use bednet for sleeping				
Yes (ref)	9607	299 (3.1)	9308	172 (1.8)
No	11438	410 (3.6)	11028	451 (4.1)
Living and hygienic conditions				
Non-poor (ref)	5099	200 (3.9)	4899	95 (1.9)
Poor	9442	318 (3.4)	9124	292 (3.2)
Extremely poor	6504	191 (2.9)	6313	236 (3.7)
Year of interview				
2000 (ref)	6211	236 (3.8)	5975	242 (4.1)
2005	6605	222 (3.4)	6383	221 (3.5)
2010	8229	251 (3.1)	7978	160 (2.0)

Source: *RDHS 2000. RDHS 2005 and RDHS 2010*

In 2010, nearly 70% of women had their child with the assistance of a skilled service provider, almost always a community health centre nurse, up from 30% five years earlier. Almost all women went for some form of medical check-up in a later stage of their pregnancy. The percentage rose to 98% in 2010, but only 35% went for all four visits recommended by the WHO.

Many women (73%) used iron supplements against anaemia, took an intestinal parasite drug (39%) or got protection against neonatal tetanus (79%) during their last pregnancy. The strong growth in antenatal treatment of pregnant women and in deliveries with skilled medical assistance probably relates to the introduction of a performance-based payment of community health centres in 2006 (Basinga *et al*., 2010; Binagwaho *et al.*, 2012).

Contrary to this progress in health-seeking behaviour, the incidence of secret abortions and subsequent necessary care, and the limited healthcare received after the delivery for both mother and child remains an issue (Basinga *et al*. 2012). Only 18% of women received a postnatal check-up within two days after giving birth. Eighty per cent did not receive a check-up, according to the latest DHS.

The descriptive frequencies presented in table 8 show that foetal and neonatal death decreased over time. They also show higher frequencies of foetal and neonatal death after particular IPI lengths. The higher values do not always appear for both types of adverse outcomes in the same variable category. For instance, after the death of the preceding infant an IPI shorter than two years does not show a higher frequency for foetal mortality, but it does for neonatal death. The opposite is seen for an IPI of more than 59 months after a surviving infant.

Table 9: Inter-pregnancy interval length in months by previous pregnancy outcome (%)

Previous outcome	Inter-pregnancy interval length in months					
	<=6	7 - <=12	13 - <=23	24- <=59	>=60	Total
Foetal death	40.5	19.5	23.6	14.4	2.1	878
Infant death	18.1	19.2	31.3	26.2	5.2	1705
Surviving infant	3.6	8.0	33.1	46.7	8.6	14966
Primigravida	0	0	0	0	0	3496
Total	1206 (6.9)	1688(9.6)	5698 (32.5)	7557(43.1)	1400(8.0)	21045 17549

Sources: *RDHS 2000. RDHS 2005 and RDHS 2010*

The descriptive statistics in table 9 give an overview of spacing practices. They show that the proportion of women with IPIs of less than 24 months after a live birth and less than six months after a pregnancy loss is substantial.

Of all women in the sample who had at least two pregnancies, 16% conceived again within a year and 7% within six months. The results in the table also show that adverse previous pregnancy outcomes (pregnancy loss and infant mortality) are in particular linked with shorter IPIs. After a foetal loss, 60% of the women became pregnant within 12 months and after losing the preceding infant, the percentages is nearly 40%.

When the previous new born survived, this frequency is a bit less than one out of nine women, yet nearly 45% started the next pregnancy before the recommended recovery time of two years as indicated by the WHO was over.

4.5 Results

The results of the Heckman model confirm the existence of selection bias. The coefficient rho (0.7203) of the test for independence of both equations is statistically significant. The sign of the coefficient indicates that error terms in the pregnancy survival and neonatal mortality equations are positively correlated. And lastly, the likelihood ratio test of independence between the two equations is less than 5% (0.043), which also indicates the dependence of the equations.

Predictors for the probability of foetal survival

The constant in the selection model is 2.174, which indicates that in 2000 the probability of foetal survival was 98% after a previous live birth and a healthy IPI of 24–60 months for a mother aged 21–35 years who had a clear opinion about the wantedness of her last pregnancy. Between 2000 and 2005, the coefficient did not change significantly, but between 2000 and 2010 the probability increased slightly (+2.174+0.126), indicating a minor reduction of pregnancy losses. There are six groups of mothers who had a significant lower probability of delivering a live birth compared to the probability for the reference group. The lowest probability is found for mothers when a previous pregnancy was lost and followed by short IPI (+2.174-0.67).

The probability for mothers who responded evasively to the question about pregnancy wantedness is of the same magnitude. As expected, the probability of a live birth is also lower if the mother is 35 years or older, and to a lesser extent if it is her first pregnancy and if the mother becomes pregnant again after a long IPI (five years or longer). Remarkably, an unhealthy IPI of less than two years after a previous live birth does not give a significant lower probability of a next live birth.

Predictors for the probability of neonatal mortality

The constant of the outcome model is -2.014. This means that the probability of dying in the first month after birth of a newborn from the reference category was only 2% in 2000. Afterwards, the probability of survival changes significantly and points at a small reduction in neonatal mortality between 2000 and 2005, and a larger one in the period afterwards (-2.014 – 0.202).

Table 10: Heckman probit coefficients: Effect of IPI on neonatal mortality in Rwanda

	Selection model: Foetal survival **Total pregnancies** (n=21045) **Foetal survival** = 20336(96.70%)				Outcome model: Neonatal mortality **Total infants at risk** (n= 20336) **Dead infants** = 623(3.24%)		
Variable	***B***	***S.E.***	***Sig***		***B***	***S.E.***	***Sig (P>z)***
Interaction variables							
Previous live birth *IPI >=24 – <=59 months (Ref)							
Preceding termination							
* IPI <=6 months	**-0.670**	0.098	***		-0.074	0.134	
* IPI 7–23 months	-0.148	0.116			0.066	0.117	
* IPI >=24 months	0.224	0.234			0.182	0.174	
Preceding infant death							
* IPI <=23 months	0.065	0.084			**0.534**	0.055	***
* IPI >=24 months	-0.119	0.100			**0.410**	0.080	***
Preceding surviving live birth							
* IPI <=23 months	0.051	0.046			**0.104**	0.039	**
* IPI >=60 months	**-0.185**	0.065	**		0.107	0.065	
First pregnancy (primigravida)	**-0.155**	0.063	*		**0.188**	0.045	***
Age at conception							
21–35 years (Ref)							
<21 years	0.096	0.077			NA		
>35 years	**-0.387**	0.039	***		NA		
Pregnancy timing							
Clear answer (Ref)					NA		
Evasive answers	**-0.657**	0.036	***		NA		
Mother had antenatal check							
Yes (Ref)							
No	n/a				**0.263**	0.031	***
Use bednet for sleeping							
Yes (Ref)							
No	n/a				**0.189**	0.046	***
Living and hygienic conditions							
Non-Poor (Ref)	n/a						
Poor	n/a				**0.170**	0.044	***
Extremely poor	n/a				**0.181**	0.041	***
Year of interview							
2000 (Ref)							
2005	0.054	0.044			**-0.071**	0.036	*
2010	**0.126**	0.043	**		**-0.202**	0.051	***
Constant	**2.174**	0.046	***		**-2.014**	0.059	***
/athrho	0.9082	2.883	0.32				
rho	0.7203	1.3873					
LR test of independence(rho = 0): chi2(1) = 4.09 P = 0.043	Significance level: *<0.05; **<0.01; ***<0.001						

Sources: *RDHS 2000. RDHS 2005 and RDHS 2010*

The selection or pregnancy survival model indicates that the probability of a foetal survival was lower for mothers who are pregnant for the first time compared to mothers who went through at least two pregnancies. The outcome model shows that if these new mothers delivered a live birth, this newborn had a higher probability of dying in the first month after the delivery.

Finally, the confounding determinants – health-seeking behaviour and living and hygienic conditions – have the expected sign. The newborns of mothers who did not go for one or more antenatal check-ups or did not use a bed-net for malaria prevention had a higher probability of a neonatal death; particularly the lack of check-ups proves to be risky. Infants born in unprivileged households in terms of hygienic living conditions had a higher risk of dying in the first month.

Looking at both models, it is evident that the association between IPI duration and the adverse pregnancy outcomes is significant either for foetal survival or for neonatal mortality. Only for women who are pregnant for the first time was a significant negative result found for both outcomes: a lower probability of foetal survival and a higher probability of neonatal mortality.

4.6 Discussion and conclusion

The interaction variables (combining the effect of IPI durations and previous pregnancy outcome) for both the analysis of foetal survival and that of neonatal mortality revealed the effect on these subsequent events.

The models show that, compared to healthy intervals (24–59 months), short intervals (6 months or less) following a foetal death lead to a higher probability of the death of the next foetus without significantly affecting neonatal survival. After a previous live birth, irrespective of the survival of this child, short intervals (<24 months) are not detrimental to pregnancy survival but do increase neonatal mortality. The fact that women with a previous surviving infant showed an increased risk of neonatal death after an unhealthy interval, and not after a healthy interval, could point at maternal folate depletion, congenital anomalies associated with short IPIs, suboptimal lactation in the first month due to breastfeeding/ pregnancy overlap, or a transmitted infection from an older sibling.

The effect of a short interval on adverse pregnancy outcomes is stronger after the death of the preceding infant compared to after a surviving older sibling. This defies the hypothesis of sibling competition and that of horizontal transmission of infectious diseases as causal mechanisms, but supports the hypothesis that unmeasured causes could be responsible for the sequence of the two fatal pregnancy outcomes. By taking into account the type of event that started the interval, there is a death trap after a previous pregnancy loss and after a previous infant death: the risk of a repeated adverse event is higher. However, the relationship with IPI does not fully explain this trap for neonatal survival after a prior infant death, as both women who became pregnant within 24 months and those who did so after 24 months show high coefficients of neonatal mortality.

In case the previous sibling dies, the explanation for the increased likelihood of neonatal mortality might include more factors than only replacement mechanism, interval length and maternal folate depletion. Bhalotra and Van Soest (2007, p. 287) stated in their study on neonatal mortality in India that 'endogenously determined birth spacing is partly responsible for generating state-dependency in neonatal mortality'. They suggested that maternal depression after the death of the previous infant is a possible additional cause for repeated neonatal mortality. Stephansson *et al.* (2003) pointed at other possible maternal characteristics, such as repeated placental complications and chronic maternal diseases. Winkvist *et al*. (1992) suggested inadequate diet related to the lifelong poverty of the mother as a possible cause of maternal depletion. The results of this study also confirm that extremely poor living and hygienic conditions have a detrimental effect on the survival of a newborn.

The possible effect of physiological regression on foetal survival and neonatal mortality was explored by combining the effect of IPI durations, previous pregnancy outcome and age of the mother. The significant effect of very long IPIs (>60 months) and older mothers (>34 years) on the risk of a foetal death confirms that, due to physiological weakness and sub-fecundity, older women have more pregnancy complications and an increased probability of a pregnancy loss. However, no significant effect was found for a higher risk of neonatal mortality. It is also clear that women who are just starting their reproductive careers have an increased risk of both foetal death and neonatal mortality.

The Rwandan DHSs do not distinguish between spontaneous foetal deaths and induced abortions. As the latter are illegal in the country, they are probably underreported in the DHS. To check for this omission, the answers to pregnancy wantedness were included in the selection model. The group that gave evasive answers probably includes the women who had an induced abortion. This is reflected in the relatively high negative odd in the selection model, indicating a lower likelihood of pregnancy survival.

In order to avoid the risk of repeated pregnancy disruption, Rwandan women should wait at least six months after a foetal death before attempting another pregnancy. In the context of poor countries like Rwanda, more effort should be put into pregnancy management, encouraging family planning and the spacing of pregnancies, and promoting health-seeking behaviour in the form of antenatal and postnatal care. Community healthcare providers should pay special attention after a foetal death or the death of an infant in order to prevent a repetition of these adverse pregnancy outcomes.

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Chapter 5: Inter-pregnancy Intervals and Maternal Morbidity: New Evidence from Rwanda

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Abstract

The effects of short and long pregnancy intervals on maternal morbidity have hardly been investigated. This research analyses these effects using logistic regression in two steps. First, data from the Rwanda Demographic and Health Survey 2010 are used to study delivery referrals to District hospitals. Second, Kibagabaga District Hospital's maternity records are used to study the effect of inter-pregnancy intervals on maternal morbidity. The results show that both short and long intervals lead to higher odds of being referred because of pregnancy or delivery complications. Once admitted, short intervals were not associated with higher levels of maternal morbidity. Long intervals are associated with higher risks of third trimester bleeding, premature rupture of membrane and lower limb edema, while a higher age at conception is associated with lower risks. Poor women from rural areas and with limited health insurance are less often admitted to a hospital, which might bias the results.

Key words: inter-pregnancy intervals, previous pregnancy, maternal morbidity, Rwanda, physiological regression.

5.1 Introduction

In Rwanda, the maternal mortality ratio has dropped impressively from 750 deaths per 100,000 women in 2005 to 383 in 2010, but needs to decline further to achieve the government's target of 268 deaths per 100,000 women in 2015 [1-2]. The establishment of community health care and improved access to health facilities through a community based insurance system contributed to this improvement [3]. Further improving the quality of and access to health care will certainly help, but should be accompanied by a strategy to improve maternal health as such, not just for the sake of the mother but also for her child. Deteriorated physiological conditions of the mother during the gestation period are shown to have a negative impact on pregnancy outcome[4], and maternal morbidity is among the leading causes of perinatal mortality [5-7].

One way to improve maternal health may be to space successive pregnancies in such a way that the effects of the previous pregnancies are not carried into the next. A wide literature has shown the adverse outcomes of both short (less than two years) and long (more than five years) inter-pregnancy intervals (IPIs) for the next pregnancy, yet few studies have addressed the effect of IPIs on maternal morbidity.

The aim of this study is to analyze whether better spacing could contribute to better maternal health. The study consists of two parts. First, it analyzes the effect of the reproductive history (outcome of the previous pregnancy and the interval to the current pregnancy) on the odds of being referred to a district hospital for the delivery. Second, it uses hospital data to analyze the effects of this reproductive history on four indicators of maternal morbidity.

5.2 Relationships between IPI and maternal morbidity

Both short and long inter-pregnancy intervals are associated with an increased risk of maternal morbidity and mortality[8-9]. Possible explanations for the association between a short IPI and maternal morbidity are threefold. The first, which is widely debated in association with pregnancy complications, is maternal (nutritional) depletion due to inadequate time to restore vital resources as folate, iron and vitamins[10]. This counts for women in poor countries in particular, because many are undernourished. The second explanation is stress, given that providing care for and breastfeeding a young child during a pre-term next pregnancy is both physically and emotionally demanding. The third is insufficient time for the healing of genital injuries or for the hormonal recovery from the previous pregnancy and birth which is likely to affect the mother and index pregnancy[11]. The association between a long IPI and maternal morbidity is explained by physiological regression with subsequent risk of complications such as hypertension, (pre-) eclampsia and edema[8,12-13]. However, the effect of long IPIs could be endogenous. Reduced fecundity at higher ages could lead to both longer intervals and pregnancy complications and without controlling for age the mechanism cannot be confirmed. Yet, a poor physiological status to give birth has also been put forward as a reason why primigravida have a higher risk of pregnancy complications and why maternal morbidity is high among the (very) young [14].

While many studies have focused on adverse effects of IPI duration on pregnancy- and perinatal outcomes, thus allowing meta-studies with significant numbers of entries, too few have studied the relationship between IPI length and specific pregnancy-related illnesses in a systematic and scientific way[15]. The omission is partly due to the wide spectrum of maternal morbidity indicators that are used in existing studies[15], and to a lack of representative datasets that include both information on the core variables and important confounding factors. So far, three studies appropriately analyzed associations between IPI duration and hemorrhage (ante- or postpartum bleeding), premature rupture of membranes (PROM), hypertensive disorders, (pre-) eclampsia or proteinuria, uterine rupture, maternal infection, maternal anemia or lower limb edema (LLE)[12, 16-18]. The results of these studies do not always support a clear association between IPI duration and a particular maternal morbidity. The need for more studies from different contexts is evident.

Another lesson to be learned from research on the effects of IPIs on pregnancy outcomes is that it should include the previous pregnancy as a possible confounding factor[19]. In particular in combination with a short IPI the type of previous outcome (early pregnancy loss versus surviving breastfed child) has differential effect on the nutritional status of the mother [20-21]**.** There is already proof that induced or spontaneous pregnancy terminations in combination with a closely timed next pregnancy (IPI < 6 months) increase the risk of maternal anemia and PROM [22, 12]. Unsafe abortions can even lead to genital sepsis and -injuries that will harm the mother's health during future pregnancies. Also a previous caesarean section in combination with a short IPI – like after an unsafe induced abortion - increases the risk of a premature uterine rupture and ante-partum bleedings caused by an incomplete healing of the uterine scar[23-24].

5.3 Maternal health care in Rwanda

The current health care system in Rwanda is community based. At village level 45,000 community health workers – three per village - operate in cooperation with village leaders and medical staff of facilities at a higher level, to give simple curative care. These trained volunteers are able to diagnose and provide medication for treatment of malaria, pneumonia, and diarrheal disease[25]. Equally important is their role in preventive care by spreading information about hygiene and sanitation. They also give attention to risks of infections and play a key role in family planning, antenatal care, and childhood immunizations. In case of severe illness or emergency these grassroots medical volunteers can refer patients to local health centers and hospitals. A third of these village workers got some training in midwifery. The tasks of these (mostly) women, include amongst others to monthly visit pregnant women and to stimulate them to go for an antenatal check at the local health center during the first four months of their pregnancy. They also supervise the course of the pregnancy and in case of problems stimulate women to go to the local health center to deliver with assistance of a skilled attendant. In 2013, Rwanda had 469 local health centers each serving 20,000-25,000 people, 42 district hospitals, each with a catchment of 150,000-250,000 people, 5 referral hospitals and many private clinics. These health institutions were staffed by 625 general physicians, 8273 nurses and 240 midwives [9]. Local health centers are primary health care units with skilled staff (nurses and midwifes) and better facilities. At this type of facility, pregnant women get antenatal care including hypertension measurements, blood and urine tests, tetanus injections before delivery, assistance during a normal delivery and basic obstetrical care when needed. District hospitals provide more advanced and emergency obstetrical care such as caesarean sections and post-abortion care. These higher level facilities are staffed with 10-15 general physicians working in collaboration with other medical professionals.

To access health care one needs a health insurance. Nearly all Rwandan citizens have a *Mutuelle de Santé* with restricted access to higher level health facilities. For every family member a yearly contribution has to be paid of 1000 Rwandan Francs (USA$2) and an additional 200 RwF for every visit to the local health center. No additional costs are charged to members of the Mutuelles for a normal delivery at this place. For obstetric care at a District Hospital 10% of the costs has to be covered by the patients themselves. A small group, military, civil servants, those employed by private employers and non-governmental organizations has a more extended health insurance.

Kibagabaga District Hospital, which is the case study for this research, is located in Gasabo District, which is the biggest district of Kigali, covering an important part of the built-up area and a large peri-urban area annex to the city proper. The hospital serves 60% of the total population of Kigali and receives an average of 460 patients every day. [26].

It is important to note that access to hospitals like Kibagabaga is supposed to be needs-based, yet in practice constraints do exist. The most common insurance requires out-of-pocket contributions for treatment and poor people might therefore choose for care at the local health center, rather than being referred to a hospital. For people living farther away transportation to the hospital does not only incur a cost, but might also not be an option in case of emergency. Those who come to the hospital are to some extent a selective group. That is one of the reasons why the referral process is analyzed as a first step in this study.

5.4 Data

Two types of datasets are used in this study. The first is the latest Demographic and Health Survey (RDHS 2010). This data set is used to depict which pregnant women have higher odds to be referred to district and referral hospitals due to pregnancy related complications (morbidity). In total 6325 women who had at least one pregnancy in the calendar period 2005-2010 are included in this first analysis. One out of 5 were pregnant for the first time, 17.4% were referred to a higher level health facility due to pregnancy complications. Table 11 presents the descriptive statistics from the variables for the analysis.

The percentages in table 11 show a wide variation in referrals. Women with healthy intervals are referred far less and primigravida and women with short and long intervals are referred more. Women from the wealthier quintiles and from Kigali show higher percentages of referral, yet it is hard to envisage that this would be a result of higher morbidity.

Table 11: Incidence of referrals to district hospitals in Rwanda

		Referred	
Variable Name	Total N	No %	Yes %
Inter-pregnancy interval			
IPI (24-59 months) -Ref	2264	91.1	8.9
Primigravida	1324	71.0	29.0
<=12 months	746	77.9	22.1
13-18 months	837	86.6	13.4
19-23 months	821	88.4	11.6
>=60 months	333	80.8	19.2
Age at Conception			
>=21 and <=35 Years –Ref	4614	81.9	18.1
<=20 Years	595	76.8	23.2
>=36 Years	1116	88.4	11.6
Previous delivery			
Live birth –Ref	5812	82.9	17.1
Pregnancy disruption	210	76.2	23.8
Infant death	303	81.5	18.5
Wealth Quintiles			
Upper two –Ref	2342	73.8	26.2
Middle	1217	85.3	14.7
Lower two	2766	88.8	11.2
Location health centers			
Other regions –Ref	5594	85.8	14.2
Kigali City	731	57.9	42.1
Total	6325	82.6	17.4

Source: *RDHS 2010/11*

The second dataset is derived from the Kibagabaga District hospital files and is used to study specific gestation and delivery complications (maternal morbidity) among pregnant women who were transferred from health care centers located in the hospital's catchment area. The risk of pregnancy-induced illness is identified by the local health care centers' staff during the woman's visit for antenatal checkup or delivery. In total, hospital discharge files for 2500 women were studied. Among them, 37.2% were transferred by health centers located in Kigali city, 39.2% from centers in the peri-urban areas surrounding Kigali city and for 23.6% of the women this information was missing. The descriptive statistics of the variables in the analysis are listed in table 12. The files are filled in by Kibagabaga hospital staff and contain socio-demographic characteristics of the women (age, occupation, province, place of residence, type of insurance), reproductive history (number of previous live births, dead and living children, number of previous spontaneous abortions or stillbirths and premature births, last menstrual period) and reason of transfer or admission.

Table 12: Descriptive statistics for four indicators of maternal morbidity

Variable names	N=2500	Gestational Hypertension (%)	Third Trimester Bleeding (%)	Premature Rupture of Membrane (%)	Lower Limb Edema (%)
Inter-pregnancy Interval					
IPI(24-59 months) Ref	395	6.6	22.8	26.8	3.1
Primigravida	1054	10.0	25.1	28.6	7.1
<=12 months	180	8.9	20.6	22.2	2.8
13-18 months	238	8.6	21.8	28.2	2.9
19-23 months	267	4.5	25.1	25.8	3.4
No IPI specified	156	9.0	21.2	23.7	5.1
>=60 months	210	2.4	29.5	32.9	5.7
Age at conception					
>=21 & <=35 years Ref	1888	7.5	24.3	27.0	4.2
<=20 years	421	8.8	23.8	28.0	2.1
(>=36 years)	191	8.9	24.6	30.6	5.8
Previous delivery					
Normal delivery Ref	1990	3.3	18.6	21.4	4.0
Adverse types of delivery	510	9.0	25.7	31.7	3.9
Medical Insurance					
Private (Ref)	405	4.4	25.4	27.4	2.7
Mutual	2052	8.5	24.2	27.5	4.3
Not specified	43	7.0	16.3	20.9	2.3
Place of residence					
Urban Ref	932	5.2	18.8	20.9	4.5
Peri-Urban	979	11.7	27.0	33.0	3.8
Not specified	589	5.6	28.4	28.4	3.6
Total/Average	2500	7.8	24.2	27.4	4.0

Source: Kibagabaga hospital obstetrical records, 2012-2013

Additional health complications of the mother such as her HIV/AIDS status, her medical and surgical history and the estimated date of delivery are also registered. Not all files contained all additional information (missing values were classifies as ‘not specified’). It can be assumed that these women partly were brought in as emergency cases or came in without a medical referral which could have hampered a complete registration. For this reason they are included in the analysis. The data shows that premature rupture of membrane and third trimester bleeding are the most common complications. Older mothers and the ones with longer intervals seem to have more complications.

Strikingly, women from the city have fewer complications than those from peri-urban areas, reflecting differences in referrals.

5.5 Methods

The analysis of the referrals on the RDHS data serves two purposes. The first is to see whether women with short or long interval have higher odds to be referred to the hospital, indicating that they have more complications or that the local health center perceives the risk of complication higher. The second is to control for the confounding effects of wealth and place of residence on the odds of being admitted to a hospital. Using binary logistic regression with the referral status as the dependent variable, two analyses are made. The first includes the nulliparous women, which means that the previous pregnancy outcome cannot be included in the model. The second is restricted to multiparous women and does include the outcome of the previous pregnancy as a predictor.

The dependent variables of the morbidity analyses are four maternal morbidity indicators indicated on the patient's file for the last pregnancy: gestational hypertension, pre-mature rupture of membranes (PROM), third trimester bleeding (TTB) and lower limb edema (LLE). These four maternal morbidity indicators relate to a severe maternal morbidity and are coded as binary (yes or no) in the 4 separate logistic regression models. The main independent variables used in the next logistic regression analyses are IPI and previous pregnancy outcome, when confounding factors as age of the mother, place of residence and type of health insurance are included. The IPI in the RDHS was measured as the interval (in months) between the conception of the last pregnancy and outcome of the previous pregnancy that ended either in a pregnancy disruption or a live birth. In the DHS women provide their reproductive history. Starting from the last birth backward, she provides details on the month and year of each birth and death if the child did not survive to the time of the interview. Likewise, women who had experienced any pregnancy termination reported the month and year when this event happened. Using this information the last and the previous event could be timed and the interval defined by subtracting the dates. For the Kibagabaga dataset the IPI is measured as the time (in months) elapsed between the date of the preceding outcome (live birth, stillbirth, or miscarriage (induced or spontaneous) and the date of the last menstrual period before the current pregnancy. Intervals between the two last pregnancies were classified in accordance with the World Health Organization's recommendation, which considers an IPI of 24 to 59 months after a live birth before attempting to become again pregnant again is an ideal IPI for better maternal and neonatal outcomes. The shortest interval used here is within one year.

The variable previous pregnancy outcome is classified as a binary variable: had previously experienced a normal delivery versus an adverse pregnancy outcome (prior caesarian section or pregnancy loss - including all types -, and premature birth). The place of residence (urban) is a proxy for availability and shorter distance to various levels of maternal health care. Together these two factors are an indicator to the access and use of antenatal care services.

5.6 Results

5.6.1 Effect of IPIs and previous pregnancy outcome on maternal referrals

Of the Rwandan women with more than one pregnancy 45% (Table 13) started their index pregnancies after a healthy interval of 24-59 months in the period 2005-2010. Nearly 15% was pregnant again within 12 months, one out of three between one and two years, and only 6% after a long IPI (=> 60 months).

Table 13: Effect of IPI on pregnancy-related referrals to District Hospitals in Rwanda

		Primigravida included				Multiparous only			
Variable Names	N	B	S.E.	Sig.	Exp(B)	B	S.E.	Sig.	Exp(B)
Inter-pregnancy Interval									
>=24 & <=59 months-Ref	2264								
Primigravida	1324	**0.995**	**0.100**	***	**2.704**	n.a			
<=12 months	746	**0.513**	**0.113**	***	**1.670**	**0.351**	**0.123**	**	**1.420**
>=13 & <=18 months	837	0.055	0.123		1.056	0.016	0.124		1.016
>=19 & <=23 months	821	-0.041	0.129		0.959	-0.051	0.130		0.950
>=60 months	333	**0.432**	**0.160**	**	**1.540**	**0.430**	**0.161**	**	**1.537**
Age at conception									
21 thru 35 years-Ref	3753								
<=20 years	138	-0.229	0.120		0.795	0.257	0.227		1.293
>=36 years	1110	**-0.254**	**0.108**	*	**0.776**	**-0.288**	**0.111**	*	**0.750**
Previous delivery									
Live birth-Ref	4490	n.a							
Pregnancy loss	210	n.a				**0.505**	**0.187**	**	**1.658**
Infant death	301	n.a				**0.304**	**0.166**		1.355
Wealth Quintile									
Upper two –Ref	1816								
Middle	965	**-0.653**	**0.086**	***	**0.521**	**-0.722**	**0.103**	***	**0.486**
Lower two	2220	**-0.396**	**0.101**	***	**0.673**	**-0.382**	**0.119**	**	**0.683**
Place of Residence									
Other Regions-Ref	4483								
Kigali City	518	**1.057**	**0.096**	***	**2.877**	**1.139**	**0.113**	***	**3.122**
Constant		**-1.697**	**0.085**	****	**0.183**	**-1.712**	**0.091**	***	**0.181**

Significance level: *<0.05; **<0.01; ***<0.001

Source: *RDHS 2010/2011*

Table 13 presents the outcomes of 2 binary logistic regression analyses for the effects of IPI length on the odds of a maternal referral to a higher level health facility. The constant in the first model (which includes primigravida) presents the odds of referral for the reference category. Women who spaced their pregnancy in healthy intervals (24-59 months); aged between 21 and 35 years who are classified among rich and richest category and reside outside Kigali city show low odds of being referred (183 over 1000 which corresponds to a likelihood of being admitted of 15.5%). The odds for women who became pregnant again within a year are 1.67 times higher, compared to women who conceived after a healthy interval. For women with a long IPI (=>5 years) the odds ratio is 1.54.

The odds ratio for mothers of over 35 years of age is smaller than 1, indicating that they are less referred than younger mothers. The highest odds ratio is found for women expecting a baby for the first time (odds ratio of 2.704). Women who spaced their pregnancies between 13 and 23 months don't show significant higher odds of being referred.

Women from the middle and lower wealth quintiles have significantly lower odds (0.521 and 0.673) to be sent to a hospital, other things being equal). The model estimates that women from the middle quintile have a chance of less than 9% to be referred, compared to 18% for the more wealthy women.

Living in Kigali increases the odds to deliver in a hospital considerably, the odds are almost three times higher than for those who live outside Rwanda's capital.

When the variable outcome of the previous pregnancy is included in the model (see the second part of table 3) a new risk group emerges. Mothers who had a previous pregnancy loss (all types taken together) have the highest odds ratio of all categories within the two main independent variables (IPI length and previous pregnancy outcome).

The other coefficients in the table hardly change when primigravida are excluded and the outcome of the previous pregnancy is added as an independent variable. The only larger change is among the women younger than twenty who now have higher odds to be referred but the effect is not significant. All other variable have the same sign and comparable magnitudes. Women of less wealth have lower odds and women in Kigali have higher odds. These results do not indicate that rural and (very) poor women have less health problems during pregnancy and at their delivery, but point at differences in access to and utilization of health care. As stated above, health care given in more advanced facilities are not fully covered by the health insurance and most of these facilities are located in urban areas. Urban women who experience pregnancy or delivery complication probably go directly to a nearby hospital without visiting a local health center/post first.

5.6.2 Effect of IPI and previous pregnancy outcome on maternal morbidity

Table 14 presents odds ratios from binary logistic regressions for each morbidity status. The constant of each model gives the odds of being diagnosed and treated for the four types of morbidity for the reference category; patients in the age 20-25 from Kigali City with private insurance that had a normal delivery before and a healthy interval. Their odds are low for gestational hypertension and LLE (odds 0.023 and 0.032), but higher for TTB (0.218) and PROM (0.264). Looking at the effects of the two main independent variables of interest (IPI and previous pregnancy outcome) it becomes clear that significant deviations from the reference group occur, yet the insignificant results are just as interesting.

Table 14: Effect of Inter-pregnancy Intervals on pregnancy related morbidity

Variable name	N=2500	Gestational Hypertension Exp B		Third Trimester Bleeding Exp B		Premature Rupture of Membrane Exp B		Lower Limb Edema Exp B	
Inter-pregnancy Interval									
24-59 months Ref	395								
Primigravida	1054	**1.709**	*	1.177		1.277		1.208	
<=12 months	180	1.375		0.876		0.910		0.679	
13-18 months	238	1.206		0.971		1.090		0.723	
19-23 months	267	0.690		1.155		1.058		0.842	
>=60 months	210	**0.332**	*	**1.451**	*	**1.343**	*	1.336	
No IPI specified	156	1.558		0.965		0.978		1.406	
Age at conception									
21 - 35 years (Ref)	1888								
<=20 years	421	0.984		0.939		0.942		**0.447**	**
>=36 years	191	1.461		0.953		1.063		1.474	
Previous type of delivery									
Normal (Ref)	1990								
Abortion/Caesarian	510	**3.164**	***	**1.303**	**	**1.394**	**	1.040	
Type of Insurance									
Private	405								
Mutual	2052	**1.894**	*	0.964		1.010		1.559	
Not Specified	43	1.777		0.493		0.486		0.842	
Location health center									
Urban (Ref)	932								
Peri-Urban	979	**2.482**	***	**1.610**	***	**1.703**	***	0.819	
Not specified	589	1.183		**1.746**	***	**1.614**	***	0.837	
Model Constant		0.023		0.218		0.264		0.032	

Significance level: *<0.05; **<0.01; ***<0.001

Source: *KABAGABAGA HOSPITAL FILES 2012-2013*

The above table shows that the effects of short intervals are all insignificant and that the odds ratios are close to one. Women with very short intervals seem to have higher odds of hypertension (ratio is 1.375) but even this one is not significant at the 0.05 level. Short intervals do not lead to more morbidity. Long intervals lead to substantially lower odds of hypertension (0.332) and to higher odds of bleeding, rupture and edema (odds ratios are 1.451, 1.343 and 1.336). Becoming pregnant at higher ages is not related to bleeding or rupture. The odds ratios are higher for hypertension and edema, but nog significant. The relation of higher age to maternal morbidity is clearly different from the relation of long intervals with morbidity. Primigravida seem to have higher odds of bleeding, rupture and edema, but the effects are too small to be significant. They do have significant higher odds of hypertension.

The type of previous pregnancy and delivery is related to morbidity in the next pregnancy. Women with a previous premature/abortion or birth by caesarian section show significant higher odds ratios for gestational hypertension (3.164), for TTB (1.303), and for PROM (1.394) relatively to those with a previous normal delivery.

The type of health insurance used by the mother and her place of residence were used as proxies of her socioeconomic status. In this context, women enrolled in mutual health insurance have a significantly higher odds ratio for gestational hypertension (1.894) and a higher, yet not significant odds ratio for LLE (1.559) relatively to women with private insurance.

Compared to women from Kigali city, those referred by health care centers located in the peri-urban and rural areas of Gasabo district have significantly higher odds ratios for gestational hypertension (2.482), for TTB (1.610) and for PROM (1.703). A significant increase in odds of TTB (1.746), in the odds of PROM (1.614) is also observed to women whose referring health care center was not mentioned on the hospital's obstetrical files.

5.7 Discussion and Conclusion

Results of the referral analysis indicate that primigravida, those with a short IPI (<=12 months) and a long IPI (>=60 months) have higher odds of being referred to district hospitals in Rwanda because of pregnancy and delivery complications. These results corroborate findings of previous studies which indicated that short IPIs are correlated with adverse obstetrical and perinatal outcomes, while long IPIs are associated with increased risk of pre-eclampsia and TTB[13,30]. After excluding primigravida and considering the type of previous delivery, it is clear that adverse previous delivery outcomes (pregnancy loss, premature birth or neonatal death) lead to increased odds of being referred to a district hospital. Yet this does not imply that short and long intervals are always related to maternal morbidity.

The analyses of the Kibagabaga district hospital data do not show a consistent relationship between IPI length and all maternal morbidities. Short intervals (<12months) are not associated with TTB, PROM or

LLE, but might be related to hypertension. This might seems surprising given the fact that the odds of referral are 1.5 times the odds of those with a healthy interval. This outcome could mean two things. The first is that (very) short intervals are related to the health status of the child but not to the health of the mother. The second is that local health centers, aware of the risks of pregnancy complications after a short interval, also refer mothers whose health status is not at stake.

The evidence for the effects of long intervals is far more convincing. The high odds of TTB and PROM support the physiological regression hypothesis[13]. These findings correspond to those who posited that the effect of long inter-pregnancy intervals is due to the fact that the protective effect that women might have acquired along the previous pregnancy is lost after a long interval [8,12,31].

The evidence is less strong for primigravida who show a significant increase in gestational hypertension, but less strong and non-significant effects for TTB and PROM. Again this might be obscured by the higher odds of referral for the primigravida. The primigravida status is known to be critical in terms of obstetrical performance; women who conceive for the first time will receive more antenatal, natal and post natal care to help them reach a good start of their reproductive health life[31] and might therefore be referred more often regardless of their health status.

The lower odds of being referred and the equal odds of maternal morbidity among older women (age=>35) in Rwanda provide further support for the physiological regression hypotheses[32]. Unlike the situation in developed countries, older women in Rwanda are mostly experienced mothers who have had several pregnancies before they conceive at higher age. Many of them enjoy the protective effects of the previous pregnancy. That could be the reason why the effect of long intervals did show up in the analyses, while the effect of higher age did not.

As socioeconomic proxy indicators, this study considered the wealth quintile and the place of residence (Kigali city vs other Regions) for the first analysis on delivery referrals. The type of insurance and the location of the health centers (Kigali City vs peri-urban or rural areas) were used for the second model on maternal morbidity. In the first analysis, women in the middle and poor wealth quintiles were referred less than more wealthy women. The same is observed for women not living in Kigali, they were also referred less. In the second analysis, women on mutual health insurance had significantly higher odds of gestational hypertension and (not significantly) higher odds of lower limb edema. Women from the in peri-urban and rural area of the Gasabo district had higher odds of gestational hypertension, of TTB, and of PROM. This obviously means that wealthy women, living in urban areas have more chances of being referred to or to utilize higher level health care institutions relatively to poor women on mutual health insurance who reside far away in the peripheral areas of Kigali. The results correspond to the findings of Chambers and Booth[33] who identified three reasons for these lower referral rates. The first is linked to poverty, making women and their families slow in seeking medical assistance because of difficulties to pay transport and referral costs. The second is transfer delays, caused by either a late decision of the medical staff or the lack of ambulances to facilitate an immediate emergency obstetrical intervention. The third delay is caused by the shortcomings in the quality of care, inadequately trained and poor staff motivation at the level of the health care center. Despite the improvements in health care in Rwanda, access to high quality reproductive health care for the poor is still problematic.

To conclude, we did not find clear evidence that avoiding short birth intervals will help to reduce maternal morbidity, but we did find a strong effect of long intervals and of the adverse outcomes of previous pregnancies on this morbidity. However using hospital data to assess the role of the reproductive history has some clear limitations. Even in Rwanda the referral process is highly selective which may bias the results. More formal models, like the Heckman model that can simultaneously estimate the probability of referral and the probability of morbidity once admitted could control this selection bias, but would require data that link patients of local health centers directly to the hospital to which they are (not) referred.

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Chapter 6: Effect of Inter-pregnancy Interval and Maternal Morbidity on Perinatal Mortality: A Mediation Perspective

Paper submitted

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Abstract

Objective: To estimate the effect of primigravid status, short and long Inter-pregnancy Interval effects on perinatal mortality when Maternal Morbidity is mediated.

Study Design: 2344 women's obstetrical files of Kibagabaga District hospital are analyzed. Using a mediation analysis, we estimate the effect of inter-pregnancy interval on maternal morbidity and perinatal mortality.

Result: In contrast to other findings linking IPI length and maternal or perinatal mortality, no significant effect of short IPI is observed in this study. We find a mediation effect of primigravida status and long IPI on perinatal mortality, and a consistent effect of these factors on both maternal morbidity and perinatal mortality.

Conclusion : Findings of this study show a lien between first pregnancies and those conceived after 59 months, and therefore call for more efforts in the improvement of the availability and accessibility of good quality antenatal care and delivery services that are urgently needed, with a special focus on sensitizing primigravid women to use regular antenatal checks.

6.1 Introduction

This study analyzes the hypothesized chain of effects of Inter-Pregnancy Interval (IPI) duration on Maternal Morbidity (MM) and subsequent on Peri-Natal Mortality (PNM). Several studies have reported that short and very long IPIs increase the risk of among others small for gestational age, low birth weight and preterm birth, which on their turn relate to a higher risk of perinatal mortality as a culminant outcome ***(***Conde-Agudelo A., et al. 2012***;*** Sachar RK, et al. 2000; Adams MM, et al. 1997; Zhu BP, et al. 1999; Fortney JA, et al.1984). IPI duration effects as well the health of the mother during pregnancy, and again short and long intervals are found to be harmful for the health status of a pregnant woman and relate to specific maternal morbidity (Conde-Agudelo & Bélizan 2000; Conde-Agudelo et al 2007, DaVanzo et al. 2007). Maternal morbidity during the pregnancy on its turn is also associated with pregnancy termination and risks of perinatal mortality (Pattinson R.C, et al. 1995; World Health Organization 2007, Wendt et al. 2012). The above mentioned associations indicate that maternal morbidity is probably a mediator of the relationship between IPI and peri-natal mortality. To analyse this hypothesized chain of effects, this article presents a case study on Rwanda, a small and poor African country where the access of the population to the improved health care system increased remarkably during the last decade. Based on data of 2344 obstetrical files of women who have been treated in the Kibagabaga District hospital located in the capital Kigali, this study explores the direct and indirect effect of IPI duration on peri-natal mortality. As mediators for the measurement of the indirect effect we focused on two types of Maternal Morbidity: Premature Rupture of Membranes (PROM) and Third Trimester Bleeding (TTB).

6.2 Inter-pregnancy Interval, Maternal Morbidity and Perinatal Mortality

In poor countries perinatal deaths originate, besides from genetic defects of the foetus, from poor maternal health, inadequate prenatal health care, inappropriate management of complications during labour and delivery as well as during the postpartum period (Pattinson R.C, et al. 1995; World Health Organization 2007). A foetus or neonate who have endured maternal morbidity during pregnancy, have presumably a greater risk of dying either during pregnancy (stillbirth) itself, or shortly after birth (JP Vogel, et al.; 2013; Pattinson RC, 1995; Lawn J, Kerber K, Enweronu-Laryea C. 2010). However, also the reproductive history of the mother could be of influence, in particular the spacing of her pregnancies.

Studies linking IPI and Perinatal or neonatal mortality showed that IPI shorter than 12 months and longer than 59 months are significantly associated with increased risk of adverse perinatal and neonatal outcomes (Conde-Agudelo et al. 2006, Smith GC et al. 2003). Main causes behind are low folate and iron for pregnant women, who shortly get pregnant after the outcome of the preceding before recovering from its strains (Doyle W. et al. 2001; Cikot RJ et al. 2001). Likewise, short IPIs between pregnancies is known to be a driver to maternal morbidity status through the maternal nutritional and folate depletion, incomplete healing of the uterine scar and cervical insufficiency (King, JC. 2003). Long IPI could lead to physiological regression, what points at a loss of beneficial physiological adaptations in a woman's reproductive system that occurs after her first pregnancy. Pregnancy conditions after a long IPI (> 60 months) contain more risks for a woman and resemble the conditions of primigravida. Studies have showed that first pregnancies have also higher risk of experiencing prolonged labour and that of delivering under caesarean section. Besides, this same category of nulliparous women have showed increased risk of antepartum haemorrhage, pregnancy hypertension and low birth weight of the newborn, Intra uterine growth retardation, need to Neonatal Intensive Care and resuscitation, and low neonatal APGAR score with subsequent perinatal mortality (Tavassoli Fatemeh, et al. 2010; Nazia Hashim, et al. 2012).

Most previous studies including IPI duration as an independent variable, focused on these possible relationships between IPI duration and either maternal health and pregnancy outcomes or infant survival. A few studies have however simultaneously linked the effect of IPI on maternal health and pregnancy outcome (Wendt et al 2012, Conde-Agudelo et al. 2000, and Schmidt RJ et al. 2012). Consequently, some possible dual relationships between IPI duration, maternal morbidity or perinatal mortality have been subject of study.

In few previous studies, women with inter-pregnancy intervals of less than 12 months had significantly higher rates of maternal death, hemorrhage, premature rupture of membranes, puerperal endometriosis, and anemia (Shachar BZ et al. 2012; Zhu BP, et al. 1999; Conde-Agudelo, et al. 2012). In the same way, women with inter-pregnancy intervals of more than 59 months were found to have higher rates of pre-eclampsia, eclampsia, and gestational diabetes mellitus. A systematic review of the literature found that long inter-pregnancy interval may be an independent risk factor for pre-eclampsia and is also associated with increased risk of labor dystocia (Conde-Agudelo A et al., 2006).

The premature ruptures of membranes or utero-placental bleeding disorders constitute a high risk for perinatal morbidity and mortality. In the first instance, the premature rupture of membranes (PROM) is associated with brief latency from membrane rupture to deliver, perinatal infection and umbilical cord compression due to a condition in pregnancy characterized by a deficiency of amniotic fluid(oligohydramnios). Women with oligohydramnios in the next stage are more likely to develop chorioamnionitis (inflammation of the membranes that surround the fetus) and sepsis (a bacterial infection in the bloodstream or body tissues) in the newborn, which constitutes a high risk for neonatal mortality (Vermillion S, Kooba A., 2000).

The rupture of membranes is associated with placenta previa (which occurs when the placenta is implanted over the internal cervical os) and placenta abruption (which is the premature separation of normally implanted placenta. Both placenta previa and placenta abruption are major causes of antepartum haemorrhage in the third trimester of pregnancies and major contributors of obstetric haemorrhage in general. The effect of these last obstetrical complications on perinatal adverse outcome is related to blood loss of the fetus, the risk of perinatal asphyxia, the risk of sepsis and that of third trimester bleeding (Yang Q., et al. 2009; Rozenberg T., et al. 2011). The effects of IPI become complicated when are combined with that of older or very young age of mothers. In most developing countries' settings, the socioeconomic status of women combined with the delay in attaining the premises of health care due to either poor infrastructure or health care facilities is more likely prevent women in timely acceding maternal prenatal and delivery care.

6.3 Study Population

The data for this study derives from Kibagabaga District Hospital maternal obstetrical files. This data is used to show specific gestation and delivery complications (morbidities) among 2500 pregnant women who were transferred to Kibagabaga District hospital in Kigali city between 2012 and 2013. These women come mainly from health care centers located in the catchment area of Kibagabaga District hospital, as cases susceptible to severe complications if not clearly monitored by a higher level service delivery unit than a community health care center. The risk of pregnancy-induced illness was identified by the community health care centers' nurses or midwives along their third trimester visit for antenatal checkup. Among these women, 1054 women, estimated at 42, 7% of all women were primigravid while 156 women did not have complete information on duration between pregnancies, even if they were multi-parous. This last category of women was excluded from the analysis and only 2344 cases remained in the analysis for easy, computation of the Inter-pregnancy Interval.

These files also contained socio-demographic characteristics (age, occupation, province, district, sector and cell, her type of insurance, her reproductive history-number of previous live births, dead and living children, number of previous spontaneous abortions or stillbirths and premature births) of referred pregnant women are registered. The medical history of the mother such as her HIV/AIDS status, the reason of transfer and admission, her medical and surgical history, her last menstrual period and the estimated date of delivery for the subsequent pregnancy are also registered on the hospital files. After the record of women's medical and reproductive anamnesis, they are admitted and other improved clinical tests are performed to identify the plausible reasons of pregnancy complications and thereafter, a plan is made by the gynaecologist whether to further monitor women on labour, whether to induce the labour or whether to administer caesarean section. At the end of the labour support and before the discharge of the admitted woman, an observation was made and written on her obstetric file, whether the infant was born alive or not, whether the born alive infant was transferred to neonatology due to asphyxia and apnea (breathing problems) and low APGAR scores. Thereafter, it is also written on the file whether the infant died or survived before or after neonatology intervention (mainly reanimation).

On the basis of the above information, this analysis is based on identified pregnancy related illness (Maternal Morbidity) and perinatal mortality for the last pregnancy to control the strength of the independent effect of Inter-pregnancy Interval on these adverse outcomes.

6.4 Methods

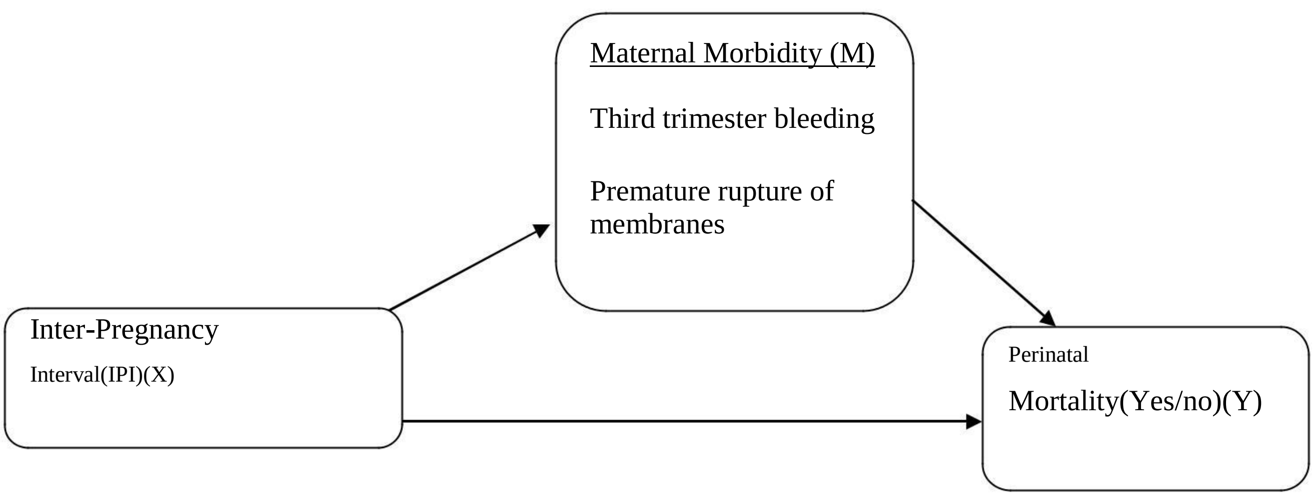
Analytical method definition

As it has been observed by prior mediation studies, any mediation analysis should evidence causal relationships between the predictor, the mediator and the outcome variables. Thus, an association between the predictor (X: short and Long IPI or Primigravida status in our case) and the mediator variable (M: Maternal Morbidity) is a pre-condition to any mediation study.

Using Andrew F. Hayes(2013)' process procedure for SPSS, a simple mediation analysis was performed. Mediation analysis is a statistical method used to help answer the question as to how some causal agent X (IV) transmits its effect on Y(DV) through a single or multiple mediator variables. A simple mediation model is any causal system along which one causal antecedent X variable is proposed as influencing Y through a single intervening Mediator variable (M).

On the basis of the process Method for SPSS as suggested by Andrew F. Hayes, which is a useful computational tool for path analysis-based mediation and its integration into conditional process modelling. The table below illustrates the logic of our model construction on the basis of the process Method.

Figure 3: Relationship between Inter-pregnancy Intervals (IPI)(X), Maternal Morbidity(Mediator) and Perinatal Mortality(Y)



In mediation analysis like in other structural Equations modelling, two or more equations are combined to estimate their effects on the dependent variable. Hence, in the simple mediation analysis, three equations/pathways are suggested in estimating the effect of X on Y. The first relationship goes from X to Y without passing through M(Y=cX+E1) to show the direct effect of X on Y. The second relationship then goes from X to M (M=aX+E2) to distil the effect of X on M to explain the direct effect of X on M. The third relationship passes from predictor X to consequent M and then from antecedent M to consequent Y(Y=bM+c'X+E3). This last relationship constitutes a combined effect of both X and M on Y and is called indirect effect of X on Y through M.

Process also produces estimates of conditional effects direct and indirect effects. The total effect quantifies how much two cases that differ by one unit on X are estimated to differ on Y. The direct effect estimates how much two cases that differ by one unit (higher if c'= +) or one unit(lower if c'= -) on X is estimated to be simultaneously higher and lower on Y. Because in the case of this study X values are dichotomous (Primigravidity(1) versus healthy IPI(0), Short IPI(1) versus healthy IPI(0), Long IPI(1) versus healthy IPI(0)), the direct effect estimated the difference between each critical IPI and healthy IPI means, when the mediator variable(M) is held constant. Given that a coefficient and p-values are provided for both the total and direct effect will be interpreted in reference to the sign of the relationship as well as the significance of p-value. The indirect effect on its part, bootstrapping (which proceeds by constructing a large number of resample of the original sample size N=2344 to B=1000 in our case) is the better inference estimation along which bootstrap confidence intervals provide a 95% bias-corrected bootstrap Confidence Interval (Hayes A. F. and Preacher K.J. 2010).

Variables definition and operationalization

Dependent variables

Mediation analysis involves more than one dependent variables, be it for simple or for multiple mediation. In this study, maternal morbidity is on one hand a dependent variable when related to Primigravid status and IPI length. On the other hand, maternal morbidity is an intermediate variable while perinatal mortality is dependent variables. Maternal Morbidity was defined by the WHO

Maternal Morbidity Working Group as 'any health condition that is attributed to or aggravated by pregnancy and childbirth that has a negative impact on the woman's wellbeing'(Firoz T., et al. 2013).

This health condition in this study is measured in terms of two severe obstetrics and delivery complications namely Premature Rupture of membranes and Third trimester bleeding. This mediator-dependent variable was made continuous by moving from not having experienced any of the chosen indicators (PROM and third trimester bleeding), having experienced any or both of them as the second and third category. Perinatal mortality was kept binary with a 0, 1 values. Value 0 standing for having survived after birth and value 1 for having died at Kibagabaga district hospital.

Independent variables

The crucial independent variable is the Inter-pregnancy interval. This category was initially grouped into primigravida, those with IPI of less than 12 months, those with IPI between 13 and 18 months, those with IPI between 19 and 23 months, those with IPI between 24 months and 59 months and those with IPI from 60 months and higher. IPI between 24 and 59 months was considered to be a healthy IPI in reference to the previous empirical findings. For a better estimation of the effect of IPI on both maternal morbidity and perinatal mortality, IPI was cut into three different dichotomous categories. The first category was made of a binary variable being primigravid (1) versus having spaced the last pregnancy between 24 and 59 months(0), the second category was that of having spaced the last pregnancy to less than 12 months- short IPI(1) versus having spaced the last pregnancy between 24 and 59 months(0) and the last category was that of having spaced the last pregnancy to 60 or more months(1) versus having spaced the last pregnancy between 24 and 59 months(0).

Age of the mother was also controlled for and coded into critical or high risk (those age below 20 and those aged beyond 36 years)(1) versus healthy reproductive age(those aged between 21 and 35 years)(0).

As a proxy to socio-economic status of the mother, the type of health insurance that is used by the parturient mother was considered. In this regards, mothers referred to Kibagabaga hospital without or with a community health insurance were controlled (1) in reference to those with improved health insurance (RAMA, MEDIPLAN, SORAS, UR, etc.)(0). In fact, the structure of the health insurance in Rwanda subdivides insurance beneficiaries according to their occupation and socio-economic status. Most of government employees or those employed by private companies are covered by best insurance schemes covering from 100% to 85% and constitutes roughly 15% of the total population. In the Government of Rwanda's effort to increase the coverage of health insurance to all Rwandans, a

Community Health Insurance was instituted since year 2000. Community Based Health Insurance(CBHI) mechanisms of community financing based on pre-payment and on risk pooling, has been very successful in reducing access to health care disparity among Rwandans. The Rwandan Government aims to increase access to health care, including chronic care, for all people. The new CBHI policy was established in 2010 and introduced a system that now provides coverage to over 90 percent of Rwanda's population. The majority of the insurance system, 55 percent, is paid for through premium payments from the population, with 21 percent of the system covered by the government, 11 percent from donors, and other system fees making up the rest. The poorest citizens, about 25 percent of Rwanda's population, have now been identified and receive free medical care through CBHI.

Referral hospitals also accept the insurance, allowing the poorest citizens with chronic diseases to afford specialized treatment.

6.5 Results

The table below present the characteristics of women that were transferred to Kibagabaga district hospital as a result of obstetrical complications. Among them, 932 (37,2%) were transferred by health centres located in Kigali city, 979 (39,2%) were transferred by those located in rural or peri-urban areas surrounding Kigali city and for 598 (23,6%) women, no referring health care center was mentioned on the hospital discharge files.

Table 15: Descriptive statistics

Covariates	N=2344	Third Trimester bleeding		Premature Rupture of Membranes	
		No(%)	Yes(%)	No(%)	Yes(%)
Interpregnancy Interval(Months)					
IPI(24-59 months)Ref	395	76.2	22.8	74.2	26.8
Primigravida	1054	74.9	**25.1**	71.4	**28.6**
<=12 months	*180*	79.4	20.6	77.8	22.2
13-18 months	*238*	78.2	21.8	71.8	26.2
19-23 months	267	74.9	23.1	74.2	25.8
>=60 months	210	70.5	**29.5**	67.1	**32.9**
Age of the mother at conception					
(>=21 & <=35 years) Ref	1888	75.7	24.3	73	27
(<=20 years)	421	76.2	23.8	72	**28**
(>=36 years)	191	75.4	**24.6**	69.6	**30.6**
Type of Medical Insurance					
(RAMA, MMI, CORAR,MEDIPLAN)Ref	249	74.6	**25.4**	72.6	27.4
(Mutuelle/sante)	2052	75.8	24.2	72.5	**27.5**
(Notspecified)	43	83.7	16.3	79.1	20.9
Total/Average		75.8	24.2	72.6	27.4

The table below summarizes two built in mediation models. The first model presents the effect of Primigravida status, Short and long IPI and confounding factors (age of the mother, type of Insurance) on perinatal mortality in Rwanda. The second model presents a combined effect of Primigravida status, short IPI, long IPI and Maternal Morbidity status on perinatal mortality. The last part of the table summarizes mediation effects of the models.

Effect of Primigravida status, short and long IPIs on Maternal Morbidity (M=aX+E2)

In case of this study, Primigravida status and long IPI have significantly increased the risk of maternal morbidity relatively to women with healthy IPI (between 24 and 59 months after the end of preceding pregnancy), which confirms the existence of the mediation effect in our model. Even though with an expected sign, no significant effect of Short IPI is observed on maternal morbidity. No effect of the age of the mother on perinatal mortality is observed in the model.

The type of health insurance shows on its part an increased risk of maternal morbidity for primigravid poor women without mutual health insurance or with mutual health insurance relatively to their counterparts insured by better health insurances such as RAMA, SORAS, and MEDIPLAN etc. No significant effect of short and long IPI is observed on maternal morbidity.

Table 16: ***Effect of IPI and Maternal Morbidity on Perinatal Mortality in Rwanda***

	Model 1: Primigravida			Model 2: Short IPI			Model 3: Long IPI		
Full Model	**Outcome 1: Maternal Morbidity**								
	Coeff	**Sig**	**S.E**	**Coeff**	**Sig**	**S.E**	**Coeff**	**Sig**	**S.E**
Constant	0.515	***	0.045	0.506	***	0.047	**0.540**	***	**0.048**
Primigravidity	**0.106**	*	**0.051**	====	====	====	**====**	====	**====**
Short IPI	**====**	**===**	**====**	0.016	n.s	0.075	**====**	====	**====**
Long IPI	**====**	**===**	**====**	====	====	====	**0.161**	*	**0.074**
Age of the mother (0, 1)	-0.035	n.s	0.050	0.005	n.s	0.092	-0.101	n.s	0.089
Type health Insurance (0,1)	**0.156**	**	**0.060**	0.177	n.s	0.096	0.070	n.s	0.096
Full Model	**Outcome 2: Perinatal Mortality**								
Constant	-4.731	***	0.448	-4.630	***	0.549	-5.091	***	0.576
Maternal Morbidity	**0.465**	**	**0.151**	0.469	n.s	0.328	**0.707**	**	**0.265**
Primigravidity	**1.053**	*	**0.441**	====	====	====	**====**	====	**====**
Short IPI	**====**	**====**	**====**	0.595	n.s	0.616	**====**	====	**====**
Long IPI	**====**	**====**	**====**	====	====	====	**1241**	*	**0.517**
Age of the mother (0, 1)	0.306	n.s	0.289	0.541	n.s	0.691	0.964	n.s	0.511
Type health Insurance(0,1)	**0.732**	*	0.305	0.084	n.s	0.797	0.488	n.s	0.596
	TOTAL, DIRECT AND INDIRECT EFFECTS								
	Effect		**S.E**	**Effect**		**S.E**	**Effect**		**S.E**
Total Effect on P M	**1.088**	*	**1.088**	0.595	n.s	0.614	**1.287**	*	**0.512**
Direct Effect on P M	**1.053**	*	**0.441**	0.595	n.s	0.616	**1.242**	*	**0.517**
Indirect Effect on P M	0.049		0.029	0.007		0.039	0.114		0.071
	BootLLCI = 0.0056; /BootULCI = 0.1271			BootLLCI = -0.059; /BootULCI = 0.102			BootLLCI = 0.0047; /BootULCI = 0.283		

Significance level: n.s: Not Significant; *<0.005; **<0.01; *<0.001; =====: not applicable**

**** Model Summary: Primigravida(R=0.088; Sig: *; F=3.778); Short IPI(Short IPI(R=0.078; Sig: n.s; F=1.171); Long IPI(Long IPI(R=0.099; Sig: *; F=1.196).** ***Abreviations : IPI: Inter-pregnancy Interval***

Effect of Primigravida status, short /long IPIs and Maternal Morbidity on Perinatal Mortality (Y=bM+c'X+E3)

The constant of this second model outcome is respectively -4.731, -4.630 and -5.091 for Primigravid women, for those who spaced their index pregnancies in less than 12 months and for those who spaced their index pregnancy in 60 or more months. This implies that women who did not experience any premature rupture of membranes and third trimester bleeding during pregnancy, who were not primigravid, who did not space their index pregnancies to less than 12 or to more than 60 months, who were not aged below 20 or more than 36 years, who used an improved health care insurance (RAMA, MEDIPLAN, SORAS etc) have a decreased likelihood of experiencing perinatal mortality. Besides, the second outcome of the mediation model presents the effect of Primigravida status, short and long IPI on one hand and that of maternal morbidity on perinatal mortality on the other hand. As in the first model, primigravida and long IPI also show an increased risk of perinatal mortality. In the same way, maternal morbidity (premature rupture of membranes and third trimester bleeding) show an increased risk of perinatal mortality for both primigravid women and those with IPI longer than 60 months after the preceding pregnancy outcome. Short IPI and age of the mother do not show any significant relationship with perinatal mortality, though bearing an expected positive sign of the relationship. Primigravid women who did not have any or who were insured in the mutual health insurance have also increased the risk of perinatal mortality relatively to their counterparts who used an improved health care insurance. No significant effect is observed on the effect of using community health care insurance or none on perinatal mortality when the latter spaced their index pregnancies to less 12 or to more than 60 months.

Estimation of the total, direct and indirect effects within the models

The total, the direct and indirect effects of the model weigh the strength of the relationship between the antecedent predictor variable (X:IPI); the mediator (M: Maternal Morbidity-Premature rupture of membranes, third trimester bleeding) and the outcome variable (Y: Perinatal mortality).

The total effect is a combined effect of the direct and indirect effect and partitions how differences in the predictor variable are mapped on differences in the outcome variable. Therefore the total effect in the model above shows strong positive effects of Primigravida status and long IPI on Perinatal mortality in Rwanda. The direct effect on its part, explains that one case higher on the predictor variable is subsequently higher on Y. Results of our logit mediation models also shows a strong positive effect of Primigravida status and long IPI on perinatal mortality.

Lastly, the indirect effect is relevant through the existence of a causal inference between the predictor variable(X: IPI) and the mediator variable (Maternal morbidity) on Perinatal mortality. As it was indicated in the first part of the analysis, a significant effect of Primigravida status and Long Inter-pregnancy Interval on maternal morbidity explained a first sine qua none condition for a mediation analysis. However, this is not enough, a conclusive estimation of the strength of mediation effect is to be found in the estimation of bootstrapping with a 95% bias corrected confidence interval. The bootstrap generates the lower and the upper confidence limits of the parameter under estimation. If zero is outside of the lower and the upper limits, then the parameter under estimation is different from zero at 0.05 for a 95% Confidence Interval.

Since the bootstrap estimates do not show any zero in the confidence interval for both Primigravida women (Boot Lower Level CI = 0.0056; /Boot Upper Level CI = 0.1271) and those with long IPI (Boot Lower Level CI = 0.0047; /Boot Upper Level CI = 0.283), a small significant indirect effect of 4,9% for Primigravid women and 11,4% for Long Inter-pregnancy interval. No significant effect is observed for women with short IPI, given that there is a zero indirect effect between lower level (-0.059) and upper level (0.102) confidence interval.

6.6 Discussion, conclusion and policy recommendation

Results of this study indicate three important findings. The first is a significant mediation effect of primigravida status and long IPI through maternal morbidity on perinatal mortality. This effect explains that, a portion of this effect caused by primigravidity status or long IPI after first causing maternal morbidity (premature rupture of membranes and third trimester bleeding) is respectively 4,9% and 11,4%. This motivates the rationale for considering the mediation perspective along the analysis of the effect of Inter-pregnancy interval on maternal morbidity and neonatal mortality. The second is that, besides the mediation effect, that of Primigravida status and Long IPI show consistently the same strong similar patterns on maternal morbidity and perinatal mortality. These similar obstetric complications and perinatal adverse outcome for are self-explained by the fact that in the first instance, primigravid women are known to be a high risk group for experiencing prolonged first and second stage of labour, for increasing the chances of foetal distress during labour and for increasing the risk of either operative vaginal delivery or emergency caesarian section compared to their multiparous counterparts (Hashim N, et al. 2012). This might be caused by a low physiological orchestration of the maternal stamina to expel the fetus and a lack of responsiveness of the pelvic along the dilation process. In the second instance, previous studies have hypothesized that long IPI are related to the physiological regression status of the mother during the long period between the end of the previous and the index pregnancy. This hypothesis relates to the physiological adaptations of the reproductive system including an increase in blood flow to the uterus in a way that, after an IPI longer than 60 months, the subsequent pregnancy can no longer benefit from these temporary beneficial adaptations and becomes vulnerable as for first pregnancies (Agustin Conde-Agudelo, et al. 2012)**.**

And thirdly and lastly, no significant effect of short IPI or any significant indirect effect (mediation) is observed on both maternal morbidity and perinatal mortality. In reference to the findings of Habimana I. et al. (2014-fourthcoming) and A. Razzaque (2005), short IPIs are associated with high blood pressure. A pregnancy becomes less risky when women under gestational hypertension are properly managed and monitored before it develops proteinuria and pre-eclampsia.

Findings of this study call for more efforts in the improvement of the availability and accessibility of good quality antenatal care and delivery services in Rwanda, with a special focus on sensitizing primigravid women to start antenatal care since the first trimester and use regular antenatal checks. The recent revision of the health insurance scheme intending to group the mutual health insurance within other improved ones such as RAMA, MMI, SORAS AND MEDIPLAN, gives hope that even poor women will accede district hospital for pregnancy and delivery care. This will reduce the proportion of perinatal deaths given the increased adequate antenatal care utilization and will increase deliveries assisted by trained attendants in improved standard health facilities.

6.7 Limitation of the study

The weakness of this study lays in two corners. The first is that we use inpatient hospital discharge data, which does not allow the selection a random sample of respondents. It drew a selected sample of women, those who were referred (to) or who simply visited Kibagabaga district hospital, for delivery assistance or who underwent a special treatment after stillbirth by skilled birth attendants as a result of severe complications during pregnancy. The second is that, due to an existing poor filing system at Kibagabaga district hospital, cases considered in this study are those with gynecologic and obstetrical files that were available between 2012 and 2013. A better filing system (may be an electronic filing system) might have allowed us to use a bigger sample and this might have improved the statistical inference and representativeness of delivery-related referred women in Rwanda.

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Chapter 7: Conclusions: A focus on pregnancy spacing will improve maternal health, reduce fetal loss and perinatal mortality in Rwanda

7.1 Introduction

This dissertation aims at demarcating the role of inter-pregnancy interval and the previous pregnancy or infant survival outcomes on maternal health, pregnancy outcome and Neonatal Mortality in Rwanda. The motivation to undertake this research is double-fold. The first is to contribute to the ongoing debate on the role of pregnancy spacing on the survival of newborn children and the health of their mothers by providing empirical findings for Rwanda, a country without sufficient evidence in this matter. The second is to give an insight to policy makers and health practitioners in Rwanda about the role of pregnancy spacing in reducing the risks of maternal morbidity and that of neonatal mortality. Different approaches are adopted to respond to the objectives of this dissertation. On the basis of DHS 2000, 2005 and 2010 data, the first study focuses on the replacement desire of women with three living children of only one gender (a.o only girls or only boys) or whose only last son or daughter dies. Secondly, the effect of the IPI on fetal loss is estimated by taking into account the type of pregnancy outcome that preceded the index pregnancy to understand the moderating role of IPI in preventing repeated fetal losses. Third, in a bid to avoid selectivity bias in the study on the effect of IPI on infant mortality, a heckman selection model is used to estimate the combined effect of IPI and the type of previous pregnancy outcome on neonatal mortality. Fourth, using DHS 2010 and Kibagabaga district hospital maternity record data, the effect of IPI on delivery-related referrals in Rwanda and the role of IPI on maternal morbidity (gestational hypertension, third trimester bleeding, premature rupture of membranes and lower limb edema) for women who were transferred to Kibagabaga district hospital from health centers are studied. Fifth and last, on the basis of Kibagabaga district hospital maternity record data, the role of IPI is estimated as well as the mediating role of maternal morbidity on perinatal mortality. The expectation is that women are more likely to be kept in a vicious cycle of maternal morbidity, fetal and neonatal death traps as outcomes of short and long inter-pregnancy intervals.

7.2 Research findings

The objective of this research is to analyze the effect of short and very long inter-pregnancy intervals on the risks of losing a pregnancy, of perinatal mortality and of (pregnancy related) maternal morbidity, and as such contribute to the debate on the role of pregnancy spacing on the survival of newborn children and the health of their mothers by providing empirical findings for Rwanda.

The results of this study bring a stone to this debate but also are useful for programs geared to improving maternal/child health and give information on the relevance of family planning methods for pregnancy spacing in Rwanda.

While adopting different approaches in estimating the plausible effect of IPI on maternal and infant's health, we show the extent to which women are caught in a vicious cycle of reproductive behavior and outcomes. In the first four chapters, the analyses are based on data from the Rwanda Demographic and Health Surveys (2000, 2005 and 2010), which means that the same analysis can be replicated in other countries with such datasets. In the last chapters, Kibagabaga district hospital data are used, obviously on a selected sample of women who were referred for improved delivery care.

Each chapter below embeds findings that are helpful in providing a response to our initial hypothesis.

The second chapter dealt with the role of Gender Preference on the replacement behavior of women

On the basis of the hypothesis that improved health and survival can motivate families to alter their gender specific replacement behavior, we estimated the replacement behavior of women, after the death of a child and which reduces the waiting time to the next pregnancy. In contrast to studies from other Sub-Sahara African countries on gender preference which point mostly at son preference, we found that both sons and daughters are equally important for mothers in Rwanda, and this leads to a replacement strategy driven by the desire for a mixed gender offspring in the family. This pattern of mixed gender preference is rather versed to the Rwandan culture, with an outmost wish for new couples to bear both genders as a complete blessing. In this perspective, findings of this study highlight the replacement strategy after the loss of the only son or daughter. In the understanding that the existing effect of narrowed Interval after the loss of a pregnancy or the death of an infant, other parts of the analysis highlighted to what extent IPI is more likely to affect the outcome of the next pregnancy, the survival of the index infant and the health of the mother.

Effect of Inter-pregnancy Interval and Previous pregnancy outcome on pregnancy loss in Rwanda

Studies presented in the World Health Organization expert consultation meeting in 2005 on Inter-pregnancy Interval (IPI) have contributed to a consensus that women should postpone the next pregnancy to at least 6 months after a fetal loss and 24 months after a live birth. Our findings show that a pregnancy preceded by a fetal loss is more likely to lead to another fetal loss, if women became pregnant within two years after a previous pregnancy loss. The reason of this recurrent adverse pregnancy outcome is likely related to a lack of post-abortion care and as a consequence, women might become pregnant again before recovering from the causes of the previous fetal death, and therefore they are caught in a fetal death trap. Our findings also show higher risk of fetal death when IPIs are longer than 5 years, which confirms the physiological regression hypothesis.

Effect of Inter-pregnancy Interval on Fetal Survival and Neonatal Mortality: A Heckman Selection Analysis

The studies on infant mortality ignored the fact that fetal death removes pregnancies from the 'population at risk' of infant mortality, which might lead to biased results. In a bid to dodge this methodological weakness, this study used a two-step heckprobit models to control for selection bias by simultaneously estimating the combined effect of IPIs lengths and the type of event that started the interval on both pregnancy survival and neonatal mortality. After controlling for the selection effect, we don't find any relationship between IPIs and neonatal mortality when the preceding event is a fetal death. We therefore understood that, even though the two models were interlinked (in reference to the significant selection effect), no simultaneous effect of IPIs exists on both fetal survival and neonatal mortality, especially when the preceding event is a fetal loss. In this way, we understand that fetal death trap is completely moderated by IPI length, and no relation between the previous fetal death and the last is observed if women wait at least 24 months before becoming again pregnant. Yet, in order to avoid the risk of repeated pregnancy disruption, an IPI of at least 6 months after a fetal death is recommended to Rwandan women. Even though IPI shorter than 24 months does not affect neo-natal survival, it increases the risks of fetal death. Women with an IPI less than 2 years have not necessarily experienced an infant death trap, and in case the previous child died in infancy the highest odds are found for neonatal death regardless the duration of the IPI.

Effect of IPI on Maternal Morbidity in Rwanda: A retrospective analysis of RDHS (2010) and Kibagabaga district hospital maternity records, 2012-2013

There is a lack of sufficient empirical evidence on the effect of IPI on Maternal morbidity to resolve the current scientific debates deemed to understand the existing relationship between IPI length and maternal pregnancy and birth outcome worldwide. On the basis of RDHS 2010, the results show that primigravid women, those with short and long intervals have increased odds of being referred because of pregnancy or delivery complications. The Kibagabaga district hospital's maternity records analysis also shows that, once admitted, short intervals were not associated with higher levels of maternal morbidity. However, Long intervals as well as first pregnancies (primigravid) are associated with higher risks of third trimester bleeding, premature rupture of membrane and lower limb edema, while a higher age at conception is associated with lower risks. And lastly, findings of this study show that, poor women from rural areas and with limited health insurance are not often referred unless they show serious complications. These women however show increased risks of maternal morbidity relatively to their counterparts from Kigali city. This outcome is mostly related to the difference in access to and utilization of health care during pregnancy. In most cases, pregnant women from rural areas are delayed to reach the district hospital because of ignorance and poverty (especially related to the lack of transport fees) as well as the transfer delay from the referring health care centers. Consequently to these delays, they reach the district hospital in a critical status and the intervention reduces delivery-related morbidity to a lower extent, relatively to their counterparts who easily afford to come immediately to this hospital in due time.

Effect of Inter-pregnancy Interval and Maternal Morbidity on Perinatal Mortality: A Mediation Perspective

Perinatal mortality is intimately linked to maternal health throughout the continuum of pregnancy.

Previous studies have assessed the relationship between IPI, maternal and perinatal morbidity and mortality separately, but few have showed the mechanism through which IPI affect first the mother, thus leading to her morbidity which then affects perinatal survival through subsequent sequalae from intrapartum complications including the premature ruptures of membranes or utero-placental bleeding disorders (the mediation perspective) which critically affect fetal survival. Our finding demarcates no indirect effect of short IPI on perinatal mortality. However, we find a small mediation effect (contribution) of 5% and 11% caused by the morbidity of primigravid women as well as by women with very long IPIs on perinatal mortality. This meaning that, a proper antepartum care of primigravid women as well as those with very long IPI is more likely to reduce the current perinatal deaths.

7.3 Discussion and Recommendations

1) Scientific contribution of the research

The WHO 2005 consultation meeting on birth spacing recommended extended research from different countries and contexts to confirm real existing lien between IPI and adverse infant and maternal mortality. Studies following this meeting and seeking to identify the optimum IPI following a fetal death have shown contradictory findings on the relationship between IPI, pregnancy outcomes and infant mortality. While studies from low income countries (e.g Bangladesh) showed that short IPIs after a fetal loss increase the risks to lose the next pregnancy, those from high income countries (e.g Scotland, Sweden) showed that short IPI(less than 6 months) did not have adverse effects on the following pregnancy . This inconsistency might be rooted either in the contexts in which research was conducted or else in the methodological weakness which, therefore calls for more evidence on this relation. Although empirical studies have theorized that maternal morbidity is an important cause of perinatal mortality the effects of shorter pregnancy intervals on maternal morbidity has hardly been investigated empirically. To further complicate the issue, very long intervals (more than 60 months) also turn out to have adverse effects. Birth spacing of more than 5 years occurs among 10% of all pregnancies in Rwanda.

Results of this thesis shed some light on the contribution of IPI and the type of previous pregnancy outcome on fetal survival, neonatal mortality and maternal morbidity in Rwanda. We evidenced hidden mechanisms that are behind IPI length, fetal loss, perinatal, neonatal mortality and maternal morbidity. By using the combined effect of IPI and the type of previous pregnancy outcome instead of Inter-Birth Interval (IBI), it became clear that analysis using IBI leave behind possible fetal deaths that are more likely to happen in between births, which on the other hand play a role in affecting the reproductive health of the mother. On the basis of these findings, we posit that women will improve their reproductive health status and avoid the risk of fetal death trap if they wait at least two years after the previous fetal death. This finding relates to the findings from other developing countries such as Bangladesh in opposite to findings from developed countries, and might be related to the absence of post-abortion care. In a bid to avoid methodological flaw, studies on infant mortality should avoid selectivity bias by concomitantly considering fetal survival. While short IPI are not associated with maternal morbidity, primigravid women, and women with long IPIs showed increased risks of third trimester bleeding, premature rupture of membrane and lower limb edema. Delays related to go for antenatal care or delivery at health centers, or delays of these centers in transferring women are prone to play a role in the increased morbidity of women residing in peri-urban or rural areas relatively to their counterparts residing in Kigali city. Primigravid women showed adverse outcomes throughout this study. Programs geared to reduce maternal death and neonatal mortality should consider primigravid women with a particular attention. Women with very long IPI (<=5 years) have consistently showed increased risks of fetal loss, neonatal death and maternal morbidity. Our findings contribute to the debate whether older age of the mother might be hiding behind the effect of very long interval length. We found no negative effects of older age, and a remaining strong effect of long inter-pregnancy interval, which explains the physiological regression hypothesis.

2) Policy implications of the findings

The family planning policy in Rwanda has focused mainly on birth limitation since the 1983's under the ONAPO (Office National de la Population) slogan TUBYARE ABO DUSHOBOYE KURERA

"let's give birth to children we are able to raise". So far relatively little attention has been devoted to the spacing of births, yet an extra focus on pregnancy spacing in the health programs could be both beneficial and feasible. The survival of mothers, fetuses, newborn and children pictures the well-being of a society and its plausible potential for the future and securing the health of mothers and that of children is mandatory for the safety of the whole society. Short or very long IPI in most cases are linked to unmet needs for family planning and pregnancy spacing and in turn affect the health of the mother, fetuses and infants. Findings of this study showed short and very long IPI to be critically affecting fetal survival and infant mortality. Policy wise, avoiding short IPI can be achieved through the use of post-partum contraception while long IPI remain problematic to avoid, given that a desired pregnancy may be precluded by sub-fertility, availability of a partner, economic issues or illness. In its efforts to reduce infant and maternal morbidity and mortality, Rwanda has not managed any effort in increasing health infrastructure, in training community health workers and medical professionals and in putting into place a coherent, integrated and effective health system. However, many efforts need to be focused on the spacing of pregnancies to at least 2 years after both fetal death and birth, together with women's access to a continuum of care for a better reproductive health. This means, women undergoing medical tests and treatment before pregnancy, during pregnancy through childbirth up to childhood period. By doing this, women who undergo a pregnancy disruption will be advised to wait at least 6 months before attempting a next pregnancy or else, any illhealth status of the mother originating from the previous pregnancy disruption will be properly identified and treated medically and psychologically before any attempt for the next pregnancy. Women who have had a pregnancy disruption should be counseled with regard to contraceptive options so that they can avoid another unintended pregnancy.

This study revealed that when the preceding pregnancy ended in a miscarriage or stillbirth, there is an elevated risk that the index pregnancy will end with the same outcome. Women with a preceding fetal loss deserve special attention in counseling and monitoring. In the context of poor countries like Rwanda, a full reproductive health package is necessary, and implies more efforts put into pregnancy management, into encouraging family planning for spacing pregnancies, and into promoting health seeking behavior in the form ante- and post-natal care. While high proportion of Rwandan women attends at least one antenatal visit during pregnancy (98%), most of these receive their first antenatal visit late in pregnancy and few of them attend the full scope of four antenatal visits during pregnancy, this full package will encourage women to start necessary antenatal care early in pregnancy and proceed to a maximum 4 antenatal care during pregnancy. Women will also be encouraged to come for post-abortion or post-natal tests for their reproductive safety. Special attention by community health care providers is needed after a fetal death and after the death of an infant to prevent a repetition of these adverse pregnancy outcomes. Other worth recommendation is that hospitals and their staff should accord a particular attention to abortions by encouraging post-abortion medication, while at the same time properly recording abortions in the obstetrical records of women visiting hospitals. Last but not least, in line with the Government of Rwanda's effort to promote women's health, health centers in remote areas of the country should not be reluctant in transferring pregnant women and wait until their situation becomes critical, rather they should provide a timely benefit of emergency obstetrical care.

3) Future research and limitations of this research

To a certain extent, this study has contributed to the ongoing academic debate on the relationship between IPI and fetal, infant and maternal morbidity and mortality. It has explained the interplay between IPI, fetal loss, infant mortality, gendered replacement strategy and maternal morbidity and has provided necessary insights to Rwandan Policy makers and stakeholders in the reproductive health care system. Even though efforts were oriented to addressing previous similar studies' methodological shortfalls, this study also, has encountered some limitations. For example, one would doubt about the accuracy of the total number of reported pregnancy losses in the Demographic and Health Surveys used in this study (2000, 2005 and 2010) is accurate, given that the measurements were made over a rather diffuse period of time and women might have not mentioned pregnancy losses that occurred in the first or the second month of their pregnancy, when they were not fully aware of being pregnant. It is also expected that Rwandan women will not easily indicate that they had an induced abortion as it is illegal, except when the physical health of the mother is in great danger. Also, the RDHS-data do not make a distinction between induced and spontaneous pregnancy losses, which is an omission seen different relations between the two types of abortions at the beginning of the IPI, length of the IPI, and pregnancy outcome found in other research. Apart from the DHS data, the Kibagabaga district hospital women's obstetrical files do not accurately register previous abortions, which hamper a proper IPI estimation. Therefore, a similar study, using primary data and in a country where abortion is legally accepted might provide more insight on the relationship between IPI, fetal, infant and maternal mortality and morbidity.

4) Final remarks

The health status of mothers, pregnancies, newborn and children constitutes the well-being of a society and its potential for the future. Failure to meet their minimum health status will harm the welfare of the whole society. The Rwanda Ministry of Health and its stakeholders need to keep synergizing so that all families have access to a continuum of care that extends from pregnancy (and even before), through childbirth and on into childhood by focusing on the contribution of pregnancy spacing on the reproductive health status of the mother, her survival and that of her pregnancy and infants. Efforts deemed to building a coherent, integrated and effective health system will eliminate financial barriers to care, and protect people from the poverty that is both a cause and an effect of ill-health. A focus on pregnancy spacing will improve maternal health; reduce fetal loss and perinatal mortality in Rwanda.

Nederlandse samenvatting

Zwangerschapsverlies en zuigelingensterfte in Rwanda:
De effecten van het interval tussen opeenvolgende zwangerschappen

Inleiding

Rwanda heeft sinds 2005, goede resultaten geboekt met het verbeteren van de gezondheid van de bevolking door het opzetten van een systeem voor 'community based' gezondheidszorg. Tegelijkertijd werd een bijbehorende ziektekostenverzekering geïntroduceerd. Huishoudens betalen hiervoor naar draagkracht, waardoor ook het armste deel van de bevolking toegang kreeg tot simpele basiszorg. Moeders en kinderen krijgen bovendien via het nieuwe systeem meer preventieve medische zorg van lokale medewerkers. Tezamen heeft dit bijgedragen tot een daling van zowel de sterfte onder kraamvrouwen en zuigelingen als onder kinderen jonger dan vijf jaar. Rwanda lijkt daardoor als één van de weinige landen in sub-Sahara Afrika de VN Millennium Ontwikkelingsdoelen op dit terrein te halen.

Bij de voorlichting aan de bevolking over persoonlijk gedrag dat de (reproductieve) gezondheid kan verbeteren, is tot nu toe nauwelijks aandacht voor 'gezonde' intervallen tussen zwangerschappen, noch in voorlichtingsprogramma's over gezinsplanning, noch in die over de gezondheid van moeder en kind.

Zwangerschappen die te kort op elkaar volgen geven volgens de Wereld Gezondheid Organisatie (WHO 2007) een groter risico op ziekte en sterfte van de moeder, haar ongeboren vrucht en pasgeborene. Ook heel lange geboorte intervallen verhogen de kans op complicaties en sterfte. In Rwanda wordt één op de vijf kinderen met rangnummer twee of hoger geboren binnen twee jaar na de geboorte van het oudere broertje of zusje en één op de tien pas na een interval van vijf jaar (NISR en ICF Int 2012).

Eén van de redenen voor het gebrek aan aandacht voor het plannen van zwangerschappen is de onzekerheid over wat nu precies als een 'gezond' zwangerschapsinterval moet worden aanbevolen.

Studies over het onderwerp geven deels tegenstrijdige uitkomsten. Dit komt onder andere door verschil in regionale context, landen met een goed versus een beperkte gezondheidssysteem, en door verschil in gevolgde methodologie. Veel studies gaan uit van het interval tussen opeenvolgende geboorten. Zwangerschappen die niet leiden tot een (levende) geboorte worden dan buitenbeschouwing gelaten. Hierdoor wordt niet alleen de lengte van geboorte intervallen verlengd, maar worden ook de effecten van zwangerschapsafbrekingen op de lichamelijke en emotionele conditie van de moeder genegeerd.

Bij onderzoek naar 'wenselijke' intervalduur is het daarom beter om zwangerschapsintervallen als uitgangspunt te nemen en ook de uitkomst van de vorige zwangerschap als variabele in de analyse te gebruiken (Da Vanzo et al. 2007, 2008).

Het effect van de lengte van het zwangerschapsinterval op maternale morbiditeit is weinig bestudeerd, zeker in relatie tot kansen op perinatale sterfte. Deze studie wil daarom bijdragen aan meer inzicht in het effect van korte en lange zwangerschapsintervallen op zwangerschapsverlies, neonatale sterfte en op zwangerschap gerelateerde ziekten van vrouwen in Rwanda.

Theorie en methodologie

Twee mogelijke verklarende kern variabelen staan centraal in deze studie. De eerste is de lengte van het interval tussen het einde van de vorige zwangerschap en de start van de volgende. De tweede is de uitkomst van de vorige zwangerschap die is geoperationaliseerd in drie categorieën: zwangerschapsafbreking (miskramen en doodgeboorten), levend geboorte van een kind dat sterft als zuigeling en een levend geboorte van een kind dat blijft leven. Deze geconstrueerde classificatie houdt verband met het advies van de WHO (2007) over geboorteplanning en het debat in de literatuur over de achterliggende mechanismen van het effect van de intervalduur op het verloop van de zwangerschap en de conditie van moeder en kind. De WHO adviseert na een zwangerschapsverlies zes maanden en na een geboorte twee jaar te wachten met de volgende zwangerschap. Zo'n periode is nodig om de lichamelijke conditie van de moeder volledig te laten herstellen van de zwangerschap en bevalling. Als de moeder na de geboorte borstvoeding geeft, en in Rwanda krijgt in 2010 meer dan 80% van de kinderen nog (aanvullende) borstvoeding in de eerste twee levensjaren, wordt van de moeder nog een langere periode extra energie gevraagd.

Als de moeder te snel weer zwanger wordt, is het mogelijk dat haar lichamelijke conditie onvoldoende is door bijvoorbeeld tekorten aan bepaalde mineralen ('maternal completion') en dat er een competitie ontstaat tussen het nog ongeboren kind en het oudere kind ('sibling competition') dat nog aan de borst is (overlap van zwangerschap en borstvoeding). Ook zou er een grotere kans zijn dat via de moeder infectieziekten worden overgedragen ('vertical transfer of deseases') (Conde-Agudelo et al. 2012).

Het idee bestaat dat speciaal in arme landen vrouwen in een vicieuze reproductieve cirkel terecht komen door snel opnieuw zwanger te worden na een zwangerschapsverlies of na de dood van een zuigeling. Door de dood van een zuigeling stopt de borstvoeding, eindigt de post-partum amenorrhea en komt de ovulatie weer op gang. De nieuwe snelle zwangerschap kan een bewuste keus zijn (vervangingseffect), maar ook ongewenste door onvoldoende toegang tot of kennis van methoden voor geboorteregeling. Door het ontstane korte zwangerschapsinterval zouden de moeders een hoger risico hebben dat de volgende zwangerschap opnieuw ongunstig of met complicaties eindigt. Kortom het verdient aanbeveling rekening te houden met de uitkomst van de vorige zwangerschap als het effect van zwangerschapsinterval op ongunstige uitkomsten van een nieuwe zwangerschap worden bestudeerd.

Bij een zwangerschap na een interval langer dan 5 jaar lijkt ook een groter risico te bestaan op een ongunstige afloop of complicaties voor moeder en kind. De veronderstelling daarbij is dat na zo'n lange periode de lichamelijke conditie van de moeder weer lijkt op die van een vrouw die voor het eerst een kind verwacht (fysiologische regressiehypothese). Fysiologische aanpassingen als gevolg van vorige zwangerschappen zijn na een lang interval te niet gedaan. Het lichaam van vrouwen die voor het eerst zwanger zijn en dat van moeders die opnieuw zwanger zijn geworden na een lang interval is als het ware minder goed ingesteld op zwangerschap en bevalling.

De analyses in dit proefschrift zijn gebaseerd op secondaire data uit drie opeenvolgende Nationale Demografische en Gezondheidsonderzoeken uit 2000, 2005 en 2010. In de laatste twee analyse hoofdstukken zijn (ook) primaire data gebruikt over vrouwen die in 2011 zijn opgenomen en behandeld in het Kibagabaga District Ziekenhuis in het Gasabo District (provincie Kigali) op de afdeling Gynaecologie.

De data van de drie RDHS zijn veelal samengevoegd tot één data set. Het jaar van onderzoek is als controle variabele opgenomen in de analyse om veranderingen in de afhankelijke variabele (risico op sterfte van de foetus, op neonatale sterfte of op zwangerschap gerelateerde ziekten) in de tijd te traceren. De uitkomsten voor deze variabelen laten zien dat de kans op een zwangerschapsverlies (met name voor verlies in de laatste maanden van de zwangerschap) of neonatale sterfte tussen 2000 en 2010 beperkt maar significant is afgenomen in Rwanda. Dit bevestigt de gunstige effecten van het gevoerde gezondheidszorgbeleid.

Resultaten

In relatie tot de hoofdvraag van deze studie wordt in hoofdstuk 2 gekeken naar het voorkomen van genderspecifieke vervanging van een overleden kind. Voor de analyse zijn moeders gekozen met drie levende kinderen. De uitkomsten laten zien dat moeders met drie kinderen van het zelfde geslacht die een kind hebben verloren van het andere geslacht een sterke wens hebben om nog een kind te krijgen. Moeders die na de dood van een kind minimaal één dochter en één zoon hebben hadden die wens niet. Het vervangingseffect hangt dus sterk samen met de samenstelling van het kindertal naar sekse in het gezin. Deze uitkomst toont aan dat het vervangingseffect niet in alle situaties geldt en dat beslissingen van ouders met betrekking tot vruchtbaarheidsgedrag in relatie tot verlies van een kind in een bredere context moeten worden gezien zoals ook andere onderzoekers hebben gesteld (Randall en LeGrand 2003). Een van die contexten is de samenstelling van het bestaande gezin.

De keuze om voor de analyse moeders met drie levende kinderen te nemen heeft overigens als achtergrond dat de Rwandese overheid in haar streven de bevolkingsgroei te verlagen een gezin met drie kinderen als ideaal propageert.

In hoofdstuk 3 wordt zwangerschapsverlies bekeken in samenhang met interval lengte en uitkomst van de vorige zwangerschap. De uitkomsten tonen aan dat vrouwen die heel snel zwanger werden na een vorige miskraam of doodgeboorte het hoogste risico liepen opnieuw een zwangerschap te verliezen. In feite bleek zelfs dat vrouwen die binnen twee jaar opnieuw zwanger werden na een miskraam of doodgeboorte een significant verhoogd risico hadden in vergelijking tot vrouwen in de referentiegroep (met een levend geboren kind uit de vorige zwangerschap en een gezonde intervallengte tussen 24 en 60 maanden). Wachten de vrouwen langer dan twee jaar met een nieuwe zwangerschap hebben zij geen hoger risiko meer op sterfte van de foetus.

Na de geboorte van een levend kind, ongeacht of dit in leven blijft of niet, is het risico op een zwangerschapsverlies na een te kort interval (< 2 jaar) niet hoger dan die van de referentiegroep met een voldoende lange intervalperiode voor herstel. Voor moeders die binnen één respectievelijk twee jaar opnieuw zwanger werden na de vorige geboorte was het teken van de regressie coëfficiënt negatief, maar alleen significant voor moeders wier kind in leven bleef na een interval van minder dan een jaar. Korte intervallen geven in dit opzicht dus geen ongunstiger resultaat dan een als gezond aanbevolen zwangerschapsinterval. Dit effect verdwijnt als de interval duur boven de 5 jaar komt. Deze moeders hebben een 1,6 keer hoger risico op een zwangerschapsverlies, een even grote kans als vouwen die voor de eerste keer zwanger waren (1,5 maal).

Leiden de korte intervallen na een levend geboorte niet tot een groter significant risico op een miskraam of doodgeboorte, dan betekent dit nog niet dat er zich geen andere ongunstige effecten kunnen voordoen zoals zwangerschap gerelateerde morbiditeit, een te laag geboortegewicht van het kind, een voortijdige geboorte, een lage APGAR score of perinatale sterfte. In hoofdstuk 4 is daarom gekeken naar een gecombineerd effect van intervalduur en uitkomst van de vorige zwangerschap (via interactievariabelen) op zowel de sterfte van de foetus als die van de pasgeborene in de eerste levensmaand.

De Heckman selectie modellen tonen aan dat in vergelijking met een gezond interval (24-59 maanden) zwangerschapsintervallen korter dan een half jaar na een zwangerschapsverlies leiden tot een hogere kans op een volgend zwangerschapsverlies (lagere overlevingskans tijdens de zwangerschap in het selectiemodel), maar geen significant negatief effect hebben op het overleven van de eerste levensmaand.

Na een levend geboren kind, ongeacht of het blijft leven of als zuigeling sterft, zijn kortere intervallen (minder dan 24 maanden), niet schadelijk voor het overleven van een zwangerschap door de foetus, maar verhogen ze de kans wel op sterfte in de eerste levensmaand van de laatst geborene. De uitkomst dat een kind van moeders, waarvan het vorige kind in leven bleef en die binnen twee jaar weer zwanger werd, een hogere kans heeft om in de eerste levensmaand te overlijden in vergelijking tot een kind verwekt na een gezond interval, kan duiden op een onvoldoende herstel en conditie van de moeder (‘maternal depletion’) of verticale overdracht van een infectieziekten.

Het effect van een ongezond interval op de kans op neonatale sterfte is echter sterker als het vorige kind als zuigeling is gestorven. Deze uitkomst ondergraaft hypotheses over competitie tussen twee opvolgende kinderen of overdracht van infectieziekten tussen de twee als mogelijke oorzaak voor de relatie tussen een kort zwangerschapsinterval en neonatale sterfte. Het ondersteunt daarentegen de hypothese dat ongemeten oorzaken waarschijnlijk verantwoordelijk zijn een herhaling van dezelfde ongunstige uitkomst. Zowel moeders die binnen twee jaar opnieuw zwanger werden als moeders die een gezond interval in acht namen hadden een hogere kans hun kind in de eerste levens maand te verliezen als het vorige kind als zuigeling was overleden.

Er zijn meer factoren die kunnen bijdragen aan de boven beschreven herhaling van zuigelingen/neonatale sterfte dan het vervangingseffect, lengte van het zwangerschapsinterval of gebrek aan nutriënten van de moeder (zoals foliumzuur, ijzer) . Andere onderzoekers wezen o.a. op mogelijke effecten van post-natale depressie na de dood van een kind (Bhalotra en Van Soest 2007), herhaalde placenta complicaties of andere chronische zwangerschap gerelateerde ziekten van de moeder (Stephansson *et al.* 2003), een onvoldoende gevarieerde en arm e voeding of een leven in extreme armoede (Winkvist *et al*. 1992). Ook de uitkomsten in deze studie bevestigden dat zeer slechte hygiënische en woonomstandigheden een ongunstig effect hebben op de overlevingskansen van een pasgeborene in de eerste levensmaand.

Het mogelijke effect van fysiologische regressie op sterfte van foetus en pasgeborene werd verkend door leeftijd van de moeder (> 34 jaar) te combineren met het effect van een lang interval (meer dan 59 maanden) en de uitkomst van de vorige zwangerschap. Er werd een significant verhogend effect gemeten voor verlies van de foetus, maar geen significant effect voor neonatale sterfte. Vrouwen die voor het eerst in verwachting zijn hebben wel een verhoogde kans voor zowel verlies van de foetus als voor het verlies van haar kind in de eerste maand na de geboorte.

In de hoofdstukken 5 en 6 richt de aandacht zich vervolgens op het effect van zwangerschapsinterval en uitkomst van de vorige zwangerschap op de gezondheid van de moeder. De gegevens voor het analyseren van het effect van de kernvariabelen op de kans van vrouwen op het krijgen van bloedingen tijdens het laatste trimester van de zwangerschap (TTB), het voortijdig breken van de vliezen (PROM), vochtophoping in de onderbenen (LLE) of hoge bloeddruk zijn afkomstig uit de datafiles van één Districtsziekenhuis gelokaliseerd in het hoofdstedelijk district Kigali. De vrouwen in deze dataset vormen geen aselecte steekproef van de Rwandese vrouwen in de vruchtbare leeftijd. Het is geen gewoonte om in het ziekenhuis te bevallen in Rwanda, laat staan in één van de beter uitgeruste ziekenhuizen met medische specialisten. Bovendien wonen de meeste Rwandezen in landelijke en niet in stedelijke gebieden.

Om beter zicht te hebben op welke vrouwen door lokale gezondheidsmedewerkers worden doorverwezen naar zulke ziekenhuizen is allereerst de kans hierop geanalyseerd met behulp van gegevens uit de dataset van nationaal representatieve DHS (NISR 2012).

De resultaten laten zien dat alle hierboven al aangeduide risicogroepen (zwangere vrouwen met een kort of lang zwangerschapsinterval, primigravida) inderdaad een grotere kans hebben om te worden door verwezen wegens zwangerschaps- en bevallingscomplicaties. Voor de multigravida met een ongunstige afloop van de vorige zwangerschap (zwangerschapsverlies, vroegtijdige geboorte en neonatale sterfte) gelden ook hogere verwijzingskansen. Opvallende uitkomsten waren verder dat er sociaaleconomische ongelijkheid bestaat bij het doorverwijzen naar een Districtsziekenhuis. Arme vrouwen worden verhoudingsgewijs minder doorverwezen, terwijl rijkere vrouwen, vrouwen met meer dan een basisverzekering en vrouwen wonend in de stad een grotere kans hebben op zo’n doorverwijzing. Gezien de extra eigen kosten die behandeling in een Districtsziekenhuis met zich meebrengt kan het zijn dat vrouwen hier een eigen stem in hebben, d.w.z. dat het geen keus hoeft te zijn geweest van de gezondheidsmedewerkers.

De analyses van de Kibagabaga Districtsziekenhuis data laten geen consistente relatie zien tussen interval lengte en alle typen zwangerschap gerelateerde aandoeningen. Korte intervallen (< 12 maanden) tonen geen verband met TTB, PROM of LLE, maar zouden verband kunnen houden met hoge bloeddruk. Dit lijkt in tegenstrijd met het gegeven dat deze vrouwen een 1,5 maal hogere kans hadden op een doorverwijzing in vergelijking tot vrouwen die zwanger werden na een gezond interval. De uitkomst zou op twee zaken kunnen wijzen. Ten eerste: korte intervallen zijn gerelateerd aan de gezondheidsstatus van het kind en niet aan die van de moeder. Ten tweede: lokale gezondheidscentra verwijzen, bewust van de risico’s op complicaties bij de bevalling na een kort interval, ook zwangere vrouwen met een kort interval maar zonder zwangerschaps-aandoeningen naar een medische instelling die een meer geavanceerde behandeling kan leveren.

Het bewijs voor de ongunstige effecten na een lang interval zijn overtuigender. De hogere risico’s voor bloedingen laat in de zwangerschap (TTB) of het voortijdig breken van de vliezen (PROM) ondersteunen de fysiologische regressie hypothese, net als de hogere risico’s gevonden voor oudere vrouwen (>34 jaar). Het bewijs is minder sterk voor primigravida, die wel een significant hoger risico op hoge bloeddruk hebben maar minder sterke en niet-significante voor TTB en PROM. Ook voor primigravida zou kunnen gelden dat zij gezien het algemene risico dat zij complicaties bij de bevalling kunnenkrijgen, vaker worden door gestuurd zonder dat er maternale aandoeningenzijn geconstateerd.

In de tweede analyse werd de aard van de ziektekostenverzekering en plaats van het verwijzende gezondheidscentrum in het district gebruik als indicators voor sociaaleconomische positie. Vrouwen met een simpele ziektekosten verzekering hadden een significant hoger risico op zwangerschap gerelateerde hoge bloeddruk en wel een hoger maar niet significant risico op LLE. Vrouwen afkomstig uit de peri-urbane en landelijke delen van het district leden relatief vaker aan hoge bloeddruk, bloedingen en vroegtijdig breken van de vliezen dan vrouwen wonend in de hoofdstad zelf. Ook dit is een indicatie dat rijke inwoners van Rwanda levend in de stad meer toegang hebben tot een goede gezondheidsvoorzieningen. Deze uitkomsten samen met die uit de analyse van de verwijzingen sluiten aan bij de bevindingen van anderen (Chambers en Booth 2012) die stellen dat armen veelal te laat medische hulp zoeken van wege de extra kosten, en dat op het moment dat ze het doen het moeilijk is om transport te regelen.

In hoofdstuk 6 zijn de data uit van het Kibagabaga ziekenhuis gebruikt om de driehoeksrelatie tussen intervalduur, maternale morbiditeit en peri-natale sterfte te onderzoeken via een mediation analyse. De resultaten van die analyse wijzen op drie zaken. Allereerst is er een significant, zij het klein effect van de primigravida status en van een lang zwangerschap interval via maternale morbiditeit op perinatale sterfte. Het gaat hierbij om de aandoeningen van vroegtijdig breken de vliezen (PROM), en bloedingen in de laatste fase van de zwangerschap (TTB). De mate van het effect is veel kleiner dan verwacht (4,9 en 11,4%). Dit kan een gevolg zijn van de gebruikte data set (geen representatieve steekproef). Het betreft ziekenhuis data en we mogen aannemen dat de gespecialiseerde medische staf door adequate obstetrische zorg de risico's van de maternale aandoeningen op ongunstige effecten voor het ongeboren kind sterk heeft verkleind.

Ten tweede blijkt opnieuw dat de primigravida status en een zwangerschap na een interval van vijf jaar of meer bij multigravida vergelijkbare risico's voor moeder en kind met zich meebrengen.

De laatste bevinding is dat opnieuw geen significant effect van een kort interval (< 12 maanden) op maternale morbiditeit (PROM, TTB en LLE) werd gevonden maar ook niet met hoge bloed druk zoals in het vorige hoofdstuk. Het lijkt erop dat ook deze aandoening goed wordt behandeld en daardoor geen extra negatief effect heeft op perinatale sterfte van het kind.

Conclusie

De belangrijkste conclusie van dit onderzoek is dat na een zwangerschapsverlies (miskraam of doodgeboorte) een veel langer zwangerschapsinterval dan 6 maanden in acht moet worden genomen om de kans op een volgende miskraam of doodgeboorte te verkleinen. Deze bevinding komt overeen met die uit andere ontwikkelingslanden zoals in de Matlab Surveys in Bangladesh (Da Vanzo et al. 2007,2008). Het advies van de WHO om 6 maanden te wachten is waarschijnlijk voldoende om problemen met een volgende zwangerschap te voorkomen voor vrouwen wonend in landen met een toegankelijk en hoogwaardig gezondheidszorg systeem en betere sociaaleconomische levensomstandigheden. In Rwanda is het ontbreken van speciale zorg en voorlichting na een zwangerschapsverlies waarschijnlijk debet aan het hogere risico op een herhaling van deze ongunstige ontwikkeling bij een zwangerschapsinterval korter dan 2 jaar. Ook het feit dat veel vrouwen te lang wachten met de eerste antenatale controle draagt wellicht bij aan dit vergrote risico.

In een poging om bij de bestudering van de kernvariabelen (zwangerschapsinterval en uitkomst van de vorige zwangerschap) op neonatale sterfte het vraagstuk van selectiviteit te voorkomen is tegelijkertijd het risico geschat van deze variabelen op zwangerschapsverlies en neonatale sterfte. Het Heckman selectiemodel gaf aan dat er inderdaad sprake is van selectie. We vonden echter weinig bewijs voor het tegelijkertijd optreden van een significant effect van een kort interval op zowel het risico op dood van een foetus als op het risico op neonatale sterfte. Een kort interval had invloed op het verlies van een zwangerschap, maar niet op neonatale sterfte. Lange intervallen (>60 maanden) en een hogere leeftijd van de vrouw (>34 jaar) hebben daarentegen wel een ongunstig effect op beide. De fysiologische regressie hypothese wordt door deze bevindingen ondersteund. Ook het feit dat vrouwen die voor het eerst zwanger zijn dezelfde hogere risico's hebben wijzen in die richting.

Ook bleken korte zwangerschapsintervallen de risico's op zwangerschapsaandoeningen niet significant te verhogen, maar vrouwen die opnieuw zwanger werden na een interval langer dan 5 jaar en primigravida hadden een verhoogd risico op bloedingen tijdens de late zwangerschap, voortijdig breken van de vliezen en vochtophopingen in de onderbenen.

Beide groepen kunnen op grond van dit onderzoek bestempeld worden tot vrouwen die tijdens hun zwangerschap extra aandacht moeten krijgen om hun hoger risico op zwangerschapsaandoeningen, op sterfte van de foetus en van hun pasgeborene te voorkomen. Programma's gericht op geboorteplanning dienen ook meer aandacht teven aan planning van een gezond interval na een miskraam of doodgeboorte. Deze vrouwen zouden net als oudere vrouwen die na een lange periode opnieuw zwanger worden door de lokale gezondheidswerkers moeten worden gestimuleerd vanaf het begin van de zwangerschap regelmatig medische controles te ondergaan om ongunstige uitkomsten van hun zwangerschap te voorkomen.

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Curriculum Vitae

Ignace Habimana-Kabano was born at Mubuga-Karongi, in the Western Province of Rwanda on July 31rst 1973. He studied his Primary school at Kalungu-Kalehe, and his secondary school at Mwanga College in the Democratic Republic of Congo.

After finishing his secondary education, he worked as a secondary school teacher before joining the National University of Rwanda in 1998.

At the National University of Rwanda, he pursued a bachelor's degree in Social Sciences that he completed in 2002. From 2002 to April 2004, he worked as a deputy coordinator of the Rwanda Network of Christian Organizations, a consortium of Christian NGos fighting HIV/AIDS and Poverty. From May 1rst 2004 he was hired by the University of Rwanda as an Assistant Professor in the department of Social Sciences. Shortly after starting this teaching career, he was appointed to be the assistant to the head of the department as a secretary. From September 2005 to December 2006, he completed his Master's degree in Population Studies at the Population Research Centre of the State University of Groningen. Since January 2007, he taught demography and statistics at the newly created department of applied statistics. In 2008, was promoted to Lecturer of demography and statistics, a position that he occupies till today.

Besides teaching duties at the University of Rwanda, he participated in the evaluation of development and policy-oriented programs in Rwanda and in the East-African Community.

In 2009, he enrolled for a PhD program at Utrecht University in The Netherlands on a 6 months shift sandwich mode, thus combining thesis research and teaching duties at the University of Rwanda. His doctoral research – *"Pregnancy loss and neonatal mortality in Rwanda: The differential role of inter-pregnancy intervals".* While doing his PhD, he participated in international conferences and workshops on demographic curriculum development and research. In 2011, he was selected for a Summer School on Longitudinal and Life Course Research at University of Antwerp in Belgium.

With a rich experience in teaching and strong acquired skills in statistical methods and software, he will continue to apply these knowledge and technical skills in teaching, research and community services in Rwanda. His current research interest is to analyze the complex relationships between pregnancy spacing, maternal and perinatal mortality, poverty and economic development in Sub-Sahara Africa. He is happily married to Madam Uwase Marie Claire. Together they have two sons.

Table 4: (a) Results from other studies concerning the effect of IPI duration on pregnancy loss after a previous spontaneous or induced termination. (b) Results from studies concerning the effect of IPI duration on pregnancy loss after various previous pregnancy outcomes.

(a)

Study period/country	Sample	Effect of IPI	Reference category for statistical analysis	Controlled for
Wong et al. 2015 [6] USA (EAGeR trial) period 2006–2012	724 pregnant women with 1-2 prior pregnancy losses	No association between adverse pregnancy outcomes including pregnancy loss and IPI (<3 months or > 3 months)	Unknown	Demographic and reproductive history characteristics
Makhlouf et al. 2014 [7] USA, period 2003–2008	Nulliparous women 7681 primigravida 1240 with 1-2 previous spontaneous pregnancy losses (SAB) 817 with a previous induced abortion (IAB)	On fetal/neonatal death and other adverse outcomes after SAB and IAB No statistically significant difference for various IPI (<6, 6–12, >12 months) on risk of fetal loss and neonatal death	Primigravida Women with one previous SAB and IPI < 6 months	Maternal age, race, education, smoking, marital status, BMI, and use of vitamins C and E
DaVanzo et al. 2012 [4] Bangladesh (Matlab), period 1977–2008	9214 women with a miscarriage (spontaneous abortion prior to gestation of 28 weeks)	The shorter the IPI following a miscarriage is, the more likely the next pregnancy results in a live birth No significant effects of IPI duration on risks of a stillbirth Relative risk of a subsequent miscarriage increases with IPI duration	Women with a previous miscarriage and IPI of 6–12 months	Maternal age, education, gravidity, and calendar year
Love et al. 2010 [5] Scottish hospital data, period 1981–2000	30,937 women with a miscarriage in first recorded pregnancy	On miscarriage, ectopic pregnancy, IAB, and stillbirth Women with IPI < 6 months had less likely a miscarriage, highest sign Risk for women with IPI > 24 months No significant effect of IPI duration on risk of stillbirth	Women with a miscarriage and IPI of 6–12 months	Maternal age, socioeconomic status, year of first conception, and smoking
Conde-Agudelo et al. 2005 [9] Latin America period 1985–2002	258,108 women with a previous abortion	On fetal death and other adverse outcomes No significant difference of effect of IPI on fetal death or on neonatal death	Women with an IPI of 18–23 months	Maternal age, parity, education, smoking, marital status, BMI, year of delivery, hypertension, nbr antenatal checks, hospital type, and geographical area

IPI = interpregnancy interval, SAB = spontaneous abortion, IAB = induced abortion, and BMI = Body Mass Index.

(b)

Study	Sample	Effect of IPI	Reference category	Controlled for
Conde-Agudelo et al. 2006 [3] Rich and poor countries from all over the world	Meta-analysis	On various adverse perinatal outcomes Less clear is the association between pregnancy spacing and the risk of fetal (and neonatal) death Curves suggest that IPI < 6 months and IPI > 50 months are associated with increased risks	Differs per included study	Various factors Not standard for previous pregnancy outcome

(b) Continued.

Study	Sample	Effect of IPI	Reference category	Controlled for
DaVanzo et al. 2007 [11] Bangladesh (Matlab) period 1982–2002	66759 pregnancies including multiple births of 28540 women	On various pregnancy outcomes An IPI < 6 months after a live birth lead to a 7.5 fold increase for miscarriages, and 1.6 fold increase for stillbirths. An IPI >75 months showed a less increased risk on fetal losses. After a fetal loss a higher likelihood of a subsequent same fetal loss regardless of the IPI duration Highest OR on a miscarriage after IPI < 6 months after a life birth	Women with live birth after IPI of 27–50 months	Socioeconomic status, maternal age, education both spouses, religion, and calendar year
Stephansson et al. 2003 [12] Sweden, period 1983–1997	410,021 women with two deliveries	Stillbirths and early neonatal death Previous reproductive history and maternal characteristics substantially confounded the association between IPI and risks of stillbirth Risks are only found for long intervals Role of short intervals may have been overestimated in previous studies	IPI of 12–35 months	Outcome of first pregnancy (*stillbirth/early neonatal death, preterm delivery,* etc.) Maternal age, education, presence of partner, country of origin, diabetes, hypertension, period of delivery, and smoking