



Published in final edited form as:

Vaccine. 2018 July 16; 36(30): 4517–4524. doi:10.1016/j.vaccine.2018.06.009.

Assessment of vaccine wastage rates, missed opportunities, and related knowledge, attitudes and practices during introduction of a second dose of measles-containing vaccine into Cambodia's national immunization program

Aaron S. Wallace^{a,*}, Kong Krey^b, John Hustedt^c, Eleanor Burnett^a, Narin Choun^c, Danni Daniels^a, Margaret L. Watkins^a, Sann Chan Soeung^b, and Richard Duncan^d

^aGlobal Immunization Division, Centers for Disease Control and Prevention, Atlanta, GA, USA

^bImmunization Division, Ministry of Health, Phnom Penh, Cambodia

^cWorld Health Organization, Phnom Penh, Cambodia

^dUNICEF, New York, NY, USA

Abstract

Introduction—Missed opportunities for vaccination (MOV) can result in inadequate protection against disease. Although healthcare provider reluctance to open multi-dose, lyophilized vaccine vials (particularly the measles-containing vaccine [MCV]) for every eligible child due to concerns about wasting vaccine is a known reason for MOV, little is known about providers' related attitudes and practices.

Methods—In 100 randomly selected health facilities and 24 districts of Cambodia, we surveyed healthcare providers and their district supervisors regarding routine vaccine administration and wastage knowledge and practices, and child caregivers (five per facility) regarding MOV. Vaccine stock management data covering six months were reviewed to calculate facility and district level wastage rates and vaccine usage patterns for six vaccines, including a recently introduced second dose of MCV (MCV2).

Results—Response rates were 100/100 (100%) among facility staff, 48/48 (100%) among district staff, and 436/500 (87%) among caregivers. Mean facility-level wastage rates varied from 4% for single-dose diphtheria-tetanus-pertussis-hepatitis B-Haemophilus influenzae type b vaccine to 60% for 10-dose MCV; district-level wastage rates for all vaccines were 0%. Some vaccines had lower wastage rates in large facilities compared to small facilities. The mean MCV wastage rate was the same before and immediately after MCV2 introduction. Providers reported waiting for a mean of two children prior to opening an MCV vial, and 71% of providers reported offering MCV vaccination less frequently during scheduled vaccination sessions than other vaccines. Less than 5% of caregivers reported that their child had been turned away for vaccination, most frequently (65%) for MCV.

*Corresponding author. ccu7@cdc.gov (A.S. Wallace).

Discussion—Although the MCV wastage rate in our study was in line with national targets, providers reported waiting for more than one child before opening an MCV vial, contrary to vaccine management guidelines. Future research should explore the causal links between provider practices related to vaccine wastage and their impact on vaccination coverage.

Keywords

Measles; Vaccination; Cambodia; Wastage

1. Introduction

Since the beginning of the Expanded Program on Immunization (EPI) in 1974, an important strategy for reaching high immunization coverage is ensuring eligible individuals are vaccinated at every opportunity [1]. Missed opportunities for vaccination (MOV) occur when a vaccination-eligible individual interacts with a healthcare provider for any type of healthcare visit (preventative or curative care) but is not vaccinated. MOV can occur due to a wide range of issues related to both healthcare provider and caregiver knowledge, beliefs and practices [2,3]. For instance, MOV have been associated with providers' reluctance to open multi-dose vials of lyophilized vaccines, including measles-containing vaccine (MCV) and Bacillus Calmette-Guérin (BCG) vaccine, which must be discarded six hours after reconstitution or at the end of a vaccination session (whichever comes first), per World Health Organization (WHO) recommendations. Provider reluctance to open multi-dose vials when only one child or a few children are present may stem from concerns about incurring high vaccine wastage rates, but few studies have examined such provider behavior in depth.

Vaccine wastage is generally defined as the proportion of doses discarded in opened or unopened vaccine vials that are not used to vaccinate an eligible individual [4]. Generally, countries use a single nationwide estimated wastage rate per vaccine for forecasting national vaccine need and as a benchmark for monitoring wastage [5]. The WHO provides wastage-related guidance, including avoidable and unavoidable reasons for discarding vaccine. Doses discarded from an opened lyophilized vaccine vial at the end of a vaccination session are considered unavoidable wastage. Globally, recommended maximum wastage rates for multi-dose vials of preserved lyophilized vaccines range from 30 to 50% versus 5–10% for preserved liquid vaccines, since the latter type of vaccine can generally be re-used up to 28 days after opening per the WHO multi-dose vial policy (MDVP) [6]. However, some evidence indicates that these global wastage recommendations can sometimes result in healthcare providers being reluctant to open a multi-dose MCV vial for only one child or a few children due to concern about wasting a high number of doses [7–9].

Concerns about high vaccine wastage stem largely from the costs associated with discarding unused vaccine. Recent modeling analyses have examined potential ways to address wastage by modifying vaccine supply chain practices and other assumed determinants; however the models have relied heavily on assumptions due to lack of empirical data on the factors that drive wastage rates at health facility level [10–13]. Assumed determinants of wastage include size of a facility's target population, number of children expected per vaccination session, number of doses in a vial and type of vaccine. These assumptions may be better

informed by empirical data about how well providers in a variety of low and lower-middle income country settings adhere to vaccine wastage-related policies. Another concern about wastage is the potential for children to be turned away for vaccination due to healthcare providers' attempts to reduce vaccine wastage, leading to a negative effect on vaccination coverage levels and ultimately increasing the programmatic cost of vaccinating each child from both health sector and societal perspectives. Lastly, countries may benefit from a better understanding of wastage rates and the factors that drive these rates by applying this information to improve vaccine forecasting approaches. For instance, countries often use a single wastage rate for each vaccine when forecasting vaccine need; however, it may be unsuitable to apply a single rate to all areas of a country if results indicate certain operational factors (such as population density) can influence wastage rates and subsequent vaccine supply needs.

In mid-2012, Cambodia's National Immunization Program (NIP) began a rolling introduction of the second dose of measles-containing vaccine (MCV2) and initiated preparations to transition away from subsidized vaccine purchasing through external partner funding in the near future. Vaccination coverage in Cambodia is among the highest of all low and lower-middle income countries (>85% for most vaccines in 2011 when this study occurred). In Cambodia, hepatitis B and pentavalent (diphtheria-tetanus-pertussis-h epatitis B-*Haemophilus influenzae* type b) vaccines are in 1 dose vial presentations, oral polio, MCV and tetanus toxoid vaccines are in 10 dose vial presentations, and BCG vaccine is in a 20-dose vial presentation. Aiming to maintain high coverage and contain vaccine costs, the Cambodia NIP expressed interest in examining vaccine wastage rates and associated provider knowledge and practices. To do so, CDC and WHO assisted the NIP to evaluate vaccine wastage rates at the health facility (where routine vaccination sessions occur) and district level, and to assess providers' and their district supervisors' knowledge, attitudes and practices regarding vaccine wastage, usage, and management; special focus was put on MCV1 and MCV2 due to past concerns about provider reluctance to open an MCV vial whenever an eligible child is present. In addition, because MCV2 was introduced on a rolling basis throughout the country during the latter half of 2012, the study design allowed for measurement of MCV wastage immediately before and after MCV2 introduction in a portion of sampled facilities.

2. Methods

2.1. Sampling

We obtained a multi-stage random sample of districts and facilities; facilities are where routine vaccinations are provided in Cambodia. We randomly selected 19 of 79 total districts outside Phnom Penh using population proportional-to-size sampling. All five districts in Phnom Penh were purposively selected, for a total of 24 sampled nationally. For selection of facilities, the 19 selected districts outside Phnom Penh were treated as clusters; five facilities were randomly selected from each district using simple random sampling. In the five selected Phnom Penh districts, one facility was randomly selected from each, for a total of 100 sampled facilities.

2.2. Data collection

A team of trained national immunization officers collected data during May 2013. At both the district and facility levels, teams retrospectively abstracted routine vaccine stock records for the six-month data review period of July–December 2012 for an expectation of 600 monthly records across all facilities (i.e. facility-month data points) and 144 monthly records across all districts (i.e. district-month data points). No vaccination campaigns occurred during this time period. At the time of our survey, BCG, hepatitis B vaccine, oral polio vaccine (OPV), pentavalent vaccine, and MCV were provided to children, and tetanus toxoid (TT) to women of childbearing age [Table 1]. A rolling MCV2 introduction began in May 2012 and was completed by April 2013. For each vaccine, the abstracted data included monthly number of doses administered, monthly opening and closing stock balances for each vaccine and monthly number of vaccine doses received by the facility from the district.

Teams used a structured questionnaire to interview the immunization officer and cold chain officer at each district and the healthcare provider who was the primary staff member providing vaccinations at each facility. The questionnaire included self-reported knowledge, attitudes and practices related to vaccine stock management and monitoring, vaccine vial usage policies and vaccine wastage. Respondents at the district level also answered questions as to why wastage occurred at facility level and suggested approaches for managing wastage at facility level. Lastly, a convenience sample of five caregivers of children aged under 24 months and attending health services on the day of the facility data collection visit were targeted for interviews about MOV. In these interviews, they were asked whether they had ever been turned away for their child's vaccinations, if they returned after being turned away, and for which vaccines they were turned away.

2.3. Data analysis

Teams collected data on paper and then entered the data into Microsoft Excel. Before analyses, we assessed the monthly availability of data for each indicator in the formula. All analyses used SAS v9.3 (Cary, NC) survey procedures to account for the multistage stratified cluster design. Results are presented as frequencies and weighted proportions. A monthly wastage rate from a facility was excluded if the monthly stock records showed the number of vaccine-specific doses administered was greater than the stock available during the month, e.g. if the following formula used for calculating a vaccine usage rate per WHO recommendations was greater than 1:

$$\text{Vaccine usage rate} = \frac{\text{Number of doses administered in month}}{\text{Starting balance of doses} + \text{Number of doses received in month} - \text{Ending balance of doses}}$$

To measure stock record data validity, we used the previous formula. If the vaccine usage rate was negative, then the facility monthly record was defined as invalid and excluded from vaccine wastage rate calculations.

3. Calculation of facility level vaccine wastage

We used WHO-recommended formulas for calculating wastage [14]. A facility-level, vaccine-specific wastage rate was calculated based on monthly vaccine stock records and using the following formula:

$$= 1 - \left[\frac{(\text{number of doses administered})}{(\text{monthly opening balance of doses} + \text{number of doses received in month}) - (\text{monthly closing balance of doses})} \right]$$

This formula is equivalent to 1 – (vaccine usage rate).

We calculated monthly unopened and opened vaccine wastage rates using the following formulas:

$$\begin{aligned} \text{Unopened vaccine wastage rate} &= \frac{(\text{Doses discarded unopened})}{(\text{monthly opening balance of doses} + \text{number of doses received}) - \text{monthly closing balance of doses}} \\ \text{Opened vaccine wastage rate} &= \frac{(\text{Doses opened for use}) - (\text{number of children immunized})}{(\text{monthly opening balance of doses} + \text{number of doses received}) - \text{monthly closing balance of doses}} \end{aligned}$$

To obtain a monthly mean of wastage rates across facilities, we averaged across all monthly wastage rates (up to 6 rates per vaccine, per facility) available from all 100 facilities. Facility data points for a particular vaccine were excluded if a wastage rate for one or more months was below zero or above one.

For analysis of MCV wastage before and after MCV2 introduction, we excluded a facility if we were unable to determine the month the facility introduced MCV2. A pre-MCV2 facility-month was defined as a month during the data collection period when a facility had not yet introduced MCV2; a post-MCV2 facility-month was defined as a month during the data collection period when a facility had introduced MCV2; the month of introduction was defined as a post-MCV2 facility-month. To further examine how MCV2 may have affected MCV wastage rates, we conducted a sub-analysis of wastage rates among facilities with both pre-MCV2 introduction and post-MCV2 introduction stock data.

To examine skewness of the wastage rate data, we also calculated the minimum, maximum, median, and 25% and 75% quartiles for total facility-level wastage rate per vaccine over the 6-month period. We classified facility by catchment population size based on the annual under one-year-old target population; if the facility target population was >1000, it was classified as a large facility (per NIP classification) and if the target population was ≤ 1000, it was classified as a small facility.

3.1. Calculation of district-level vaccine wastage

Since vaccines are only stored at the district health office level (i.e., no vaccination occurs at this level), we used the following formula to calculate district-level, unopened, vaccine-specific wastage rates:

$$= \frac{\text{number of doses discarded unopened for any reason}}{(\text{monthly opening balance} + \text{number of doses received}) - \text{monthly closing balance}}$$

We then averaged across all district monthly wastage rates available, up to 144 (24 districts × 6 months) monthly rates per vaccine.

3.2. Analysis of KAP survey data

Frequencies and weighted percentages with confidence intervals (CI) were reported for facility- and district-level categorical KAP responses from providers and caregivers. Statistical comparisons of means between groups were conducted using p-values from t-tests, as described under survey procedures, while statistical comparisons of proportions between groups were conducted using Rao-Scott chi-square tests.

This project was determined to be non-research program evaluation by the CDC Human Subjects Office and by the national ethics committee of health research in the Cambodia Ministry of Health.

4. Results

Of the target sample, 24 (100%) district immunization officers (supervisors) and 24 (100%) district cold chain officers at 24 districts, 100 (100%) healthcare providers at 100 facilities, and 436 (87%) caregivers of children < 24 months of age were included in the KAP survey. Vaccine wastage rate data were collected from all except two districts, which did not have stock management records available [Table 2]. Five facilities were classified as large (mean under one-year-old target population of 1173); the other 95 facilities (mean under one-year-old target population of 306) were classified as small. Among facilities, 36 introduced MCV2 prior to the six-month retrospective review period, 52 during the period, and 3 after the period; 9 had an unknown date of MCV2 introduction. Of the 100 facilities, two were missing all BCG, hepatitis B and OPV vaccine stock data needed to calculate wastage for any of the six months; data were complete for all 100 facilities for MCV and TT vaccine stock data. Of the 100 facility, both data completeness and validity needed to calculate wastage for all six reviewed months varied by vaccine, ranging from a high of 84% (492) of facility-months for BCG and MCV to a low of 62% (372) of facility-months for TT. For MCV wastage analysis during MCV2 introduction, data from 45 and 405 facility-months were available for the pre- and post-MCV2 introduction periods, respectively; data from 42 facility-months from 7 facility were excluded, as it could not be determined which month the facility introduced MCV2. The mean age of children among surveyed caregivers was 10 months (age range, 2–23 months) and all but two children had received at least one vaccine.

4.1. Vaccine stock management and monitoring knowledge and practices

At almost all facilities (98%; 95% CI, 94–100%), providers reported that they request vaccine from district as they need it; the remaining providers were given vaccine based on targets predetermined by the district. When determining the amount of vaccine to request, 60% (95% CI, 43–76%) of providers reported estimating vaccine needs from the number of vaccines administered during previous months and 30% (95% CI, 13–46%) used the target

population minus the current stock. Vaccine stockouts during the previous six months were reported by 51% (95% CI, 34–68%) of providers; the majority of stockouts were hepatitis B vaccine. A slight majority of providers (59%; 95% CI, 40–78%) reported using the number of villages in their catchment area to determine the number of routine vaccination sessions to schedule each month.

4.2. Knowledge and implementation of vaccine usage policies

Among healthcare providers, 74% (95% CI, 61–87%) reported opening an OPV vial whenever an eligible child came to the facility whereas 18% (95% CI, 8–28%) reported opening an MCV vial whenever an eligible child came to the facility; 48% (95% CI, 33–66%) waited for > 1 child before opening an MCV vial. Official NIP policy is to open a vial for every eligible child irrespective of the vaccine or number of eligible children present. Providers reported they waited for a mean of 2 (95% CI, 1.8–2.6) children to be present before they opened an MCV vial and offered to vaccinate. The first dose of MCV (MCV1) was reportedly administered to children up to 24 months of age by 90% (95% CI, 81–98%) of providers. Among providers, 71% (95% CI, 55–87%) reported offering MCV at fewer vaccination sessions per month than pentavalent vaccine; pentavalent vaccine was offered a mean of 21 (95% CI, 20.1–21.5) sessions per month compared to 11 (95% CI, 8.9–12.6) sessions per month for MCV. Overall, 68% (95% CI, 53–82%) of providers reported MCV was offered 8 times per month.

Nearly all providers reported behavior consistent with MDVP guidelines; 98% (95% CI, 94–100%) re-used an open vial of OPV for up to 28 days and 84% (95% CI, 74–93%) discarded MCV 6 h after reconstitution or at the end of the vaccination session, whichever comes first. Additionally, most (86%; 95% CI, 73–99%) providers knew the MDVP applies to OPV and 63% (95% CI, 47–78%) listed at least three of five appropriate conditions for vial re-use under the MDVP.

4.3. Knowledge, attitudes and practices regarding wastage

Most providers (90%; 95% CI, 82–99%) reported that their district supervisors discussed the need to reduce vaccine wastage; on average, facility respondents reported that the target maximum wastage rate to be achieved at the facility level for MCV was 52% and district respondents responded similarly (51%). The main reasons that providers reported for vaccine wastage during the last six months were discarding of BCG and MCVs six hours after reconstitution (61%; 95% CI, 47–76%) and vial breakage (31%; 95% CI, 15–47%) [Table 3]. The majority of district respondents reported the most important reasons for wastage in their district was doses discarded six hours after reconstitution (54%; 95% CI, 30–77%) and exposure to high temperature (51%; 95% CI, 27–74%). Among facility respondents, the most frequently cited wastage management strategies were improved organization of outreach vaccination sessions (47%; 95% CI, 33–60%) and ‘batching’ or waiting for a group of children prior to opening a vial (34%; 95% CI, 20–47%). Among district respondents, the most frequently cited wastage management strategy was ‘batching’ children (65%; 95% CI, 43–87%).

4.4. Vaccine wastage rates

Mean liquid vaccine wastage rates varied between 0% and 27% whereas lyophilized vaccine wastage rates varied between 60% and 81% [Table 1]. Single-dose vaccine vials (hepatitis B and pentavalent) had the lowest mean facility-level wastage (4% and 6% respectively), whereas wastage for 10-dose vaccine vials varied between 25% and 27% for the liquid 10-dose vaccines and 60% for lyophilized 10-dose vaccines. The mean facility-level wastage rate for 20-dose BCG was highest among all vaccines at 81%. Mean wastage rates in large facilities were lower than those in small facilities for all vaccines; these comparisons reached statistical significance ($p < 0.004$) for all except MCV ($p = 0.10$). Mean facility-level wastage rates were positively skewed by 4–7 percentage points compared to median facility-level wastage rates for all vaccines except BCG and MCV, for which mean facility-level wastage rates were negatively skewed by 4 and 6 percentage points, respectively [Fig. 1]. The range for facility-level wastage rates was 0% to >90% for all vaccines except OPV. The mean unopened facility-level wastage rate ranged between 0% and 2% for all vaccines. The mean monthly district-level wastage rate was 0% (95% CI, 0–0%) for all vaccines.

The mean facility-level MCV wastage rate was 60% (95% CI, 54–67%) before MCV2 introduction (across 45 facility-months) and 58% (95% CI, 56–61%) after MCV2 introduction (across 405 facility-months); this difference was not statistically significant ($p = 0.46$). In months prior to MCV2 introduction, facilities that offered MCV 8 times per month had a wastage rate of 60% (95% CI, 52–68%) while facilities that offered MCV > 8 times per month had a wastage rate of 62% (95% CI, 51–72%). After MCV2 introduction, MCV wastage rates were 58% (95% CI, 56–61%) and 61% (95% CI, 57–64%), respectively, at facilities offering MCV 8 and > 8 times per month. Fifteen facilities had at least 1 month of vaccine stock data for both pre- and post-MCV2 introduction periods; in a sub-analysis of only these facilities, we observed no distinct temporal patterns in the facilities' MCV wastage rates before and after MCV2 introduction [Fig. 2].

4.5. Caregivers' experiences with vaccination services

Of the 436 caregivers of children < 24 months of age included in this survey, <5% reported that their child had been turned away or asked to return at another time for vaccination services; of these, 65% reported having brought their child to the facility for MCV, 25% for pentavalent vaccine and 20% for BCG vaccine. These children had a mean age of 10 months (range, 3–19 months). The most frequently mentioned reason for not receiving the vaccination on the first attempt was that no vaccination was offered on that day (35%); three respondents (15%) indicated their child had not yet reached the recommended age for the vaccine. Fifteen percent of caregivers who had been turned away reported their child had not subsequently received the missed vaccine.

5. Discussion

In our study, the majority of providers had accurate knowledge and correct practices regarding vaccine management and usage techniques related to vaccine wastage, including implementation of the MDVP, and were aware of national maximum wastage targets and strategies for reducing wastage. Mean wastage rates varied by type of vaccine and type of

facility, with overall wastage rates generally in line with the nationally recommended maximum rates for each vaccine but higher than globally recommended rates. Large facilities generally had lower wastage rates than did small facilities, lyophilized vaccines had higher rates than liquid vaccines, and wastage rates generally trended higher with a greater number of doses per vial. While providers stated that they offered MCV at fewer scheduled sessions than other vaccines, they also indicated that they only waited for 1–2 children prior to opening an MCV vial. Additionally, MOV due to being turned away for vaccination was uncommon among interviewed caregivers which may help explain the high routine vaccination coverage observed in Cambodia. Lastly, MCV wastage rates were little changed during the months immediately following MCV2 introduction, although this could be due to a lag in changes in health worker practices and slow MCV2 uptake.

How well national policies minimizing MOV are supported and prioritized over efforts to minimize wastage may play a role in the results we observed in Cambodia compared to other settings. In this study, healthcare providers indicated that they wait for 1–2 children prior to opening a vial; this number is substantially lower than the 6–7 children that providers in our Nigeria study indicated they require before opening an MCV vial [7]. The mean MCV wastage rate in our Cambodia study was also much higher than the estimated rate in the Nigeria study (19% wastage rate for MCV), which could reflect the lower threshold in Cambodia for opening an MCV vial along with other vaccine management factors. In the Nigeria study, 30% of the interviewed caregivers reported being turned away for vaccination, whereas among the interviewed Cambodian women in the current study, being turned away for vaccination was relatively rare. We hypothesize this could provide additional evidence of the linkage between wastage concerns and MOV; however, additional work is needed to test these hypotheses under a causal study design.

Another critical issue is the interplay among vaccine stockouts, wastage concerns and MOV. In Cambodia, national program managers use vaccine forecasting calculations with a substantially higher wastage rate for MCV and BCG than used in Nigeria [7]. As a result, providers in Cambodia are likely provided with substantially more vaccine stock compared to those in Nigeria, and this would allow the Cambodian providers to administer these vaccines more frequently and thus minimize MOV from turning children away. Additionally, by being provided substantial MCV buffer with the high MCV wastage rate used in the forecasting calculation, providers could have less concern about vaccine stockouts caused by opening MCV vials for only a few children, further lessening hesitancy to open an MCV vial which, in turn, minimize MOV. Such differences are an indication of how national-level authorities should think through all the levels of support needed for implementing strategies designed to minimize MOV, for instance through ensuring sufficient vaccine is ordered so healthcare providers are not forced to decide when to open a vial to vaccinate an eligible child.

This study is the first to document MCV wastage rates during MCV2 introduction in a nationally representative sample of health facilities. We collected vaccine wastage data during a period when Cambodia was introducing MCV2, which provided an opportunity to measure the possible immediate impact on MCV wastage. We did not observe a significant decrease in MCV wastage during the period immediately following MCV2 introduction as

the MCV2 introduction guidelines predict[15] given expected efficiencies when vaccinating a broader age range. Several reasons could explain such results. Any downward effects on MCV wastage after introduction of MCV2 may have a substantial lag period during which vaccine supply management and caregivers demand adapt to the additional dose in the schedule; however, we were able to analyze MCV wastage rates for only 3–4 months following MCV2 introduction, so we could not measure effects that would occur after that period. WHO/UNICEF estimates of coverage in Cambodia indicate steady MCV2 uptake that lags MCV1 coverage by 20–40%. National MCV2 coverage was 41% in 2012, the year in which MCV2 was rolled out, 49% in 2013, the first full year with MCV2 in the schedule, 59% in 2014 and 58% in 2015. By comparison, MCV1 coverage was 79% in 2012, 76% in 2013, 80% in 2014 and 81% in 2015. MCV2 is administered during the second year of life which is a new age for childhood vaccination in Cambodia, so caregivers and providers may take a while to adjust to new second-year of life vaccination visit. Secondly, the quality of administrative records for capturing MCV2 results used as the data source in this study is unknown and lapses in quality could have masked a change in vaccine wastage.

Since this survey, Cambodia changed the MCV1 dose from measles single-antigen vaccine to measles-rubella (MR) vaccine, while the MCV2 dose remained measles single-antigen vaccine; Cambodia has plans to change the second dose to MR vaccine in 2017 [16]. The wastage implications of using different formulations for the two doses, and of the transition to the same formulation for both doses, are unknown; however, rates could be monitored during this transition.

Our study is subject to several limitations. This study improved upon the methods used in our Nigeria study [7] by increasing the sample size to include nearly 10% of the facilities and 25% of all districts in Cambodia. However, we had to exclude approximately 20% of vaccine stock records because the number of children vaccinated in a month was greater than the doses available, invalidating these records for use in our analysis; we are uncertain the direction of bias in our rate estimates potentially caused by these excluded data points. The caregivers selected to participate in our study were a convenience sample among only those who attended the facility for childhood vaccination visits and thus cannot be generalized to any other populations; additionally fewer caregivers were interviewed than our target number due to fewer caregivers attending health facilities than anticipated. Healthcare providers' reported vaccination practices were based on recall rather than direct observation, thus providers may have answered in ways they believed were more correct rather than their actual practices. The time difference between the KAP surveys and the months for which wastage data were abstracted limits our ability to draw conclusions about the impact of knowledge, attitudes, and practices on wastage rates, particularly since the program introduced MCV2 during this period and that introduction could have influenced KAP. Our wastage data were collected retrospectively, which may have contributed to the lack of data completeness, and for a relatively short period, which limits our ability to understand potential temporal patterns such as seasonality or the impact of MCV2 introduction. Furthermore, data were not collected on the organization of MCV1 delivery or on the number of MCV2 doses administered at facilities where pre- and post-MCV2 introduction wastage data were available, so we cannot assess the direct relationship between MCV2 introduction and MCV wastage. Lastly, our wastage rate analysis found that

vaccine wastage rates were skewed positively or negatively for 4–7 percentage points, indicating the presence of outlier data points. In a sub-analysis of outlier data, we found that a small proportion of facilities consistently reported very low BCG and MCV wastage rates, while a small number consistently reported very high pentavalent, hepatitis B and OPV wastage rates.

The results of this survey highlight the challenges faced by front-line healthcare providers to minimize MCV wastage while eliminating missed opportunities for MCV. Future research to understand how variations in wastage practices affect coverage is needed, as are interventions to decrease provider hesitancy to open an MCV vial. Though MCV2 introduction promises to increase the number of children eligible to receive vaccine, potentially reducing wastage and increasing opportunities for vaccination, our results suggest that these benefits may not materialize immediately. More robust evaluations of wastage are needed as countries introduce MCV2, particularly addressing the forecasting of MCV needs in the context of MOV, lagging MCV2 uptake and within-country variation in wastage. Common wastage modeling assumptions, including how a smaller MCV vial size (e.g. 5-dose vial versus a 10-dose vial) may influence wastage and provider reluctance to open a vial, should also be evaluated.

References

1. Expanded Programme on Immunization. World health organization global advisory group meeting summary. *Wkly Epidemiol Rec.* 1984; 59:85–9.
2. Hutchins SS, Jansen HA, Robertson SE, Evans P, Kim-Farley RJ. Studies of missed opportunities for immunization in developing and industrialized countries. *Bull World Health Organ.* 1993; 71(5): 549–60. [PubMed: 8261558]
3. Sridhar S, Maleq N, Guillermet E, Colombini A, Gessner BD. A systematic literature review of missed opportunities for immunization in low- and middle-income countries. *Vaccine.* 2014; 32(51): 6870–9. [PubMed: 25444813]
4. Monitoring vaccine wastage at country level: Guidelines for programme managers. World Health Organization; Geneva, Switzerland: 2005.
5. WHO vaccine-preventable diseases: joint reporting form summary. World Health Organization; Geneva, Switzerland: 2015.
6. WHO Policy Statement: The use of opened multi-dose vials of vaccine in subsequent immunization sessions. World Health Organization; Geneva, Switzerland: 2000.
7. Wallace A, Willis F, Nwaze E, Dieng B, Sipilanyambe N, Daniels D, et al. Vaccine wastage in Nigeria: an assessment of wastage rates and related vaccinator knowledge, attitudes and practices. *Vaccine.* 2017; 35(48):6751–8. [PubMed: 29066189]
8. Fisker AB, Hornshøj L, Rodrigues A, Balde I, Fernandes M, Benn CS, et al. Effects of the introduction of new vaccines in Guinea-Bissau on vaccine coverage, vaccine timeliness, and child survival: an observational study. *Lancet Glob Health.* 2014; 2(8):e478–87. [PubMed: 25103521]
9. World Health Organization, African Regional Office. Mid-Level Management Course for EPI Managers. 2004. p. 1-54.
10. Parmar D, Baruwa EM, Zuber P, Kone S. Impact of wastage on single and multi-dose vaccine vials: implications for introducing pneumococcal vaccines in developing countries. *Human Vaccines.* 2010; 6(3):270–8.
11. Assi TM, Brown ST, Djibo A, Norman BA, Rajgopal J, Welling JS, et al. Impact of changing the measles vaccine vial size on Niger's vaccine supply chain: a computational model. *BMC Public Health.* 2011; 11:425. [PubMed: 21635774]

12. Lee BY, Assi TM, Rookkapan K, Connor DL, Rajgopal J, Sornsrivichai V, et al. Replacing the measles ten-dose vaccine presentation with the single-dose presentation in Thailand. *Vaccine*. 2011; 29(21):3811–7. [PubMed: 21439313]
13. Lee BY, Norman BA, Assi TM, Chen SI, Bailey RR, Rajgopal J, et al. Single versus multi-dose vaccine vials: an economic computational model. *Vaccine*. 2010; 28(32):5292–300. [PubMed: 20566395]
14. Monitoring vaccine wastage at country level: guidelines for programme managers. World Health Organization; Geneva, Switzerland: 2005.
15. A Guide to Introducing a Second Dose of Measles Vaccine into Routine Immunization Schedules. World Health Organization; Geneva, Switzerland: 2013.
16. GAVI Annual Progress Report 2012. Cambodia Ministry of Health; 2013. Available from: <http://www.gavi.org/country/cambodia/documents/#approvedproposal>

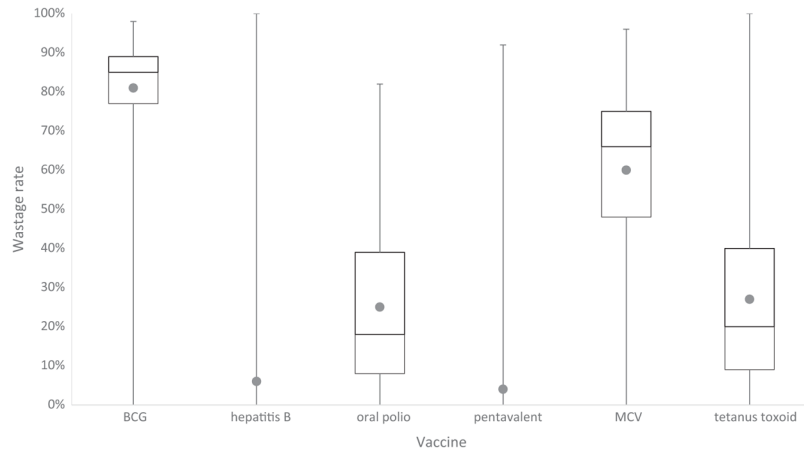


Fig. 1. Mean and median monthly vaccine wastage rates for six vaccines in 100 health centers; Cambodia, July-December 2012. Dot indicates mean wastage rate per vaccine; boxplot for each vaccine includes minimum, 25%, 50% and 75% quartiles, and vertical bars indicate minimum and maximum wastage values across the 100 health facilities. Definitions: BCG = bacillus Calmette Guerin vaccine; OPV = oral polio vaccine; MCV = measles-containing vaccine; pentavalent = diphtheria-tetanus-pertussis-HepB-*Haemophilus influenzae* type b vaccine; TT = tetanus toxoid.

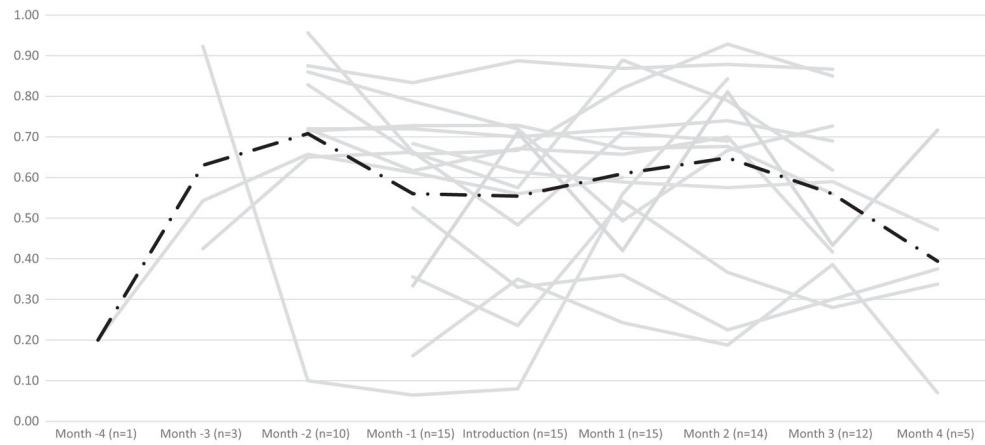


Fig. 2. Monthly measles-containing vaccine wastage rates for fifteen health facilities in Cambodia that introduced an MCV second dose (MCV2) during the data collection period, organized by time to MCV2 introduction. The dotted line indicates the mean vaccine wastage rate. *n indicates the number of health facilities with data points for the month prior to or after MCV2 introduction.

Table 1
Mean monthly vaccine wastage rates in 100 health centers; Cambodia, July–December 2012.

Vaccine and timeframe given (n = number of facility-months ^a analyzed)	Type	Doses in series	Doses in vial	National target maximum wastage rate ^e	Total wastage rate, mean % (95% CI)	Total wastage rate in large ^b health centers, mean % (95% CI)	Total wastage rate in small ^b health centers, mean % (95% CI)	Open vial wastage rate, mean % (95% CI)
<i>Birth</i>								
hepatitis B (n = 378)	Liquid	1	1	0	6 (5, 8)	1 (0, 1)	6 (5, 8)	1 (1, 2)
BCG (n = 492)	Lyophilized ^e	1	20	75	81 (79, 82)	75 (72, 79)	81 (80, 82)	78 (77, 80)
<i>Childhood</i>								
pentavalent (n = 420)	Liquid	3	1	0	4 (2, 5)	1 (0, 2)	4 (2, 5)	1 (0, 1)
polio (n = 390)	Liquid	3	10	25	25 (23, 27)	13 (6, 21)	25 (23, 27)	22 (20, 24)
MCV (n = 492)	Lyophilized	2 ^f	10	50	60 (57, 62)	45 (33, 57)	60 (57, 62)	56 (54, 58)
MCV, pre-MCV2 ^c (n = 45)	Lyophilized	2 ^f	10	50	60 (54, 67)	NA ^d	62 (56, 68)	59 (52, 66)
MCV, post-MCV2 ^c (n = 405)	Lyophilized	2 ^f	10	50	58 (56, 61)	53 (48, 58)	61 (58, 63)	56 (54, 58)
<i>Maternal</i>								
tetanus toxoid (n = 372)	Liquid	5	10	25	27 (25, 30)	14 (8, 21)	27 (25, 30)	23 (20, 25)

Definitions: CI = confidence interval; BCG = bacille Calmette-Guerin vaccine; MCV = Measles-containing vaccine; MCV2 = Measles-containing vaccine, second dose; pentavalent = diphtheria-tetanus-pertussis-hepatitis B-*Haemophilus influenzae* type b vaccine; open vial wastage = waste of vaccine that occurs after a vial has been opened for use; total wastage = sum of open and unopened vaccine wastage.

^aFacility months = 6 months of vaccine stock records were abstracted from each health center for a total target of 600 facility-months of records; some monthly records for certain vaccines were excluded due to data inconsistencies.

^bLarge health center defined as serving an estimated under one-year old population > 1000 (mean size = 1173); small health center defined as serving an estimated under one-year old population of 1000 (mean size = 305).

^cPre-MCV2 is during the period prior to MCV2 introduction and post-MCV2 is after MCV2 introduction.

^dNot applicable: All large health facilities had introduced MCV2 by the start of this study's data review period so no pre-MCV2 data were collected.

^eRate used by country for forecasting vaccine need and provided to health sector for performance monitoring purposes.

^fCambodia began a rolling introduction of a second routine dose of measles-containing vaccine throughout the 2nd half of 2012, completed by end of April 2013.

Table 2

Characteristics of districts and health centers surveyed for a study of vaccine wastage rates and related healthcare provider knowledge, attitudes and practices in Cambodia, 2013.

	Number	% or (range)
<i>District (N = 24)</i>		
Mean annual births (range)	160,448	(3359, 361,279)
Mean number of health centers per district (range)	14	(3, 26)
Number of districts with complete and valid data available to calculate wastage rate over 6-month period ^a		
BCG vaccine	22	92
Hepatitis b vaccine	17	71
Oral polio vaccine	21	88
Pentavalent vaccine	21	88
Measles-containing vaccine	21	88
Tetanus toxoid	18	75
<i>Health centers (N = 100)</i>		
Large (under 1-year old population > 1000)	5	5
Mean under 1-year old population (range)	1173	(560, 2139)
Small (under 1-year old population < 1000)	95	95
Mean under 1-year old population (range)	306	(235, 393)
Timing of MSD ^b introduction at facility		
Before data review period ^c	36	36
During data review period ^c	52	52
After data review period ^c	3	3
Unknown introduction date	9	9
Number of facilities with complete and valid data available to calculate wastage rate over 6-month period ^a		
BCG Vaccine	84	84
Hepatitis B Vaccine	65	65
Oral polio vaccine	67	67
Pentavalent vaccine	70	70
Measles-containing vaccine	82	82
Tetanus toxoid	62	62

Definitions: facility = health center; BCG = Bacillus Calmette-Guérin vaccine; pentavalent vaccine: diphtheria-tetanus-pertussis-hepatitis B-*Haemophilus influenzae* type b.

^aDistrict or facility has all data needed to properly calculate a monthly vaccine wastage rate for 6-month study period.

^bMCV2 = measles second-dose. Pre-MCV2 is during the period prior to MCV2 introduction and post-MCV2 is after MCV2 introduction.

^cData review period = 6-month period (July–December 2012) for which vaccine stock data were abstracted.

Vaccine wastage knowledge and practices among health sector staff at 100 health facilities and 20 districts in Cambodia, 2013.

Table 3

	Health center			District		
	No.	%	95% CI	No.	%	95% CI
<i>Reported reasons for wastage</i>						
Discard 6 h after reconstitution or end of vaccination session, whichever first occurs (BCG, MCV only ^a)	60	61	47, 76	12	54	30, 77
Discard after opened, MDVP-eligible ^b vaccines at end of session	19	18	4, 31	8	41	18, 65
Breakage	29	31	15, 47	11	44	21, 67
Expiry date has passed	20	20	5, 34	12	47	24, 70
Exposure to high temperature	20	18	7, 30	13	51	27, 74
Inability to get all doses from vial	9	10	0, 19	4	17	0, 37
Exposure to freezing	5	5	1, 9	7	18	4, 33
Spillage	3	2	0, 4	3	9	0, 19
Do not know	2	2	0, 4	0	0	0, 0
Other	6	6	0, 11	10	57	35, 80
<i>Reported strategies for managing wastage</i>						
Improve stock management	30	33	14, 51	9	28	8, 48
Batch children	35	34	20, 47	14	65	43, 87
Better organize outreach vaccination sessions	47	47	33, 60	10	39	16, 62
Improve community mobilization	30	31	13, 48	4	18	2, 35
Implement FIFO/EEFO ^c	19	21	10, 31	4	22	0, 43
Implement MDVP	19	21	8, 34	9	36	13, 58
Change number of vaccination sessions	26	27	13, 41	5	19	1, 37
Request change in number of doses per vial	27	25	6, 44	8	30	10, 50
Other	6	6	0, 12	4	26	5, 48

Definitions: CI = confidence interval; BCG = bacille Calmette-Guerin vaccine; MCV = measles-containing vaccine.

^aBoth BCG and MCV are lyophilized and must be reconstituted for use.

^bMDVP = multi-dose vial policy, which indicates that certain vaccines (polio vaccine, tetanus vaccine) can be reused up to 28 days once opened, provided they are stored under certain conditions.

^cFIFO/EEFO = First in, first out/earliest to expire, first out. A practice designed to ensure those vaccine vials that are the soonest to expire and/or the earliest ones placed in the cold chain, are prioritized for use above any other vaccine vial.