



# Human Immunodeficiency Virus type 1 (HIV)-Exposure and Risk of Sudden Infant Death Syndrome (SIDS)

Victoria Nankabirwa, Halvor Sommerfelt, Olive Namugga, Joan Murungi, Andrew Kirabo, Hans Steinsland

Centre for Intervention Science in Maternal and Child Health (<https://www.uib.no/en/cismac>), Makerere University School of Public Health, Cluster for Global Health-Norwegian Institute of Public Health

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# Infant HIV-exposure

- Globally: 1.2 million HIV-exposed (**HE**) infants born/year
- Well-performing Prevention of mother-to-child HIV transmission programs: >95% of **HE** infants remain HIV uninfected (**HEU**)
- Even **HEU** infants: Substantially higher risk of serious bacterial infection/death than unexposed (**HU**) infants

# Sudden Infant Death Syndrome (SIDS)

- ❑ sudden unexplained death between one week and one year of age
- ❑ most common cause of post-neonatal infant death in Europe, Australia/NZ and US/Canada

# Idea and Evidence before our study

- From 2016: Large (n=4500) randomized controlled trial of possible non-specific effects of the BCG vaccine in **HE** infants (“Does BCG reduce risk of severe infections or death?”)
- When assessing the verbal autopsies: Some mothers reported their babies were found “dead in their sleep”.  
Too many?
  1. Sudden infant death syndrome (SIDS). Unexplained
  2. Sudden unexpected infant death (SUID): SIDS plus accidental suffocation, sepsis, severe pneumonia++



# Previous studies **HIV-exposure** → SUIDs/SIDS

1. Author, Year	Country or region	SUID / SIDS	Cases / enrollees	
			HE infants	HU infants
1. European Collaborative Study team, 1991	Europe	SUID & SIDS	3/600	nd
2. Kind, 1992	Switzerland	SIDS	2/100	nd
3. Bulterys, 1993	Rwanda	SUID	3/410	0/426
4. Mayaux, 1995	France	SIDS	6/944	nd
5. Starc, 1999	USA	SUID & SIDS	1/432	nd
6. Dominguez, 2000	USA	SIDS	7/8,465	nd
7. Bulterys, 2000	USA	SIDS	37/23,265	nd
8. Kahlert, 2007	Switzerland	SIDS	7/466	nd
9. Madhi, 2017	South Africa	SIDS	1/184	0/100

# Opportunity

In parallel to our BCG trial in **HE** infants, we undertook:

- A trial of cleansing the umbilical cord stump in **HU** neonates with Chlorhexidine
- We expanded the follow-up up to 1 year of age (infancy) for death/survival
- A cohort study of COVID-19 (both **HE** and **HU** infants)



# Our research questions:

1. To what extent do **HE** infants have an increased risk of SIDS compared to their **HU** peers?
2. How common is the most important modifiable SIDS risk factor, prone/side sleeping and unprotected bed-sharing?

2. Most common sleeping position in our sub-cohort of 1,876 infants:

- Prone: 50% [**HU**(>)**HE**]
- Side: 43%
- Supine: 7%

Bedsharing: Almost ubiquitous (>90%)

A systematic review of the burden and risk factors of sudden infant death syndrome (SIDS) in Africa

Godwin K Osei-Poku<sup>1</sup>,  
Sanya Thomas<sup>1</sup>, Lawrence  
Mwananyanda<sup>1,2</sup>, Rotem

Lapidot<sup>3,4</sup>, Patricia A Elliott<sup>5</sup>,  
William B Macleod<sup>1</sup>, Somwe  
Wa Somwe<sup>6</sup>, Christopher J Gill<sup>1</sup>

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# Accruing HE and HU babies into our cohort:

4483 HE infants followed for 4239 child-years

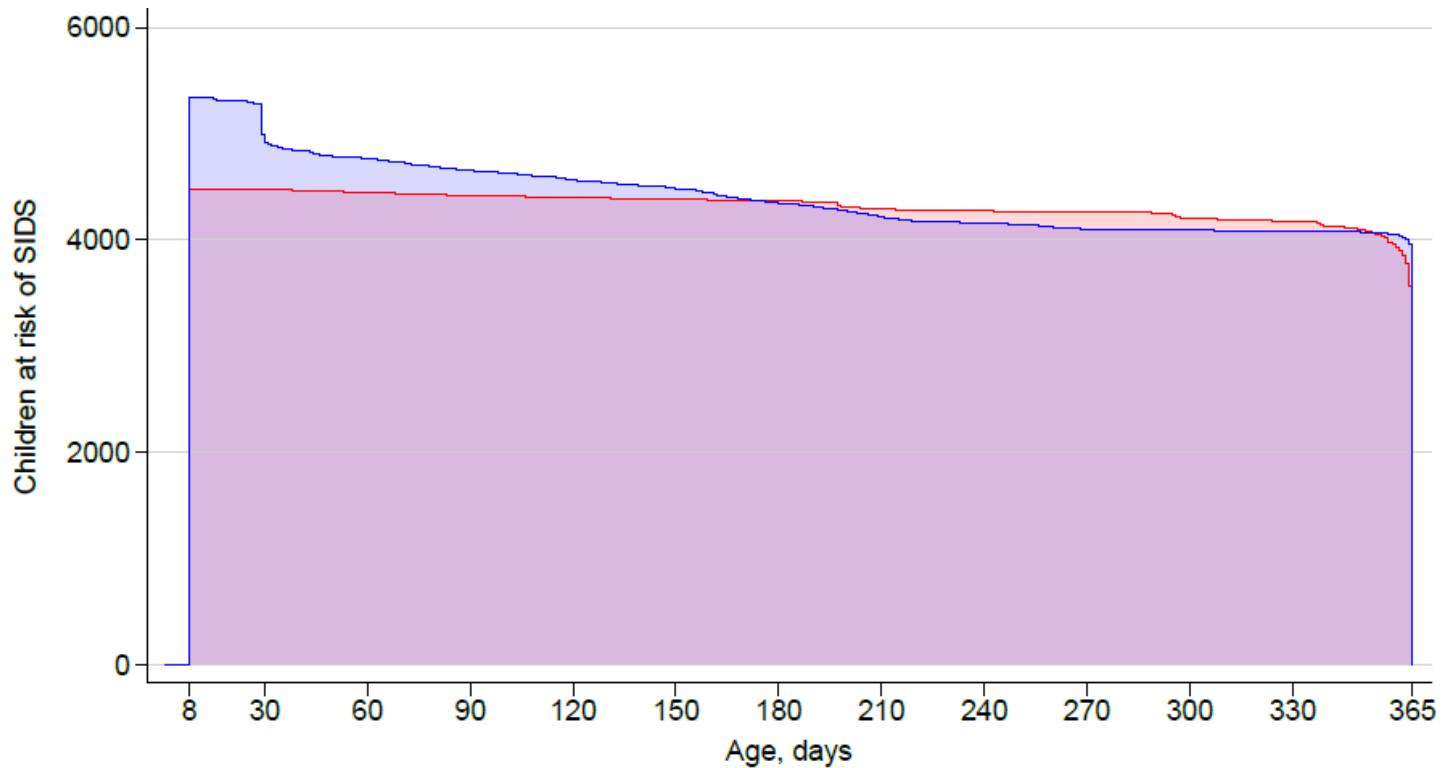
5354 HU infants followed for 4331 child-years



# Following up the cohorts:

4483 **HE** infants followed for 4239 child-years

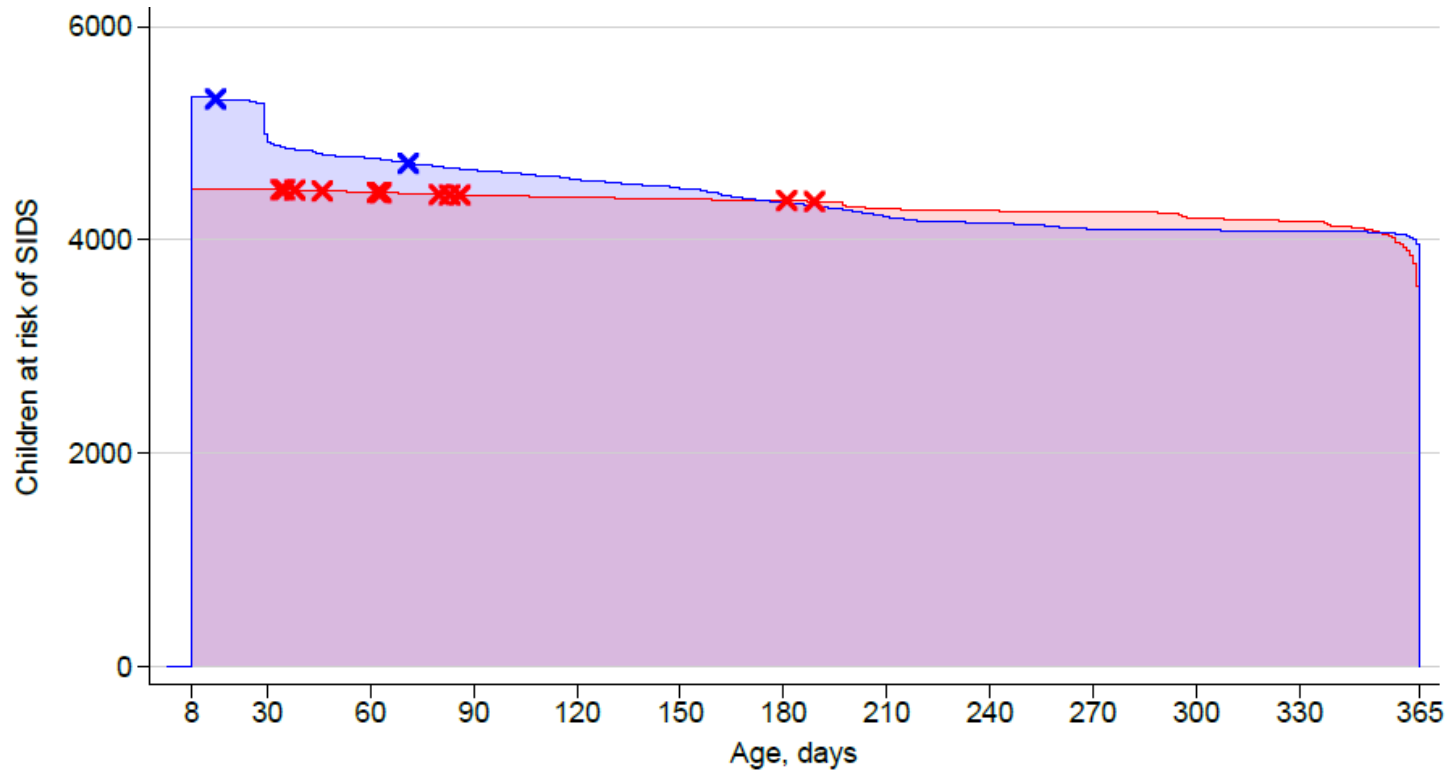
5354 **HU** infants followed for 4331 child-years



# Findings: SIDS in HE × and HU × infants

4483 HE infants followed for 4239 child-years

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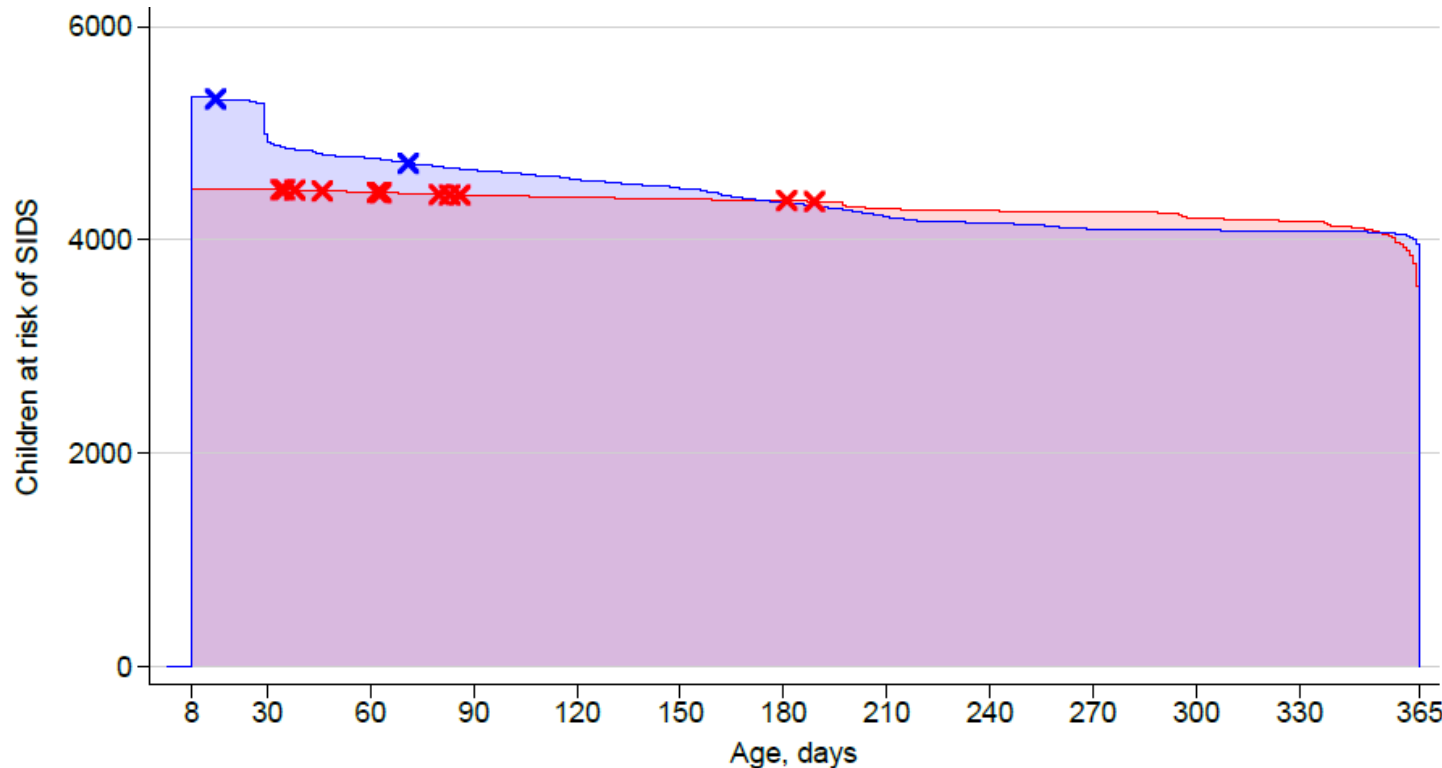


# Findings: SIDS in HE × and HU × infants

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SIDS
12
2



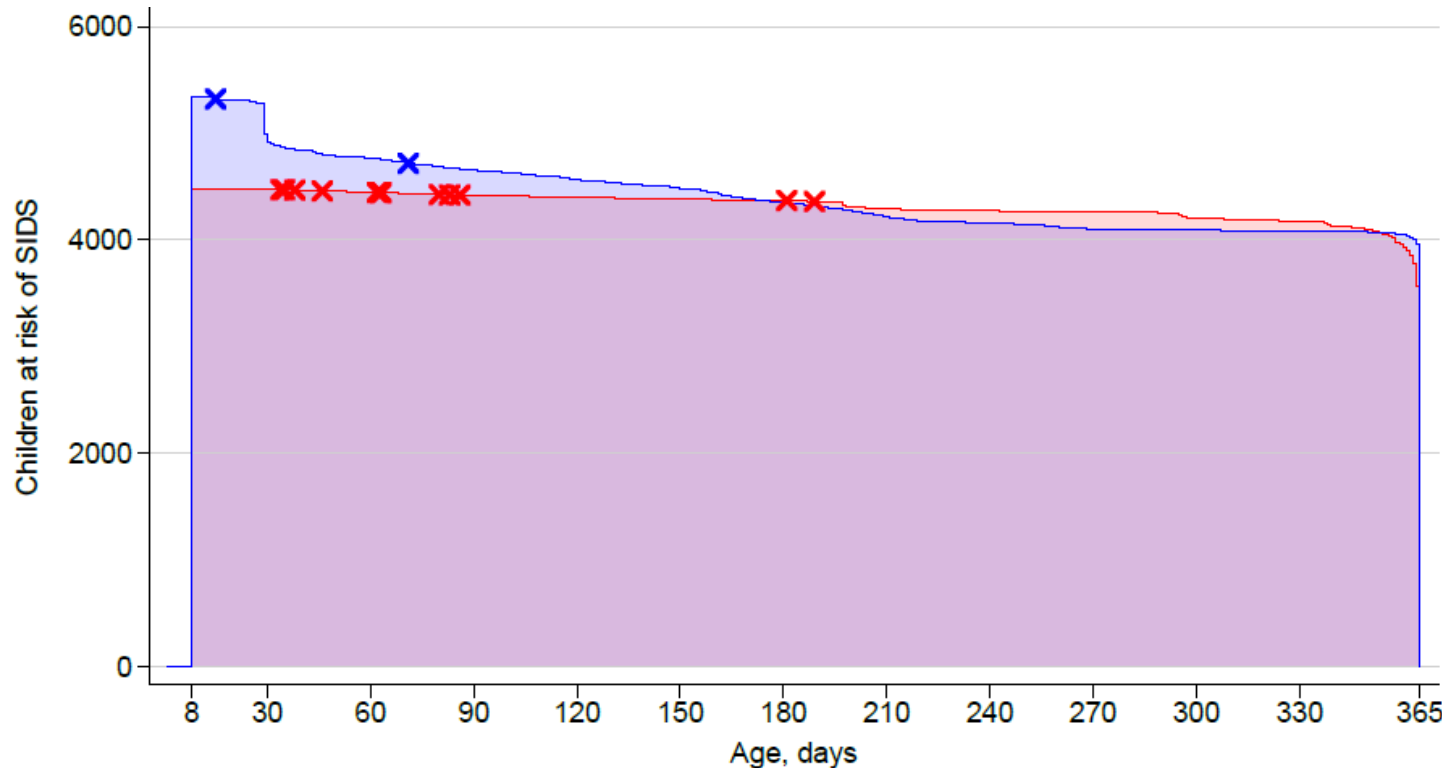
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SIDS
12
2

$$12/2=6$$



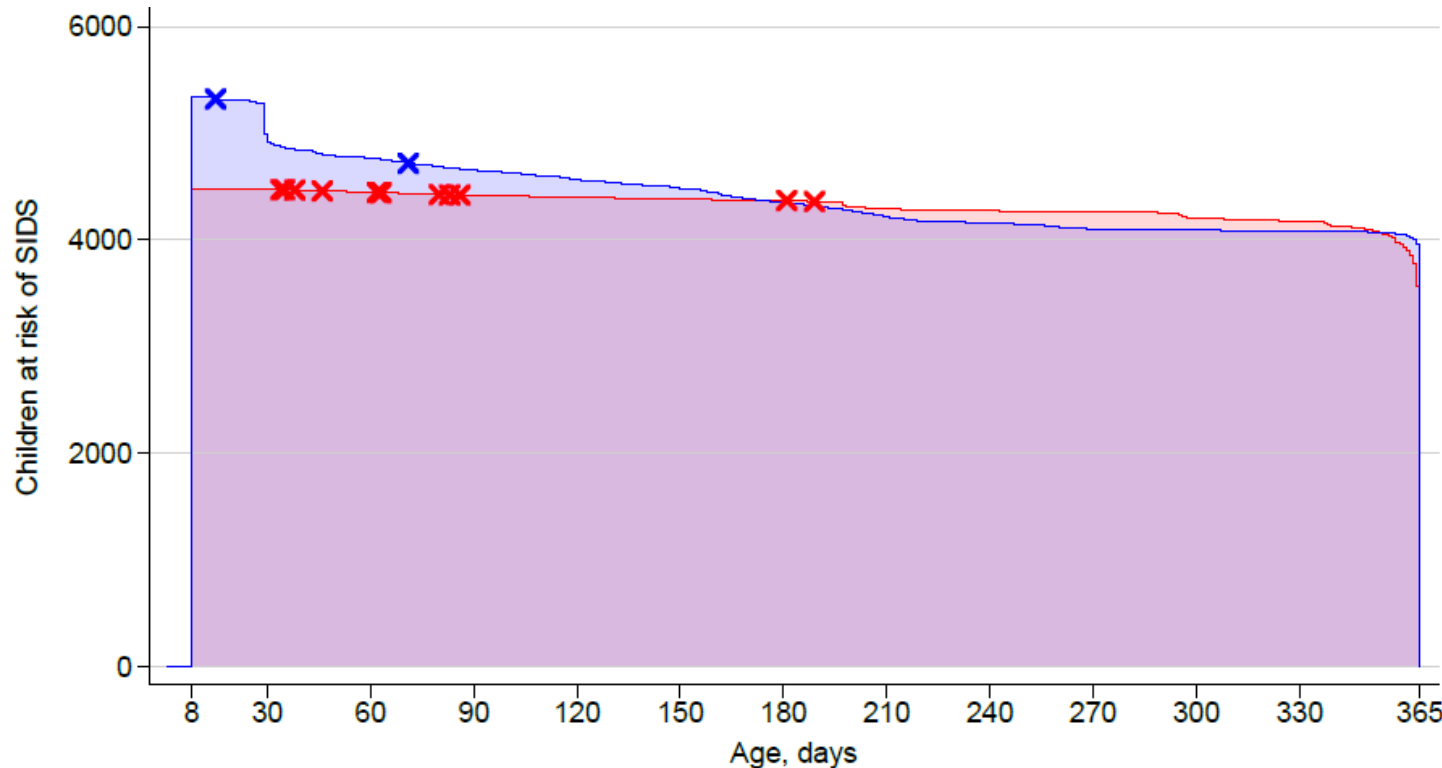
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Incidence rate of SIDS per 1000 child-years:  
HE: 2.8  
HU: 0.46

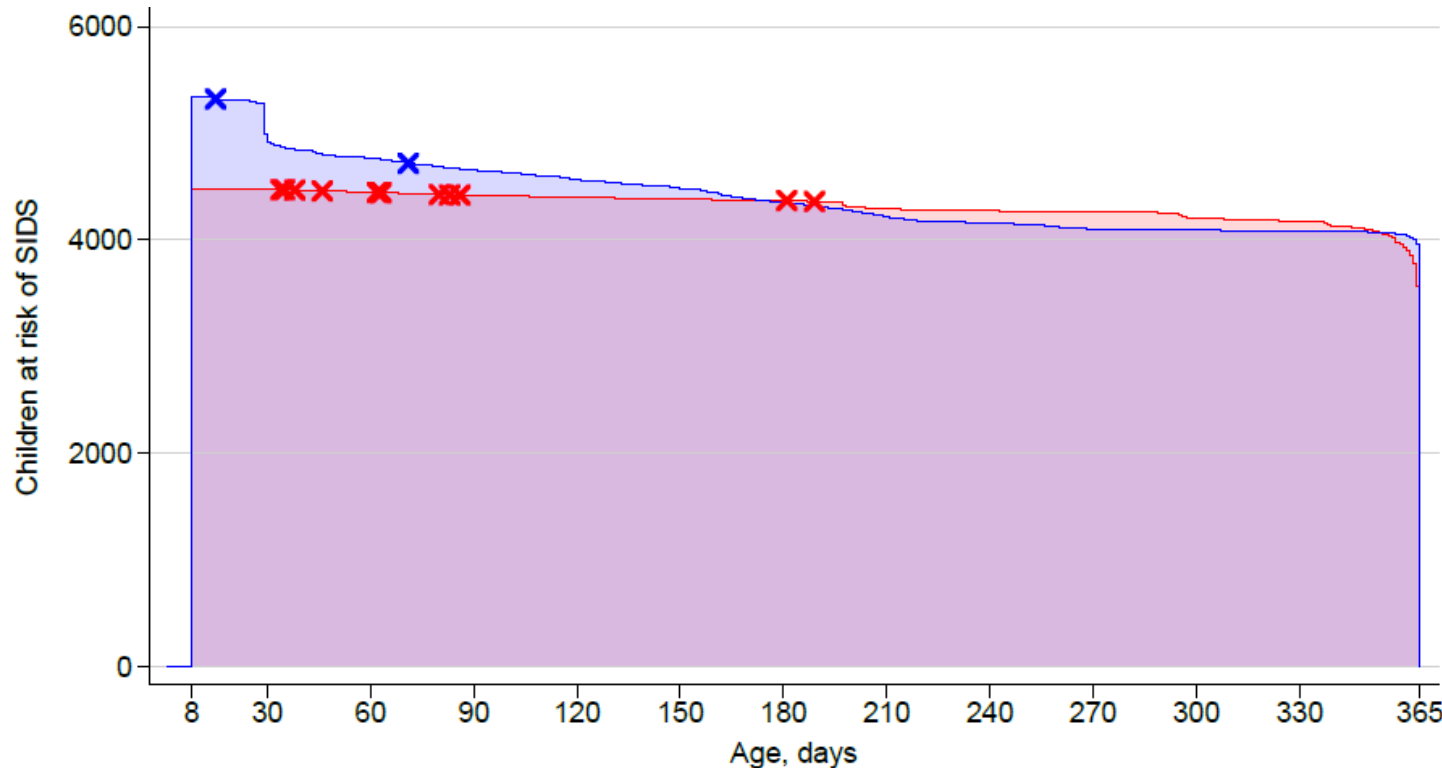
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Incidence rate of SIDS per 1000 child-years:

HE: 2.8

HU: 0.46

$$IRR: 2.8/0.46 = 6$$

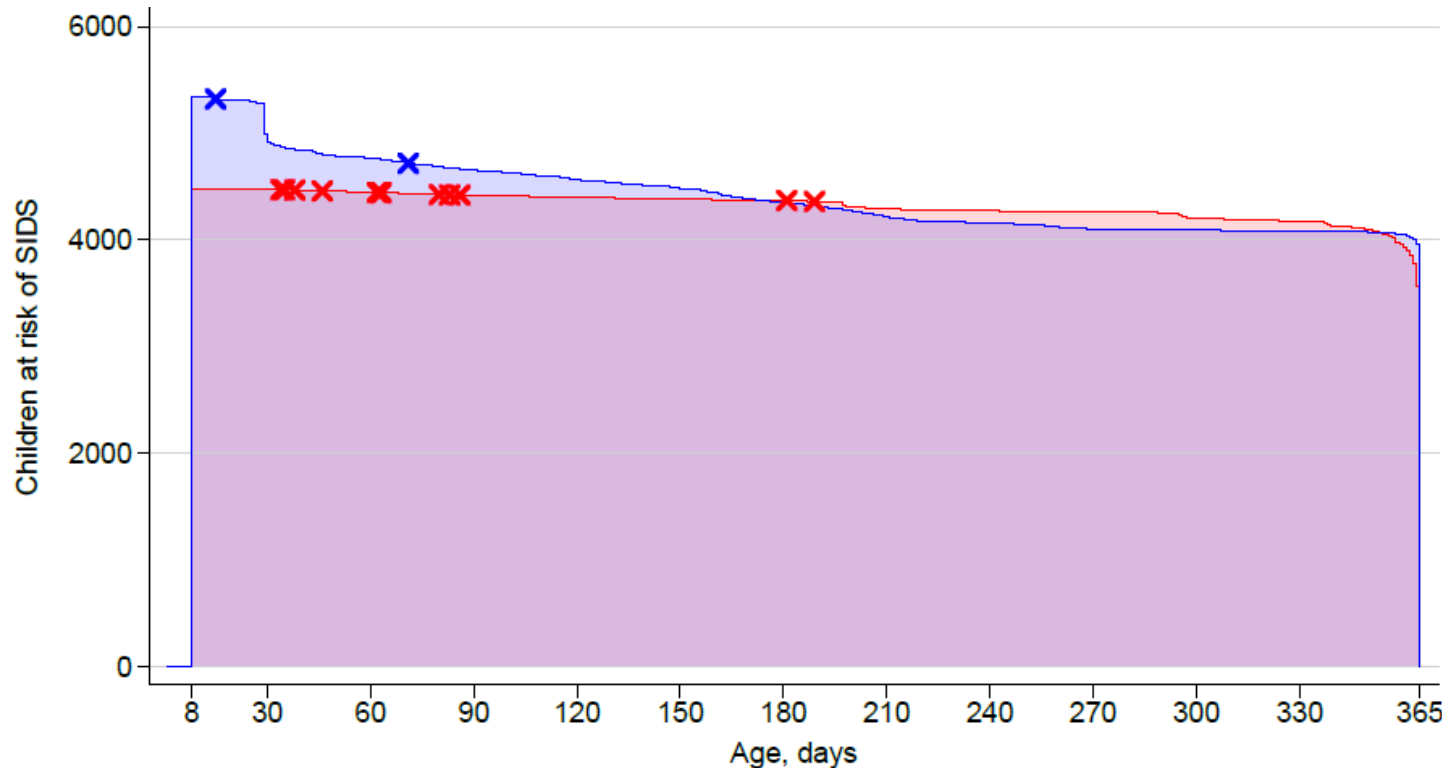
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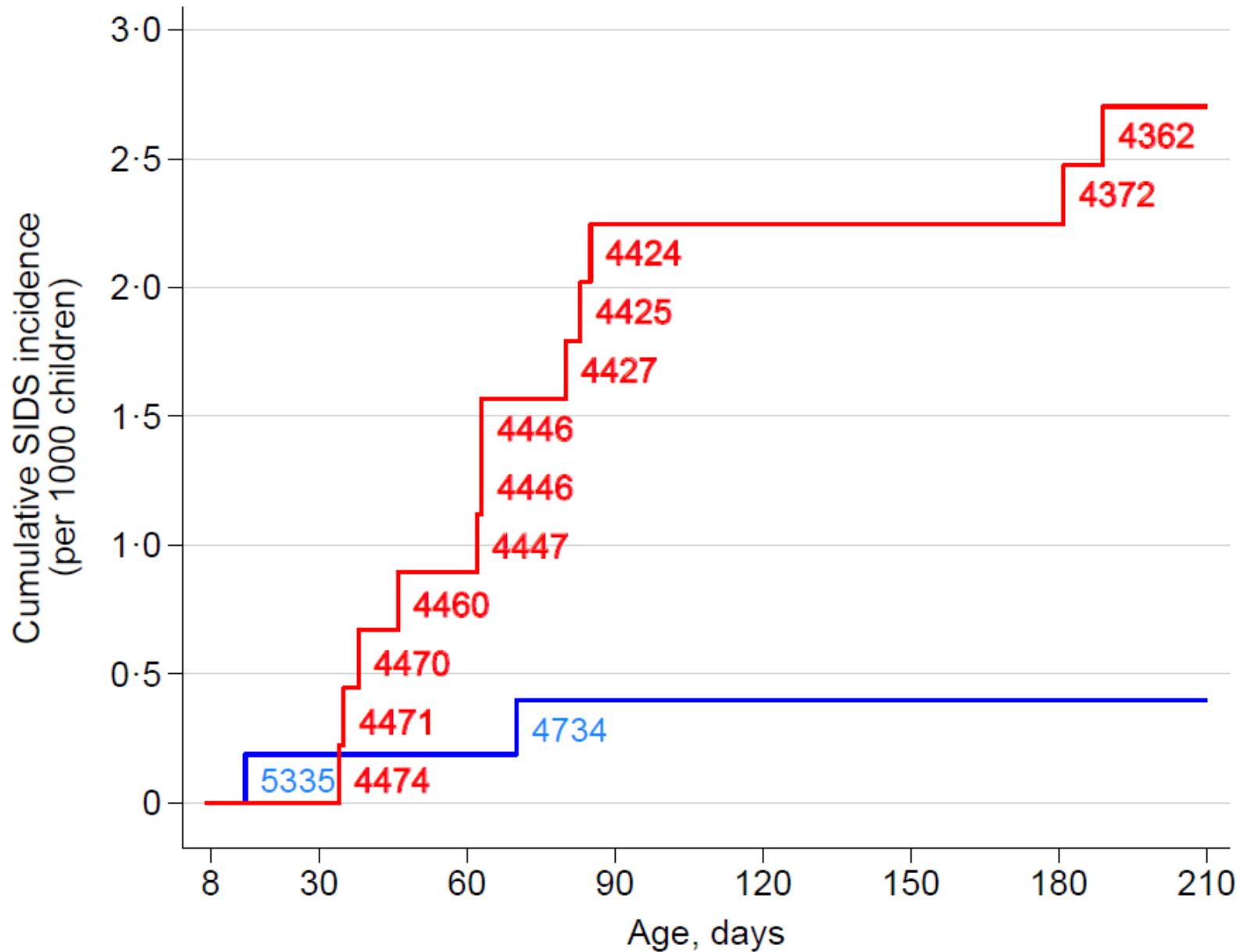
$$12/2=6$$



Incidence rate of SIDS per 1000 child-years:  
HE: 2.8  
HU: 0.46  
IRR:  $2.8/0.46 = 6$

IRR = 6 (95% CI 1.5–40)

# Findings: SIDS in HE and HU infants



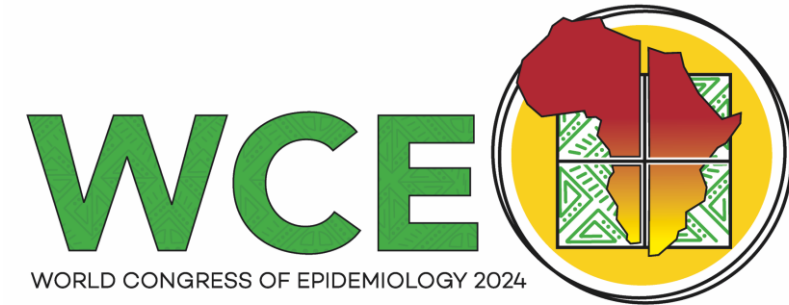


# Conclusions/way forward

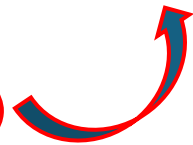
- Hypothesis based on studies in 1980/90ies of **HE** as a possible risk factor for SIDS is strengthened
- Our hope and aspiration:
  - Others (in this audience?) will do similar studies
  - If promoting supine and protected sleep is as effective in **HE** as in **HU** infants, “**Safe-to-sleep**” programs may greatly reduce their:
    - SIDS risk
    - and
    - infant mortality



# Thank you for listening.....



And, again, many thanks to study mothers, families and infants (now children)

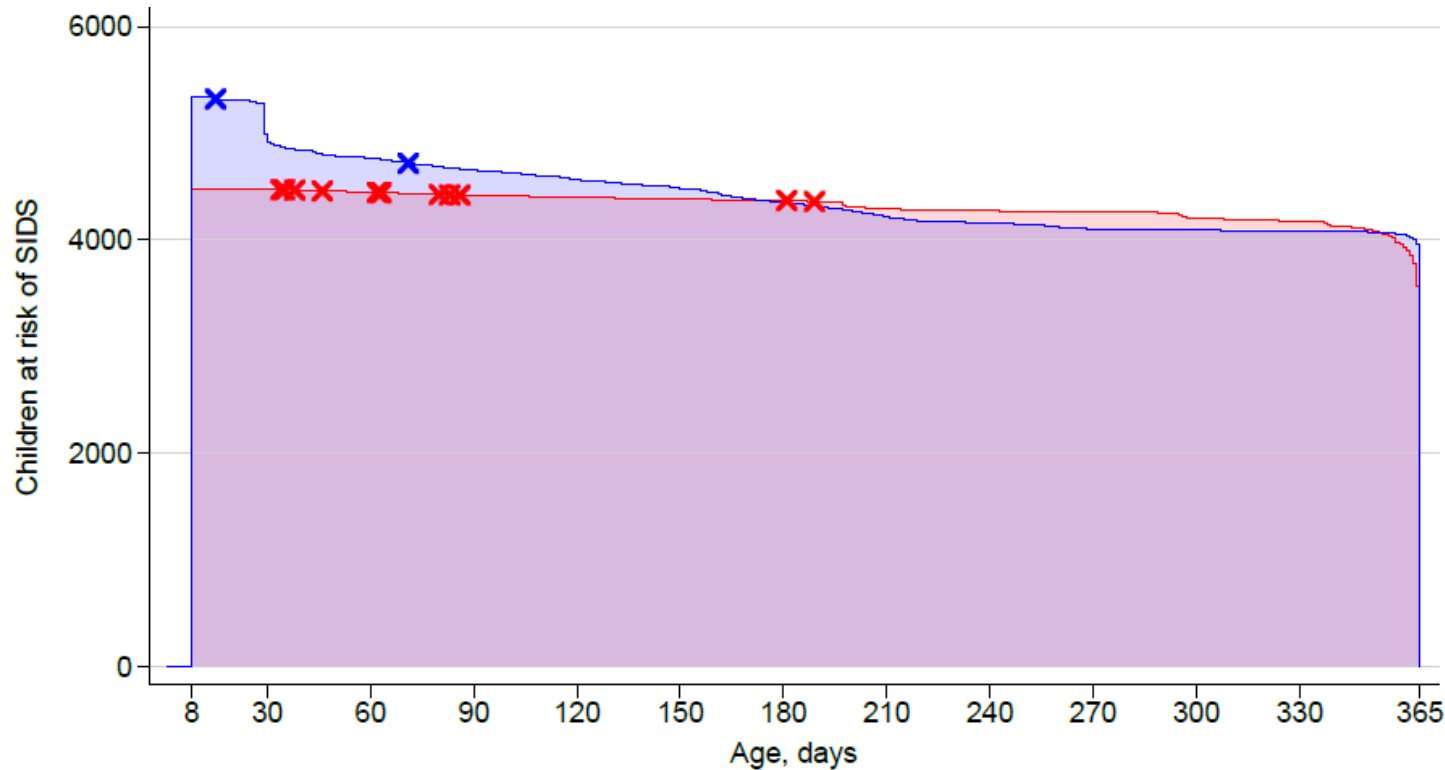


# Findings: SIDS in HE × and HU × infants

4483 HE infants followed for 4239 child-years

5354 HU infants followed for 4331 child-years

All Deaths	SIDS	%
79	12	15
33	2	6



# Other findings

- Incidence rate difference was 2.4: Preventing 422 maternal HIV infections could avert one SIDS event.
- The  $AF_{exp}$  was 0.84: 10 of the 12 SIDS events among HE infants could be ascribed to their HIV exposure.
- Post-hoc observation → analysis: SIDS incidence rate dropped considerably following the national COVID–19 lockdown: IRR=0.14

	<b>HIV-1 exposed</b>	<b>HIV-1 unexposed</b>
	(N=4483)	(N=5354)
<b>Mean number of people in household</b>	3.5 (1.7)	3.6 (1.7)
<b>Unknown</b>	30	11
<b>Wealth quintile</b>		
<b>1</b>	1078 (24.0%)	1053 (19.7%)
<b>2</b>	1074 (24.0%)	1460 (27.3%)
<b>3</b>	629 (14.0%)	912 (17.0%)
<b>4</b>	718 (16.0%)	927 (17.3%)
<b>5</b>	967 (21.6%)	993 (18.5%)
<b>Unknown</b>	17 (0.4%)	9 (0.2%)
<b>House ownership</b>		
<b>Own</b>	1007 (22.5%)	1105 (20.6%)
<b>Renting</b>	3345 (74.6%)	4100 (76.6%)
<b>Other</b>	114 (2.5%)	140 (2.6%)
<b>Unknown</b>	17 (0.4%)	9 (0.2%)
<b>Drinking water</b>		
<b>Protected natural spring</b>	746 (16.6%)	791 (14.8%)
<b>Covered well</b>	159 (3.5%)	177 (3.3%)
<b>Borehole</b>	225 (5.0%)	226 (4.2%)
<b>Public tap</b>	2498 (55.7%)	3112 (58.1%)
<b>Piped into plot</b>	493 (11.0%)	646 (12.1%)
<b>Piped into house</b>	106 (2.4%)	124 (2.3%)
<b>Other*</b>	239 (5.3%)	269 (5.0%)
<b>Unknown</b>	17 (0.4%)	9 (0.2%)

Data are n (%) or mean (SD)

	<b>HIV-1 exposed</b>	<b>HIV-1 unexposed</b>
	(N=4483)	(N=5354)
<b>Cooking fuel</b>		
<b>Wood</b>	303 (6.8%)	237 (4.4%)
<b>Charcoal</b>	4098 (91.4%)	5030 (93.9%)
<b>Other</b>	65 (1.4%)	78 (1.5%)
<b>Unknown</b>	17 (0.4%)	9 (0.2%)
<b>Electricity</b>		
<b>No</b>	753 (16.8%)	692 (12.9%)
<b>Yes</b>	3713 (82.8%)	4653 (86.9%)
<b>Unknown</b>	17 (0.4%)	9 (0.2%)
<b>Mother's education level</b>		
<b>None</b>	179 (4.0%)	87 (1.6%)
<b>Primary school</b>	1846 (41.2%)	1583 (29.6%)
<b>O level</b>	2007 (44.8%)	2743 (51.2%)
<b>A level</b>	240 (5.4%)	442 (8.3%)
<b>Certificate or Degree or Other</b>	189 (4.2%)	482 (9.0%)
<b>Unknown</b>	22 (0.5%)	17 (0.3%)
<b>Marital status</b>		
<b>Single, Separated/Divorced /Widowed</b>	601 (13.4%)	607 (11.3%)
<b>Married or cohabitating</b>	3865 (86.2%)	4738 (88.5%)
<b>Unknown</b>	17 (0.4%)	9 (0.2%)

Data are n (%) or mean (SD)

	HIV-1 exposed	HIV-1 unexposed
	(N=4483)	(N=5354)
<b>Bednet use by mother</b>		
<b>No</b>	254 (5.7%)	270 (5.0%)
<b>Always</b>	3999 (89.2%)	4829 (90.2%)
<b>Sometimes</b>	213 (4.8%)	246 (4.6%)
<b>Unknown</b>	17 (0.4%)	9 (0.2%)
<b>Antenatal visits during pregnancy</b>	4.0 (1.5)	3.5 (1.2)
<b>Unknown</b>	12	8
<b>Antenatal visits during pregnancy</b>		
<b>0-2</b>	555 (12.4%)	1026 (19.2%)
<b>3-4</b>	2495 (55.7%)	3448 (64.4%)
<b>≥5</b>	1421 (31.7%)	872 (16.3%)
<b>Unknown</b>	12 (0.3%)	8 (0.1%)
<b>Mother's age in years</b>	27.9 (5.1)	24.8 (4.8)
<b>Unknown</b>	15	9
<b>Mother's age</b>		
<b>&lt;25 years</b>	1253 (28.0%)	2801 (52.3%)
<b>≥25 years</b>	3215 (71.7%)	2544 (47.5%)
<b>Unknown</b>	15 (0.3%)	9 (0.2%)
<b>Parity</b>		
<b>Primiparous</b>	541 (12.1%)	1566 (29.2%)
<b>Multiparous</b>	3925 (87.6%)	3779 (70.6%)
<b>Unknown</b>	17 (0.4%)	9 (0.2%)

IRR 6.1 virtually unchanged (to 5.9) when adjusting for the only two preconception baseline features which were markedly different between the HE and HU infants

Data are n (%) or mean (SD)

	<b>HIV-1 exposed</b>	<b>HIV-1 unexposed</b>
	(N=4483)	(N=5354)
<b>Baby sex</b>		
<b>Boy</b>	2256 (50.3%)	2655 (49.6%)
<b>Girl</b>	2227 (49.7%)	2699 (50.4%)
<b>Breast feeding initiation within 1 h. of birth</b>		
<b>Yes</b>	3760 (83.9%)	4913 (91.8%)
<b>No</b>	723 (16.1%)	416 (7.8%)
<b>Unknown</b>	0 (0.0%)	25 (0.5%)
<b>Baby given other feed than breast milk on day1</b>		
<b>No</b>	4338 (96.8%)	5234 (97.8%)
<b>Yes</b>	145 (3.2%)	110 (2.1%)
<b>Don't know</b>	0 (0.0%)	5 (0.1%)
<b>Unknown</b>	0 (0.0%)	5 (0.1%)
<b>Baby weight when enrolled, kg</b>	3.1 (0.4)	3.2 (0.4)
<b>Unknown</b>	2	5
<b>Enrollment weight</b>		
<b>&lt;2.5 kg</b>	313 (7.0%)	263 (4.9%)
<b>2.5-&lt;3 kg</b>	1441 (32.1%)	1481 (27.7%)
<b>3-&lt;3.5 kg</b>	1867 (41.6%)	2444 (45.6%)
<b>&gt;=3.5 kg</b>	860 (19.2%)	1161 (21.7%)
<b>Unknown</b>	2 (0.0%)	5 (0.1%)

\*pond, stream, unprotected natural spring, rain water, unprotected well, misc.