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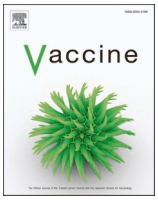

Vaccine coverage and timeliness among children of adolescent mothers: A community-based study in the Eastern Cape, South Africa

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ABSTRACT

Background: Children born to adolescent mothers are more vulnerable to infant mortality and morbidity than those born to adult mothers. HIV-exposed children have lower antibody protection against vaccine-preventable diseases at birth compared to unexposed children. In South Africa, 17 % of adolescent girls aged 15–19 years are mothers, yet vaccination coverage and timeliness among their children is underreported.

Methods: This study estimated age-appropriate vaccination coverage and timeliness among children ($n = 1080$) of adolescent mothers ($n = 1015$) in the Eastern Cape, South Africa. Mother-child dyads were recruited through healthcare and community-based sampling strategies. Vaccination data were abstracted from 1013 home-based child health records (2017–2019). Coverage is reported for Diphtheria-Tetanus-Pertussis 3rd dose (DTP3), under-1 vaccination among children over 12 months ($n = 613$) and measles 2nd dose (MCV2) among children over 24 months ($n = 382$) using proportions with 95 % confidence intervals (95 %CI). Timeliness is defined as receiving each vaccination within 4 weeks of recommended age. Findings are disaggregated by maternal HIV-status.

Results: Overall, 27.3 % of adolescent mothers were living with HIV. Coverage of DTP3 was 85.6 % (95 %CI: 82.6–88.3 %), under-1 coverage was 53.2 % (95 %CI: 49.1–57.2 %), and MCV2 coverage was 62.3 % (95 %CI: 57.2–67.2 %). Vaccination coverage was lower among children of adolescent mothers living with HIV (AMLHIV) than unexposed children (DTP3 80.3 % vs 88.2 % *p*-value: 0.01; under-1 46.5 % vs 56.4 % p-value: 0.02; MCV2 55.4 % vs 67.1 % p-value: 0.02). Timeliness of vaccinations declined over time from 98.0 % at birth, 70.7 % at 14 weeks, 71.9 % at 9 months and 37.3 % at 18 months.

Conclusion: Vaccination coverage among children of adolescent mothers in the Eastern Cape are below national targets. Children of AMLHIV had lower coverage than HIV-unexposed children. Further research is needed to identify risk factors associated with incomplete and delayed vaccinations among this group, particularly among HIV-exposed children. Enhanced vaccination campaigns may be required for children of adolescent mothers.

Abbreviations: AMLHIV, Adolescent mothers living with HIV; BCG, Tuberculosis vaccine; DHIS, District health information system; DHS, Demographic and Health Survey; DTP3, Diphtheria-Tetanus-Pertussis 3rd dose coverage; DTaP1, DTaP2, DTaP3, DTaP4, Pentavalent vaccine (DTaP-IPV-Hib: Diphtheria, tetanus, acellular pertussis, inactivated polio vaccine, haemophilus influenzae type B dose 1, 2, 3 and 4); DTaP-HepB1, DTaP-HepB2, DTaP-HepB3, DTaP-HepB4, Hexavalent vaccine (DTaP-IPV-Hib-HBV: DTaP-IPV-Hib combined with Hepatitis B dose 1, 2, 3 and 4); Hep B1, Hep B2, Hep B3, Hepatitis B Vaccine dose 1, 2 and 3; HIV, Human immunodeficiency virus; MCV2, Measles containing vaccine 2nd dose coverage; Measles 1, Measles 2, Measles containing vaccine dose 1 and 2; OPV0, OPV1, Oral Polio Vaccine dose 1 and 2; PCV1, PCV2, PCV3, Pneumococcal Conjugated Vaccine dose 1, 2 and 3; RV1, RV2, Rotavirus Vaccine dose 1 and 2.

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1. Introduction

Children born to adolescent mothers are more vulnerable to infant mortality and morbidity than children of adult mothers [1–3]. Timely childhood vaccination is a central component of reducing infant mortality and morbidity [4]. This is particularly important in high HIV-burden settings where HIV-exposed infants have a higher risk of negative outcomes caused by vaccine-preventable diseases due to lower antibody levels at birth [5–7]. By 2050, sub-Saharan Africa will be home to 36 % of the world's adolescent population (10–19 years), with the highest adolescent birth rate globally [8,9]. In South Africa, high rates of early childbearing exist in a context of the largest HIV epidemic [10] and where adolescent girls and young women have the highest HIV incidence [11,12]. Persistent rates of early childbearing and HIV incidence among adolescent girls are predicated by poor access to quality health services [13–15]. Despite this, coverage of child health services, including vaccination, among children born to adolescent girls is underreported.

In South Africa, national childhood vaccination coverage targets are not met despite the provision of free vaccination services for all children [16]. The performance of a country's routine vaccination program is typically determined by two indicators: (1) the coverage of the 3rd dose of the Diphtheria-Tetanus-Pertussis (DTP3) vaccine (i.e., the percentage of children under the age of 1 year who have completed three scheduled doses) and (2) the coverage of the 2nd dose of the measles containing vaccine (MCV2) [17]. In 2018/2019, national coverage rates of the DTP3 vaccine, offered in a hexavalent formulation containing the inactivated polio, *Haemophilus influenzae* type B and hepatitis B vaccines (DTaP-IPV-Hib-HBV), was 83.0 %. The coverage rates for under-1 and MCV2 were 81.9 % and 76.5 %, respectively [16]. DTP3 and MCV2 coverage was lowest in the Eastern Cape province, followed by KwaZulu-Natal – both provinces with the highest burden of antenatal HIV prevalence (36.5 % and 40.9 %, in 2019 respectively) and high adolescent birth rates (60.1 and 69.7 deliveries per 1000 adolescent girls, respectively) [18]. Vaccination coverage reporting in administrative data is not disaggregated by maternal age and HIV-status [19–21] which masks the potential gaps in coverage and the identification of groups such as children of adolescent mothers and children of adolescent mothers living with HIV (AMLHIV). Survey data show that vaccination timeliness is highly variable across South Africa [22–25]. Untimely vaccination delays protection against vaccine-preventable diseases and contributes to insufficient levels of herd immunity necessary to prevent outbreaks. Recent outbreaks of measles and rubella in South Africa, signal gaps in timely immune protection [26].

Studies conducted in the Eastern Cape, Gauteng, KwaZulu-Natal and the Western Cape province report mixed findings about the association between adolescent maternal age, HIV-status and childhood vaccination coverage and timeliness. In 2013, a health-facility based study conducted in rural Eastern Cape found no significant difference in vaccination coverage in children of adolescent mothers (≤19 years; $n = 76$) compared to adult mothers ($n = 382$) [27]. A more recent health-facility based study (2012–2016) conducted in the Western Cape found that children of adolescent caregivers had higher odds of delayed vaccination compared to children of adult caregivers ($n = 652$; adult vs. adolescent caregiver sample size unreported) [22]. Both studies did not disaggregate analyses by maternal HIV-status and the latter only included children with mild to severe respiratory tract infections which limits the generalisability of these findings. Two other studies also found inconsistent results when examining maternal HIV-status as a potential risk factor for vaccination coverage and timeliness [23,28]. The earlier community-based study in Kwazulu-Natal (2005–2006), found that positive maternal HIV-status reduced the odds of vaccination after adjusting for maternal age, distance to clinic and wealth (adolescent mothers ≤19 years old $n = 36$ and adult mothers ≥20 years old $n = 239$) [28]. Another hospital-based study was conducted at two urban respiratory infection surveillance sites in 2012 in Kwazulu-Natal and Gauteng [23]. It reported contrary findings that unknown maternal HIV-status was associated with delayed vaccination compared to positive maternal HIV-status.

There is an evidence gap on whether adolescent maternal age and HIV-status are risk factors for childhood vaccination coverage and timely vaccine uptake. In response to these evidence gaps, this study estimates age-appropriate vaccination coverage and timeliness among children of adolescent mothers, including AMLHIV, in the Eastern Cape, South Africa.

2. Methods

2.1. Study design & setting

This research uses cross-sectional data (2017–2019) drawn from an observational cohort study of adolescent and young mothers (10–24 years) ($n = 1045$) and their children ($n = 1144$) residing in the Eastern Cape, South Africa [29]. The study was located within a peri-urban and rural health district with one of the highest antenatal HIV prevalence rates (36.5 %) in South Africa in 2019 [30]. It is also one of ten health districts in South Africa with the lowest DTP3 (68.0 %) and MCV2 coverage (64.9 %) in 2019 [16]. Adolescent birth rates are high in the Eastern Cape where approximately 17.1 % of facility-based deliveries in 2020/21 were among adolescent girls (10–19 years) [31].

2.2. Recruitment

Adolescent and young mothers (10–24 years) who had their first child before the age of 20 were eligible to participate. All children born to eligible mothers were enrolled in the cohort regardless of their cohabitation arrangements with their biological mother. Six parallel recruitment strategies were implemented to ensure representation of mother-child dyads who may or may not have had existing access to health services during recruitment. In collaboration with on-site researchers and an advisory group of adolescent mothers, we mapped potential access points (e.g., clinics, schools, salons, churches, social services, and community groups) to request contact details of mothers. This process followed relevant approvals, with ethical considerations described below. Subsequently, mothers were traced and enrolled into the study. Further details about recruitment for the cohort and research governance are described elsewhere [32,33].

Due to the age distribution of children at the time of data collection, vaccination coverage outcomes are only reported for applicable subgroups of children. For example, under-1 coverage excluded all children who were under 12 months at the time of data collection. DTP3, under-1 and MCV2 coverage were compared with population-level data (i.e. children of all mothers) reported in the District Health Information System (DHIS) in 2018/19 for the Eastern Cape [16] and 2016 DHS estimates for the Eastern Cape [20]. As illustrated in Fig. 1, children born to mothers 20 years or older were excluded from analysis. Second and third order children born to mothers 20 years or older were also excluded from analysis ($n = 34$). Children were excluded from analysis if no Road to Health booklet was available ($n = 60$) or vaccination records were missing due to damaged or missing immunisation page and lost original booklet that included immunisation data ($n = 7$).

2.3. Data collection procedures

In South Africa, vaccinations are recorded in government-issued home-based child health records, known as Road to Health booklets. Pages within the booklet were photographed, monitored for quality and uploaded to a secure server. Data including visits, immunisation dates and HIV-related data, were extracted from the images onto an electronic Open Data Kit survey. Socio-demographic and healthcare access factors were collected from mothers or primary caregivers using self-administered electronic surveys (Open Data Kit) on tablets (available

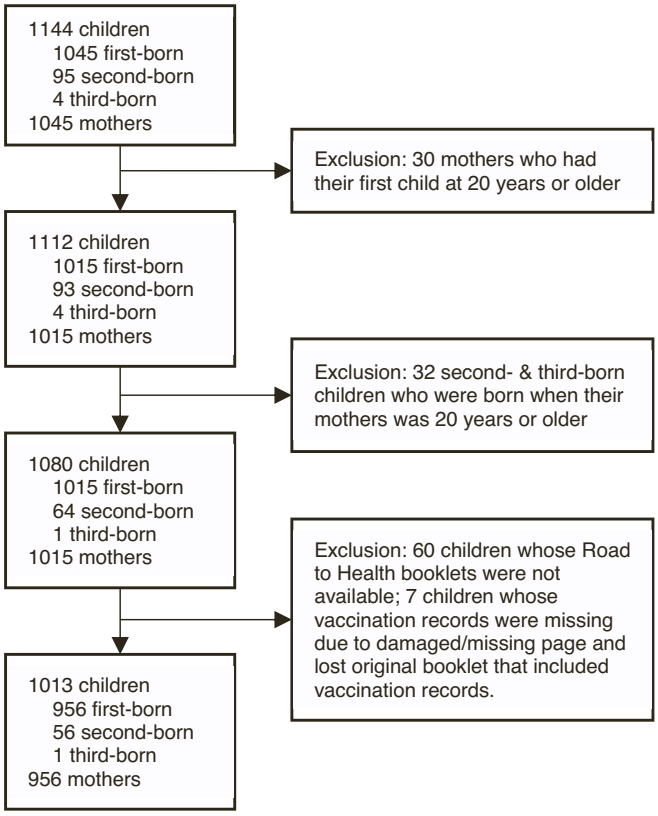

Fig. 1. Flowchart of sample inclusion.

at www.heybaby.org.za/research) with support by trained research assistants. Questionnaires assessed maternal and child health, access to health services, access to social grants and child caregiving arrangements. HIV-status and dates of birth were validated using data from Road to Health booklets and patient files [34].

2.4. Outcome definitions

A child was considered vaccinated when a date was recorded against each vaccine in the Road to Health booklet [22]. Illegible dates were coded to indicate that the vaccine was administered but date is unknown. Invalid dates were manually reviewed against photographs of the booklets and recoded as appropriate. Age of vaccination was calculated by subtracting the child's date of birth from the date of vaccination.

Following the definitions from the 2016 South Africa Demographic and Health Survey (DHS), all vaccination coverage estimates measured the proportion of children who received age-appropriate vaccinations as per the South African Expanded Programme for Immunisation Schedule (Table 1) [20].

The DTP3 vaccination coverage was defined as the proportion of children who received DTaP dose 1, 2 and 3 by 12 months (≤51 weeks old) as a proportion of children over 12 months (≥48 weeks old). Children were considered to have complete *under-1 vaccination coverage* if they received all scheduled vaccinations by 12 months (i.e., all vaccines except measles dose 2 and DTaP/Hep B 4). *Under-1 vaccination coverage excluding Hep B 1, 2 and 3* was also reported to account for the replacement of the pentavalent (DTaP-IPV-Hib) vaccine with hexavalent (DTaP-IPV-Hib-HepB) vaccine in 2015. The *MCV2 vaccination coverage* measured the proportion of children who received dose 1 and 2 of the measles vaccine by 24 months as a proportion of children over 24 months. *DTaP dose 3 to measles dose 1 drop-out rate* was measured as the proportion of children over 12 months who did not receive measles dose 1 as a proportion of all children who received DTaP dose 3 by 12 months.

Table 1
Expanded Programme on Immunisation (EPI) in South Africa (December 2015).

Age	Vaccines[1]	Timeliness threshold (child age in weeks)
Birth	BCG; OPV0	0–3
6 weeks	OPV1; RV1; PCV1; DTaP1/DTaP-HepB1; HepB1[2]	6–9
10 weeks	DTaP2/DTaP-HepB2; HepB2[2]	10–13
14 weeks	RV2; PCV2; DTaP3/DTaP-HepB3; HepB3[2]	14–17
6/9months[3]	Measles1	24-31/36-43
9 months	PCV3	36–43
12/18 months[3]	Measles2	48–55/72–79
18 months	DTaP4/DTaP-HepB4; HepB4[2]	72–79

[1] BCG (Tuberculosis); OPV0, OPV1 (Oral Polio Vaccine dose 1 and 2); RV1, RV2 (Rotavirus dose 1 and 2); PCV1, PCV2, PCV3 (Pneumococcal Conjugated Vaccine dose 1,2 and 3); DTaP1, DTaP2, DTaP3, DTaP4 (Pentavalent vaccine DTaP-IPV-Hib: Diphtheria, tetanus, acellular pertussis, inactivated polio vaccine, haemophilus influenzae type B dose 1,2,3 and 4); Hep B1, Hep B2, Hep B3 (Hepatitis B dose 1,2 and 3); Measles 1, Measles 2 (Measles containing vaccine dose 1 and 2); DTaP-HepB1, DTaP-HepB2, DTaP-HepB3, DTaP-HepB4 (Hexavalent vaccine DTaP-IPV-Hib-HBV: DTaP-IPV-Hib combined with Hepatitis B dose 1,2,3 and 4).

[2] The pentavalent vaccine (DTaP-IPV-Hib) was replaced by the hexavalent vaccine (DTaP-IPV-Hib-HBV) in 2015. Vaccination guidelines were updated and specified that when hexavalent vaccine is used, Hep B vaccine should not be administered.

[3] The national Expanded Programme for Immunisation schedule changed after December 2015 recommending that measles dose 1 and 2 should be given at 6 and 12 months.

Timeliness of vaccinations was categorically defined as early, timely and late. Vaccinations were classified as timely if administered within 28 days/4 weeks of recommended age as per the vaccination schedule [22,23] (Table 1). Any vaccinations administered either before or after this threshold were categorised as early or late, respectively. In December 2015, the South African Expanded Programme for Immunisation schedule lowered the recommended ages for measles vaccination from 9- and 18-months to 6- and 12-months [35]. To account for this programmatic switch, coverage and timeliness of the first and second dose of measles containing vaccine are reported separately for children born before and after the vaccination schedule changed.

2.5. Data analysis

We report sociodemographic and healthcare access characteristics of the sample, disaggregated by maternal HIV-status (positive and negative). Outcomes are reported on using proportions (as percentages) with 95 % confidence intervals (CI). We compared children of AMLHIV and children of HIV-negative adolescent mothers using Pearson's chi-squared test, Wilcoxon rank-sum test and *t*-test, as appropriate, and to obtain the corresponding *p*-values. To assess potential confounding by maternal age category (≤15, 16–17 and 18–19 years) and maternal HIV-status, Mantel-Haenszel chi-square test was used to compute summary odds ratios and corresponding p-values [36]. Data were analysed using Stata/SE 17.0.

2.6. Ethical considerations

Ethical approvals for this study were obtained from the Universities of Oxford (R48876/RE003) and Cape Town (HREC226/2017), and the London School of Hygiene & Tropical Medicine Research Ethics Committee (26,703/RR/28131). The Departments of Health, Social Development and Basic Education reviewed the ethics protocol, approved recruitment, and data collection activities. In accordance with ethical and legal requirements for research among children in South Africa, full

informed consent was obtained from all parents for their children and, where adolescent parents are aged under 18, additionally from their primary caregiver. The informed consent and assent process were administered by trained research staff. A referral protocol facilitated health and social services referrals for participants who reported untreated illness, abuse, and food insecurity (available at www.heybaby.org.za/research). Among children with available records none had zero vaccinations.

3. Results

Overall, 1080 children of adolescent mothers were enrolled in the study, and data were abstracted from 1013 (93.8 %) Road to Health booklets. Children accessed vaccination services across 61 different health facilities. Sample characteristics are described in Table 2. AMLHIV (27.3 %; $n = 261$) and their children (28.6 %; $n = 290$) were older than HIV-negative adolescent mothers (72.7 %; $n = 695$) and their children (71.4 %; $n = 723$). The median child age at data collection was 1.3 years [interquartile range (IQR) 0.5–2.5 years] with 60.5 % ($n = 613$) being over 12 months old. Children of AMLHIV (n = 290) had median age of 2.0 years [IQR 0.6–3.2] compared to children of HIV-negative adolescent mothers with a median age of 1.1 years [IQR 0.5–2.1]. The median age of mothers at the birth of their first child was 17.2 years [IQR 16.1–18.3]. Similarly, maternal age at birth of first child was older among AMLHIV compared to HIV-negative adolescent mothers (18.1 years [IQR 16.9–19.1] versus 16.9 years [IQR 15.9–18.0]). Children of AMLHIV were more likely to have siblings than children of HIV-negative adolescent mothers, most likely because AMLHIV were older. Most children were living in an urban community (71.5 %) with a slightly higher proportion of children of AMLHIV living in an urban area compared to children of HIV-negative adolescent mothers. The majority of children (93.8 %) were cohabiting with their biological mother at least 4 nights per week. Approximately 75.2 % of the children travelled less than 30 min to the clinic and 79.4 % of adolescent mothers were attending secondary school (grade ≥ 9) at the time of their first pregnancy. Attendance to antenatal care services was high with 79.3 % of adolescent mothers attending 5 or more appointments during their first pregnancy. However, a third (33.9 %) of adolescent mothers did not report attending any postnatal care visits after their first birth. There was no other evidence of differences in characteristics by maternal HIV-status.

3.1. Age-appropriate vaccination coverage

Age-appropriate vaccination coverage by ages 12 and 24 months among children ≥12 months and ≥ 24 months old in the study is reported in Table 3. There was a decline in coverage as the schedule progresses, particularly after the 6-month vaccination. Up to 6 months in the schedule, coverage remained relatively high, ranging between 86.8 % and 98.0 %. This was followed by a steep downward trend, declining to approximately 75.2 % for 9-month vaccines and approximately 60 % for 18-month vaccines. Hep B doses 1, 2, and 3 had lower coverage compared to other vaccines at the same schedule intervals. Measles dose 1 and 2 coverage was higher among children born before the 2015 vaccination schedule change compared to children born after (83.9 % and 61.5 % compared to 79.1 % and 3.2 % respectively). Among the children born after the schedule change who received the measles dose 2 vaccine, 63.2 % received it on time. Vaccination coverage did not significantly differ by maternal HIV-status up to week 10 in the vaccination schedule. However, from week 14 in the schedule, children of AMLHIV had significantly lower coverage compared to children of HIV-negative adolescent mothers (Table 3).

Table 4 presents DTP3, under-1 and MCV2 vaccination coverage, by maternal HIV-status. DTP3 coverage was 85.6 % (95 %CI: 82.6–88.3) and 53.2 % (95 %CI: 49.1–57.2) had complete under-1 coverage by 12 months. After excluding Hep B 1, 2 and 3 coverage to account for distribution of the hexavalent vaccine which combined Hep B and DTaP vaccines, under-1 coverage increased to 59.4 % (95 %CI: 55.4–63.3). Only 62.3 % (95 %CI: 57.2–67.2) had complete MCV2 coverage by 24 months. The drop-out rate for DTaP dose 3 to measles dose 1 was 9.4 % (95 %CI: 7.1–12.1). We found that vaccination coverage was significantly lower among children of AMLHIV compared to children of HIV-

Table 2
Socio-demographic and healthcare access characteristics of children and adolescent mothers by maternal HIV status in the cohort.

Children	Total ($n = 1013$)	Children of AMLHIV[1] ($n = 290$)	Children of HIV-negative adolescent mothers ($n = 723$)	p-value
Frequency, n (%)				
Child sex				
Female	502 (49.6)	153 (52.8)	349 (48.3)	0.20
Male	511 (50.4)	137 (47.2)	374 (51.7)	
Sibling				
Only child	884 (87.3)	217 (74.8)	667 (92.3)	<0.001
Has sibling	129 (12.7)	73 (25.2)	56 (7.7)	
Child age at data capture				
≤11 months	400 (39.5)	92 (31.7)	308 (42.6)	<0.001
12–23 months	231 (22.8)	41 (14.1)	190 (26.3)	
≥24 months	382 (37.7)	157 (54.1)	225 (31.1)	
Child age in years (median [IQR])[2]	1.3 [0.5–2.5]	2.00 [0.6–3.2]	1.1 [0.5–2.1]	<0.001
Child year of birth				
2009–2015	242 (23.9)	110 (37.9)	132 (18.3)	<0.001
2016–2019	771 (76.1)	180 (62.1)	591 (81.7)	
Birth order				
First	956 (94.4)	261 (90.0)	695 (96.1)	<0.001
Second & third	57 (5.6)	29 (10.0)	28 (3.9)	
Location				
Urban	724 (71.5)	219 (75.5)	505 (69.8)	0.07
Rural	289 (28.5)	71 (24.5)	218 (30.2)	
Child lives with biological mother				
≥4 nights/week	950 (93.8)	275 (94.8)	675 (93.4)	0.68
≤3 nights/week	21 (2.1)	5 (1.7)	16 (2.2)	
None	42 (4.1)	10 (3.4)	32 (4.4)	
Child distance to clinic (minutes)				
≤20	441 (44.7)	130 (46.4)	311 (44.0)	0.72
21–30	301 (30.5)	85 (30.4)	216 (30.6)	
31–59	74 (7.5)	17 (6.1)	57 (8.1)	
≥60	171 (17.3)	48 (17.1)	123 (17.4)	
Mother	Total ($n = 956$)	AMLHIV (n = 261)	HIV-negative adolescent mothers (n = 695)	
Maternal age at first birth (years, median [IQR])[3]	17.2 [16.1–18.3]	18.1 [16.9–19.1]	16.9 [15.9–18.0]	<0.001
Maternal education level at first pregnancy[4]				
Primary (grade ≤ 8)	174 (20.6)	40 (20.5)	134 (20.6)	0.98
Secondary (Grade 9–12)	672 (79.4)	155 (79.5)	517 (79.4)	
Antenatal care visits[5]				
≥5	680 (79.3)	178 (79.8)	502 (79.2)	0.05
1–4	147 (17.2)	32 (14.3)	115 (18.1)	
None	30 (3.5)	13 (5.8)	17 (2.7)	
Postnatal care visits[6]				
≥2	349 (34.7)	91 (32.0)	258 (35.7)	0.27
1	316 (31.4)	86 (30.3)	230 (31.9)	
None	341 (33.9)	107 (37.7)	234 (32.4)	

[1] Unconfirmed if these children were HIV-exposed at birth as adolescent mothers may have acquired HIV after child's birth; [2]Child age at the time of data collection; [3]Maternal age at birth of first child; [4]School grade when pregnant with first child; [5]Number of antenatal visits attended during pregnancy for all children; [6]Number of postnatal visits attended for all children.

Table 3
Comparison of age-appropriate vaccination coverage for children aged ≥12 months (born 2009–2018) and ≥ 24 months (born 2009–2017) for all immunisations recommended up to 18 months in the EPI in South Africa by maternal HIV status.

Age	Vaccine	Age-appropriate vaccination coverage Proportion (95 % CI)			
		Total	Children of AMLHIV[1]	Children of HIV-negative adolescent mothers	p-value[2]
Among ≥ 12 months		n = 613	*n* = 198	*n* = 415	
Birth	BCG	96.2 (94.4–97.6)	94.9 (91.9–98.0)	96.9 (95.2–98.5)	0.24
	OPV0	98.0 (96.6–99.0)	97.5 (95.3–99.7)	98.3 (97.1–99.6)	0.48
6 weeks	OPV1	91.4 (88.8–93.5)	90.9 (86.9–94.9)	91.6 (88.9–94.2)	0.79
	RV1	95.3 (93.3–96.8)	93.9 (90.6–97.3)	95.9 (94.0–97.8)	0.28
	PCV1	95.8 (93.8–97.2)	95.5 (92.6–98.4)	95.9 (94.0–97.8)	0.80
	DTaP1	95.3 (93.3–96.8)	94.4 (91.3–97.6)	95.7 (93.7–97.6)	0.51
	Hep B1	90.5 (87.9–92.7)	90.4 (86.3–94.5)	90.6 (87.8–93.4)	0.94
10 weeks	DTaP2	93.5 (91.2–95.3)	91.4 (87.5–95.3)	94.5 (92.3–96.7)	0.15
	Hep B2	87.3 (84.4–89.8)	88.4 (83.9–92.8)	86.7 (83.5–90.0)	0.57
	DTaP3	88.7 (86.0–91.1)	82.3 (77.0–87.6)	91.8 (89.2–94.4)	0.001
14 weeks	Hep B3	83.2 (80.0–86.1)	78.3 (72.5–84.0)	85.5 (82.2–88.9)	0.02
	RV2	87.4 (84.6–90.0)	81.8 (76.4–87.2)	90.1 (87.2–93.0)	<0.01
	PCV2	91.4 (88.8–93.5)	85.9 (81.0–90.7)	94.0 (91.7–96.3)	0.001
6 months	Measles1[3]	79.1 (73.3–84.1)	71.7 (63.1–80.3)	85.2 (79–91.3)	0.01
9 months	PCV3	75.2 (71.6–78.6)	67.2 (60.6–73.7)	79.0 (75.1–83.0)	<0.01
	Measles1[4]	83.8 (80.7–86.7)	74.2 (68.2–80.3)	88.4 (85.4–91.5)	< 0.001
12 months	Measles2[3]	3.2 (1.7–5.5)	3.3 (−0.4–6.9)	3.1 (1.1–5.2)	0.95
Among ≥ 24 months		n = 382	*n* = 157	*n* = 225	
18 months	DTaP4	58.9 (53.8–63.9)	53.5 (45.7–61.3)	62.7 (56.3–69.0)	0.07
	Measles2[5]	61.5 (55.9–67.8)	56.6 (47.2–66.0)	65.6 (57.4–73.9)	0.16

[1] *Unconfirmed if these children were HIV-exposed at birth as adolescent mothers may have acquired HIV after child's birth;* [2]*Obtained using Pearson's chi-squared test.*
[3] *Reported for children born after 1 December 2015 only to account for the vaccination schedule change. Total n = 379; Children of AMLHIV n = 92; Children of HIV-negative adolescent mothers n = 287.*
[4]*Reported for children before 30 November 2015 only to account for the vaccination schedule change. Total n = 234; Children of AMLHIV n = 106; Children of HIV-negative adolescent mothers n = 128.*
[5] *Reported for children born after 1 December 2015 only to account for the vaccination schedule change. Total n = 148; Children of AMLHIV n = 51; Children of HIV-negative adolescent mothers n = 97.*

negative adolescent mothers. Among children of AMLHIV and HIV-negative adolescent mothers, DTP3 coverage was 80.3 % (95 %CI: 74.8–85.8) compared to 88.2 % (95 %CI: 85.1–91.3), respectively (*p*-value <0.01). Only 46.5 % (95 %CI: 39.5–53.4) of children of AMLHIV had complete under-1 coverage compared with 56.4 % (95 %CI: 51.6–61.2) of children of HIV-negative adolescent mothers (p-value <0.05). MCV2 coverage was 55.4 % (95 %CI: 47.6–63.2) among children of AMLHIV and 67.1 % (95 %CI: 61.0–73.2) among children of HIV-negative adolescent mothers (p-value <0.05). The proportion of children who did not receive the first dose of measles vaccine after receiving the DTaP dose 3 vaccine offered at 14 weeks was significantly lower among children of AMLHIV (14.7 % vs 7.1 %; p-value <0.01). Analyses adjusting for possible confounding by adolescent maternal age group (≤15 years; 16–17 years and 18–19 years) indicate that maternal age only had a weak influence on the association between maternal HIV-status and vaccination status (Supplement A).

As illustrated in Fig. 2, vaccination coverage indicators followed a different trend compared with District Health Information System (DHIS) reports for the same period (2018/19) in the Eastern Cape [16]. The DTP3 coverage was 18.5 % higher (85.6 vs 67.1), but under-1 coverage was 18.7 % lower (53.2 vs 71.9). By 2 years old, MCV2 coverage among children in our study was only 2.8 % lower compared to DHIS data (62.3 vs 65.1). However, our measurement of under-1 and MCV2 coverage were comparable with 2016 DHS estimates for the Eastern Cape and followed a more similar pattern of decline (see Fig. 2) [20].

3.2. Vaccination timeliness

Timeliness of each vaccination declined gradually along the schedule and steeply dropped between the 9-month and 18-month vaccinations for all children (Fig. 3). As reported in Table 5, there was weak evidence of a difference in vaccination timeliness between children of AMLHIV and children of HIV-negative adolescent mothers. Timely uptake of measles dose 1 and 2 was higher among children born after the vaccination schedule changed. Of the children born before the measles vaccination schedule changed, only 62.0 % received their 9-month measles dose 1 vaccine on time. However, among the children born after the measles vaccination was lowered to 6 and 12 months, 79.4 % received measles dose 1 vaccine on time. The same trend emerges for timeliness of the second dose of measles vaccine. Approximately 29.5 % received measles dose 2 vaccine on time among children born before the schedule changed. Meanwhile, among those children born after the change, 63.2 % received measles dose 2 vaccine on time.

4. Discussion

This study contributes evidence on the coverage of lifesaving childhood vaccinations among children of adolescent mothers in the Eastern Cape province of South Africa. We estimated age-appropriate vaccination coverage and timeliness among children of adolescent mothers, by maternal HIV-status. Despite high vaccination uptake and timeliness for birth vaccinations, children of adolescent mothers living in peri-urban and rural health districts in the Eastern Cape had sub-optimal coverage and failed to reach the national vaccination targets set out in the 2014/15 to 2018/19 Department of Health Strategic Plan [37]. Both vaccination coverage and timeliness declined with child age along the vaccination schedule. Children of AMLHIV had lower vaccination coverage, suggesting a heightened vulnerability to vaccine-preventable infections compared with children of HIV-negative adolescent mothers. Further efforts are required to improve vaccination coverage and timeliness among children of adolescent mothers, particularly children of AMLHIV.

Table 4
Comparison of DTP3, Under-1 and DTaP dose 3 to measles dose 1 dropout rate among children ≥12 months (born 2009–2018) and MCV2 vaccination coverage among children ≥24 months (born 2009–2017) by maternal HIV status.

		Age-appropriate vaccination coverage Proportion (95 % CI)			
	Vaccination target[1]	Total	Children of AMLHIV[2]	Children of HIV-negative adolescent mothers	p-value[3]
Among ≥ 12 months		*n* = 613	n = 198	n = 415	
DTP3	90 %	85.6 (82.6–88.3)	80.3 (74.8–85.8)	88.2 (85.1–91.3)	0.01
Under-1		53.2 (49.1–57.2)	46.5 (39.5–53.4)	56.4 (51.6–61.2)	0.02
Under-1 (excl. Hep B1,2,3)[4]	N/A	59.4 (55.4–63.3)	51.5 (44.6–58.5)	63.1 (58.5–67.8)	0.01
DTaP dose 3 to measles dose 1 drop-out rate	<5 %	(*n* = 544) 9.4 (7.1–12.1)	(n = 163) 14.7 (9.3–20.2)	(*n* = 381) 7.1 (4.5–9.7)	0.01
Among ≥ 24 months		*n* = 382	n = 157	n = 225	
MCV2	95 %	62.3 (57.2–67.2)	55.4 (47.6–63.2)	67.1 (61.0–73.2)	0.02

[1] Department of Health Strategic Plan, 2014/15 to 2018/19; [2]Unconfirmed if these children were HIV-exposed at birth as adolescent mothers may have acquired HIV after child's birth; [3]Obtained using Pearson's chi-squared test; [4]Under-1 vaccination coverage excluding Hep B dose 1, 2 and 3 reported to account for the replacement of the pentavalent (DTaP-IPV-Hib) vaccine with hexavalent (DTaP- IPV-Hib-HepB) after December 2015.

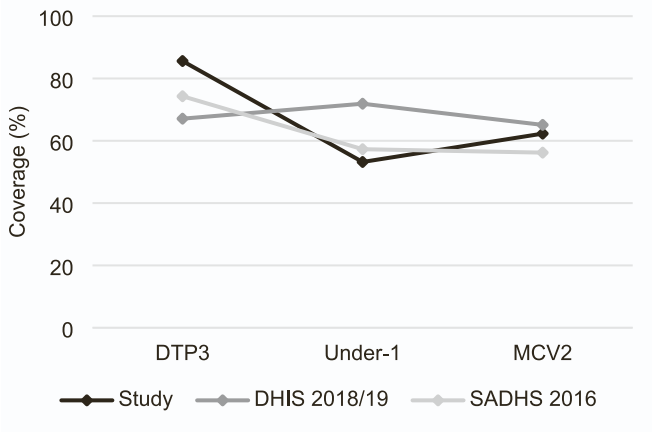

Fig. 2. Comparison of DTP3, Under-1 and MCV2 vaccination coverage with DHIS and DHS reports.

4.1. Age-appropriate vaccination coverage

Vaccination coverage among children in this study were comparable to 2016 DHS estimates for the Eastern Cape [20]. This supports the validity of under-1 and MCV2 coverage estimates in our study. Several factors could explain the remaining differences between our data and DHIS and DHS reports. Firstly, DHIS estimates are derived from routine data collected at health facilities while our study used a survey approach which could have resulted in different measurements. The accuracy of DHIS estimates, especially under-1 coverage, has been disputed [38,39]. A 2011–2014 surveillance study conducted in Gauteng with 692 caregivers reported a comparable estimate for under-1 coverage of 55.1 % which was explained by vaccine stock-outs [40]. Given that vaccine stock-outs also coincided with our study in the Eastern Cape [41], we consider our measurement of under-1 coverage to be reliable. Second, coverage could be overestimated due to missing data for approximately 6 % ($n = 67$) of children who may have had lower vaccination coverage due to not having a Road to Health booklet available. Conversely, reports using DHIS data may be inaccurate due to data management issues at health-facility level [21]. Both data sources could be prone to recording errors due to manual data entry. Third, differences in health seeking behaviour among adolescent mother-child dyads may also underpin discrepancies between our measurement of vaccination coverage and DHIS and DHS estimates. As reported in other populations [22,42], young maternal age may be a risk factor for lower vaccination coverage. Children in this study had meaningfully higher uptake of DTaP dose 1, 2 and 3 vaccines. Adolescent mothers' heightened sense of responsibility and determination to protect their child may be reflected in the higher uptake of vaccines early in the schedule [43,44]. Despite this, the steep decline in vaccination coverage by 12 months suggests that children of adolescent mothers may be disengaging from the vaccination schedule sooner than children represented in DHIS and DHS reports. Harsh treatment by healthcare workers and stigma may also discourage attendance [45]. This highlights that DHIS data may not be sufficiently age disaggregated to identify potential risk groups such as children of adolescent mothers.

We found lower or equivalent DTP3, under-1 and MCV2 coverage compared to other published population-based studies in South Africa. DTP3 coverage was similar to studies in KwaZulu-Natal [28] and the Western Cape [22]. This supports the validity of our measurement of DTP3 coverage. Unexpectedly, DTP3 coverage was comparable to the Western Cape survey, despite the Western Cape typically having higher coverage than the Eastern Cape. DTP3 coverage may have been lower in the Western Cape study because it included children of adolescent caregivers which were found to have significantly lower coverage compared to children of adult caregivers. Additionally, the Western Cape study sampled children attending hospitals for respiratory illness, potentially impacting health-seeking behaviours and interfering with vaccination uptake. DTP3 coverage was higher among children in two urban sites in Gauteng and KwaZulu-Natal [23]. Prevailing differences in sampling approaches and vaccination coverage between provinces in South Africa limit comparability of these findings. This emphasises the importance of implementing tailored approaches to improve vaccination coverage for different sub-groups and geographic areas.

Under-1 coverage in our study was only 53.2 %, while coverage per individual vaccine among the cohort ranged between 59 and 98 %. This discrepancy may be linked to vaccination delays and stock-outs [24,40]. Issues with vaccination stock management in the Eastern Cape during the survey period [41], may account for the lower under-1 coverage in our study compared to children of adolescent mothers surveyed in a rural health district of the Eastern Cape in 2013 [24]. Similarly, lower coverage of Hep B dose 1, 2 and 3 compared to other vaccines at the same schedule intervals, may be due to stock-outs and the transition from the pentavalent vaccine to the hexavalent vaccine which combined Hep B with DTaP.

MCV2 coverage was lower in our study compared to children in the 2013 Eastern Cape survey [24] and the 2012–2016 Western Cape survey [22]. Vaccination stock-outs, which mainly affected the BCG, rotavirus, and measles vaccines, could have impacted coverage observed in our study. The very low coverage (3.2 %) for age-appropriate measles dose 2 among children born after the 2015 vaccination schedule change can be attributed to delayed vaccination. Age-appropriate measles dose 2 vaccination required administration by the age of 12 months (i.e., by 51 weeks old). Our findings show that only 63.2 % of the same subgroup of

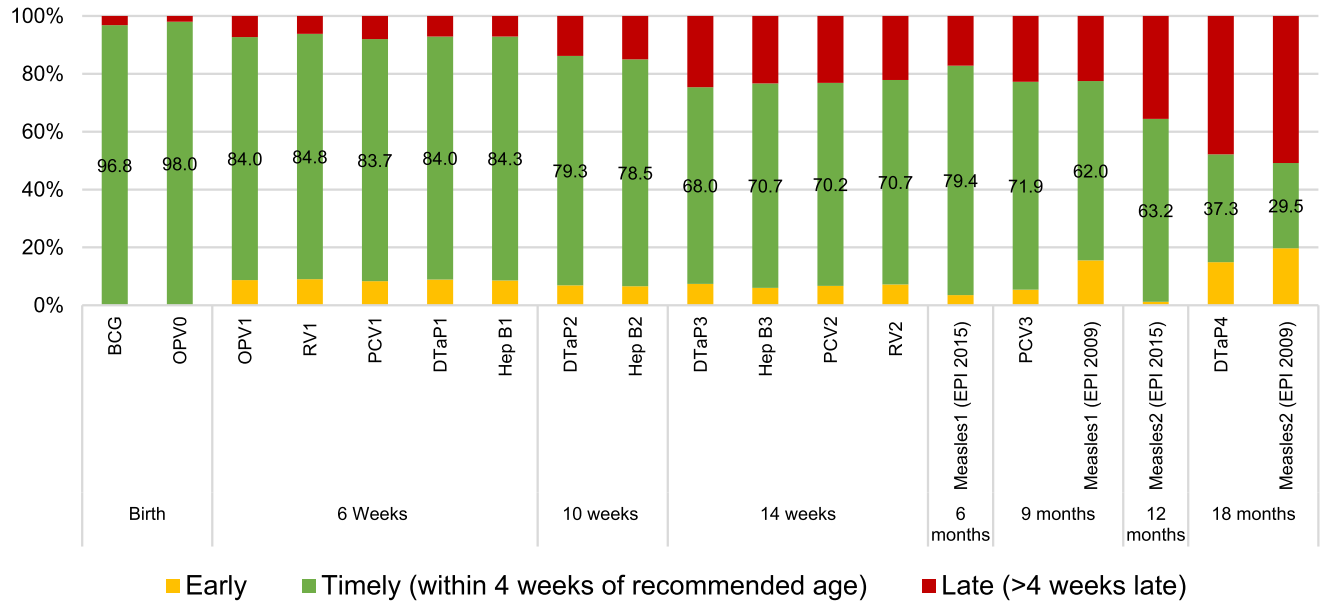

Fig. 3. Timeliness of vaccination for all immunisations recommended up to 18 months in the South African EPI for vaccinated children (born 2009–2019).

Table 5
Comparison of vaccination timeliness for all immunisations recommended up to 18 months in the South African EPI among for vaccinated children (born 2009–2019) by maternal HIV status.

Age	Vaccine	Timeliness of vaccination (%)[1]								
		Children of AMLHIV[2]				Children of HIV-negative adolescent mothers				
		n	Early	Timely	Late	n	Early	Timely	Late	p-value[3]
Birth	BCG	271	-	95.2	4.8	670	-	97.5	2.5	0.07
	OPV0	285	-	2.5	97.5	710	-	1.8	98.2	0.53
6 weeks	OPV1	267	7.1	83.9	9.0	640	9.4	84.1	6.6	0.27
	RV1	276	6.5	85.5	8.0	674	9.9	84.6	5.5	0.10
	PCV1	280	5.4	84.6	10.0	668	9.6	83.2	7.2	0.05
	DTaP1	277	6.1	84.1	9.8	669	10.0	84.0	6.0	0.03
10 weeks	Hep B1	262	5.7	85.1	9.2	622	9.8	83.9	6.3	0.06
	DTaP2	262	5.3	76.7	17.9	638	7.5	80.4	12.1	0.04
	Hep B2	249	4.8	76.7	18.5	573	7.3	79.2	13.4	0.09
14 weeks	DTaP3	225	5.3	66.2	28.4	587	8.2	68.7	23.2	0.15
	Hep B3	210	4.3	69.5	26.2	537	6.7	71.1	22.2	0.28
	RV2	229	4.4	66.8	28.8	592	7.6	71.5	21.0	0.02
	PCV2	221	5.4	65.6	29.0	568	7.9	72.7	19.4	0.01
6 months	Measles1[4]	98	4.1	72.5	23.5	362	3.3	81.2	15.5	0.15
9 months	PCV3	165	4.9	68.5	26.7	393	5.6	73.3	21.1	0.36
	Measles1[5]	93	17.2	58.1	24.7	120	14.2	65.0	20.8	0.59
12 months	Measles2[4]	65	3.1	47.7	49.2	182	0.6	68.7	30.8	0.01
18 months	DTaP4	112	12.5	38.4	49.1	204	16.2	36.8	47.1	0.68
	Measles2[5]	76	17.1	27.6	55.3	107	21.5	30.8	47.7	0.58

[1] As a proportion of those vaccinated. Timeliness threshold: Early = date of vaccination before recommended age; Timely = vaccinated within 28 days/4 weeks of the recommended age; Late = date of vaccination more than 28 days/4 weeks after recommended age; [2]Unconfirmed if these children were HIV-exposed at birth as adolescent mothers may have acquired HIV after child's birth; [3]Obtained using Pearson's chi-squared test; [4]Reported for children born after 1 December 2015 only to account for the vaccination schedule change; [5]Reported for children before 30 November 2015 only to account for the vaccination schedule change.

children received measles dose 2 vaccination on time (between 48 and 55 weeks old). Therefore, the low estimate for age-appropriate measles dose 2 is most likely a reflection of children receiving measles dose 2 after age of 51 weeks. Measles vaccination timeliness was better among the sub-group of children who were born after the recommended age for measles vaccination was lowered. Lowering vaccination age of the measles vaccine may have improved coverage and timeliness by capitalising on higher uptake of vaccinations earlier in the schedule. Higher adherence to the vaccination schedule among children born after the schedule changed, is also reflected by the reduced drop-out between DTaP dose 3 and measles dose 1.

4.2. Children of adolescent mothers living with HIV

Few studies have examined childhood vaccination coverage and timeliness by maternal HIV-status [46]. These descriptive analyses suggest that vaccination coverage and timeliness may be influenced by positive maternal HIV-status among children of adolescent mothers in the Eastern Cape. This is consistent with studies conducted in Gauteng and KwaZulu-Natal [23,28]. Further research is required to determine

the underlying drivers of the association between maternal HIV-status and vaccination coverage among their children. Timely vaccination has been demonstrated to ensure antibody responses that are equivalent in HIV-exposed uninfected and HIV-unexposed infants [47]. Given that HIV-exposed infants are more vulnerable to poor outcomes from vaccine-preventable diseases compared to HIV-unexposed children [5,6], targeted vaccination campaigns may be required to promote timely vaccination for this group. Risk factors for low vaccination coverage among children of AMLHIV were not explored in this study. HIV-exposed children may face additional barriers to accessing vaccination services as ill health could limit their mothers' capacity to bring them to vaccination clinics. Accessing antiretroviral treatment also necessitates more frequent clinic visits, reducing financial resources available for transport to vaccination visits. Previous studies have suggested that young maternal age, low maternal education, lack of awareness about timely vaccination, barriers to access including transportation costs, and lack of childcare support may contribute to incomplete or delayed vaccination among children born to women living with HIV [23,28,48,49]. More advanced statistical methods should be employed to examine potential mediating and confounding effects of other sociodemographic, maternal and healthcare service risk factors (e.g., maternal age, education, birth order, distance to facility) on vaccination coverage and timeliness among children of AMLHIV and HIV-negative adolescent mothers. Qualitative research could explore what influences vaccination uptake among children of adolescent mothers, and to further understand the unique circumstances of AMLHIV.

4.3. Declining coverage and timeliness

Due to inconsistent use of definitions for timely vaccination, comparison with other studies is restricted to those using the same measurement for timeliness. In line with other studies in South Africa [22,23], this study considered vaccinations within 28 days/4 weeks of the recommended age as timely. The observed decline in vaccination coverage and timeliness was anticipated [20–22,24,25]. Timeliness of DTaP dose 3 was comparable to a household level study in KwaZulu-Natal and Gauteng [23]. However, children included in our study achieved better timeliness for vaccines up to 6 months, compared to children attending hospital in the Western Cape [22]. Child ill health in the Western Cape study may have influenced health-seeking behaviours and vaccination uptake. Our findings indicate that children of adolescent mothers, especially children of AMLHIV, are at risk of vaccine-preventable diseases for longer due to delayed vaccination. Consequently, this group of children may be contributing to the risk of outbreaks in the Eastern Cape. Implementing interventions such as caregiver education, communication campaigns, and recall strategies through text messages could improve both vaccination timeliness and uptake [50]. Such interventions could leverage existing platforms including clinics offering youth, HIV, and maternal health services.

Children of AMLHIV were more likely to have missed the 6-month measles dose 1 vaccine after receiving the 14-week DTaP dose 3 vaccine compared to children of HIV-negative adolescent mothers. This reveals a critical window where children of AMLHIV are disengaging from the vaccination schedule (i.e., before their first measles vaccine dose). Timely vaccination is vital for maintaining herd immunity, especially for highly contagious diseases like measles. Identifying when children are disengaging from the vaccination schedule, and associated risk factors, would help immunisation providers in delivering timely support to enhance vaccine uptake and timeliness.

4.4. Limitations

This study has several limitations. First, the absence of a comparison group (i.e., children of adult mothers) prevents us from examining whether children of adolescent mothers have lower vaccination coverage compared to children of adult mothers. Second, the proportion of AMLHIV in this study is higher than maternal HIV prevalence among 15–19 year old women in South Africa [12]. This may have been influenced by higher maternal HIV prevalence in the Eastern Cape [12] and our sampling approach which aimed to include AMLHIV. An over-representation of children of AMLHIV who have lower vaccination coverage and timeliness could therefore result in an underestimation of coverage in this sample of children of adolescent mothers. Third, AMLHIV were older than HIV-negative adolescent mothers. Given that HIV prevalence increases with age this was anticipated. Maternal-age stratified analyses (Supplement A) found that maternal age was not an important confounder in the association between maternal HIV-status and vaccination. Nevertheless, maternal age could influence children's access to health services. For example, younger mothers may be benefiting from additional support from family than older adolescent mothers. Fourth, vaccination documentation was missing for 6 % of children which could result in an overestimation of coverage. Vaccination history was not obtained from caregivers during data collection. Although vaccinations reported by caregivers are susceptible to recall bias, it is recommended to obtain vaccination history directly from caregivers in cases where vaccination documentation is not available. Fifth, within the scope of this study, we were unable to account for the impact of vaccination stock-outs and schedule changes on coverage and timeliness. Future research should investigate whether inequalities in vaccination coverage and timeliness exist by maternal age and HIV-status using a representative sample of HIV-exposed and HIV-unexposed children of adolescent and adult mothers.

Notwithstanding, this study has several strengths. First, we distinguish between vaccination coverage and timeliness since crude vaccination coverage can conceal delays in timely vaccination uptake. Our findings signal gaps in immune protection among a group at high risk of vaccine-preventable diseases. Second, this study's large sample size and sampling method uniquely reduces the risk that findings are biased by adolescent mother's health-seeking behaviour. Due to the combination of health facility and community-based sampling methods across peri-urban and rural settings, these results may be generalisable to other populations of children of adolescent mothers, including children of AMLHIV, especially those who are not accessing healthcare services. Additionally, vaccination coverage in the study is less likely to be affected by variations in the quality of services within individual facilities, as it includes children accessing services across 61 primary healthcare facilities.

5. Conclusion

Children born to adolescent mothers (10–19 years) are a rapidly growing demographic in Southern Africa. Suboptimal vaccination coverage is a concern for this group, particularly HIV-exposed children who disproportionately experience poor outcomes. While vaccination coverage and timeliness are high for early vaccines in the schedule, children of adolescent mothers are behind on vaccination targets and experience increasing delays in vaccination uptake over time. Positive maternal HIV-status may be an important risk factor contributing to incomplete and delayed vaccinations in children of adolescent mothers in the Eastern Cape, South Africa. Immunisation programmes should consider targeting children of adolescent mothers to improve vaccination coverage and ensure groups at highest risk of poor health outcomes are protected against vaccine-preventable diseases, especially children of AMLHIV. A critical research gap remains and requires further exploration to understand how and why timeliness and coverage decline over time, particularly among children of adolescent mothers.

Availability of data

Data are available on reasonable request - visit the team's website for further information (www.heybaby.org.za/).

Contributions

CW conceptualised this study, managed data collection, curated the dataset, conducted analysis, and prepared the manuscript. AD, ET, and HW supported conceptualisation of the study, interpretation of the results, and contributed to writing the manuscript. ET and LC are co-Principal Investigators of the HEY BABY Study and implemented the overall study. EA-D and CC supported interpretation of the data and provided input on the manuscript. All authors reviewed and approved the final manuscript.

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CRediT authorship contribution statement

Camille Wittesaele: Writing – review & editing, Writing – original draft, Visualization, Supervision, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Elona Toska:** Writing – review & editing, Supervision, Methodology, Investigation, Funding acquisition, Conceptualization. **Lucie Cluver:** Writing – review & editing, Methodology, Investigation, Funding acquisition. **Helen A. Weiss:** Writing – review & editing, Supervision, Methodology, Conceptualization. **Courteney Collins:** Writing – review & editing, Visualization, Validation. **Edina Amponsah-Dacosta:** Writing – review & editing, Visualization, Validation. **Aoife M. Doyle:** Writing – review & editing, Supervision, Methodology, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Camille Wittesaele reports financial support was provided by Horowitz Foundation for Social Policy. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

All authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2024.126318.

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