Delivering R21 vaccine through seasonal malaria chemoprevention: coverage and qualitative insights from cluster-randomised trials in Burkina Faso, Mali, and Chad

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Conflict of interest: the authors have declared no conflict of interest.

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Background

Malaria in children in the Sahel

(WHO 2023 estimates)

Children under five represent ~40% of all malaria cases and ~80% of malaria deaths

- Burkina Faso: 10.8 million malaria cases overall; 25,000 deaths in children under five
- Mali: 3.6 million cases; 12,000 deaths in children under five
- Chad: 3.9 million cases; 15,000 deaths in children under five

R21/Matrix-M malaria vaccine

- Recommended by WHO since 2023
- Offers **75%** reduction in malaria episodes
- Target age group: generally 6-11 months, can extend to up to 24 months
- Three doses primary series one month apart, booster required at ~one year
- Not aligned with other vaccines, requires additional visits
- High coverage <u>across all doses</u> is essential to maximise impact, although challenging to achieve through the Essential Immunisation Programme (EPI)

2025 administrative coverage data from early adoption countries (Dose 3)

Niger	**39%**
Cote d'Ivoire	**43%**
Benin	**44%**
Burkina Faso	**72%**

HOW to deliver R21 at scale, efficiently, and equitably?

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Can Seasonal Malaria Chemoprevention (SMC) be leveraged to deliver R21?

Seasonal malaria chemoprevention (SMC) is a well-functioning, trusted platform

- Antimalarials (sulfadoxine-pyrimethamine plus amodiaquine) given monthly during the rainy season in areas of seasonal transmission
- Reaches over 50 million children aged **3–59 months** annually in West Africa
- Has proven effectiveness and strong community acceptance

Integration of the R21 vaccination with existing SMC campaigns aims to create a synergy

Hypotheses: The integrated approach will

- **Enlarge the vaccine eligible age group**
- **Improve vaccine coverage and reduce dropout**
- Offer protection extending post SMC
- Ultimately, show reduction in incidence of uncomplicated and complicated malaria during the peak season and limit rebound
- Improve access and cost-effectiveness

Trial settings

	IMVACS trial* June 2025-Oct 2028		CoSAV-R21/ INTEGREVAC trial* June 2025-Dec 2027
Country	**BURKINA FASO**	**MALI**	**CHAD**
Implementing partner	MoH, Unité de recherche clinique de Nanoro	MoH, University of Sciences and Techniques of Bamako	MoH, **MSF OCP**
District	Bousse	Dioila	Moissala and Dembo
Number of study clusters (health areas)	10+10	8+8	13+13
Estimated under-five population	~ 15,000	~ 33,000	~ 100,000
Routine SMC strategy	Target: 3 to 59 months Delivered door-to-door 4 rounds in July, Aug, Sep, Oct	Target: 3 to 59 months Delivered door-to-door or at fixed point 4 rounds in July, Aug, Sep, Oct	Target: 3 to 59 months Delivered door-to-door 5 rounds in June, July, Aug, Sep, Oct
Routine R21 vaccination strategy	Target: 3 to 36 months Delivered at health facility all year	Target: 3 to 36 months Delivered at health facility all year Sensitisation campaign in June Advanced vaccination in villages a few days per month	Target: 6 to 11 months Delivered at health facility all year

*Study protocols were approved by national ethics committees, by the Médecins Sans Frontières Ethics Review Board (MSF ERB) and by ethics committee of the Liverpool School of Tropical Medicine

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Trial design

Cluster randomised trials

Health areas randomised to intervention or routine arm

Participants enrolled during 2025 malaria season (vaccinations started in June 2025)

evaluating two R21 delivery strategies

Nested coverage surveys and qualitative surveys

Intervention

R21 vaccination integrated into SMC

- Three doses of the primary series of R21 vaccine delivered alongside SMC in 2025 and booster at 1st SMC round in 2026 **SEASONAL**

- **R21 target age groups: 3-59m (Burkina Faso, Mali) 6 –59m (Chad)**
- Location of vaccination:
  - At home (door-to-door) in Burkina Faso
  - Fixed sites in villages in Mali and Chad

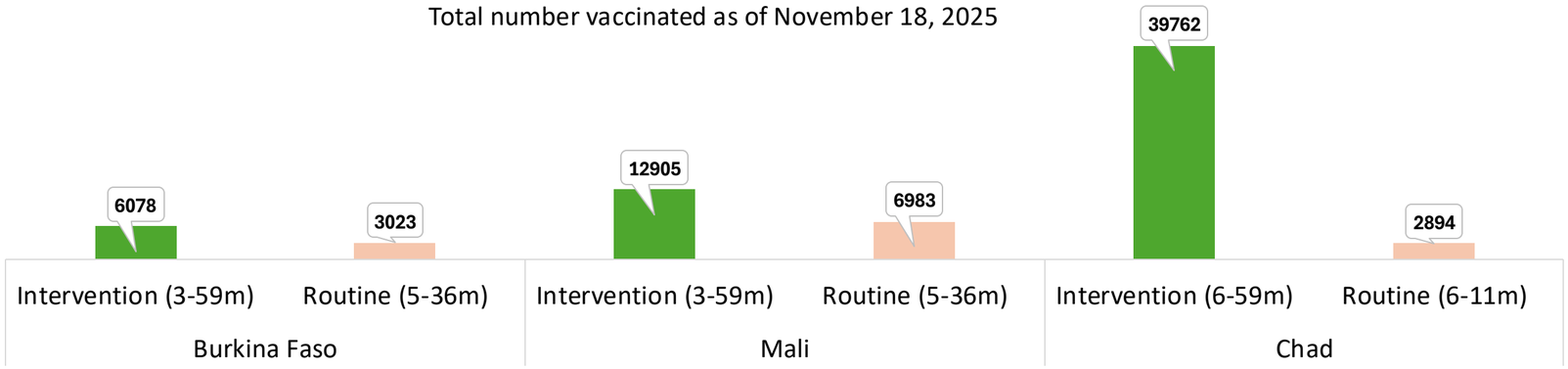
Routine

R21 through Essential Immunisation Programme (EPI)

- R21 vaccination aged-based, **ALL YEAR**, at health centre
- SMC in campaign, according to the strategy in place (business as usual)

- **R21 target age groups: 5-36m (Burkina Faso, Mali) 6-11m (Chad)**

Total number vaccinated as of November 18, 2025



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Coverage survey methods

Primary objective

to estimate the vaccine's primary series coverage and SMC coverage during 2025 season

Design

Cross-sectional household surveys nested in trials, conducted in Nov-Dec 2025

- **Simple** random sampling in Burkina Faso and Mali

- **Two-stage** cluster geopoint sampling in Chad

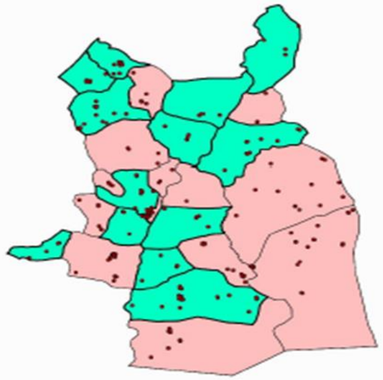
Data collection

Caregiver interviews with vaccination and SMC status recorded (card-verified when available)

Analysis

Coverage estimated accross different arms/ countries/ strategies/ rounds

Results in percentage and 95% confidence interval



Geographical distribution of mini-clusters of 5-7 households surveyed in Moissala and Dembo, Chad.
Green: Intervention areas

Survey denominators

	BURKINA FASO		MALI		CHAD	
	Intervention	**Routine**	**Intervention**	**Routine**	**Intervention**	**Routine**
Total numbers of children surveyed	412	412	412	412	902	1254
Numbers in target age groups						
Vaccination	408	239-254*	410	216-235*	858	175-218*
SMC	399-407*	404-405*	406-409*	405-407*	832-874*	1978-2107*

*Denominators used for the different coverage estimates can vary depending on vaccine doses and SMC rounds (ranges shown)

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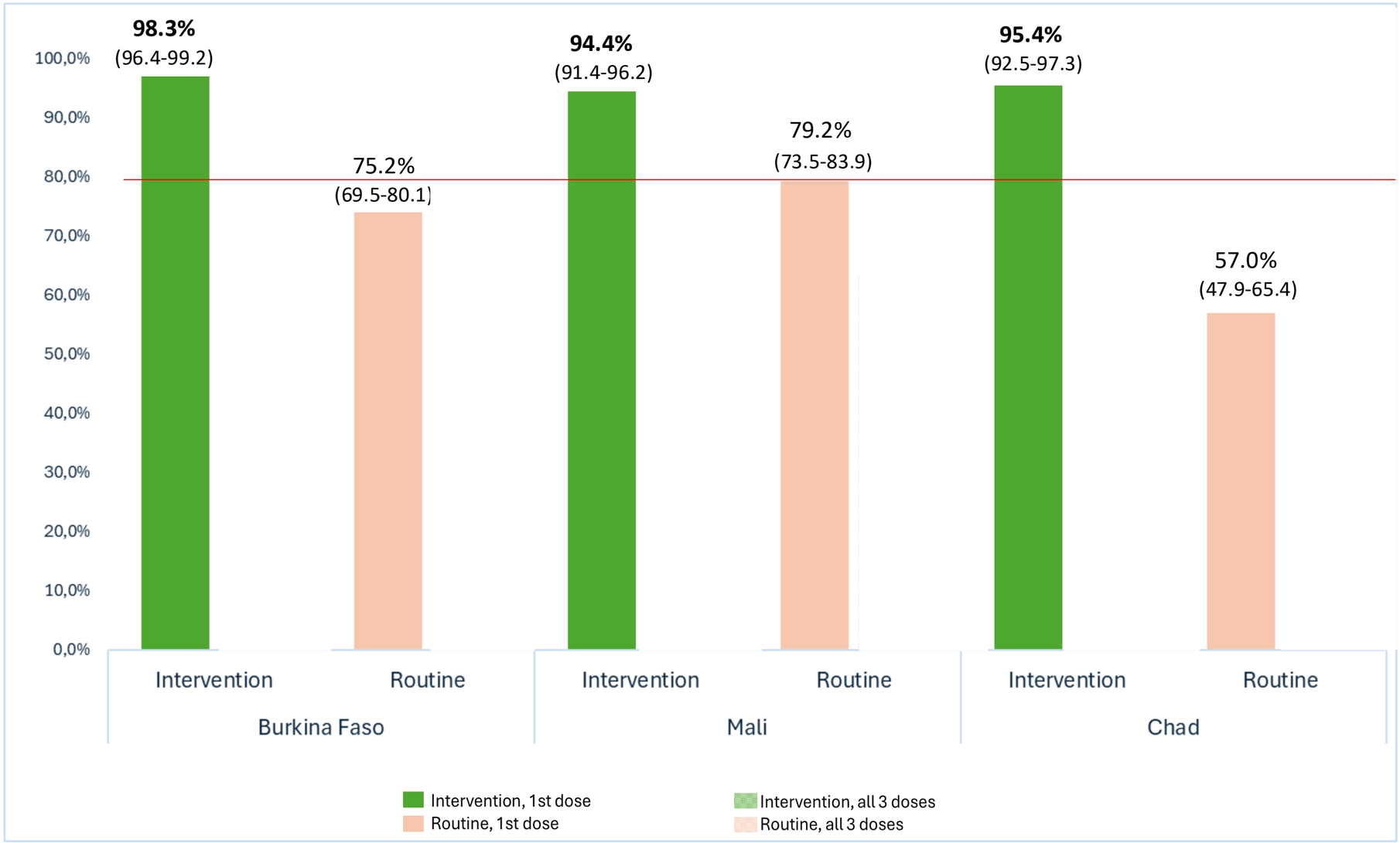
Survey results: Vaccine coverage

In all countries, intervention arms achieved **higher R21 coverage of first dose**

Data are based on vaccination cards and verbal recall



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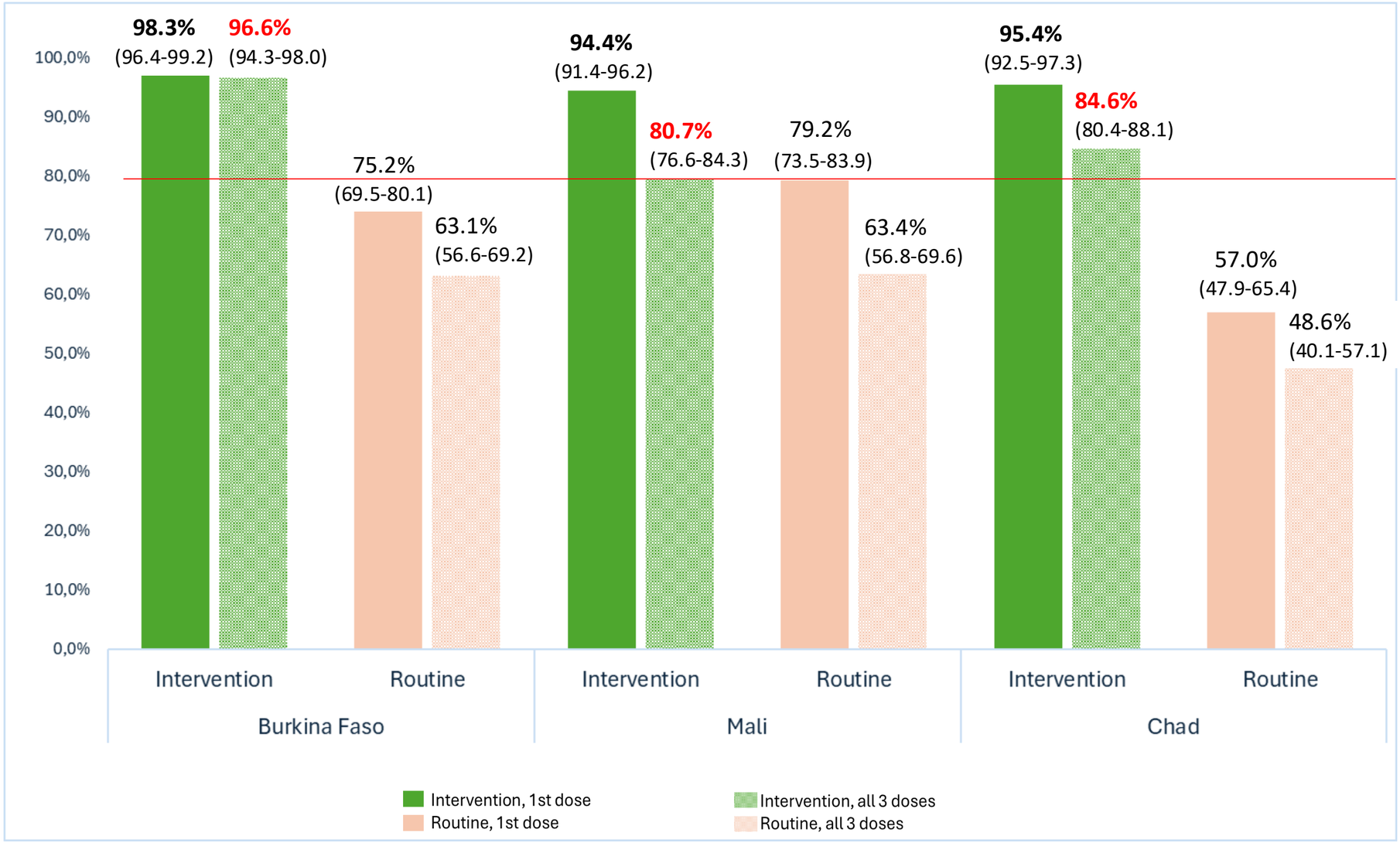
Survey results: Vaccine coverage

In all countries, intervention arms achieved **higher R21 coverage of first dose** and **higher coverage of the full 3-dose primary series**

Data are based on vaccination cards and verbal recall



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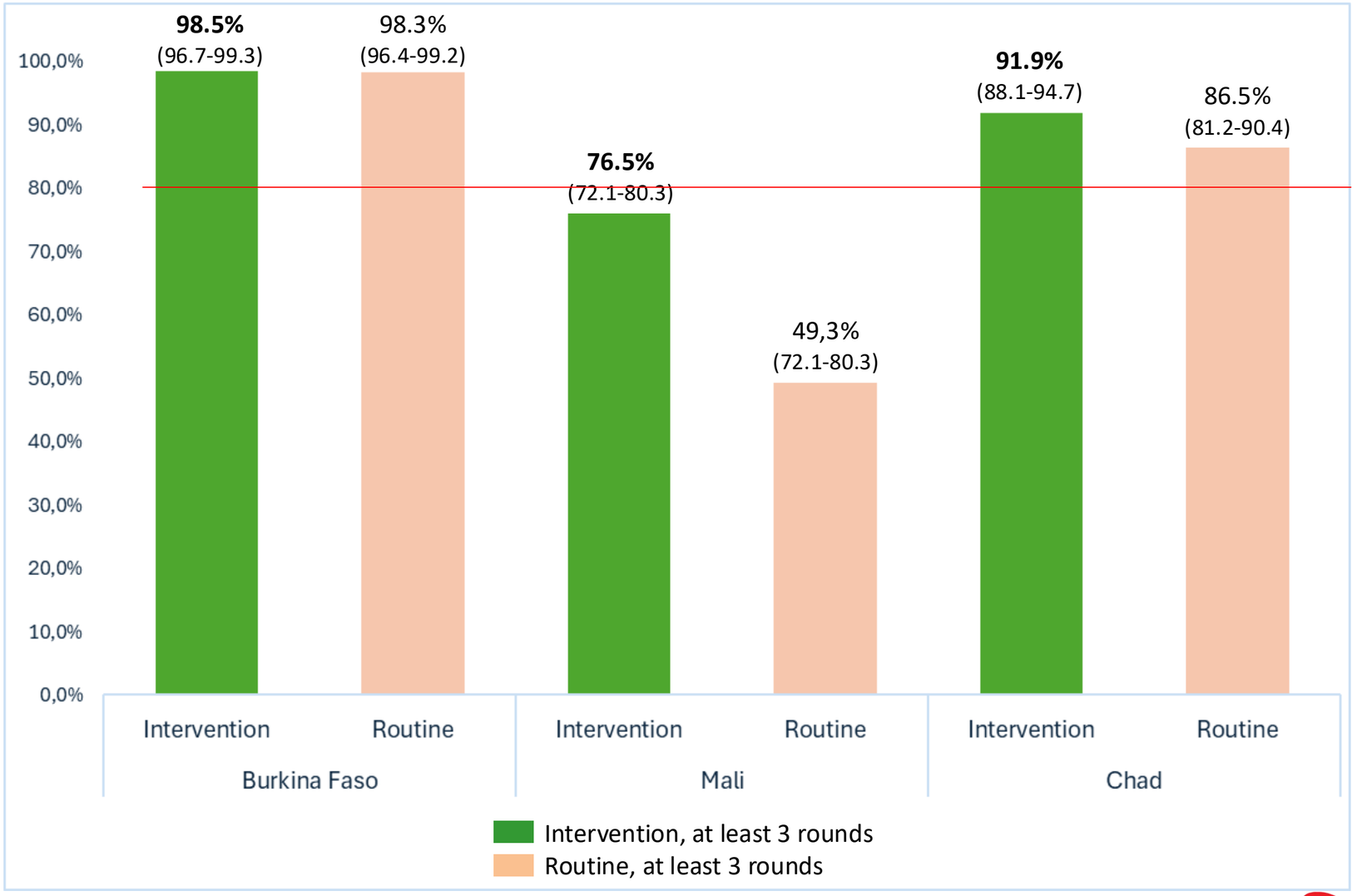
Survey results: SMC coverage

- **Synchronised delivery did not reduce SMC uptake:** coverage was similar or higher in intervention arms
- Substantial variation across countries

Data are based on vaccination cards and verbal recall



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Qualitative methods

OBJECTIVE

To assess the acceptability and feasibility of each vaccination strategy among policy makers, health managers, health providers and caregivers

DESIGN

Cross-sectional design, November 2025 to January 2026 (after the primary series vaccination)
In-depth interviews and focus group discussions

METHODS

Caregivers

- Caregivers of eligible children 3-59 months (intervention) and 5-36 (control)
- Randomly sampled caregivers for cohort included 40 in Burkina Faso, 24 in Mali, total across both arms
- Purposively sampled caregivers included 30 in Burkina Faso, 24 in Mali and 34 in Chad, total across both arms

Health managers, providers and SMC agents

- Purposive selection across both intervention arms included 30 in Burkina Faso, 32 in Mali, and 49 in Chad
- Health providers - in EPI facilities (control) and R21 vaccinators (intervention)
- CHW/SMC agents (control & intervention)

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Acceptability: stakeholder perceptions of routine delivery

"The difficulty is if it becomes too much for the children in a single day. There are vaccination days when there are many injections, so if this is added on top, it could become too much for them…" **Caregiver, Mali**, routine arm, 2 doses

"I prefer the strategy of vaccinating in the routine arm. That way, the child can receive the vaccine at any time. Now, with the SMC Campaign, it's only when the SMC is due that the child receives it". **R21 vaccinator**, **BF** intervention arm

CAREGIVERS

- Added benefits of attending EPI – health education, other interventions
- Health providers at facilities are better skilled
- Better facilities, waiting areas
- Long wait times
- **Too many injections at some appointments**

HEALTH PROVIDERS

- **Continuous availability of R21 at EPI clinics is an advantage**
- Demand for R21 provides opportunities to catch up missed vaccines
- Narrower age range for receiving the R21 compared to integrated arm

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Acceptability: stakeholder perceptions of integrated delivery

" … administering the malaria vaccine and the SMC together would be more effective and provide better protection. That is indeed the idea behind administering these two products at the same time." **Caregiver, Chad,** Intervention arm

"The strategy of the masses is better because…there are constraints, but it allows us to reach a large number of children. It even makes sure to touch all the children, since these are door to door. But when it's at the health facility you don't know who came, who didn't come." **Health manager, BF**, Intervention arm

CAREGIVERS

- Improves access for children who do not go to EPI
- **Giving R21 and SMC together provides better protection**
- Some concerns about overdosing when given together

HEALTH PROVIDERS

- **Will reach more children across a wider age range**
- Increased protection during high transmission season
- Inaccessible villages during rainy season

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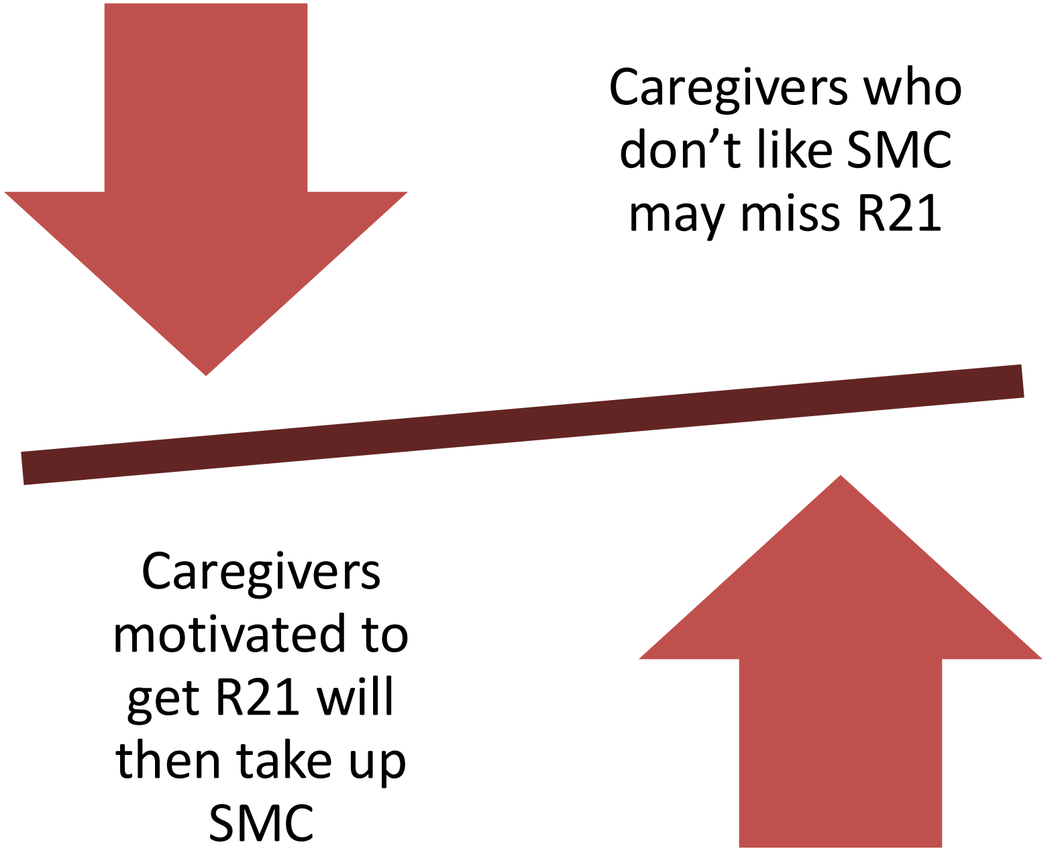
Perceived potential impact of integrated delivery on uptake of either SMC or R21

"It has been beneficial for SMC and not a drawback, because thanks to R21 many people now come for SMC administration…

… But with the introduction of R21, those who completed the first round were able to complete the third round, meaning they received the third dose."
(**CHW, Mali**, intervention)



Caregivers who don't like SMC may miss R21

Caregivers motivated to get R21 will then take up SMC

"…that it becomes the injection, the vaccine, you see what I mean. That's what they prefer more than the tablets. So, if these tablets are not phased out, it could create difficulties for the R21."
(**HP, Mali**, routine)

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Summary of stakeholder perceptions of integrated delivery versus routine delivery

ADVANTAGES

- Access hard-to-reach children & those who do not attend EPI
- R21 with SMC is complementary, optimises duration of protection

DISADVANTAGES

- R21 availability limited to campaigns
- Missed opportunity to catch up on other missed vaccines compared to EPI

Discussion: study limitations

Inherent limitations

- Missing vaccination and SMC cards (recall bias)
- Hard-to-define denominators
- Vaccination still ongoing in routine arms at the time of the survey
- Qualitative data are preliminary, analysis is ongoing

We don’t have the full picture yet

Some evidence is still needed to inform the integrated strategy

- **Primary outcome: Impact on malaria incidence** 12 months after the first dose, including severe disease and hospitalisations **Results expected in 2027**
- Other key secondary outcomes: **Results expected in 2028**
  - **Equity**
  - **Costs** and **cost-effectiveness**
  - Effectiveness and feasibility of **delivering the booster dose through SMC**

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Take away messages

- Integrating malaria vaccination with SMC **increases coverage of the full primary series**
- Integration **does not impair SMC coverage**
- Integrated delivery of the primary doses **is valued by health providers and caregivers**
- Integration **expands access to older and hard-to-reach children** often missed by routine vaccination services

Potential operational implications and impact

- **Settings with existing SMC**
  - Integrated vaccination may improve effectiveness and efficiency
    - Extended protection beyond SMC cycles and reduced end-of-season rebound
    - **Greater timing flexibility**, enabling earlier SMC start
  - **Hybrid delivery models** allowing some doses to be given with SMC and others via routine EPI

- **Settings without SMC (displaced populations or sharp seasonal peaks)**
  - Evidence supports **feasible and acceptable campaign-based vaccine delivery**
  - Vaccination can be integrated into non-SMC prevention campaigns

- **Beyond MSF**
  - Findings inform advocacy and national, global, and WHO guidance on integrated seasonal strategies

Thank you

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Caregivers, children and the communities

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Other results on costs incurred by caregivers, malaria prevalence, coverage of other antigens etc could not be presented here, happy to discuss during the coffee break

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