

Calvert, C; Ronsmans, C (2013) The contribution of hiv to pregnancy-related mortality: a systematic review and meta-analysis. AIDS (London, England), 27 (10). pp. 1631-9. ISSN 0269-9370 DOI:  $10.1097/\mathrm{QAD.0b013e32835fd940}$ 

Downloaded from: http://researchonline.lshtm.ac.uk/617521/

DOI: 10.1097/QAD.0b013e32835fd940

## Usage Guidelines

 $Please\ refer\ to\ usage\ guidelines\ at\ http://researchonline.lshtm.ac.uk/policies.html\ or\ alternatively\ contact\ researchonline@lshtm.ac.uk.$ 

Available under license: http://creativecommons.org/licenses/by-nc-nd/2.5/

## **Supplementary Files – File S1**

#### **PUBMEB SEARCH STRATEGY**

## Search 1: HIV terms

HIV OR "human immunodeficiency virus" OR AIDS OR "acquired immunodeficiency syndrome" OR HIV/AIDS OR HIV[MeSH] OR "HIV Infections" [MeSH] or "acquired immunodeficiency syndrome" [MeSH]

#### Search 2: Maternal/pregnancy terms

matern\* OR pregnan\* OR childbirth OR intrapartum OR intra-partum OR postpartum OR post-partum OR puerperal OR puerperium OR parturition OR "expectant mother" OR "expectant mothers" OR "maternal health services" [MeSH] OR "delivery, obstetric" [MeSH] OR parturition [MeSH] OR pregnancy [MeSH] OR "Delivery, Obstetric" [MeSH] OR "postpartum period" [MeSH]

## Search 3: Objective 1 specific terms (mortality)

mortalit\* OR fatalit\* OR "fatal outcome" OR death OR deaths OR death[MeSH] OR mortality[MeSH]

## Search 4: Objective 2 specific terms (obstetric complications)

morbidit\* OR "pregnancy complication" OR "complication of pregnancy" OR "obstetric complication" OR "obstetric labor complication" OR "obstetric labour complication" OR "adverse pregnancy outcome" OR ((postpartum OR post-partum) AND (haemorrhage OR hemorrhage)) OR ((obstetric) AND (haemorrhage OR hemorrhage)) OR hemorrhage OR "vaginal bleeding" OR ((antepartum OR ante-partum) AND (haemorrhage OR hemorrhage)) OR dystocia OR ((obstructed OR prolonged) AND (labour OR labor)) OR "retained placenta" OR "pregnancy induced hypertension" OR hellp OR eclampsia OR preeclampsia OR "preeclampsia" OR "gestational diabetes" OR "abruptio placent\*" OR "placental abruption" OR "placenta previa" OR "placenta praevia" OR "ruptured uterus" OR sepsis OR septic OR septicemia OR septicemic OR endometritis OR "puerperal infection" OR "near miss" OR "near-miss" OR "caesarean section" OR c-section OR "caesarian section" OR "cesarean section" OR anaemia OR anemia OR "iron deficien\*" OR "obstetric labor complications" [MeSH] OR "pregnancy complications" [MeSH] OR hemorrhage [MeSH] OR "postpartum haemorrhage" [MeSH] OR "uterine inversion" [MeSH] OR "uterine hemorrhage" [MeSH] OR dystocia [MeSH] OR "placenta, retained" [MeSH] OR "hypertension, pregnancy-induced" [MeSH] OR "hellp syndrome" [MeSH]

Terms] OR eclampsia[MeSH] OR pre-eclampsia[MeSH] OR "diabetes, gestational"[MeSH] OR "abruptio placentae"[MeSH] OR "placenta previa"[MeSH] OR "uterine rupture"[MeSH] OR sepsis[MeSH] OR "cesarean section"[MeSH Terms] OR "anemia"[MeSH Terms]

# Search 5: Objective 3 specific terms (HIV disease progression)

"CD4 lymphocyte count" OR "CD4 count" OR (HIV AND "disease progression") OR "HIV severity" OR "aids defining" OR "AIDS-related opportunistic Infections" OR "kaposi's sarcoma" OR lymphoma OR "wasting syndrome" OR cachexia OR "pneumocystis carinii" OR tuberculosis OR to OR "symptomatic HIV" OR "opportunistic infection" OR "opportunistic infections" OR "CD4 lymphocyte count" [MeSH] OR "AIDS-related opportunistic Infections" [MeSH] OR "lymphoma" [MeSH] OR "cachexia" [MeSH] OR "tuberculosis" [MeSH]

#### Search 6: Objective 4 specific terms (HIV incidence)

seroconversion OR incidence OR "incidence" [MeSH] OR "HIV infections/transmission" [MeSH]

FINAL SEARCH: (#1 AND #2 AND (#3 OR #4 OR #5 OR #6))

#### **EMBASE SEARCH STRATEGY**

#### Search 1: HIV terms

HIV OR human immunodeficiency virus OR HIV infections OR AIDS OR acquired immunodeficiency syndrome OR HIV/AIDs OR exp human immunodeficiency virus/ OR exp human immunodeficiency virus infection/ OR exp acquired immune deficiency syndrome/

## Search 2: Maternal/pregnancy terms

matern\* OR mother\* OR pregnan\*OR childbirth OR intrapartum OR intra-partum OR postpartum OR puerperal OR puerperium OR parturition OR expectant mother\* OR exp expectant mother/ OR exp birth/ OR exp childbirth/ OR exp pregnancy/ OR exp delivery/

## Search 3: Objective 1 specific terms (mortality)

mortalit\*OR maternal mortality OR fatalit\* OR fatal outcome OR death\* OR exp mortality/ OR exp maternal mortality/ OR exp fatality/ OR exp death/

## Search 4: Objective 2 specific terms (obstetric complications)

morbidit\* OR pregnancy complication OR complication of pregnancy OR obstetric complication OR obstetric labor complication OR obstetric labour complication OR adverse pregnancy outcome OR ((postpartum OR post-partum) AND (haemorrhage OR hemorrhage)) OR ((obstetric) AND (haemorrhage OR hemorrhage)) OR hemorrhage OR vaginal bleeding OR ((antepartum OR ante-partum) AND (haemorrhage OR hemorrhage)) OR dystocia OR ((obstructed OR prolonged) AND (labour OR labor)) OR retained placenta OR pregnancy induced hypertension OR hellp OR eclampsia OR pre-eclampsia OR pre-eclampsia OR gestational diabetes OR abruptio placent\* OR placental abruption OR placenta previa OR placenta praevia OR ruptured uterus OR sepsis OR septic OR septicemia OR septicemic OR endometritis OR puerperal infection OR near miss OR near-miss OR caesarean section OR c-section OR caesarian section OR cesarean section OR anaemia OR anemia OR iron deficien\* OR exp morbidity/ OR exp maternal morbidity/ OR exp pregnancy complication/ OR exp labor complication/ OR exp postpartum hemorrhage/ OR exp bleeding/ OR antepartum hemorrhage/ OR exp obstetric hemorrhage/ OR exp dystocia/ OR exp retained placenta/ OR exp maternal hypertension/ OR exp HELLP syndrome/ OR exp "eclampsia and preeclampsia"/ OR exp pregnancy diabetes mellitus/ OR exp placenta previa/ OR exp uterus rupture/ OR exp sepsis/ OR exp septic shock/ OR exp septicemia/ OR exp endometritis/ OR exp puerperal infection/ OR exp cesarean section/ OR exp anemia/ OR exp iron deficiency anemia/

## Search 5: Objective 3 specific terms (HIV disease progression)

CD4 lymphocyte count OR CD4 count OR HIV disease progression OR HIV severity OR aids defining OR AIDS-related opportunistic Infections OR kaposi's sarcoma OR lymphoma OR wasting syndrome OR cachexia OR pneumocystis carinii OR tuberculosis OR to OR symptomatic HIV OR opportunistic infection\* OR exp CD4 lymphocyte count/ OR exp disease course/ OR exp AIDS related complex/ OR exp kaposi sarcoma/ OR exp lymphoma/ OR exp wasting syndrome/ OR exp cachexia/ OR exp pneumocystis carinii/ OR exp tuberculosis/ OR exp opportunistic infection/

## Search 6: Objective 4 specific terms (HIV incidence)

seroconversion OR incidence OR exp seroconversion/ OR exp incidence/ OR exp disease transmission/

FINAL SEARCH: (#1 AND #2 AND (#3 OR #4 OR #5 OR #6))

#### **POPLINE SEARCH STRATEGY**

#### Search 1: HIV terms

(HIV/"human immunodeficiency virus" / AIDS / "acquired immunodeficiency syndrome" / "HIV Infections")

## Search 2: Maternal/pregnancy terms

(matern\* / pregnan\* / childbirth / intrapartum / intra-partum / postpartum / post-partum / puerperal / puerperium / parturition / "expectant mother" / "expectant mothers")

## Search 3: Objective 1 specific terms (mortality)

(mortalit\* / fatalit\* / death\*)

# Search 4: Objective 2 specific terms (obstetric complications)

(morbidit\* / "pregnancy complication" / "obstetric complication" / "obstetric labor complication" / "obstetric labour complication" / "adverse pregnancy outcome" / "postpartum haemorrhage" / "postpartum hemorrhage" / "obstetric haemorrhage" / "obstetric hemorrhage" / hemorrhage / "vaginal bleeding" / "antepartum haemorrhage" / "antepartum hemorrhage" / dystocia / "obstructed labour" / "obstructed labor" / "prolonged labor" / "retained placenta" / "pregnancy induced hypertension" / hellp / eclampsia / preeclampsia / "pre-eclampsia" / "gestational diabetes" / "abruptio placent\*" / "placental abruption" / "placenta previa" / "placenta praevia" / "ruptured uterus" / sepsis / septic / septicemia / septicemic / endometritis / "puerperal infection" / "near miss" / "near-miss" / "caesarean section" / c-section / "caesarian section" / "cesarean section" / anaemia / anemia)

## Search 5: Objective 3 specific terms (HIV disease progression)

("CD4 lymphocyte count" / "CD4 count" / "HIV disease progression" / "HIV severity" / "aids defining" / "AIDS-related opportunistic Infections" / "kaposi's sarcoma" / lymphoma / "wasting syndrome" / cachexia / "pneumocystis carinii" / tuberculosis / tb / "symptomatic HIV" / "opportunistic infection\*")

# Search 6: Objective 4 specific terms (HIV incidence)

(seroconversion / incidence)

## FINAL SEARCH (advanced search in title/keywords and abstract)

(HIV/"human immunodeficiency virus" / AIDS / "acquired immunodeficiency syndrome" / "HIV Infections") & (matern\* / pregnan\* / childbirth / intrapartum / intra-partum / postpartum / post-partum / puerperal / puerperium / parturition / "expectant mother" / "expectant mothers") & ((mortalit\* / fatalit\* / death\*) / (morbidit\* / "pregnancy complication" / "obstetric complication" / "obstetric labor complication" / "obstetric labour complication" / "obstetric pergnancy outcome" / "postpartum haemorrhage" / "postpartum hemorrhage" / "obstetric haemorrhage" / "obstetric hemorrhage" / hemorrhage / "vaginal bleeding" / "antepartum haemorrhage" / "antepartum haemorrhage" / "obstructed labour" / "obstructed labor" / "prolonged labor" / "prolonged labor" / "retained placenta" / "pregnancy induced hypertension" / hellp / eclampsia / preeclampsia / "pre-eclampsia" / "gestational diabetes" / "abruptio placent\*" / "placental abruption" / "placental previa" / "placenta praevia" / "ruptured uterus" / sepsis / septic / septicemia / septicemic / endometritis / "puerperal infection" / "near miss" / "near-miss" / "caesarean section" / c-section / "caesarian section" / "cesarean section" / anaemia / anemia) / ("CD4 lymphocyte count" / "CD4 count" / "HIV disease progression" / "HIV severity" / "aids defining" / "AIDS-related opportunistic Infections" / "kaposi's sarcoma" / lymphoma / "wasting syndrome" / cachexia / "pneumocystis carinii" / tuberculosis / tb / "symptomatic HIV" / "opportunistic infection\*") / (seroconversion / incidence))

#### **AFRICAN INDEX MEDICUS SEARCH STRATEGY**

#### **HIV terms:**

HIV, human immunodeficiency virus, AIDS, acquired immunodeficiency syndrome

# Maternal/pregnancy terms:

Maternal, Pregnancy, childbirth, intrapartum, intra-partum, postpartum, post-partum, puerperal, puerperium, parturition

# Searches conducted:

- 1. Maternal HIV
- 2. Pregnancy HIV
- 3. Puerperium HIV
- 4. Maternal human immunodeficiency virus
- 5. Maternal AIDS
- 6. Pregnancy AIDS
- 7. Maternal acquired immunodeficiency syndrome
- 8. Pregnancy acquired immunodeficiency syndrome
- 9. Puerperium acquired immunodeficiency syndrome

# <u>Supplementary Information – Table S1</u>

Table S1. Summary of studies of HIV and pregnancy-related mortality

Reference	Study design	Study Setting	Study Population	ART	Prevalence	Definition of	Risk of	Risk of	Risk Ratio	Attributable	Population
				Available	of HIV <sup>2</sup>	pregnancy-	pregnancy-	pregnancy-	(95% CI)	Risk per	Attributable
						related	related death	related death		100,000	Fraction
						mortality <sup>3</sup>	amongst HIV+	amongst HIV-		women (95%	
							women per	women per		CI)	
							100,000 women	100,000 women			
							(total number	(total number			
							of HIV+	of HIV-			
							women)	women)			
Black et al.,	Retrospective	A single tertiary	All women with known HIV status	Both	20.7%	Maternal	776 <sup>4</sup> (7,605)	124 <sup>4</sup> (13,694)	6.25 (3.65-	652 (446-	52.1%
2009[12]	Cohort	hospital in	who gave birth; any maternal deaths			Death			10.71)	857)	
		Johannesburg, South	during pregnancy until 42 days								
		Africa (2003-2007)	postpartum included								
Chilongozi et	Prospective	Multiple hospitals	All HIV+ women enrolled and 1	No	NA	Pregnancy-	1824 (1,864)	0 (367)	13.64	1832 (1164-	NA
al., 2008[33]	Cohort (from an	and antenatal clinics	HIV- woman enrolled for every 5			related death			(0.84-	2501)	
	RCT)	in Malawi (Blantyre	HIV+ women; followed up from						221.19)		
		and Lilongwe) and	between 20 and 24 weeks of								
		Zambia (Lusaka)	pregnancy to 12 months postpartum								
		(2001-2003)									

Coley et al.,	Prospective	Three hospitals and	HIV+ women recruited from	No <sup>1</sup>	13.1%	Pregnancy-	760 (526)	206 (486)	3.70 (0.41-	555 (-290-	26.1%
2001[15]	Cohort	one clinic in Dar es	control arm of an RCT and HIV-			related death			32.95)	1399)	
		Saalam, Tanzania	women from psychosocial study;								
		(1995-1997)	followed up from between 12 and								
			27 weeks of pregnancy until								
			delivery								
De Groot et	Retrospective	A single high risk	All HIV+ women and 2 HIV-	No¹	30.1% in	"Maternal	3704 (81)	1176 (170)	3.15 (0.54-	2528 (-1893-	39.3%
al., 2003[13]	Cohort	obstetric unit in	controls for every HIV+ women		2001 in Free	death",			18.47)	6948)	
		Bloemfontein, South	enrolled from a high risk obstetric		State	unclear					
		Africa (2001)	unit; all information extracted from		Province [a]						
			medical records and no information								
			on follow-up time given								
Figueroa-	Prospective	Institute of	44 HIV+ women and 2 controls for	Both	No estimate	"Maternal	2273 (44)	0 (88)	5.93 (0.25-	2273 (-3197-	NA
Damian,	Cohort	Perinatology in	every HIV+ women, match on age		available	death",			142.74)	7742)	
1999[32]		Mexico City,	and socioeconomic status; followed			unclear					
		Mexico (1989-1997)	up from enrolment in pregnancy to								
			the end of delivery								
Khan et al.,	Retrospective	A single tertiary	Total number of deliveries to HIV+	No¹	29.4%	Maternal	202 (14,849)	280 (35,669)	7.21 (3.52-	174 (100-	64.6%
2001[14]	Cohort	hospital in Durban,	and HIV- women was calculated			death			14.74)	248)	
		South Africa (1996-	based on reported HIV prevalence			(including					
		1998)	and no. of deliveries in hospital;			late maternal					
			HIV status of maternal deaths (up to			deaths)					
			1 year postpartum) known through								
			HIV tests								

Kourtis et al.,	Retrospective	20% of all	All HIV+ and HIV- pregnant	Yes	0.14%	Pregnancy-	299 (12,378)	14 (8,784,767)	21.38	285 (189-	2.8%
2006[30]	Cohort	community hospitals	women between 15-44 years of age			related death			(15.43-	381)	
		in the USA (1994	who were hospitalised; all						29.64)		
		and 2003)	information extracted from medical								
			records and no information on								
			follow-up time given								
Kumar et al.,	Prospective	A single tertiary	160 HIV+ women and 160 HIV-	No	0.3% in 1992	Maternal	6000 (150)	0 (152)	19.25	6000 (2023-	5.2%
1995[27]	Cohort	hospital in Manipur,	mothers (matched for age and		in all urban	death			(1.13-	9977)	
		India (1992-1993)	parity); followed up from less than		areas of India				327.84)		
			28 weeks of pregnancy to 42 days		[b] <sup>2</sup>						
			postpartum								
Le Coeur et	Census	Pointe Noire,	Total number of deliveries to HIV+	No <sup>1</sup>	6.3%	Pregnancy-	1813 (386)	471 (5734)	3.85 (1.69-	1343 (0-	15.2%
al., 2005[16]		Republic of Congo	and HIV- women was calculated			related			8.79)	2686)	
		(2001)	based on the total number of live								
			and still births and assuming a HIV								
			prevalence 6.3%; HIV status of								
			maternal deaths (up to 42 days								
			postpartum) known through HIV								
			tests								
Lepage et al.	Prospective	A single hospital in	All HIV+ women and an equal	No	30.3%	Maternal	0 (215)	463 <sup>4</sup> (216)	0.33 (0.01-	-463 (-1738-	NA
1991[22]	Cohort	Kigali, Rwanda	number of HIV- women matched			death			8.17)	812)	
		(1988-1989)	for age and parity. Women had to								
			have lived for at least 6 months in a								
			district within a diameter of <10								
			Km from the hospital and delivered								

			1. 1 6.11 6								
			a live newborn; follow-up from								
			delivery to 15 days postpartum								
Leroy et	Prospective	A single tertiary	All HIV+ women and a equivalent	No	34.4%	Pregnancy-	824 (364)	274 (365)	3.01 (0.31-	550 (-522-	40.9%
al,1998[5]	Cohort	hospital in Kigali,	number of HIV- women matched			related			28.79)	1623)	
		Rwanda (1992-	for age who attended the antenatal								
		1993)	clinic for 2 days each week, who								
			were resident in Kigali and who								
			wished to deliver in the hospital;								
			followed up from 21-28 weeks of								
			gestation to 42 days postpartum								
Lionel et al,	Retrospective	A single hospital in	All HIV+ and HIV- women; all	Yes	0.5%	"Maternal	917 (109)	125 (23,277)	7.36 (1.01-	793 (-998-	3.1%
2008[28]	Cohort	Vellore, India	information extracted from medical			death",			53.58)	2583)	
		(2000-2002)	records and no information on			unclear					
			follow-up time given								
Louis et al.,	Prospective	19 different	All women having a c-section with	Yes <sup>1</sup>	0.69%	"Maternal	794 (378)	61 (54,281)	13.05	733 (-162-	7.7%
2007[31]	Cohort	academic medical	a gestational age of >20 weeks at			death",			(4.02-	1628)	
		centres in the USA	delivery and who delivered an			unclear			42.38)		
		(1999-2002)	infant of at least 500g birth weight								
			with known HIV status; only look								
			at mortality around delivery								
Maiques-	Retrospective	A single maternity	All HIV+ women having a c-section	No	0.49%	"Maternal	2222 (45)	0 (90)	5.93 (0.25-	2222 (-3130-	2.4%
Montesinos et	Cohort	hospital in Valencia,	and a sample of HIV- women			death",			142.84)	7575)	
al., 1999[29]		Spain (1987-1996)	undergoing c-section matched for			unclear					
			indication for c-section, stage of								
			labour, number of foetuses and date								

			postpartum								
			weeks of pregnancy to 6 weeks								
et al., 2006[24]		(2002-2004)	enrolled; followed up from 36								
Biribonwoha	Cohort	Kampala, Uganda	nulliparous and uniparous women		[e] <sup>2</sup>	related			65.80)	3431)	
Nuwagaba-	Prospective	A single hospital in	132 HIV+ and 399 HIV-	Yes	8.5% in 2002	Pregnancy-	1527 (131)	254 (394)	6.02 (0.55-	1273 (-885-	29.9%
		1995)	weeks postpartum								
		Zimbabwe (1991-	followed up from delivery to 6								
2004[19]	Cohort	hospital in Harare,	mothers (matched for age) enrolled;		1995 [d] <sup>2</sup>	related			22.39)	1232)	
Nathoo et al.,	Prospective	A single tertiary	384 HIV+ women and 374 HIV-	No <sup>1</sup>	32.0% in	Pregnancy-	562 (356)	275 (363)	2.04 (0.19-	286 (-659-	25.0 %
			discharge after delivery								
			followed up from pregnancy until								
			agree to deliver in the hospital;								
		Uganda (1988-1990)	lived within 15km of Mulago and								
1993[23]	Cohort	hospital in Kampala,	10% sample of HIV- women who			related			53.40)	1586)	
Mmiro et al.,	Prospective	A University	All HIV+ women and a random	No <sup>1</sup>	27.7%	Pregnancy-	898 (557)	143 (697)	6.26 (0.73-	754 (-78-	59.3%
		(1987-1989)	postpartum								
		District, Malawi	antenatal visit to 6 weeks								
al., 1996[18]	Cohort	clinics in Mangochi	followed up from their first		1994 [c] <sup>2</sup>	related			9.48)	1424)	
McDermott et	Prospective	Four antenatal	All HIV+ and HIV- women;	No¹	16.5% in	Pregnancy-	735 (272)	346 (3,472)	2.13 (0.48-	390 (-644-	15.7%
			given								
			no information on follow-up time								
			extracted from medical records and								
			of delivery; all information								

Ryder et al.,	Prospective	A single hospital in	All HIV+ women, and a sample of	No <sup>1</sup>	5.5%	Pregnancy-	3239 (247)	0 (314)	21.59	3239 (932-	53.1%
1994[17]	Cohort	Kinshasa,	HIV- women matched for age and			related	,		(1.25-	5545)	
		Democratic	parity to each HIV+ women						372.30)	ŕ	
		Republic of Congo	recruited; followed up from active						ŕ		
		(1986-1987)	labour to 1 year postpartum								
Sewankambo	Prospective	Rakai, Uganda	All households in 56 communities	No	16.1%	"Maternal	1687 (415)	310 (2,582)	5.44 (1.98-	1377 (120-	41.7%
	_			140	10.170		1007 (415)	310 (2,302)			41.770
et al., 2000[25]	Cohort	(1994-1997)	located on secondary roads eligible			death",			14.93)	2634)	
			for inclusion in cohort and HIV			unclear					
			tests; continuous follow-up, but not								
			clear what time period women were								
			considered at risk of "maternal								
			death"								
Temmermann	Prospective	A single health	All HIV+ women, and a sample of	No¹	8.8%	Pregnancy-	1269 (315)	0 (311)	8.89 (0.48-	1270 (-110-	41.0%
et al., 1994[26]	Cohort	centre in Nairobi,	HIV- women matched for age and			related			164.36)	2650)	
		Kenya (1989-1991)	parity to each HIV+ women								
			recruited; followed up from less								
			than 28 weeks of pregnancy to 6								
			weeks postpartum								
Ticconi et al.,	Retrospective	A single tertiary	All woman with known HIV status;	No <sup>1</sup>	8.3%	"Maternal	30488 (82)	2102 (904)	14.51	28386	52.9%
2003[20]	Cohort	hospital in	followed up from discharge from			death",			(8.35-	(18378-	
		Centenary	hospital during pregnancy to the			unclear			25.19)	38394)	
		Zimbabwe (2000-	end of pregnancy								
		2001)									

Prospective	14 maternity clinics	All HIV+ and HIV- women were	No¹	30.0% in	Pregnancy-	3726 <i>(3,999)</i>	280 (8,577)	13.32	3446 (2849-	78.7%
Cohort (from an	and hospitals in	recruited if neither they or their		2000 [d] <sup>2</sup>	related			(8.67-	4044)	
RCT)	Greater Harare,	baby had a life-threatening						20.46)		
	Zimbabwe (1997-	condition, the baby was not from a								
	2000)	multiple birth or had a birth								
		weight<1500g; followed up from								
		within 96 hours of delivery to 1								
		year postpartum								
	`	Greater Harare, Zimbabwe (1997-	Greater Harare, baby had a life-threatening  Zimbabwe (1997- condition, the baby was not from a  2000) multiple birth or had a birth  weight<1500g; followed up from  within 96 hours of delivery to 1	Greater Harare, baby had a life-threatening  Zimbabwe (1997- condition, the baby was not from a  2000) multiple birth or had a birth  weight<1500g; followed up from  within 96 hours of delivery to 1	CCT)  Greater Harare, baby had a life-threatening  Zimbabwe (1997- condition, the baby was not from a  2000)  multiple birth or had a birth  weight<1500g; followed up from  within 96 hours of delivery to 1	CCT)  Greater Harare, baby had a life-threatening  Zimbabwe (1997- condition, the baby was not from a  2000)  multiple birth or had a birth  weight<1500g; followed up from  within 96 hours of delivery to 1	CCT) Greater Harare, baby had a life-threatening  Zimbabwe (1997- condition, the baby was not from a  2000) multiple birth or had a birth  weight<1500g; followed up from  within 96 hours of delivery to 1	CCT) Greater Harare, baby had a life-threatening  Zimbabwe (1997- condition, the baby was not from a  2000) multiple birth or had a birth  weight<1500g; followed up from  within 96 hours of delivery to 1	CCT) Greater Harare, baby had a life-threatening 20.46)  Zimbabwe (1997- condition, the baby was not from a 2000) multiple birth or had a birth weight<1500g; followed up from within 96 hours of delivery to 1	Greater Harare, baby had a life-threatening 20.46)  Zimbabwe (1997- condition, the baby was not from a  2000) multiple birth or had a birth  weight<1500g; followed up from  within 96 hours of delivery to 1

Information was not supplied in the published paper so whether antiretroviral treatment should have been available was based on the study dates and study location; for two studies it was not clear from the study dates and location whether ART would be available so the information was inferred from the literature.

- a)Pointe Noire, Congo in 2001: No ART treatment based on the UNAIDS data accessed on 31st May 2012 at http://www.unaids.org/en/regionscountries/countries/democraticrepublicofthecongo/
- b) Greater Harare, Zimbabwe in 2000: No ART treatment based on the UNAIDS data accessed on 31st May 2012 at http://www.unaids.org/en/regionscountries/countries/zimbabwe/
- c)Bloemfontein, South Africa in 2001: No ART treatment based on the UNAIDS data accessed on 7th July 2012 at http://www.unaids.org/en/regionscountries/southafrica/
- <sup>2</sup>Sources of HIV prevalence, when this information was not provided in the paper:
  - a) UNAIDS. South Africa: Epidmiological Factsheets on HIV/AIDs and Sexually Transmitted Infections 2004.
  - b) UNAIDS. India: Epidmiological Factsheets on HIV/AIDs and Sexually Transmitted Infections 2004.
  - c)UNAIDS. Malawi: Epidmiological Factsheets on HIV/AIDs and Sexually Transmitted Infections 2004.
  - d) UNAIDS. Zimbabwe: Epidmiological Factsheets on HIV/AIDs and Sexually Transmitted Infections 2004.
  - e)UNAIDS. Uganda: Epidmiological Factsheets on HIV/AIDs and Sexually Transmitted Infections 2004.

<sup>&</sup>lt;sup>3</sup>Definition of maternal death classified as" maternal death" if incidental deaths were excluded; as "pregnancy-related" if incidental deaths were not excluded or they only used the term death and as "Maternal death, unclear" if they use the term maternal death but do not define this in the paper

<sup>&</sup>lt;sup>4</sup>Use number of live births as dominator rather than number of women

# <u>Supplementary Information – Table S2</u>

Table S2. Methodological quality assessment for each of the studies included in the systematic review

			Quality Criteria		
Reference	Loss to follow up	Adjustment for confounders	Definition of pregnancy-related death	Ascertainment of maternal death	Selection of comparison group
Black et al.,	Inadequate: 28% of deaths had	Inadequate: No adjustment for	Adequate: All deaths of women at	Inadequate: Hospital record review	Adequate: Include all women with known
2009[12]	known HIV status	confounders	the facility during pregnancy or		HIV status for a single facility
			within 42 days of childbirth		
Chilongozi et al.,	Adequate: Less than 10% of HIV+	Inadequate: No adjustment for	Adequate: All pregnancy related	Adequate: Prospective cohort study	Inadequate: Unclear on exact selection
2008[33]	and HIV- women loss to follow-up	confounders	deaths up to one year postpartum		methods; however no HIV- women were
					selection from one of the study sites
Coley et al.,	Adequate: Less than 10% of HIV+	Inadequate: No adjustment for	Adequate: Any death before delivery	Adequate: Prospective cohort study	Inadequate: HIV+ and HIV- women were
2001[15]	and HIV- women loss to follow-up	confounders			recruited from different studies
De Groot et al.,	Adequate: 53 (17%) women were	Inadequate: No adjustment for	Inadequate: No information on the	Inadequate: Hospital record review	Adequate: HIV+ and HIV- women enrolled
2003[13]	excluded after study groups were	confounders	period of pregnancy in which women		from the same study site
	selected (due to HIV status unknown		were observed		
	(n=6), discharge before delivery				
	(n=45) and abortion (n=2))				
Figueroa-	Inadequate: Insufficient information	Adequate: Match for age and socio-	Adequate: Any death before delivery	Adequate: Prospective cohort study	Inadequate: Unclear on exact selection
Damian,	provided	economic status			methods; HIV-infected women were
1999[32]					recruited from a Department of Infectious

					Diseases, but do not state where HIV-
					uninfected women were recruited from
Khan et al.,	Inadequate: Over 50% of deaths had	Inadequate: No adjustment for	Adequate: All deaths of women at	Inadequate: Hospital record review	Adequate: Include all women with known
2001[14]	unknown HIV status	confounders	the facility during pregnancy or		HIV status for a single facility
			within 1 year of childbirth		
Kourtis et al.,	Inadequate: Insufficient information	Inadequate: No adjustment for	Inadequate: No information on the	Inadequate: Hospital discharge data	Adequate: Include all hospitalised,
2006[30]	provided	confounders	period of pregnancy in which women	from national database	pregnant women with known HIV status
			were observed		
Kumar et al.,	Adequate: Less than 10% of HIV+	Adequate: Match for age and parity	Adequate: Maternal deaths up to 42	Adequate: Prospective cohort study	Adequate: HIV+ and HIV- women enrolled
1995[27]	and HIV- women loss to follow-up		days postpartum		from the same study site
Le Coeur et al.,	Adequate: Over 90% of deaths had	Inadequate: No adjustment for	Adequate: All pregnancy related	Adequate: All deaths identified in	Adequate: Capture all women in Pointe
2005[16]	known HIV status	confounders <sup>1</sup>	deaths up to 42 days postpartum	city mortuary	Noire
Lepage et al.	Inadequate: Between delivery and	Adequate: Match for age and parity	Adequate: All pregnancy related	Adequate: Prospective cohort study	Adequate: HIV+ and HIV- women enrolled
1991[22]	15 days postpartum 21% of HIV+		deaths up to 42 days postpartum		from the same study site
	women were lost to follow-up				
Leroy et	Adequate: Less than 10% of HIV+	Adequate: Match for age and parity	Adequate: All pregnancy related	Adequate: Prospective cohort study	Adequate: HIV+ and HIV- women enrolled
al,1998[5]	and HIV- women loss to follow-up		deaths up to 42 days postpartum		from the same study site
Lionel et al,	Inadequate: Insufficient information	Inadequate: No adjustment for	Inadequate: No information on the	Inadequate: Hospital record review	Adequate: All women from study hospital
2008[28]	provided	confounders	period of pregnancy in which women		enrolled
			were observed		
Louis et al.,	Inadequate: Insufficient information	Inadequate: No adjustment for	Inadequate: No information on the	Inadequate: Data came from the	Adequate: All women enrolled
2007[31]	provided	confounders	period of pregnancy in which women	Maternal-Fetal Medicine Units	
			were observed	Network Caesarean registry	
Maiques-	Inadequate: Insufficient information	Inadequate: No adjustment for	Inadequate: No information on the	Inadequate: Hospital record review	Adequate: HIV+ and HIV- women enrolled
Montesinos et al.,	provided	confounders	period of pregnancy in which women		from the same study site

1999[29]			were observed		
McDermott et	Adequate: Less than 10% of HIV+	Inadequate: No adjustment for	Adequate: All pregnancy related	Adequate: Prospective cohort study	Adequate: All women enrolled
al., 1996[18]	and HIV- women loss to follow-up	confounders	deaths up to 42 days postpartum		
Mmiro et al.,	Inadequate: Insufficient information	Inadequate: No adjustment for	Inadequate: States that woman were	Adequate: Prospective cohort study	Adequate: HIV+ and HIV- women enrolled
1993[23]	provided	confounders	followed up through pregnancy until		from the same study site
			discharge after delivery -insufficient		
			information.		
Nathoo et al.,	Adequate: Less than 10% of HIV+	Adequate: Match for age	Adequate: All pregnancy related	Adequate: Prospective cohort study	Adequate: All women enrolled before
2004[19]	and HIV- women loss to follow-up		deaths up to 42 days postpartum		being tested for HIV
Nuwagaba-	Adequate: Less than 10% of HIV+	Inadequate: No adjustment for	Adequate: All pregnancy related	Adequate: Prospective cohort study	Adequate: HIV+ and HIV- women enrolled
Biribonwoha et	and HIV- women loss to follow-up	confounders	deaths up to 42 days postpartum		from the same hospital
al., 2006[24]					
Ryder et al.,	<b>Inadequate:</b> More than 20% of	Adequate: Match for age and parity	Adequate: All pregnancy related	Adequate: Prospective cohort study	Adequate: HIV+ and HIV- women enrolled
1994[17]	HIV+ women loss to follow-up		deaths up to one year postpartum		from the same hospital
Sewankambo et	<b>Inadequate:</b> About 25% of the study	Inadequate: No adjustment for	Inadequate: No information on the	Inadequate: Death data collected	Adequate: All women from study area
al., 2000[25]	cohort loss to follow-up	confounders	period of pregnancy in which women	from household census; not clear how	enrolled
			were observed	data on pregnancy was collected	
Temmermann et	Inadequate: More than 20% of	Adequate: Match for age and parity	Adequate: All pregnancy related	Adequate: Prospective cohort study	Adequate: HIV+ and HIV- women enrolled
al., 1994[26]	HIV+ and HIV- women loss to		deaths up to 42 days postpartum		from the same antenatal clinics
	follow-up				
Ticconi et al.,	Inadequate: Insufficient information	Inadequate: No adjustment for	Inadequate: No information on the	Adequate: Prospective cohort study	Adequate: All women with known HIV
2003[20]	provided	confounders	period of pregnancy in which women		status enrolled from study hospital
			were observed		
Zvandasara et	Adequate: Just over 10% of HIV+	Inadequate: No adjustment for	Adequate: All pregnancy related	Adequate: Prospective cohort study	Adequate: All women enrolled before
al., 2006[21]	and HIV- women loss to follow-up	confounders	deaths up to one year postpartum		being tested for HIV

<sup>&</sup>lt;sup>1</sup>This study presented the adjusted the rate ratio comparing mortality rates in HIV-infected with uninfected for age; however, to enable the data to be pooled with the other studies information was only extracted on the risk ratio, using number of pregnant women for the denominator, rather than number of women years