MAJOR ARTICLE

Human Papillomavirus Vaccination in Tanzanian Schoolgirls: Cluster-Randomized Trial Comparing 2 Vaccine-Delivery Strategies

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Background. We compared vaccine coverage achieved by 2 different delivery strategies for the quadrivalent human papillomavirus (HPV) vaccine in Tanzanian schoolgirls.

Methods. In a cluster-randomized trial of HPV vaccination conducted in Tanzania, 134 primary schools were randomly assigned to class-based (girls enrolled in primary school grade [class] 6) or age-based (girls born in 1998; 67 schools per arm) vaccine delivery. The primary outcome was coverage by dose.

Results. There were 3352 and 2180 eligible girls in schools randomized to class-based and age-based delivery, respectively. HPV vaccine coverage was 84.7% for dose 1, 81.4% for dose 2, and 76.1% for dose 3. For each dose, coverage was higher in class-based schools than in age-based schools (dose 1: 86.4% vs 82.0% [$P = .30$]; dose 2: 83.8% vs 77.8% [$P = .05$]; and dose 3: 78.7% vs 72.1% [$P = .04$]). Vaccine-related adverse events were rare. Reasons for not vaccinating included absenteeism (6.3%) and parent refusal (6.7%). School absenteeism rates prior to vaccination ranged from 8.1% to 23.5%.

Conclusions. HPV vaccine can be delivered with high coverage in schools in sub-Saharan Africa. Compared with age-based vaccination, class-based vaccination located more eligible pupils and achieved higher coverage. HPV vaccination did not increase absenteeism rates in selected schools. Innovative strategies will be needed to reach out-of-school girls.

Clinical Trials Registration. NCT01173900.

Cervical cancer, caused by human papillomavirus (HPV) [1, 2], is the leading cause of years of life lost from cancer in much of the developing world [3]. It is estimated that Tanzania has one of the highest rates of cervical cancer globally and the third highest mortality rate from cervical cancer (325 deaths/1 000 000) among countries eligible for support from the GAVI Alliance [4, 5]. Developing country screening programs are frequently limited or absent, leading to late presentation of cervical cancer and associated high mortality rates [6]. However, renewed hope for cervical cancer control has recently come from prophylactic HPV vaccines.

The efficacy of these vaccines against persistent HPV-16 and HPV-18 infection and cervical lesions is highest in subjects who have not yet acquired these HPV types [7, 8]. The 2 available HPV vaccines, Gardasil (Merck) and Cervarix (GlaxoSmithKline Biologicals), have primarily targeted females around 9–18 years of age. In the developed world, the vaccines are often given as part of a broader program of other vaccinations or via targeted school-based programs [9]. However, in sub-Saharan

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Africa, preadolescent school girls are not a group routinely targeted by the Expanded Programme on Immunization (EPI), and strategies for delivery of the vaccine therefore need to be explored.

We aimed to compare the coverage achieved by 2 different HPV vaccination strategies in rural and urban schools in Tanzania. Schools were cluster-randomized to receive class-based delivery, in which vaccine was offered to all girls enrolled in school class 6 in 2010, or age-based delivery, in which vaccine was offered to all girls born in 1998. The rationale for comparing these 2 strategies was related to potential challenges in identifying girls by age across all school classes in a country where many people do not know their date of birth, and the potential for schools to have a wide range of ages enrolled in a specific class.

METHODS

Study Design

This was a phase IV cluster-randomized trial (Clinical Trials Registration: NCT01173900) of 2 vaccine delivery strategies: an age-based strategy (targeting girls born in 1998) and a class-based strategy (targeting girls in school class 6). The trial was conducted in the city of Mwanza and the neighboring district of Misungwi in northwest Tanzania. Sufficient vaccine to vaccinate 5250 girls was provided from Axios Healthcare Development.

Preliminary Activities

Overall 242 schools were mapped between March and May 2010 to document the number of girls born in 1998 (age 12 years in 2010) and enrolled in class 6 (median age, 13 years in 2010). Schools were classified as urban or rural on the basis of government classifications.

We aimed to obtain an estimate of the number of potentially eligible girls for vaccination in these schools. However, although most school heads were cooperative, collection of accurate denominator data was hampered by missing register books, inconsistent data, reluctance to disrupt classes to cross-check numbers, and absence of some classes at some schools. Data on eligible pupils were therefore rechecked on the day of vaccination. Eligible pupils in schools randomized to the age-based delivery strategy were defined as girls born in 1998, whereas eligible pupils in schools randomized to the class-based strategy were defined as girls enrolled in class 6.

Teachers, parents/guardians, and girls in the target vaccination group were provided with verbal and written information about HPV vaccination through school, parent, and community meetings, through distributed leaflets and posters, through radio messages, and through community drama troupes, following qualitative research to identify locally contextualized ways of promoting and delivering HPV vaccination [10]. The project adopted an opt-out consent approach for parents, whereby parents wishing to opt-out indicated to teachers or the project team that they did not wish their daughter to be vaccinated.

The median age at sexual debut in this population is approximately 16–17 years [11]. Selection of the class and age for the 2 delivery strategies was made in consultation with the Ministry of Health and Social Welfare and was agreed on at stakeholder meetings.

To determine whether HPV vaccination would increase absenteeism at schools on vaccination days, a check of pupil attendance records across different classes was conducted at 10 randomly selected schools (5 urban government, 3 rural government, and 2 private) over 25 randomly selected school days during the 6 months prior to starting vaccination.

Randomization and Masking

In total, 134 schools (60 urban government, 60 rural government, and 14 private) were randomly allocated to either the age- or class-based delivery strategy, stratified by school type. The allocation was done by an independent statistician. The study was not blinded.

Vaccine Administration

Eligible girls were offered 3 doses of the quadrivalent L1 virus-like particle vaccine (which protects against HPV-6, -11, -16 and -18). Vaccination was performed by one EPI nurse per school. One or two teachers assisted with paperwork and organization of pupils.

Vaccination was conducted in 4 school rounds over 12 months; each school was visited on a nominated day. The first dose was offered between August and September 2010 (recipients are referred to as phase 1 girls). Dose 1 was offered at round 2 between October and November 2010 for girls who had previously missed dose 1 (ie, phase 2 girls). The second dose was offered at round 2 for phase 1 girls and at round 3 (January–March 2011) for phase 2 girls. The third dose was offered at round 3 for phase 1 girls and at round 4 (May–June 2011) for phase 2 girls. Girls who missed dose 2 or 3 were offered vaccine at subsequent rounds.

After the school vaccine day, vaccine vials were left at the health facility for 2–4 weeks only, because of cold-storage limitations. A teacher was asked to encourage pupils who had missed their vaccine dose to attend the nominated health facility.

Vaccinees were instructed to request their parents to call the team in the event of any suspected adverse event (AE) and to go to the nearest health facility. Adverse events were also recorded at each school visit, using adapted national EPI forms. Serious AEs (SAEs) or AEs that indicated potential vaccine reactions were investigated by a senior clinician and were reported to Merck.

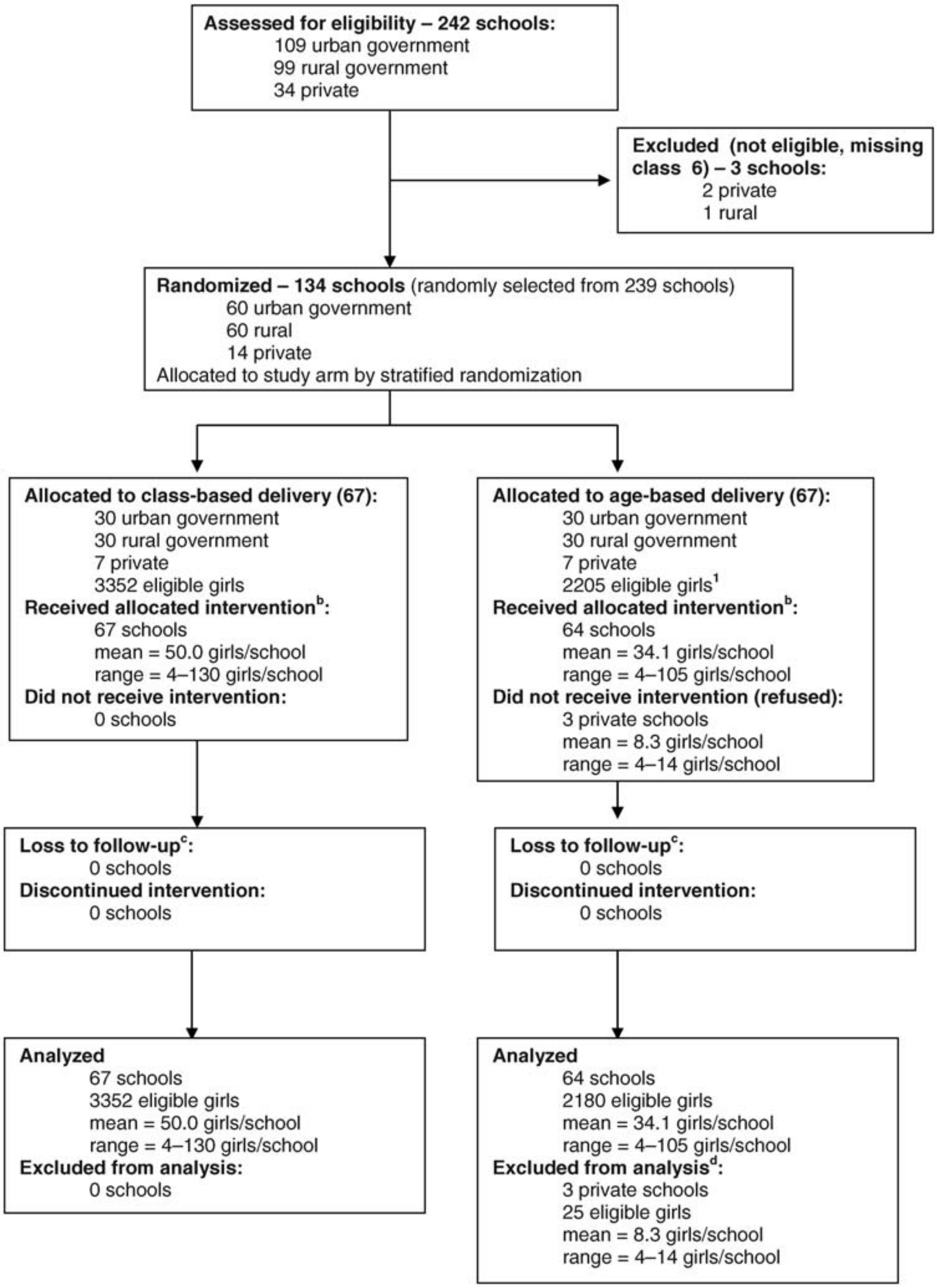

Figure 1. Study design and participant enrollment. [a]Includes the 25 girls in 3 schools that refused whose eligibility could not be reassessed on the day of vaccination. [b]"Intervention" is defined as the provision of human papillomavirus (HPV) vaccine through 2 different school-based strategies. [c]Because the outcome is defined as the receipt of 1, 2, or 3 doses of vaccine by eligible girls, the outcome is known for all eligible girls. Therefore, there is no loss to follow-up in the sense of the outcome being unknown. [d]Secondary analysis included all schools that were randomized.

Statistical Considerations

Data were double-entered in OpenClinica 3.0.1 (2009; Akaza Research; Waltham, MA) and analyzed using Stata 11.0 (StataCorp; College Station, TX).

The sample size was based on methods designed for cluster-randomized trials and assumed that 120 schools (60 urban and 60 rural) would be randomized to the 2 delivery strategies, with an average of 40–45 girls per school, and that the coefficient of variation (k) between clusters (schools) was 0.25. With an expected sample size of 5000 girls eligible for vaccination, the study had at least 80% power to detect an increase in vaccination uptake from 65% to 75%, or from 70% to 85%, between age-based and class-based strategies. Within each stratum (urban and rural), we had at least 80% power to detect an increase in vaccination uptake from 60% to 75%, or from 65% to 80%, between the 2 delivery strategies. In addition, we randomly allocated 7 private schools to each strategy, irrespective of location (urban or rural,) to obtain meaningful information about vaccine delivery in private schools. This number did not provide power to formally test the difference between strategies in private schools.

Vaccine coverage was calculated for each dose by phase and vaccination site and by delivery strategy and type of school. We examined the impact of delivery strategy on vaccine uptake, using random-effects logistic regression to account for the correlation within schools. Odds ratios (ORs) and 95% confidence intervals (CIs) were estimated for the effect of delivery strategy in all strata combined and within rural and urban government schools separately. In addition, we examined the effect of age on vaccine uptake within the class-based delivery strategy and of class within the age-based strategy, using conditional logistic regression to account for correlation within schools.

Reasons for failing to receive dose 1 were compared between delivery strategies, using the Pearson χ^2 statistic with the second-order correction of Rao and Scott to account for the clustered design.

Ethical approval was obtained from the ethics committees of the Tanzanian Medical Research Coordinating Committee and the London School of Hygiene and Tropical Medicine.

Table 1. Coverage for Each Dose Among Eligible Girls, by Phase[a] and Vaccination Site

Dose, Site (Phase)	Coverage: Eligible, No.	Coverage: Vaccinated, No. (%)
Dose 1		
Schools (phase 1)	5532	3945 (71.3)
Health facilities (phase 1)	5532	203 (3.7)
Schools (phase 2)	5532	514 (9.3)
Health facilities (phase 2)	5532	22 (0.4)
Total vaccinated with dose 1	5532	4684 (84.7)
Dose 2		
Schools (phase 1)	5532	3623 (65.5)
Health facilities (phase 1)	5532	192 (3.5)
Schools (phase 2)	5532	654 (11.8)
Health facilities (phase 2)	5532	34 (0.6)
Total vaccinated with dose 2	5532	4503 (81.4)
Total vaccinated with dose 1 who received dose 2	4684	4503 (96.1)
Dose 3		
Schools (phase 1)	5532	3486 (63.0)
Health facilities (phase 1)	5532	102 (1.8)
Schools (phase 2)	5532	608 (11.0)
Health facilities (phase 2)	5532	15 (0.3)
Total vaccinated with dose 3	5532	4211 (76.1)
Total vaccinated with dose 2 who received dose 3	4503	4211 (93.5)

[a]Phase 1 girls received dose 1 between August and September 2010; phase 2 girls received dose 1 between October and November 2010.

RESULTS

Mapping of Schools and Numbers of Eligible Pupils

In total, 67 schools were selected for age-based vaccination, and 67 were selected for class-based vaccination; there were 7 private schools, 30 urban government and 30 rural government schools per arm (Figure 1). Rechecking numbers of pupils on the day of vaccination found 2180 eligible girls (born in 1998) in the age-based schools, compared with 1931 in the mapping data, and 3352 eligible girls (enrolled in class 6) in class-based schools, compared with 3227 in the mapping data.

Head teachers at 3 private schools randomized to the age-based strategy, with an estimated 25 eligible pupils in total, would not permit vaccination, fearing negative parental feedback. The pupils in these schools could not be rechecked for eligibility and were excluded from the denominator. A sensitivity analysis was performed to examine the impact of vaccination strategy on coverage when these schools were included.

Vaccine Coverage

Results are presented for the first 12 months of the project. In total 5532 girls were eligible for vaccination in 64 age-based schools and 67 class-based schools.

Vaccine coverage for dose 1 was 84.7%, 81.4% of eligible girls received at least 2 doses of vaccine, and 76.1% received all 3 doses (Table 1 and Figure 2). Overall, 4503 of 4684 girls (96.1%) who received dose 1 received dose 2, and 93.5% of girls who received dose 2 went on to receive dose 3. Dose 1 vaccine coverage was higher in rural government schools (88.2%) than in urban government schools (82.0%) or private schools (82.0%). When the 3 private schools that did not participate were included, overall coverage for each of the 3 doses was 84.3%, 81.0%, and 75.8%, respectively.

Only 4.1% of eligible girls received dose 1 or dose 2 at a health facility; this proportion was even lower for dose 3 (2.1%). By providing another opportunity for girls who missed dose 1 in the first round to be vaccinated in the second round, another 526 girls (9.7%) received dose 1 (Table 1).

There were 2180 and 3352 eligible girls in the age-based and class-based vaccination schools, respectively (Table 2). Vaccine coverage for dose 1 was nonsignificantly higher with the class-based strategy, compared with the age-based delivery strategy (86.4% vs 82.0%; school-type-adjusted OR [AOR], 1.22; 95% CI, .84–1.78; $P = .30$). Class-based schools had significantly better coverage than age-based schools for both dose 2 (83.8% vs 77.8%; AOR, 1.37; 95% CI, .99–1.90; $P = .05$) and dose 3 (78.7% vs 72.1%; AOR, 1.36; 95% CI, 1.02–1.82;

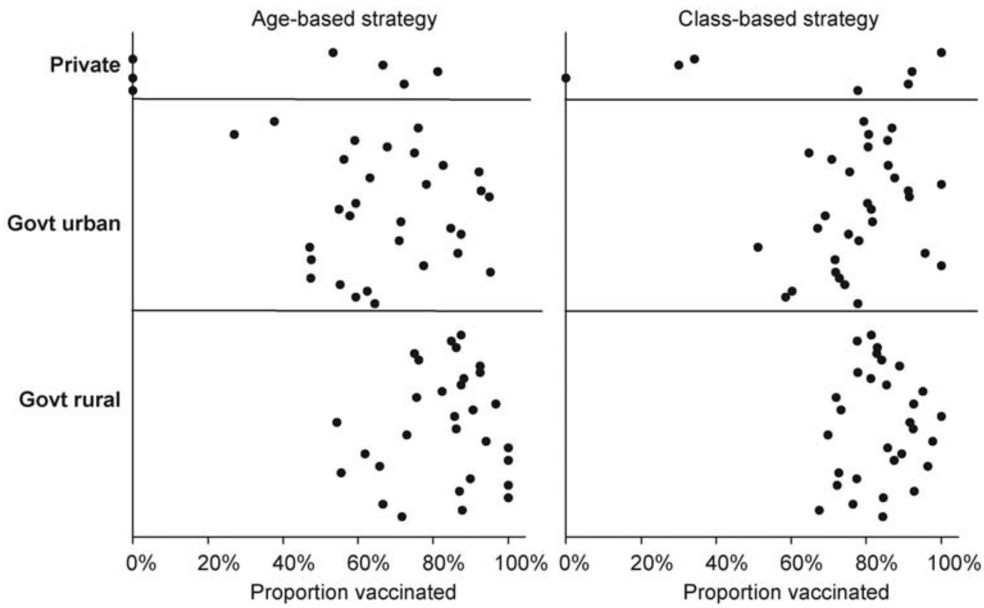

Figure 2. Coverage for dose 3 in each school, by school type and delivery strategy. Abbreviation: Govt, government.

P = .04). When the 3 private schools that refused to participate were included, the difference in coverage between the class-based and age-based strategies was even greater (dose 1: 86.4% vs 81.1% [AOR, 1.39; 95% CI, .93–2.09; *P* = .11]; dose 2: 83.8% vs 76.9% [AOR, 1.52; 95% CI, 1.08–2.15; *P* = .02]; and dose 3: 78.7% vs 71.3% [AOR, 1.48; 95% CI, 1.09–2.02; *P* = .01]).

The highest coverage was achieved in rural government schools that were allocated to the class-based delivery strategy: 89.4% for dose 1, 87.3% for dose 2, and 82.5% for dose 3 (Table 2). Private schools had better coverage with the age-based strategy than with the class-based strategy when the 3 schools that refused to participate were excluded. However, when these 3 private schools were included in the analysis, age-based private schools had the lowest coverage achieved for each dose (73.3%, 67.8%, and 61.4%, for dose 1, 2, and 3, respectively).

Within the class-based schools, there was no evidence of a difference by age in vaccine coverage for dose 1 (*P* = .34; Table 3), although there was some evidence that coverage for dose 3 varied by age (*P* = .06) and was lower in the older age groups (eg, OR, 1.78 [95% CI, 1.06–3.00] in comparison of coverage for girls aged ≤12 years to coverage for females aged ≥17 years).

Within the age-based schools, vaccine coverage for each dose was significantly lower for girls in class 7 compared with girls in class ≤4 (for dose 1, 66.7 vs 85.1%; OR, 0.47; 95% CI, .26–.87; Table 3).

Reasons for Missing Dose 1

Overall, 848 girls (15.3%) did not receive dose 1. Parent refusal (6.7%) and absence from school on the day of vaccination (6.3%) were the main reasons for failure to receive dose 1 (Table 4). Reasons differed significantly by school type (*P* < .001). Parent refusal was the major reason for not vaccinating in private schools and urban government schools (95.2% and 52.9% of vaccine nonrecipients, respectively), whereas absence from school (59.2%) was the main reason in rural government schools.

The check of pupil attendance records prior to the start of vaccination found that the proportion of pupils absent on any one day ranged from 9.6% to 19.7% for class 6 pupils and from 8.1% to 23.5% for all pupils in classes 4–7 (data not shown). The 2 private schools in this exercise had lower absenteeism rates for the 4 classes (8.1%–10.9%), compared with 10.0%–19.7% for the urban government schools and 17.6%–23.5% for the rural government schools. Absence from school as a documented reason for not receiving a vaccine dose was not higher on vaccination days, compared with absenteeism rates prior to vaccination.

Estimated Population Vaccine Coverage

On the basis of 2010 Tanzanian Demographic and Health Survey data, we estimate that 88%–89% of girls aged 10–12 years are still in school and that the proportion of all girls who ever attend class 6 is 75%–80% (85%–90% of those in school at the age of 12 years). Thus, our estimated population coverage for dose 1 with the standard 6-based approach would be 65%–70%. If the class-based approach was targeted at lower standards (eg, standard 4, which an estimated 85% of all girls would be expect to reach), then estimated coverage would be >70%, assuming uptake was similar to that in standard 6 [12].

Table 2. **Vaccine Coverage by Dose, Type of School, and Delivery Strategy**

	Proportion (%) Vaccinated,[a] by Strategy					
Dose, School Type	Age Based	Class Based	Overall	ICC	Odds Ratio (95% CI)	*P*
Dose 1						
Government						
Urban	822/1065 (77.2)	1504/1773 (84.8)	2326/2838 (82.0)	0.19	1.52 (.91–2.56)	.11
Rural	859/994 (86.4)	1276/1428 (89.4)	2135/2422 (88.2)	0.13	1.11 (.70–1.77)	.66
All government	1681/2059 (81.6)	2780/3201 (86.9)	4461/5260 (84.8)			
Private	107/121 (88.4)	116/151 (76.8)	223/272 (82.0)		…[b]	
All schools	1788/2180 (82.0)	2896/3352 (86.4)	4684/5532 (84.7)	0.21	1.22 (.84–1.78)[c]	.30
Dose 2						
Government						
Urban	765/1065 (71.8)	1449/1773 (81.7)	2214/2838 (78.0)	0.14	1.80 (1.17–2.76)	.008
Rural	831/994 (83.6)	1247/1428 (87.3)	2078/2422 (85.8)	0.12	1.12 (.72–1.73)	.61
All government	1596/2059 (77.5)	2696/3201 (84.2)	4292/5260 (81.6)			
Private	99/121 (81.8)	112/151 (74.1)	211/272 (77.6)		…[b]	
All schools	1695/2180 (77.8)	2808/3352 (83.8)	4503/5532 (81.4)	0.16	1.37 (.99–1.90)[c]	.05
Dose 3						
Government						
Urban	705/1065 (66.2)	1354/1773 (76.4)	2059/2838 (72.6)	0.11	1.72 (1.17–2.52)	.006
Rural	777/994 (78.2)	1178/1428 (82.5)	1955/2422 (80.7)	0.11	1.11 (.74–1.67)	.62
All government	1482/2059 (72.0)	2532/3201 (79.1)	4014/5260 (76.3)			
Private	90/121 (74.4)	107/151 (70.9)	197/272 (72.4)		…[b]	
All schools	1572/2180 (72.1)	2639/3352 (78.7)	4211/5532 (76.1)	0.13	1.36 (1.02–1.82)[c]	.04

Abbreviations: CI, confidence interval; ICC, intracluster correlation coefficient.

[a] Data are no. of girls eligible/no. vaccinated (%).

[b] Study was not designed to look at the effect of the strategy in private schools separately.

[c] Adjusted for school type (private, government urban, and rural).

AE Reports

Overall, 13 398 doses of vaccine were given. There were 11 AEs reported, including 3 SAEs. A generalized rash in a 12-year-old girl 24 hours after dose 1 was the only AE considered to be related to vaccination. This resolved over 1 week, and the subject was not given further doses of vaccine. There were 2 deaths. One death involved a 14-year-old girl 2 weeks after vaccination and was related to complications of paralytic ileus, and the other involved a 15-year-old girl 1 month after vaccination and was probably related to long-standing renal and cardiac disease. There were 3 episodes of proven or presumptive malaria, one of which resulted in hospital admission; 4 reports of headache and 1 report of fatigue after vaccination; and 1 presumptive chest infection.

DISCUSSION

This is the first randomized trial to evaluate alternative delivery strategies for HPV vaccination. Although there is no effective widespread targeting of younger primary school girls for vaccination programs in Tanzania, our results show that HPV vaccination is acceptable, is safe, and can be delivered with high coverage in a resource-poor setting.

Our results are comparable with those from a larger demonstration project in Uganda and with HPV vaccination programs in a number of developed countries [13–16]. The 2 studies from Uganda and Tanzania have achieved better coverage than programs in countries such as the United States, Denmark, and the Netherlands, which rely on health center visits, on-demand vaccination, or private sector provision [17–21]. A demonstration project in 2 districts in Uganda had coverage for all 3 doses of 86.3%–87.8% for its school-based delivery strategy [14]. Uganda has a long established and well-accepted program of child health interventions through its Child Days Plus activities, including tetanus toxoid immunization in school girls, delivered 2 months per annum [22, 23]. Such well-established programs are not present in many other sub-Saharan African countries, including Tanzania. Although there was a program to deliver tetanus toxoid vaccination to class 7 schoolgirls in Tanzania, this met with challenges in implementation and has recently been discontinued. In addition, public suspicion about vaccination programs arose in the mid-2000s after some pupils had adverse reactions to praziquantel

Table 3. **Findings of Logistic Regression Analysis to Examine the Effect of Class on Vaccine Uptake Within the Age-Based Strategy and of Age on Vaccine Uptake Within the Class-Based Delivery Strategy**

	Dose 1			Dose 2			Dose 3		
Strategy	Proportion (%)[a]	Odds Ratio (95% CI)	*P*	Proportion (%)[a]	Odds Ratio (95% CI)	*P*	Proportion (%)[a]	Odds Ratio (95% CI)	*P*
Age based									
Class			< .001			< .001			< .001
≤4	326/383 (85.1)	1		319/383 (83.3)	1		293/383 (76.5)	1	
5	571/688 (83.0)	1.23 (.83–1.85)		558/688 (81.1)	1.18 (.81–1.73)		522/688 (75.9)	1.35 (.96–1.90)	
6	819/1000 (81.9)	1.55 (1.02–2.34)		790/1000 (79.0)	1.37 (.93–2.02)		742/1000 (74.2)	1.57 (1.10–2.22)	
7	72/108 (66.7)	0.47 (.26–.87)		28/108 (25.9)	0.08 (.04–.15)		15/108 (13.9)	0.06 (.03–.12)	
Class based									
Age (years)			.34			.09			.06
≤12	181/211 (85.8)	1.57 (.84–2.94)		175/211 (82.9)	1.52 (.85–2.71)		167/211 (79.2)	1.78 (1.06–3.00)	
13	845/986 (85.7)	1.33 (.81–2.17)		829/986 (84.1)	1.44 (.91–2.28)		778/986 (78.9)	1.58 (1.06–2.37)	
14	805/924 (87.1)	1.32 (.82–2.14)		779/924 (84.3)	1.26 (.81–1.97)		740/924 (80.1)	1.56 (1.05–2.32)	
15	558/618 (90.3)	1.68 (1.01–2.79)		543/618 (87.9)	1.63 (1.02–2.60)		511/618 (82.7)	1.73 (1.14–2.61)	
16	293/340 (86.2)	1.14 (.67–1.93)		277/340 (81.5)	0.97 (.60–1.57)		259/340 (76.2)	1.15 (.75–1.76)	
≥17	186/215 (86.5)	1		180/215 (83.7)	1		163/215 (75.8)	1	

Analysis by conditional logistic regression, conditioning on school.

Abbreviation: CI, confidence interval.

[a] Data are no. of girls eligible/no. vaccinated (%).

as part of a deworming campaign [24]. Despite this, through a relatively limited sensitization process, we demonstrated that HPV vaccination was acceptable, and most parents at the selected schools were willing to have their daughters vaccinated.

These results are extremely encouraging for cervical cancer control program initiatives in sub-Saharan Africa. At the country level, this study has been extremely valuable for planning a national HPV immunization program. HPV vaccination is planned to be added to the national immunization program in Tanzania in 2012. Vaccine roll out is planned to take place incrementally through primary school provision, since this strategy has the best chance of achieving high coverage because, with the government's universal primary education policy, >70% of children attend primary school [25, 26].

In our setting, the class-based vaccination strategy had higher coverage and achieved vaccination of more pupils, compared with the age-based strategy. An integrated costing study has shown that this strategy was also less expensive per girl vaccinated ($52 and $67 per fully vaccinated girl in urban and rural schools, respectively), compared with the age-based

Table 4. **Reasons for Not Receiving Dose 1, by Type of School**

		Government			
Variable	Private (n = 272)	Urban (n = 2838)	Rural (n = 2422)	Any (n = 5260)	Total (n = 5532)
Vaccinated	223 (82.0)	2326 (82.0)	2135 (88.2)	4461 (84.8)	4684 (84.7)
Reasons why not vaccinated[a]					
Absent from school	0	181 (6.4)	170 (7.0)	351 (6.7)	351 (6.3)
Sick	0	2 (0.1)	2 (0.1)	4 (0.1)	4 (0.1)
Left the school	2 (0.7)	33 (1.2)	46 (1.9)	79 (1.5)	81 (1.5)
Parent refused	45 (16.5)	265 (9.3)	59 (2.4)	324 (6.2)	369 (6.7)
Pupil refused/ran away	2 (0.7)	6 (0.2)	4 (0.2)	10 (0.2)	12 (0.2)
Pregnant/suspected pregnant	0	0	1 (<0.1)	1 (<0.1)	1 (<0.1)
Allergic to vaccine	0	0	0	0	0
Other	0	22 (0.8)	5 (0.2)	27 (0.5)	27 (0.5)
Missing information	0	3 (0.1)	0	3 (0.1)	3 (<0.1)

Data are no. (%) of girls.

[a] Reason given at the last school visit by girls who were not vaccinated. Only 1 reason was recorded for each girl.

strategy ($87 and $98, respectively) [27]. Class-based delivery has several potential logistical advantages: it may be easier to liaise with parents and teachers of one specific class at a school, only one class is disrupted while vaccination is underway, and it is easier to locate pupils in one class. In this region of Tanzania, class-based delivery allowed us to vaccinate a larger number of girls than the number vaccinated during age-based delivery, not just because of better vaccine coverage but because we found substantially more girls in class 6 than girls of a single year of age in the same schools [28]. This may reflect the complexity of obtaining reliable listings of girls in a given age group when they are spread over many different classes and the relatively wide age range of girls enrolled in primary school. Disadvantages of class-based delivery include the fact that some older girls may already have become sexually active. Although the risk of acquiring HPV-16 and HPV-18 is greatest during the first few years of sexual activity, few girls are likely to have acquired both HPV-16 and HPV-18 by the time of vaccination and thus will still gain some benefit from the HPV vaccine [29]. However, the greatest effect will be obtained in sexually naive girls, and so the timing of vaccination is important. Lower vaccine coverage in older girls and those in higher classes, especially for dose 3, is likely to result from girls leaving primary school during vaccination, and this is an important consideration when selecting the appropriate national vaccination strategy.

Because of EPI capacity constraints, we were unable to pragmatically evaluate coverage through an EPI-delivery system. However, every effort was made to work with EPI staff for vaccine delivery and to mimic EPI systems.

As noted above, school-based vaccine delivery will fail to reach the 20% of girls who are not enrolled in schools and who may be especially vulnerable to acquiring HPV infection and cervical cancer. This project was not designed to deliver vaccine to out-of-school girls, and separate initiatives will need to be explored to reach this target population in sub-Saharan Africa.

We observed a higher rate of parent refusal in private schools. Some head teachers were reluctant to hold specific parent-teacher meetings. Teachers at 3 private schools were concerned about losing income from parents who might disapprove or be suspicious of activities not directly related to education of their children. Liaison with private schools, especially boarding schools, will need to be specifically addressed by any national HPV vaccination program. A national campaign of information about cervical cancer and the benefits of HPV vaccination may assist in this.

Although absenteeism from schools was the primary reason for not receiving dose 1 of the HPV vaccine in government schools, the proportion of pupils absent from school on the day of vaccination was lower than school records suggested for the previous 6 months prior to starting vaccination. There was no evidence that the presence of the vaccine team substantially increased absenteeism rates at the schools.

Attention will need to be paid to determining denominators to calculate vaccine coverage. Although the Ministry of Education & Vocational Training does collect data on the number of girls in school by age and class, more timely reporting of school statistics and checking of school class records at the time of vaccination will assist in obtaining more accurate data on vaccine coverage of eligible pupils.

In conclusion, HPV vaccination can be delivered with high coverage in sub-Saharan Africa. Class-based delivery gave higher coverage and access to more eligible girls than age-based delivery in our setting. Other countries may find specific studies to determine the best delivery strategy to use to be helpful prior to starting a national HPV vaccination program. Guidelines for the provision of HPV vaccination in Tanzania in schools are now being developed in preparation for a national vaccination program that is schedule to commence in 2012. Specific strategies will be needed to reach out-of-school girls for vaccination.

Notes

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