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1	Trends and risk factors of stillbirths and neonatal deaths in Eastern
2	Uganda (1982-2011): A cross-sectional, population-based study
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25	Shortened running title:

26 Risk factors of stillbirths and neonatal deaths in Uganda

27

## 28 Abstract

Objectives: To identify mortality trends and risk factors associated with stillbirths and neonatal
 deaths during 1982-2011.

*Methods:* Population-based cross-sectional study based on reported pregnancy history in Iganga-Mayuge Health and Demographic Surveillance Site (HDSS) in Uganda. A pregnancy history survey was conducted among women aged 15-49 living in the HDSS during May-July 2011 (n = 10,540). Time trends were analysed with cubic splines and linear regression. Potential risk factors were examined with multilevel logistic regression with adjusted odds ratios (AOR) and 95% confidence intervals (CI).

37 *Results:* A total of 34,073 births in 1982-2011 were analysed. The annual rate of decrease was 38 0.9% for stillbirths and 1.8% for neonatal mortality. Stillbirths were associated with several risk 39 factors including multiple births (AOR 2.57, CI 1.66-3.99), previous adverse outcome (AOR 40 6.16, CI 4.26-8.88) and grand multiparity among 35-49 year olds (AOR 1.97, CI 1.32-2.89). 41 Neonatal deaths were associated with multiple births (AOR 6.16, CI 4.80-7.92) and advanced 42 maternal age linked with parity of 1-4 (AOR 2.34, CI 1.28-4.25) and grand multiparity (AOR 43 1.44, CI 1.09-1.90). Education, marital status and household wealth were not associated with the 44 outcomes.

45 *Conclusions:* The slow decline of mortality rates and easily identifiable risk factors calls for 46 improving quality of care at birth and a rethinking of how to address obstetric risks, potentially a 47 revival of the risk-approach in antenatal care.

*Keywords:* Epidemiologic Factors; Perinatal Death; Pregnancy; Reproductive History; Stillbirth;
Uganda

50

# 51 Introduction

Every year, 2.6 million infants are stillborn<sup>1</sup> and 2.7 million die during their first month of life<sup>2</sup>. An estimated 98-99% of these deaths happen in low- and middle-income countries, where they remain underreported due to a lack of registration systems, births and deaths occurring outside health facilities and cultural beliefs and stigma<sup>3,4</sup>.

56 It is estimated that stillbirth and neonatal mortality rates are highest in sub-Saharan Africa and have decreased at a markedly slower pace in the region compared to the rest of the world<sup>5,6</sup>. 57 58 Uganda has the fifth highest number of stillbirths and eighth highest number of neonatal deaths in 59 sub-Saharan Africa<sup>6</sup>. Stillbirth rates in the country are based on estimates and predictions with the exception of one study that has investigated stillbirth over time<sup>7</sup>. While a large part of 60 61 stillbirths and neonatal deaths are caused by potentially preventable diseases or identifiable 62 conditions<sup>8</sup>, 50% of stillbirths and 60% of early neonatal deaths have not been linked to any maternal condition<sup>9</sup>, highlighting the importance of identifying at-risk pregnancies. 63

64 Reviews suggest that stillbirths and neonatal deaths are linked to several biological and socioeconomic risk factors<sup>4,10–12</sup>. While some studies set in sub-Saharan Africa have been 65 published, mostly from Ethiopia<sup>13-18</sup>, and Ghana<sup>19-22</sup>, a dearth of population-level studies 66 remains. An estimated 57% of deliveries in sub-Saharan Africa take place outside health 67 facilities<sup>23</sup>, rendering hospital-based studies unrepresentative. Moreover, findings from settings 68 69 outside sub-Saharan Africa may not be generalisable due to social, cultural and economic differences. Of the population-based studies on stillbirths in sub-Saharan Africa that we 70 identified<sup>7,11,19,20,24</sup>, one examined time trends<sup>7</sup> and one investigated associations with multiple 71 72 birth, previous stillbirth and infant  $sex^{20}$ , while none of the studies included birth intervals.

The Sustainable Development Goals aim to lower newborn deaths to 12/1,000 live births by 2030, while the Global Every Newborn Action Plan has set a global target of less than 10 stillbirths per 1,000 births by 2035<sup>25</sup>. Achieving these goals is unlikely without significant investments into research providing population estimates and guiding programmatic priorities<sup>5,26</sup>.
The objective of this study was to identify risk factors of stillbirths and neonatal deaths in rural
Uganda, and to depict the mortality rate trends in 1982-2011.

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80 Methods

81

## 82 *Study setting and data collection*

The data used in this study were obtained from a cross-sectional survey conducted in order to investigate the reliability of mortality tracking at Iganga-Mayuge Health and Demographic Surveillance Site (HDSS). The site is located in rural Eastern Uganda, covering 65 villages with 16,000 households. The socioeconomic profile of the area is homogenous, with 80% of people earning their living from subsistence farming and retail trading. One hospital, 15 health centres and 24 private clinics serve the 80,000 inhabitants. Nearly 70% of women give birth in a health facility and 30% of women attend four or more antenatal care visits.<sup>27</sup>

90 The study population consisted of women aged 15-49 living in the HDSS in May–July 91 2011. We used a list generated from the HDSS database as a guide showing all households in the 92 HDSS and the corresponding females in the household. The data collection team consisted of 60 93 data collectors working in groups of ten people, visiting all households in the area and identifying 94 and interviewing women aged 15-49. The interviewers asked all respondents what year and 95 month they were born in and then asked for their age in years. The answers were crosschecked 96 and the interviewers attempted to clarify any inconsistencies. If a participant was unsure of her 97 age, the interviewer requested to see documentation containing her date of birth or attempted to 98 estimate the date of birth based on any historical events the respondent was aware of that 99 occurred around the time of her birth.

A maximum of three follow-up visits were made to women who were not home during the
first visit. In total, 10,540 women were surveyed (Figure 1; study sample flow chart). During the

102 visit, the data collectors administered a pregnancy history survey. The survey recorded whether a 103 pregnancy resulted in a multiple or a single birth and what the outcome of the pregnancy was 104 (born alive, born dead, miscarriage or induced abortion). Sex of the baby and date of birth was 105 recorded for all pregnancies that did not result in a miscarriage or abortion. If the baby was 106 reported to have been born dead, the mother was asked whether the baby cried, moved or 107 breathed after birth in order to control for misclassification of stillbirths and newborn deaths. Age 108 at death was recorded for babies who were born alive but later died. If the pregnancy ended in a 109 miscarriage or abortion, the month and year of termination of the pregnancy and the duration of the pregnancy were recorded. 110



- Figure | Participant selection flowchart
- 111
- 112 Variables
- 113 The outcome variables were stillbirth, defined as giving birth to an infant who did not move, cry
- or breathe, and neonatal death, defined as death during the first 28 days of life. We used the third-

trimester stillbirth definition recommended for international comparison ( $\geq 28$  weeks of gestation)<sup>28</sup>. We used the year of birth for analysing time trends and as a potential confounder in the analysis for risk factors of stillbirth and neonatal death. Year of birth was treated as a continuous variable in time trend analysis and categorised into six-year intervals for the regression model: 1982-1987, 1988-1993, 1994-1999, 2000-2005, and 2006-2011.

120 We analysed associations between the outcomes and socioeconomic status, which was 121 reflected by education, marital status and household wealth. The woman's level of education was 122 categorised as none, primary, and secondary or higher. Marital status at the time of the survey 123 was defined as married or single/divorced. The household wealth index was obtained from a 124 separate module and divided into quartiles with ascending household wealth: lowest, second, third and highest. The index was created for an earlier study<sup>29</sup> by doing a principal component 125 analysis (PCA) on variables measuring asset ownership and household characteristics<sup>30</sup>. The 126 approach is often used in settings where it is challenging to obtain reliable estimates of income. 127 128 The final list included the following variables: number of sleeping rooms, type of floor material, 129 type of roof material, type of wall material, fuel used for cooking, source of light, and the 130 ownership of a radio, a sewing machine, an electric flat iron, type of bed, charcoal flat iron, a bed 131 net, kerosene lamp, kerosene stove, car, tea table, refrigerator, television set, sound stereo, 132 telephone, mattress, wheel barrow, cell phone and camera (Chronbach's alpha = 0.848).

133 Births were categorised as either single or multiple based on the number of infants born. 134 Sex of the infant was categorised as male, female and unknown. Birth interval was defined as the 135 time between the date of the latest birth and the date of the previous birth, categorised as  $\geq 33$ 136 months and <33 months, based on WHO recommendation of a minimum interval of two years 137 between a birth and attempting next pregnancy. Previous adverse outcome was defined as the 138 previous pregnancy resulting in a stillbirth or neonatal death. Age at childbirth was calculated 139 from the dates of birth for the mother and the baby and categorised into 15-17, 18-34, and 35-49 140 years. Parity was defined as the number of preceding pregnancies leading to a birth after 28 weeks of gestation and categorised as nulliparity, 1-4 births and grand multiparity (≥5 births). In
order to investigate whether the association between parity and stillbirth was influenced by
maternal age at birth, the variables were combined and births were divided into categories: (1)
nulliparous, 15-17 years old; (2) nulliparous, 18-34 years old; (3) parity 1-4, 15-17 years old; (4)
parity 1-4, 18-34 years old; (5) parity 1-4, 35-49 years old; (6) parity ≥5, 18-34 years old; (7)
parity ≥5, 35-49 years old.

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#### 148 Statistical analysis

149 We first analysed stillbirth and neonatal mortality rates with chi-square statistics to 150 examine the rates within different levels of the same potential risk factor without adjustment for 151 covariates. Due to the relatively high number of missing values in household wealth (n = 13,745; 152 40%), we included births with a missing value as a separate group in chi-square analysis. We 153 conducted a univariate logistic regression on the variables that displayed a difference between the 154 outcomes (p < 0.10) and included the variables that showed an association in univariate logistic 155 regression in the multivariate model. We constructed a multilevel logistic regression model with 156 odds ratios (OR) and 95% confidence intervals (CI) to identify risk factors of stillbirth and 157 neonatal deaths. The variables in this study were divided into socioeconomic and proximate 158 based on the framework by Mosley and Chen developed to study child mortality in low-income 159 countries<sup>31</sup>. We added socioeconomic variables (education, household wealth, marital status) into 160 the model first and did a backward elimination of variables not reaching p-value of 0.10 or less 161 before adding the proximate variables (age, parity, fetal sex, birth interval, single/multiple birth, 162 previous adverse outcome) and doing another backward elimination. Year of birth was included 163 as a potential confounder in order to control for higher mortality in earlier years. Adjusted odds 164 ratios are only reported for the risk factors that remained significant in the multivariate analysis. 165 We used chi-squares to investigate statistical significance of mortality decline and cubic Bsplines to visualise mortality rates with three internal knots at 25<sup>th</sup>, 50<sup>th</sup> and 75<sup>th</sup> percentile for 166

	variable year of birth. we obtained the annual decrease in mortanty rates with a nitear regression
168	on yearly mortality rates that had been transformed into a natural log scale. All analyses were
169	conducted with Stata version 13 (Stata Corporation, College Station, TX, USA).
170	
171	Ethical considerations
172	The Higher Degrees, Research and Ethics Committee at Makerere University approved the data
173	collection (ethical clearance: IRB0005876FWA, Protocol 073). Informed consent was obtained
174	from participants in writing or with an inked thumbprint for illiterate individuals after explaining
	the standay work allow and in available a
175	the study verbally and in writing.
175 176	the study verbally and in writing.
175 176 177	Results
<ol> <li>175</li> <li>176</li> <li>177</li> <li>178</li> </ol>	Results The survey intended to interview 16,410 women and 10,540 participated in the study. A large
<ol> <li>175</li> <li>176</li> <li>177</li> <li>178</li> <li>179</li> </ol>	Results The survey intended to interview 16,410 women and 10,540 participated in the study. A large number of women (4,955 women) could not be reached as they were pursuing secondary or
<ol> <li>175</li> <li>176</li> <li>177</li> <li>178</li> <li>179</li> <li>180</li> </ol>	<b>Results</b> The survey intended to interview 16,410 women and 10,540 participated in the study. A large number of women (4,955 women) could not be reached as they were pursuing secondary or tertiary education outside the HDSS; another 889 women had outmigrated and 26 died between
<ol> <li>175</li> <li>176</li> <li>177</li> <li>178</li> <li>179</li> <li>180</li> <li>181</li> </ol>	Results The survey intended to interview 16,410 women and 10,540 participated in the study. A large number of women (4,955 women) could not be reached as they were pursuing secondary or tertiary education outside the HDSS; another 889 women had outmigrated and 26 died between survey rounds.
<ol> <li>175</li> <li>176</li> <li>177</li> <li>178</li> <li>179</li> <li>180</li> <li>181</li> <li>182</li> </ol>	<b>Results</b> The survey intended to interview 16,410 women and 10,540 participated in the study. A large number of women (4,955 women) could not be reached as they were pursuing secondary or tertiary education outside the HDSS; another 889 women had outmigrated and 26 died between survey rounds.

184 All live births and stillbirths during the reproductive age range (15-49) were eligible for inclusion 185 in the analysis (births with maternal age of under 15 were excluded, n = 1,233). We excluded 186 births from the analysis if information about the year of birth (n = 61) or birth outcome (n = 73)187 was missing. Births occurring before 1982 (n = 101) were excluded as the low number of 188 observations would have made the mortality rate estimates unreliable. Of the 10,540 women 189 surveyed, 6,962 women reported at least one pregnancy leading to a stillbirth or a live birth and 190 were included in the analyses (Table 1). There were 34,073 reported births in total. Of all births, 191 515 (1.5%) were reported to have resulted in stillbirth and 899 (2.6%) in neonatal death. The 192 maternal characteristics for most births were primary school education (61.7%), currently married

8

193 (88.9%), maternal age 18-34 (80.5%; median 25 years, IQR: 20-30 years) and parity 1-4 (55.3%).

194 Of all infants that were born, 96.7% were singletons, 49.9% were female, 55.3% were linked to a

195 birth interval shorter than 33 months and 2.5% followed a previous birth that resulted in a

196 stillbirth or neonatal death.

197

Table 1. Characteristics of births at the	Iganga-Mayuge Health and	Demographic Surveillance Site (N
= 34,073)		

Item		n	%
Pregnancy outcome	Stillbirth	515	1.5
	Neonatal death	899	2.6
	Live birth	32,659	95.9
Year of pregnancy	1982-1987	2,162	6.4
	1988-1993	4,421	13.0
	1994-1999	7,475	21.9
	2000-2005	9,312	27.3
	2006-2011	10,703	31.4
Education	None	6,358	18.7
	Primary	21,013	61.7
	Secondary and above	6,702	19.7
Household wealth index quartiles	Lowest	3,578	10.5
	Second	5,467	16.0
	Third	6,292	18.5
	Highest	4,991	14.7
	Missing	13,745	40.3
Marital status	Single/divorced	3,741	11.0
	Married	30,300	88.9
	Missing	32	<0.1
Maternal age at childbirth	15-17	3,791	11.1
	18-34	27,438	80.5
	35-49	2,819	8.3
	Missing	25	<0.1
Birth type	Singleton	32,941	96.7
	Multiple	1,120	3.3
	Don't know	6	<0.1
	Missing	6	<0.1
Sex	Female	16,986	49.9
	Male	16,938	49.7
	Don't know	149	<0.5
Birth interval	<33 months	18,829	55.3
	≥33 months	8,029	23.6
Previous adverse outcome	Yes	855	2.5
	No	26,073	76.5
Parity	Nulliparity	6,962	20.4
	1–4 births	18,830	55.3
	Grand multiparity (≥5 births)	8,281	24.3

198

199 *Time trends in mortality rates* 

200	The stillbirth rate and	neonatal mortality	v rate displayed	d a slow decline (	Figure 2). Stillbirths
		2	1 2		

201 decreased from 20/1,000 births in 1982-1987 (CI 14-26/1,000) to 16/1,000 in 2006-2011 (CI 14-

19/1,000 (p = 0.121) (Table S1). There was a statistically significant decline in neonatal deaths

- 203 (p < 0.001) from 42/1,000 live births in 1982-1987 (CI 22-50/1,000) to 29/1,000 in 2006-2011
- 204 (CI 26-32/1,000). The annual rate of change for neonatal mortality was 1.8% per year (p < 0.01),
- while the stillbirth rate decreased by 0.9% per year (p = 0.19).







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208

 Table S1. Stillbirth rate (per 1,000 births) and neonatal mortality rate (per 1,000 live births) in Iganga-Mayuge HDSS in 1982-2011 with 95% confidence intervals.

Year	Stillbirths (n)	All births (n)	Stillbirth rate	CI	Neonatal deaths (n)	Live births (n)	Neonatal mortality rate	CI
1982-1987	43	2,162	19.9	14.0-25.8	88	2,119	41.5	22.0-50.0
1988-1993	72	4,421	16.3	12.6-20.0	122	4,349	28.1	23.1-33.0
1994-1999	95	7,475	12.7	10.1-15.2	194	7,380	26.3	22.6-29.9
2000-2005	135	9,312	14.5	12.1-16.9	192	9,177	20.9	18.0-23.9
2006-2011	170	10,703	15.9	13.5-18.6	303	10,533	28.8	25.6-32.0

209

## 210 Risk factors of stillbirth and neonatal death

211	In the multivariate analysis multiple births carried a 3-fold risk of stillbirth (AOR 2.57, CI 1.66-
212	3.99) (Table 2) and 6-fold risk of neonatal death (AOR 6.16, CI 4.80-7.92) (Table 3) compared to
213	singleton births. The odds of stillbirth were 41% higher for males compared to females (AOR
214	1.41, CI 1.11-1.80), while male sex was linked to 37% higher odds of neonatal death (AOR 1.37,
215	CI 1.16-1.61). A birth interval of less than 33 months was linked to increased odds of stillbirth
216	(AOR 1.47, CI 1.09-1.98) and neonatal death (AOR 1.50, CI 1.23-1.84). If the previous

pregnancy had resulted in a stillbirth or neonatal death, the odds of stillbirth were six times the odds for births not following a stillbirth or neonatal death (AOR 6.16, CI 4.26-8.88), while there was a 4-fold increase in odds for neonatal death (AOR 4.15, CI 3.02-5.72). The combination of advanced maternal age (35-49) and grand multiparity was linked with twice the odds of stillbirth compared to age group 18-35 with a parity of 1-4 (AOR 1.97, CI 1.32-2.89). For neonatal deaths, advanced maternal age was a risk factor for births linked to a parity of 1-4 (AOR 2.34, CI 1.28-4.25) and grand multiparity (AOR 1.44, CI 1.09-1.90).

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**Table 2.** Adjusted and unadjusted odds ratios for stillbirths according to year, socioeconomic and proximate characteristics (n = 34,073 births)

	Stillbirt	hs	All births		Stillbirths per 1,000 births	Unadjusted		Adjusted*	
Independent variables	n	%	n	%		OR	CI (95%)	OR	CI (95%)
Pregnancy year									
1982-1987	43	8	2,162	6	20	1		1	
1988-1993	72	14	4,421	13	16	0.82	0.55-1.23		
1994-1999	95	18	7,475	22	13	0.6 7	0.45-0.99	0.47	0.27-0.83
2000-2005	135	26	9,312	27	15	0.78	0.54-1.14	0.54	0.31-0.94
2006-2011	170	33	10,703	31	16	0.87	0.60-1.26		
Socioeconomic variables									
Education									
None	84	16	6,358	19	13	0.85	0.61-1.20		
Primary	331	64	21,013	62	16	1.07	0.83-1.39		
Secondary and above	100	19	6,702	20	15	1			
Household wealth index quartile									
Lowest	64	12	3,578	11	18	1.40	0.91-2.15		
Second	86	17	5,467	16	16	1.17	0.79-1.75		
Third	86	17	6,292	18	14	1.04	0.70-1.55		
Highest	63	12	4,991	15	13	1			
Marital status									
Single/divorced	71	14	3,741	11	19	1.35	1.00-1.82		
Married	442	86	30,300	89	15	1			
Proximate variables									
I ype of pregnancy	400	00	22.044	07	4.4	4		4	
Single	462	90	32,941	97	14	1	0.07.4.75	1	1 66 2 00
Sox of the helpy	49	10	1,120	3	44	3.30	2.37-4.75	2.57	1.00-3.99
Sex of the baby	192	25	16 096	50	11	1		1	
Mala	220	42	16,900	50	12	1 25	1 01 1 53	1 /1	1 11 1 20
Birth interval	220	43	10,950	50	15	1.20	1.01-1.55	1.41	1.11-1.00
>33 months	96	10	8 029	24	12	1		1	
<33 months	299	58	18 829	55	16	135	1 06-1 71	1 47	1 09-1 98
Previous adverse outcome	200	00	10,020	00	10	1.00	1.00 1.71	1.47	1.00 1.00
No	300	58	25,773	76	12	1		1	
Yes	132	26	855	3	154	6.85	5.06-9.27	6.16	4.26-8.88
Parity and age at birth									
Nulliparous, 15-17 years old	36	7	2,872	8	13	1.15	0.80-1.67		
Nulliparous, 18-34 years old	45	9	4,085	12	11	0.94	0.67-1.32		
Parity 1-4, 15-17 years old	15	3	919	3	16	1.49	0.85-2.62		
Parity 1-4, 18-34 years old	197	38	17,539	51	11	1		1	
Parity 1-4, 35-49 years old	6	1	354	1	17	1.36	0.56-3.32		
Parity ≥ 5, 18-34 years old	152	30	5,814	17	26	2.47	1.97-3.11		
Parity ≥ 5, 35-49 years old	64	12	2,465	7	26	2.35	1.72-3.21	1.97	1.32-2.89

\*In the adjusted model, variables were added group by group starting with socioeconomic variables. A backward elimination was performed on all variables not reaching the 0.05 significance level before proximate variables were added in the model. This was again followed by backward elimination. Finally, the year of pregnancy was added in the model. Again, a backward elimination was performed, resulting in the final model.

#### 

Table 3. Adjusted and unadjusted odds ratios for neonatal deaths according to year, socioeconomic and proximate characteristics (n = 33,558 births)

	Neonat	al deaths	All births		Neonatal deaths per 1,000 live births	Unadjusted		I deaths per Unadjusted		A	djusted*
Independent variables	n	%	n	%		OR	CI (95%)	OR	CI (95%)		
Pregnancy year											
1982-1987	88	10	2,119	6	42	1		1			
1988-1993	122	14	4,349	13	28	0.65	0.48-0.87	•			
1994-1999	194	22	7.380	22	26	0.61	0.46-0.80	0.47	0.27-0.83		
2000-2005	192	21	9.177	27	21	0.48	0.36-0.63	0.54	0.31-0.94		
2006-2011	303	34	10,533	31	29	0.67	0.52-0.88				
Socioeconomic variables			,								
Education											
None	181	20	6,274	19	29	1.29	1.00-1.67				
Primary	562	63	20,682	62	27	1.17	0.95-1.43				
Secondary and above	156	17	6,602	20	24	1					
Household wealth index quartile											
Lowest	93	10	3,514	10	27	1.13	0.82-1.56				
Second	137	15	5,381	16	26	1.07	0.80-1.43				
Third	170	19	6,206	18	27	1.18	0.89-1.56				
Highest	121	13	4,928	15	25	1					
Marital status											
Single/divorced	107	12	3,670	11	29	1.12	0.88-1.42				
Married	792	88	29,858	89	27	1					
Proximate variables											
Type of pregnancy											
Single	757	84	32,479	97	23	1		1			
Multiple	142	16	1,071	3	133	7.64	6.05-9.63	6.16	4.80-7.92		
Sex of the baby	~~-										
Female	385	43	16,804	50	23	1		1			
Male	502	56	16,718	50	30	1.32	1.15-1.52	1.37	1.16-1.61		
Birth Interval	400	45	7 000	0.4	47						
233 months	138	15	1,933	24	17	1 60	1 22 1 07	1 50	1 00 1 04		
<33 monuns	517	90	10,530	55	20	1.02	1.32-1.97	1.50	1.23-1.64		
Previous adverse outcome	560	60	25 772	77	22	1		1			
NO	100	12	20,110	2	140	2 00	2 0 2 5 45	1 15	2 0 2 5 7 2		
Parity and age at hirth	100	12	123	2	149	3.99	2.92-3.45	4.15	3.02-3.72		
			0.000	~		4 00					
Nulliparous, 15-17 years old	101	11	2,836	8	36	1.69	1.34-2.13				
Nulliparous, 18-34 years old	116	13	4,040	12	29	1.30	1.05-1.62				
Parity 1-4, 15-17 years old	26	3	904	3	29	1.27	0.83-1.95				
Parity 1-4, 18-34 years old	390	43	17,342	52	23	1		1			
Parity 1-4, 35-49 years old	15	2	348	1	43	2.16	1.22-3.83	2.34	1.28-4.25		
Parity $\geq$ 5, 18-34 years old	169	19	5,662	17	30	1.28	1.06-1.56				
Parity ≥ 5, 35-49 years old	82	9	2,401	7	34	1.57	1.21-2.03	1.44	1.09-1.90		

\*In the adjusted model, variables were added group by group starting with socioeconomic variables. A backward elimination was performed on all variables not reaching the 0.05 significance level before proximate variables were added in the model. This was again followed by backward elimination. Finally, the year of pregnancy was added in the model. Again, a backward elimination was performed, resulting in the final model.

**Discussion** 

During 1982-2011, neonatal mortality rate decreased by 1.8% and stillbirth rate by 0.9% per year.

232 The odds of stillbirth and neonatal death were higher with a multiple pregnancy, male infant,

short birth interval and previous adverse outcome. Neonatal deaths were linked to advanced
maternal age and stillbirths were linked to grand multiparity during advanced maternal age. We
detected no association with socioeconomic variables.

236 Earlier studies have reported a similar risk from multiple births<sup>20,32,33</sup> and male fetal sex<sup>12,20,34</sup>. Male sex is a risk factor for neonatal deaths<sup>35,36</sup> and it has been suggested that male 237 fetuses are also more vulnerable to stressors in utero<sup>12</sup>. The association between neonatal deaths 238 239 and birth intervals shorter than 33 months has been reported in earlier studies<sup>37</sup>. However, few 240 studies have investigated birth intervals and stillbirths exclusively. Our findings are similar to the 241 two studies we were able to identify, which reported an association between risk of stillbirth and 242 birth intervals of less than 21 months<sup>38</sup> and less than 35 months<sup>39</sup>. The association in this study 243 was controlled for previous stillbirth, suggesting that the association is not only linked to 244 maternal characteristics that may result in consecutive stillbirths. The underlying mechanism of 245 action is unclear, but it may be linked to depletion of reproductive and nutritional resources due to physical strain from short birth intervals<sup>37,40,41</sup>. 246

The odds of stillbirth and neonatal death were higher if the previous pregnancy ended in an adverse outcome, consistent with previous studies<sup>20,32,39,42–46</sup>. A recent meta-analysis on studies conducted in high-income countries reported an increased risk of subsequent stillbirth if the initial pregnancy resulted in stillbirth, but pointed out that the association is less clear when the initial stillbirth is unexplained<sup>47</sup>. In addition to being physiological, the association may also be a proxy for either environmental or socioeconomic factors that have not been fully accounted for.

Nulliparity or grand multiparity alone were not associated with stillbirths in this study, in line with findings from Bangladesh<sup>43</sup> and Egypt<sup>48</sup>, but in contrast with other studies<sup>7,11,19,46,49</sup>. However, the odds of stillbirth were higher for grand multiparous women with advanced maternal age, similar to findings from other studies<sup>10,11,20,24</sup>. Advanced maternal age is a wellestablished risk factor for stillbirths<sup>10,11</sup> and it is linked with a higher prevalence of chronic hypertension and placental pathologies<sup>50</sup>. Advanced maternal age was a risk factor for neonatal deaths regardless of parity, consistent with some previous findings<sup>32,51–53</sup> but in contrast to several others<sup>14,21,36,54,55</sup>. The association may be due to age-related birth complications resulting in early neonatal deaths, or less health-seeking behaviour and more observance of potentially harmful traditions among older generations.

While many studies have linked socioeconomic status with stillbirths and neonatal 263 mortality<sup>13,36,46,51,56–59</sup>, our findings mirror several other studies that did not find an association 264 with education<sup>19,20,24,32,43,48,49,60</sup>, household wealth<sup>19,24,56,60</sup> or marital status<sup>10,24,60</sup>. Socioeconomic 265 266 factors may have less influence in rural areas, where wealthier and more educated women still 267 face inadequate quality and availability of health services. Moreover, survival around the time of 268 birth is reliant on the availability of medical interventions such as induction and surveillance of 269 labour, assisted vaginal delivery and caesarean section. The findings of this study may be 270 generalisable to women aged 15-49 living in other rural areas in Sub-Saharan Africa, as the 271 socioeconomic and biological risk profile is similar to many other low-resource settings. In urban 272 areas, where there is generally more accessible and better quality health care, socioeconomic 273 factors might exert a larger influence.

274 To the best of our knowledge, this is one of the first population-based studies that examined 275 time trends and risk factors of stillbirths in sub-Saharan Africa. This study is also among the first 276 studies that use complete pregnancy histories rather than birth histories. The annual rates of 277 change obtained through this method are similar to global estimates overlapping the time period in this paper: 0.9% for stillbirths compared to a global estimate of 1.1% for 1995-2009<sup>61</sup>, and 278 279 1.8% for neonatal mortality compared to 2% globally for 1990-2012<sup>6</sup>, indicating that pregnancy 280 histories are a relatively reliable data collection method. The use of pregnancy histories is in line 281 with the Every Newborn Action Plan, which advocates for more comprehensive pregnancy and 282 newborn data collection in communities while routine data collection systems are being strengthened<sup>25</sup>. 283

14

284 This study has some limitations. Education level, marital status and household wealth 285 reflect the situation at the time of the survey. This may have resulted in some pregnancies to be 286 linked to incorrect socioeconomic variables and attenuated the associations, even though very 287 similar results were obtained when the analysis was restricted to births during 2006-2011 (data 288 not shown). Up to 40% of births were to households that did not have household wealth status, 289 probably due to missing asset data from the earlier survey. Moreover, the population in the area is 290 relatively homogenous, which may have diluted the associations. We missed 4,955 women for 291 interview who were schooling outside the study area and could not be reached for interview; most 292 of them in the age bracket 15-17 years. However, few births are likely to have been missed 293 because of this due to the prevailing practice of schools expelling pregnant girls.

294 Residual confounding is most likely present due to lack of information on antenatal care 295 attendance, place of delivery, maternal conditions and pregnancy complications. We did not have 296 information on pregnancies linked to maternal deaths. Pregnancies with advanced maternal age 297 are underrepresented in earlier years due to the retrospective nature of the survey. These factors 298 may have resulted in underestimated mortality rates. The apparent rise in mortality rates over the 299 more recent years may reflect recall bias, with women more likely to report more recent 300 stillbirths and neonatal deaths. Relying on mothers' recollection of the month and year of 301 termination of pregnancy or neonatal death is also subject to recall bias, which may have led to a 302 non-differential misclassification between miscarriages, stillbirths and neonatal deaths.

The stillbirth rate/neonatal mortality rate ratio was 0.58 in this study, which is in line with population-based retrospective surveys (mean ratio 0.6), but lower than high-quality civil registration and vital statistics data (mean ratio 1.03)<sup>5</sup>. However, in the absence of high quality facility-level data, pregnancy history surveys offer a viable option in resource-poor settings compared to more costly routine surveillance.

308 The apparent slow rate of decline for both neonatal mortality and stillbirths, lack of 309 association with education and household wealth and the existence of easily identifiable risk

310 factors call for a rethinking on how to address obstetric risks. The risk approach in antenatal care was criticised in the early 2000s and replaced by the statement that every pregnancy is at risk<sup>63</sup>. 311 312 In response, all mothers are today advised to deliver with a skilled attendant and in a facility. 313 However, our study indicates that multiple pregnancies and pregnancies linked to previous birth 314 complications, grand multiparity and advanced maternal age bear a much greater risk for the 315 baby. A re-positioning of the risk approach with the aim to refer higher risk pregnancies to fully 316 equipped hospitals should be considered. In high income settings around 60% of multiple pregnancies are delivered by Caesarean section<sup>64</sup> while in low-income settings this rate remains 317 318 below 40% at hospital-level<sup>65</sup>. The re-vitalisation of family planning programmes after a decade 319 of neglect will hopefully also contribute to a decrease of unwanted pregnancies that pose higher 320 risks for the neonate.

321

#### 322 Conclusion

This is one of the first population-based studies from Sub-Saharan Africa that investigated trends and risk factors of pregnancy outcomes by using a pregnancy history survey. Based on modelling, the data compared favourably to international estimates. In light of the findings, we encourage improved access and quality of care at birth, an increased focus in targeting high-risk pregnancies during antenatal care and further validation of pregnancy history data.

328

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336	
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338	The authors declare no conflicts of interest.
339	
340	Contribution to Authorship
341	SK with support from CH and PW conceptualised the study, wrote the initial and the final paper
342	draft and conduced all statistical analyses. DK, JA and GP participated in the initial study design,
343	data collection and management and reviewed and provided input to the final draft. All authors
344	read and approved the final manuscript.
345	
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347	The study received ethics approval from the Higher Degrees, Research and Ethics Committee at
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