

An integrated newborn care kit (iNCK) to save newborn lives and improve health outcomes in Gilgit-Baltistan, Pakistan: An open-label cluster-randomised controlled trial

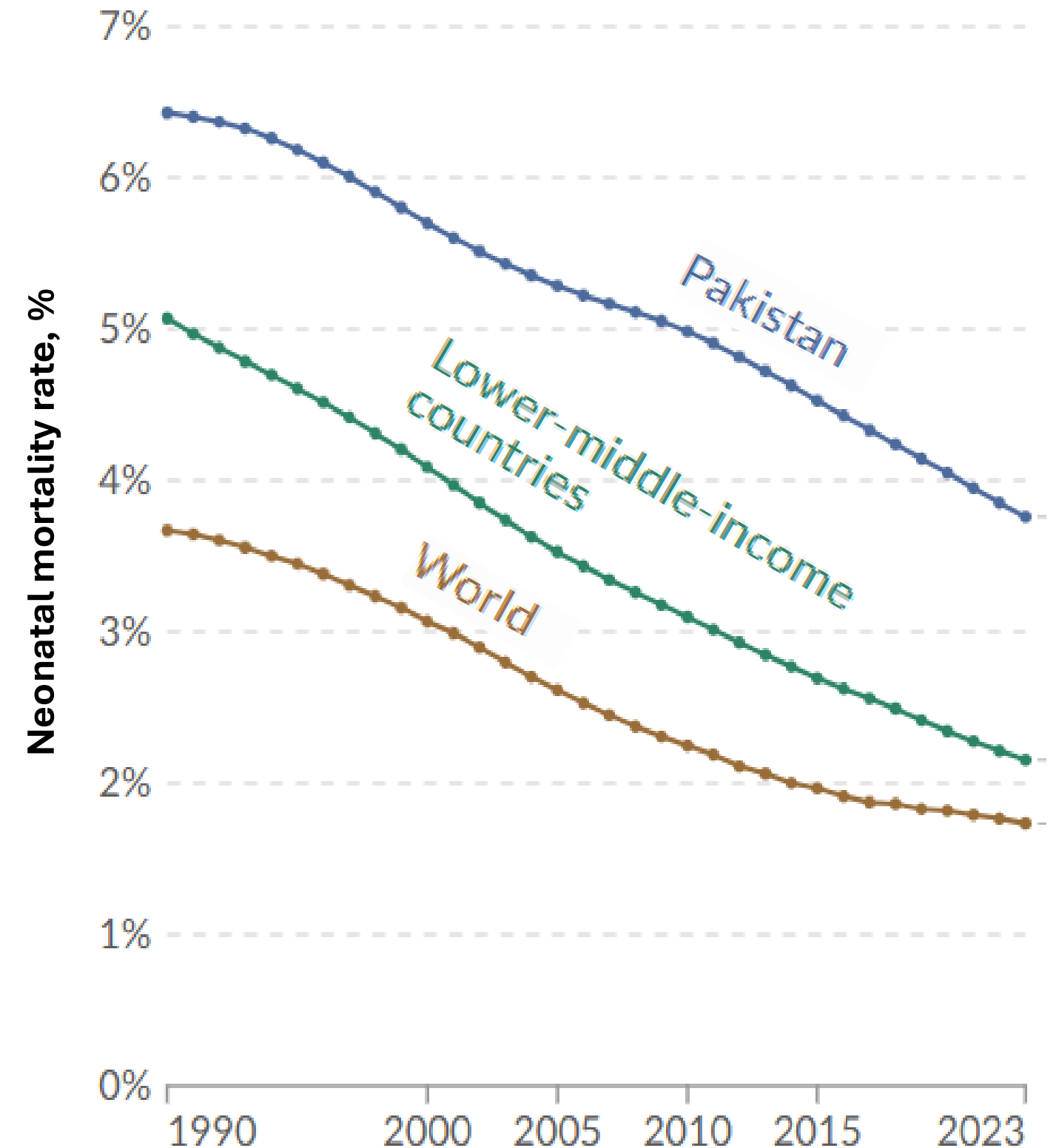
Daniel S. Farrar for the GB iNCK Study Team

COI: The author has declared no conflict of interest.



Neonatal Mortality

- Since 2000, global declines in neonatal mortality (↓44%) lag behind progress for under-5 mortality (↓51%)
- Pakistan experiences high neonatal mortality, around 38–40 newborn deaths per 1000 live births
- Most newborn deaths are from preventable causes (e.g., birth asphyxia, complications of prematurity, infection)



Neonatal mortality, 1990–2023

(Our World in Data)

<https://ourworldindata.org/grapher/neonatal-mortality-wdi>

Integrated Newborn Care Kit (iNCK)

Portable Easy-to-Use Low-Cost
Integrated Evidence-Based

(A) Clean birth kit

(B) Chlorhexidine 4% gel

(C) Three misoprostol tablets

(D) Sunflower oil emollient

(E) ThermoSpot™ thermoindicator sticker

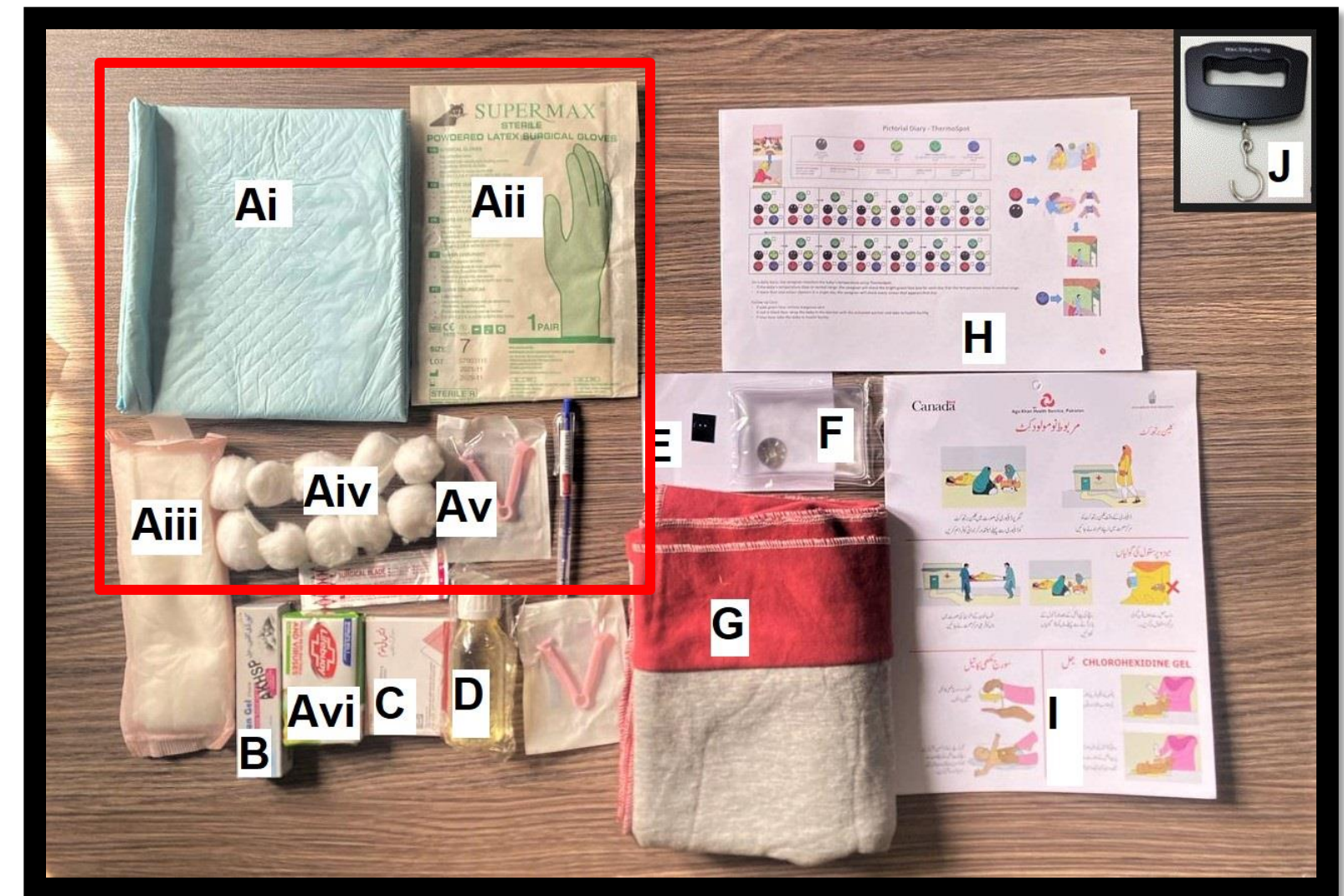
(F) Click-to-heat warmer

(G) Fleece blanket

(H/I) Pictorial diary and guide

(J) Weighing scale

**Delivered to pregnant women by Lady Health
Workers during the third trimester of pregnancy**



(A) Clean birth kit:

Used at time of delivery regardless of location of delivery. Includes plastic sheet, sterile blade, sterile cord clamp, gloves, and soap.

Integrated Newborn Care Kit (iNCK)

Portable Easy-to-Use Low-Cost
Integrated Evidence-Based

(A) Clean birth kit

(B) Chlorhexidine 4% gel

(C) Three misoprostol tablets

(D) Sunflower oil emollient

(E) ThermoSpot™ thermoindicator sticker

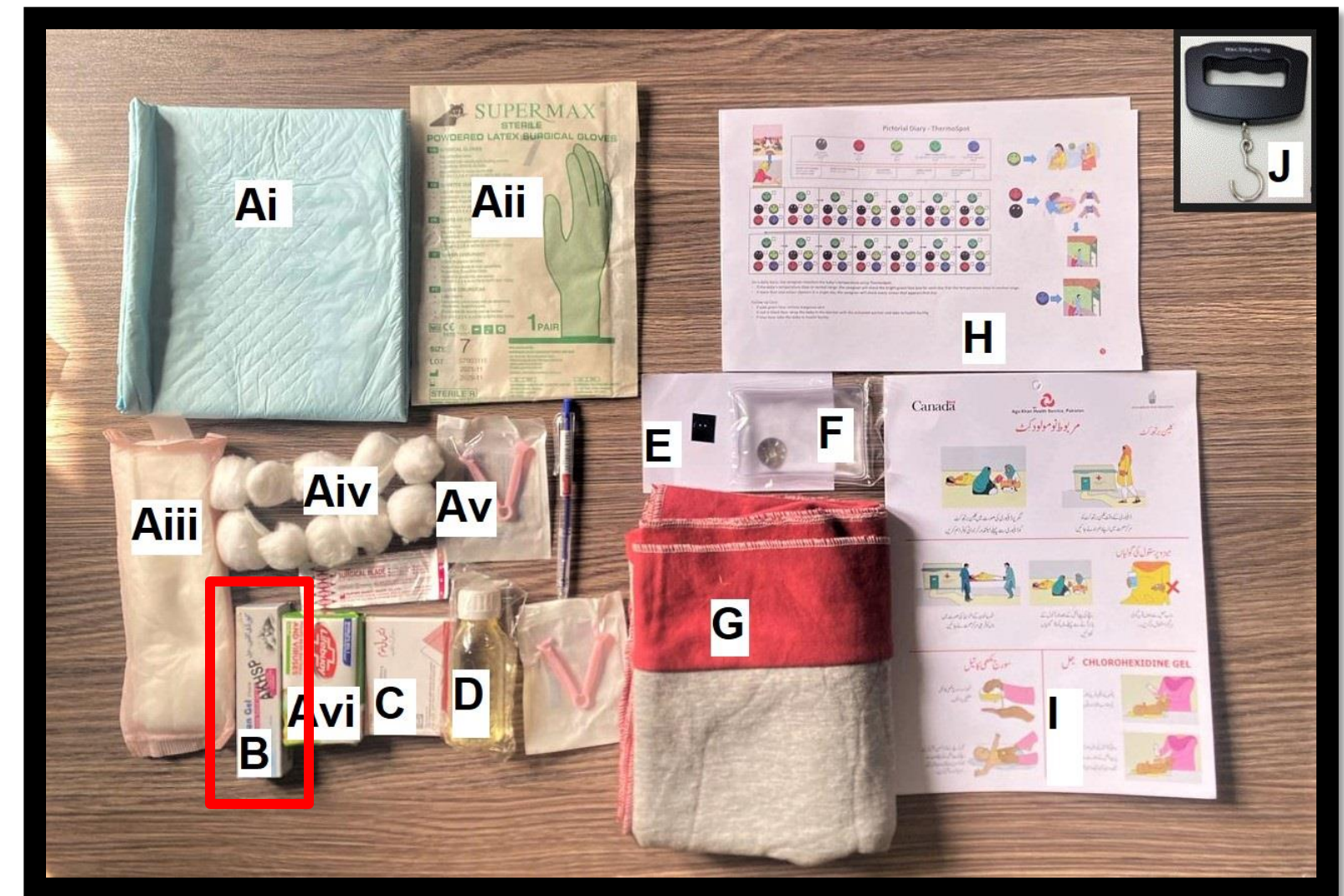
(F) Click-to-heat warmer

(G) Fleece blanket

(H/I) Pictorial diary and guide

(J) Weighing scale

**Delivered to pregnant women by Lady Health
Workers during the third trimester of pregnancy**



(B) Chlorhexidine 4% gel:

Applied to umbilical stump once daily
from days 1–10 after delivery.

Integrated Newborn Care Kit (iNCK)

Portable Easy-to-Use Low-Cost
Integrated Evidence-Based

(A) Clean birth kit

(B) Chlorhexidine 4% gel

(C) Three misoprostol tablets

(D) Sunflower oil emollient

(E) ThermoSpot™ thermoindicator sticker

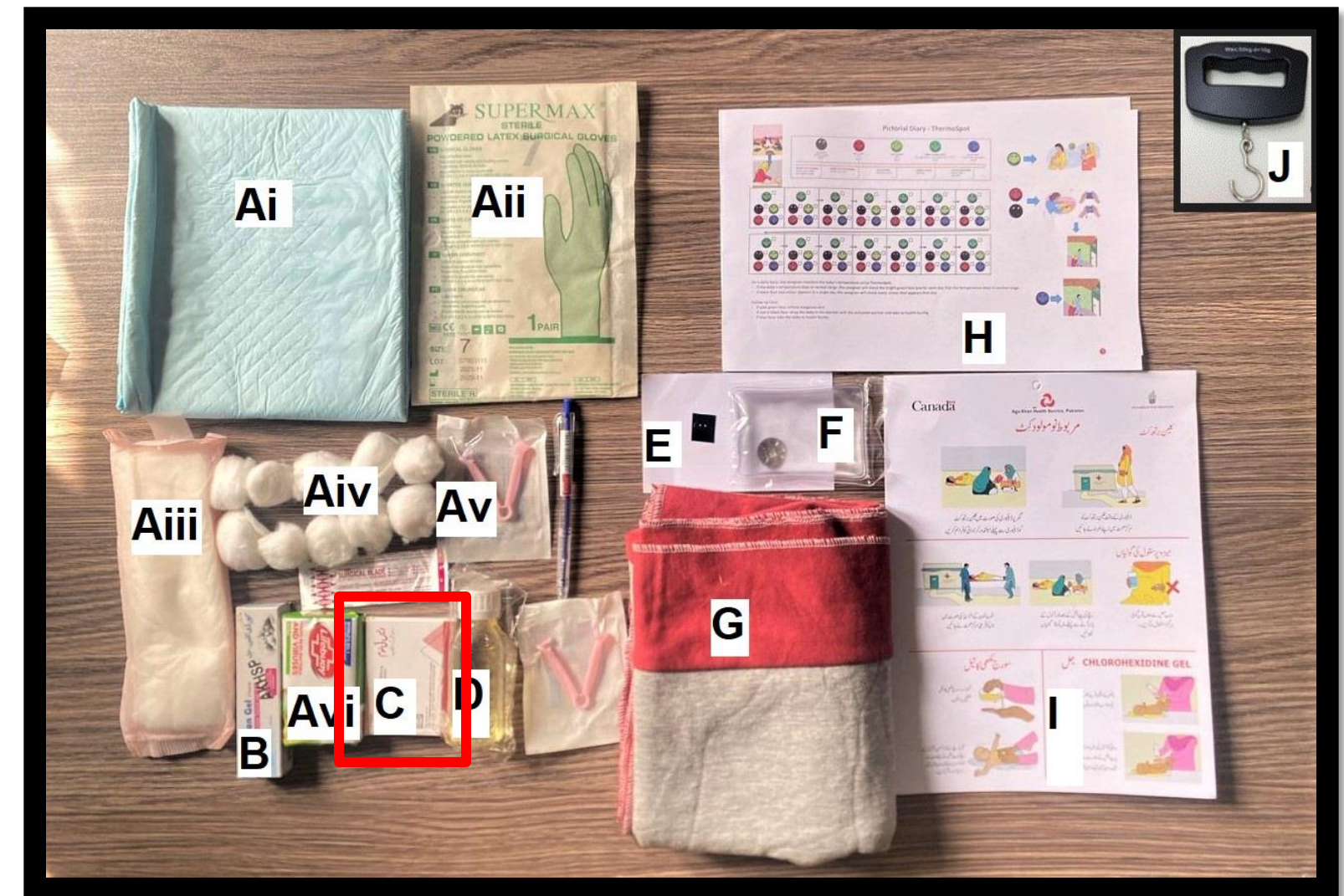
(F) Click-to-heat warmer

(G) Fleece blanket

(H/I) Pictorial diary and guide

(J) Weighing scale

**Delivered to pregnant women by Lady Health
Workers during the third trimester of pregnancy**



(C) Three misoprostol tablets:

Taken by the woman after delivery of the newborn but before delivery of the placenta.

Integrated Newborn Care Kit (iNCK)

Portable Easy-to-Use Low-Cost
Integrated Evidence-Based

(A) Clean birth kit

(B) Chlorhexidine 4% gel

(C) Three misoprostol tablets

(D) Sunflower oil emollient

(E) ThermoSpot™ thermoindicator sticker

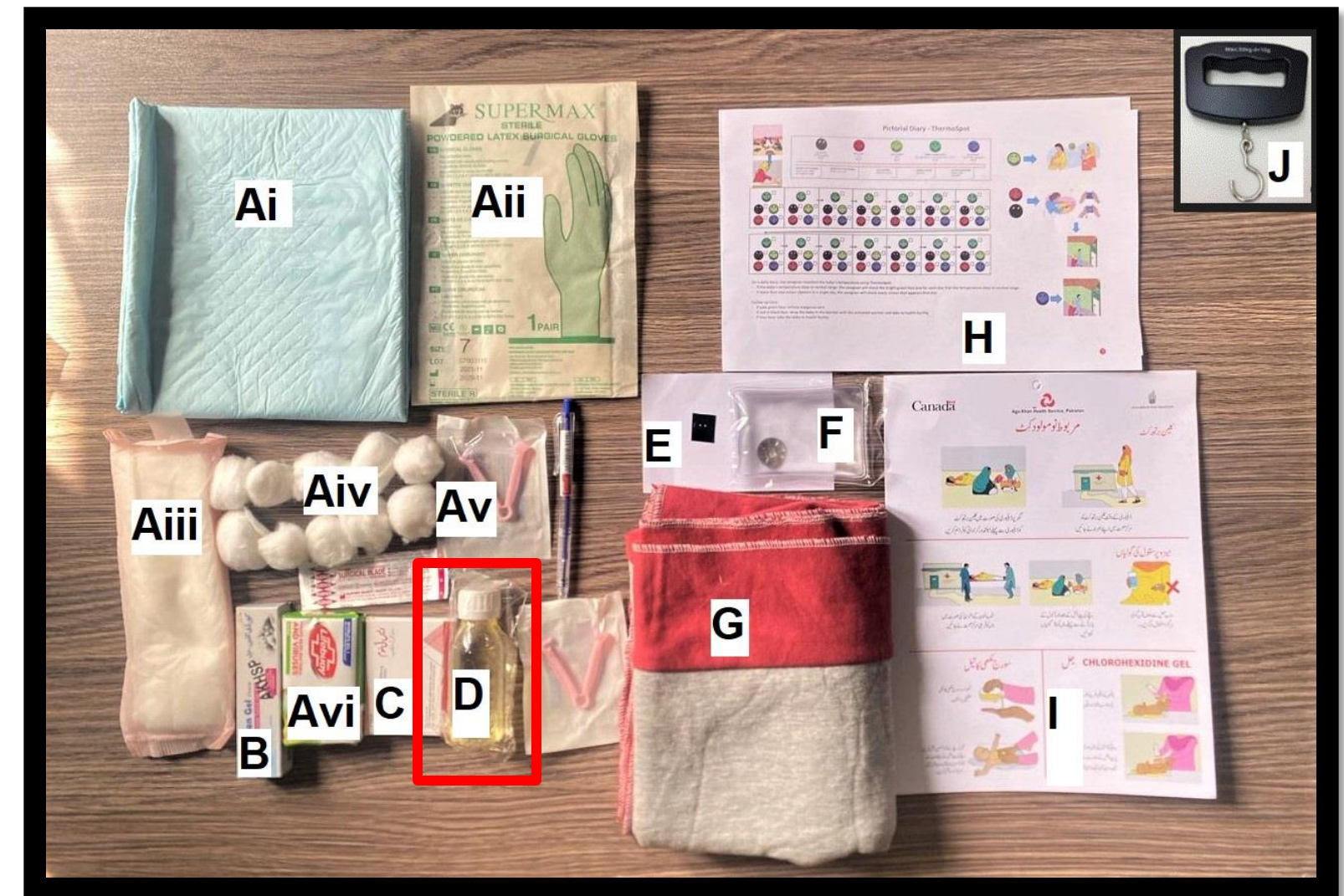
(F) Click-to-heat warmer

(G) Fleece blanket

(H/I) Pictorial diary and guide

(J) Weighing scale

**Delivered to pregnant women by Lady Health
Workers during the third trimester of pregnancy**



(D) Sunflower oil emollient:

Applied to the newborn's body once daily from days 1–28 after delivery.

Integrated Newborn Care Kit (iNCK)

Portable Easy-to-Use Low-Cost
Integrated Evidence-Based

(A) Clean birth kit

(B) Chlorhexidine 4% gel

(C) Three misoprostol tablets

(D) Sunflower oil emollient

(E) ThermoSpot™ thermoindicator sticker

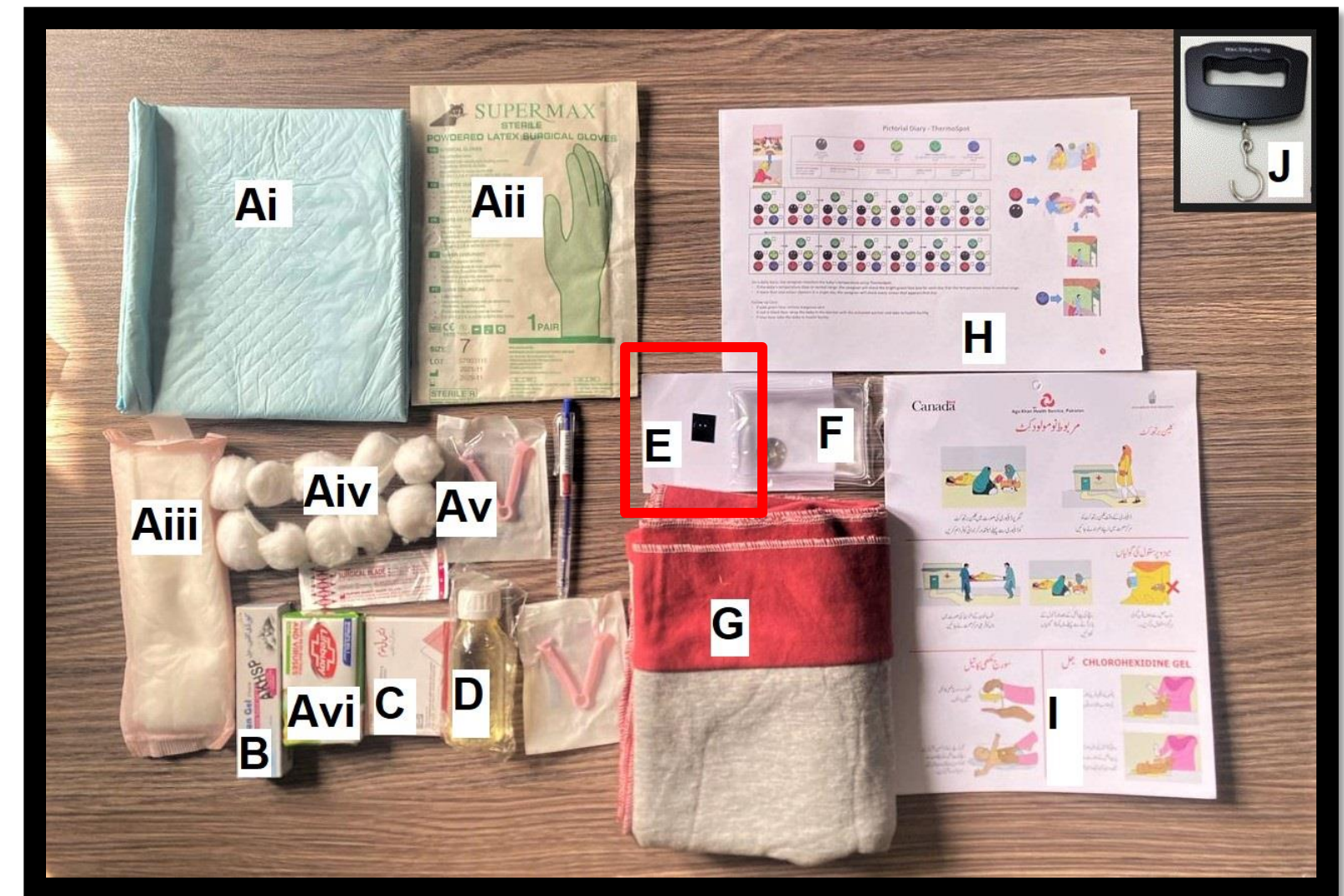
(F) Click-to-heat warmer

(G) Fleece blanket

(H/I) Pictorial diary and guide

(J) Weighing scale

**Delivered to pregnant women by Lady Health
Workers during the third trimester of pregnancy**



(E) ThermoSpot™:

Applied to the newborn's carotid artery
and monitored from days 1–14 after
delivery.

Integrated Newborn Care Kit (iNCK)

Portable Easy-to-Use Low-Cost
Integrated Evidence-Based

(A) Clean birth kit

(B) Chlorhexidine 4% gel

(C) Three misoprostol tablets

(D) Sunflower oil emollient

(E) ThermoSpot™ thermoindicator sticker

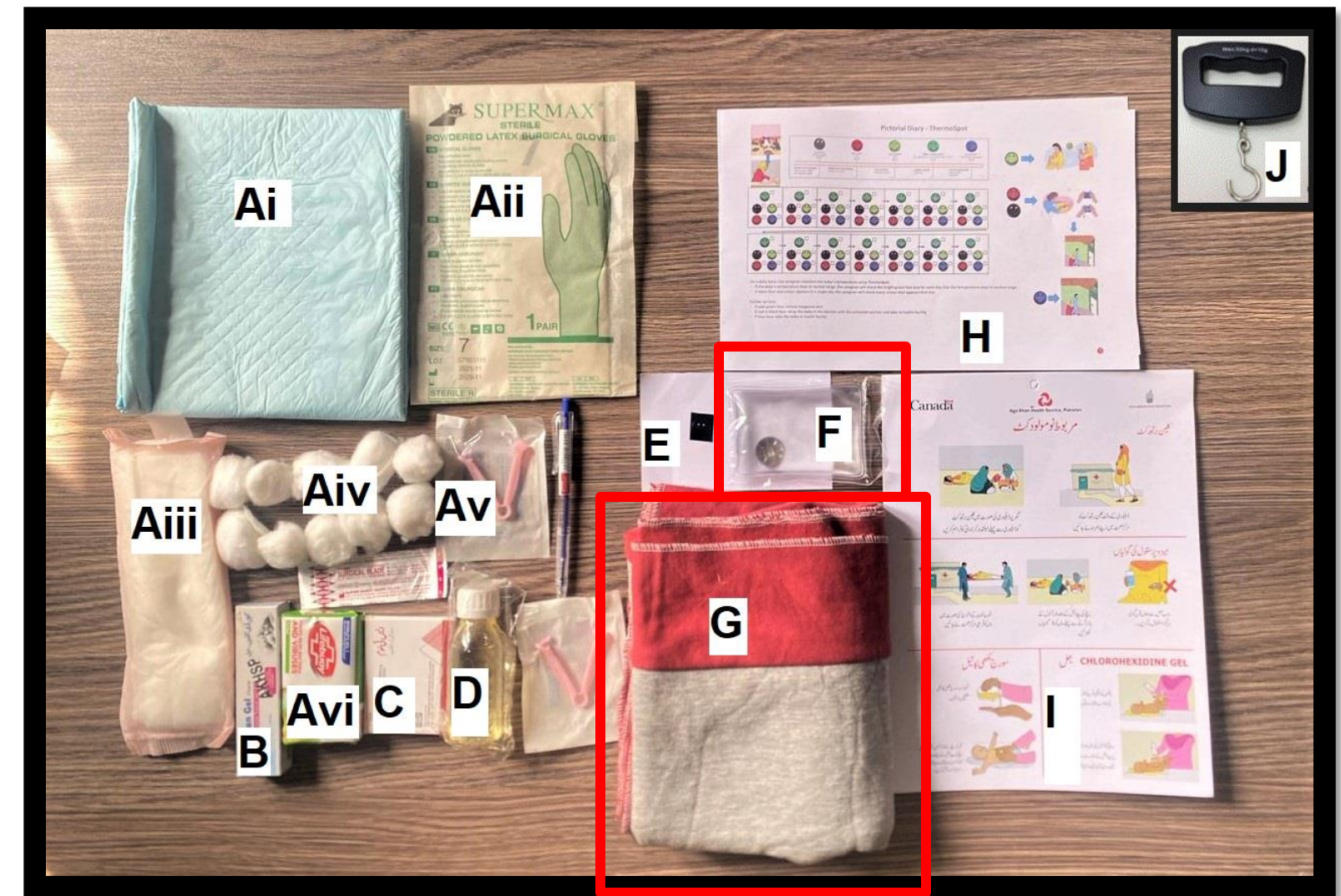
(F) Click-to-heat warmer

(G) Fleece blanket

(H/I) Pictorial diary and guide

(J) Weighing scale

Delivered to pregnant women by Lady Health Workers during the third trimester of pregnancy



(F/G) Fleece blanket and click-to-heat warmer:

Used if ThermoSpot™ indicates moderate or severe hypothermia.

Integrated Newborn Care Kit (iNCK)

Portable Easy-to-Use Low-Cost
Integrated Evidence-Based

(A) Clean birth kit

(B) Chlorhexidine 4% gel

(C) Three misoprostol tablets

(D) Sunflower oil emollient

(E) ThermoSpot™ thermoindicator sticker

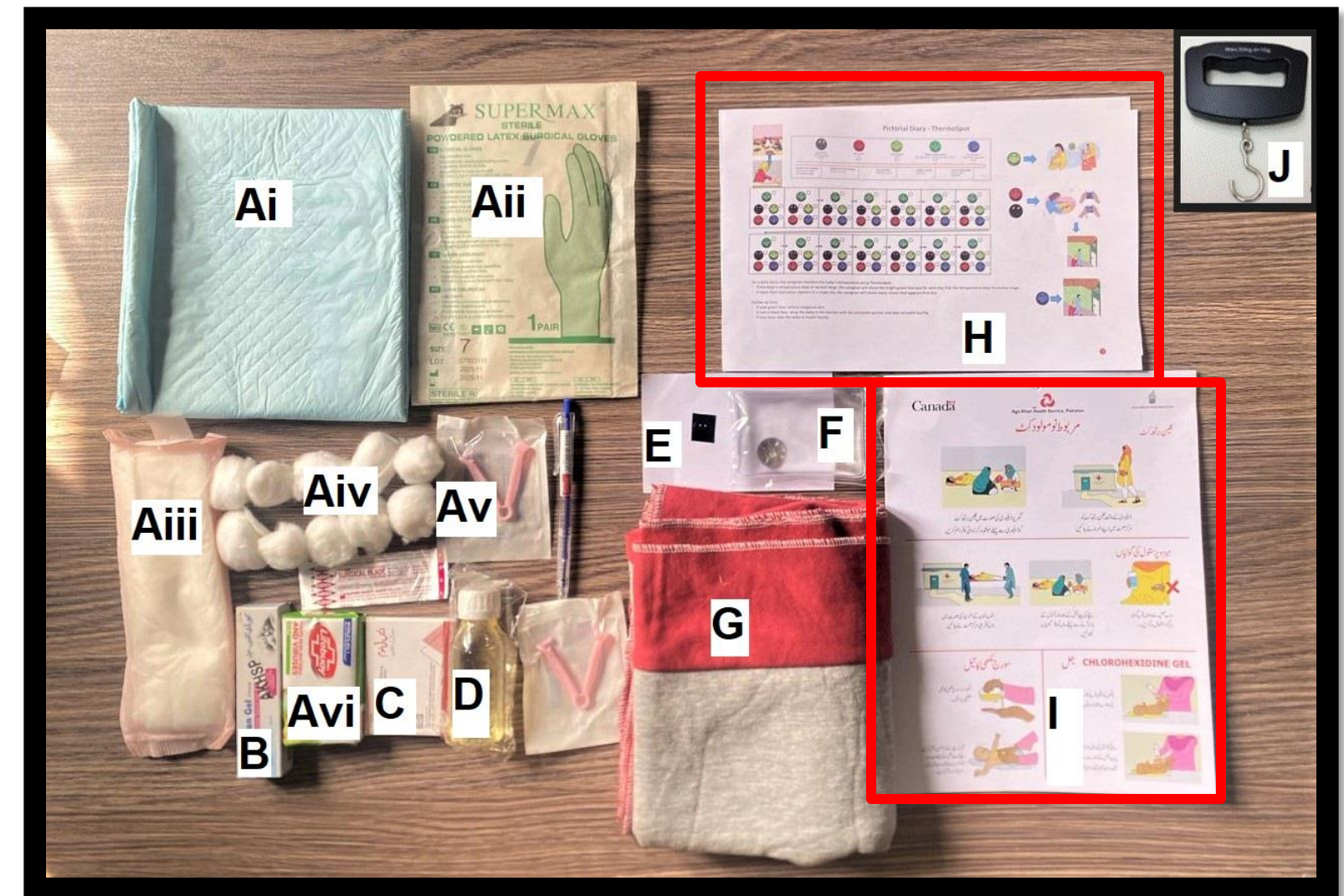
(F) Click-to-heat warmer

(G) Fleece blanket

(H/I) Pictorial diary and guide

(J) Weighing scale

**Delivered to pregnant women by Lady Health
Workers during the third trimester of pregnancy**



(H/I) Pictorial diary and guide:

Guide demonstrating the usage and timing for each component.

Integrated Newborn Care Kit (iNCK)

Portable Easy-to-Use Low-Cost
Integrated Evidence-Based

(A) Clean birth kit

(B) Chlorhexidine 4% gel

(C) Three misoprostol tablets

(D) Sunflower oil emollient

(E) ThermoSpot™ thermoindicator sticker

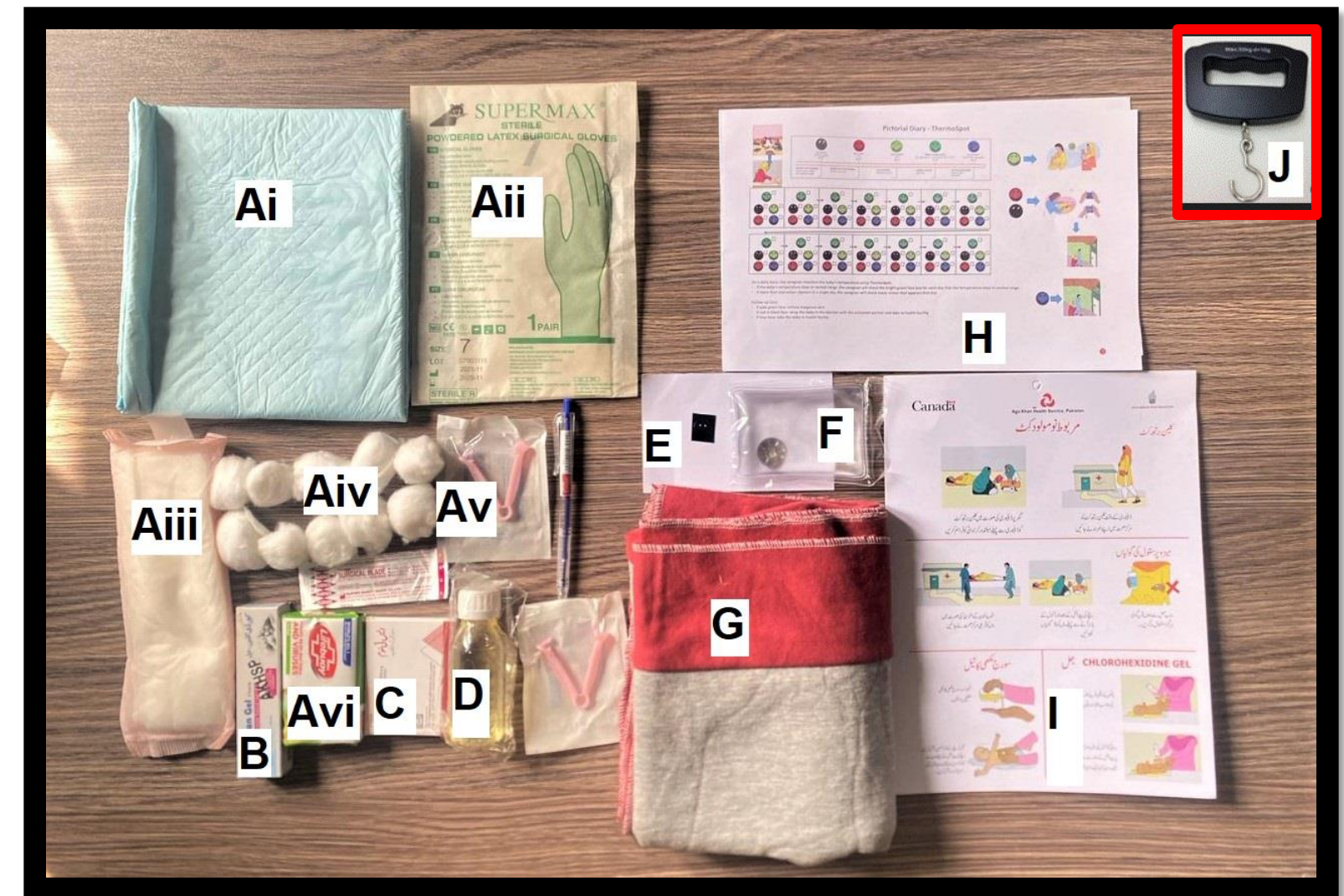
(F) Click-to-heat warmer

(G) Fleece blanket

(H/I) Pictorial diary and guide

(J) Weighing scale

Delivered to pregnant women by Lady Health Workers during the third trimester of pregnancy



(J) Weighing scale:

Used by Lady Health Workers to measure newborn birthweight.

Integrated Newborn Care Kit (iNCK)

Portable Easy-to-Use Low-Cost
Integrated Evidence-Based

(A) Clean birth kit

(B) Chlorhexidine 4% gel

(C) Three misoprostol tablets

(D) Sunflower oil emollient

(E) ThermoSpot™ thermoindicator sticker

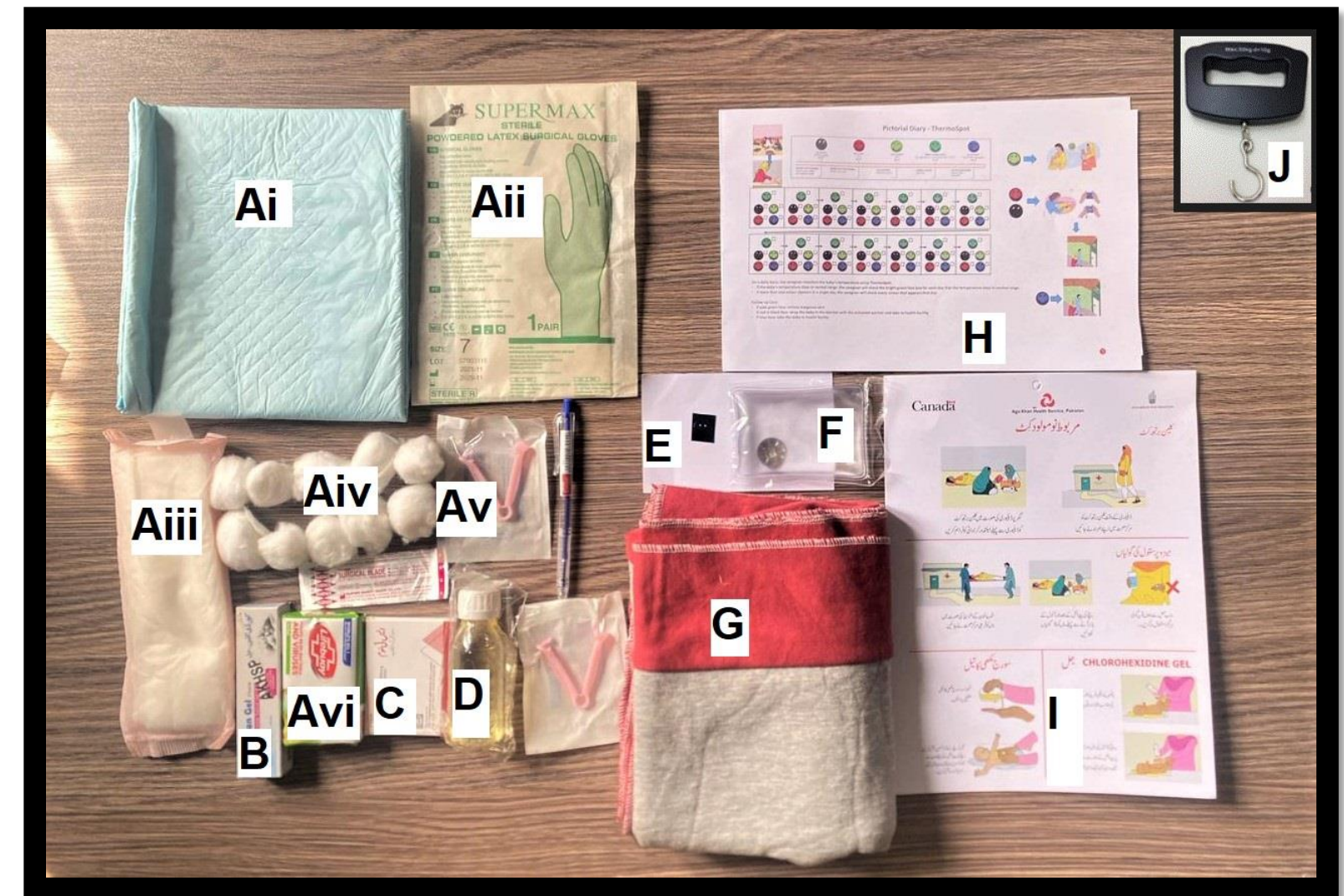
(F) Click-to-heat warmer

(G) Fleece blanket

(H/I) Pictorial diary and guide

(J) Weighing scale

**Delivered to pregnant women by Lady Health
Workers during the third trimester of pregnancy**



In a pilot trial from 2014–15,
the iNCK was associated with a
17% reduction in neonatal mortality
(not significant).

Pell et al. 2019. BMJ Global Health.

Methods – Trial Design

Objective: Estimate the effect of the iNCK on neonatal mortality, newborn omphalitis, birthweight measurement, and maternal postpartum haemorrhage when delivered to pregnant women by Lady Health Workers during the third trimester.

Study Design

Open-label, cluster randomised controlled trial

Study Setting

Seven district of Gilgit-Baltistan, Pakistan

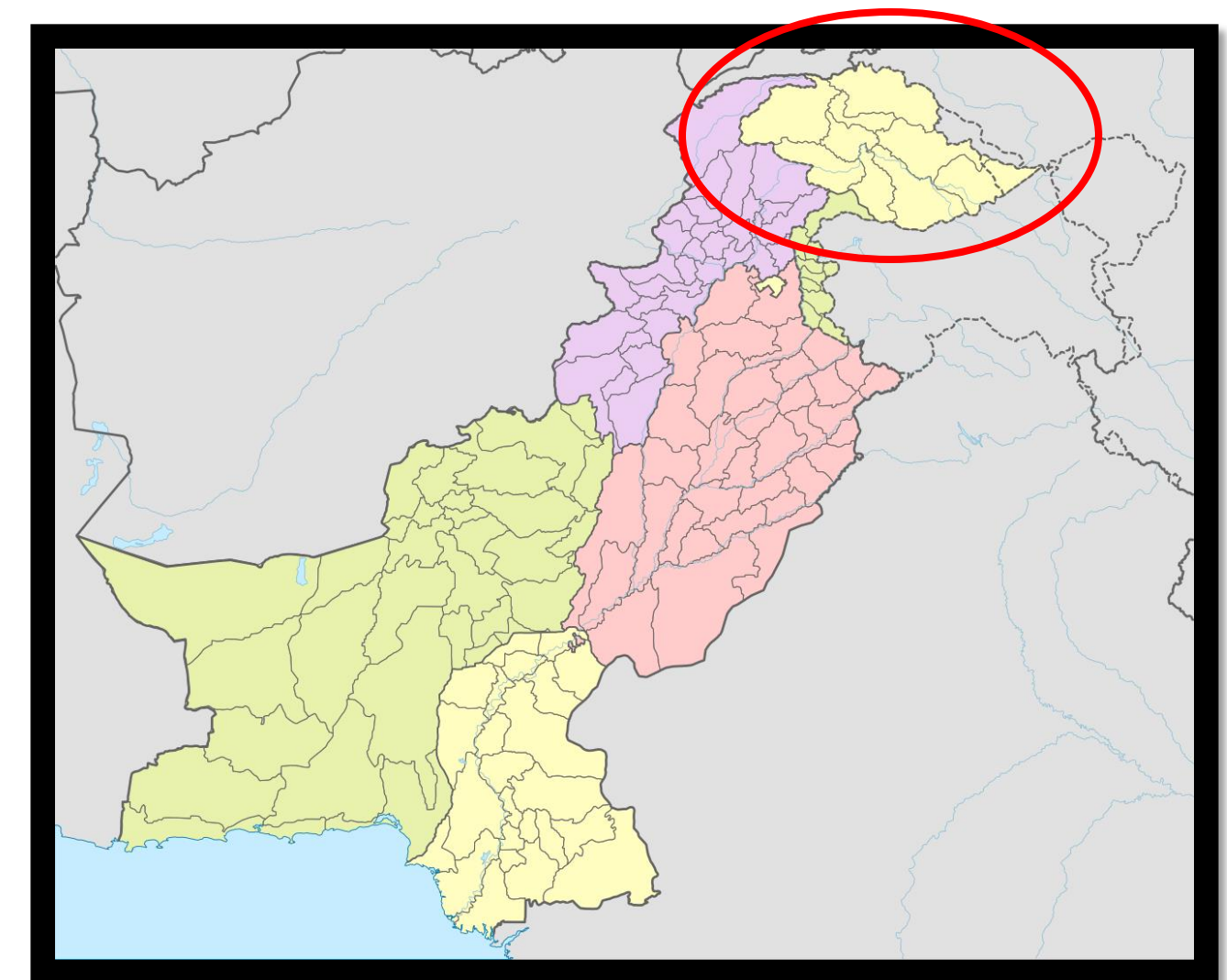
- 77 clusters (Union Councils) randomised 1:1
- 38 control vs. 39 iNCK clusters

Study Period

March 2022–June 2024

Sample Size

Target of 27,448 pregnant women



Map of Pakistan (Milenioscuro, CC BY-SA 4.0)

Methods – Procedures

Third trimester:

Pregnancy identification by LHWs

Soon after delivery:

Birth notification to study team

Third trimester:

Enrollment & intervention delivery

Days 8 and 29 after delivery:

Data collection visits



Methods – Outcomes & Analysis

- 1 Neonatal mortality rate (NMR):** Deaths of live-born children within 28 days after delivery, per 1,000 live births
- 2 Omphalitis (umbilical cord stump infection):** Proportion of live births with redness or pus on the umbilical stump or surrounding skin within 28 days after delivery
- 3 Postpartum haemorrhage:** Proportion of women who deliver vaginally with excessive vaginal bleeding within 24 hours after delivery
- 4 LHW-measured birthweight:** Proportion of live births who are weighed by a Lady Health Worker within three days after delivery

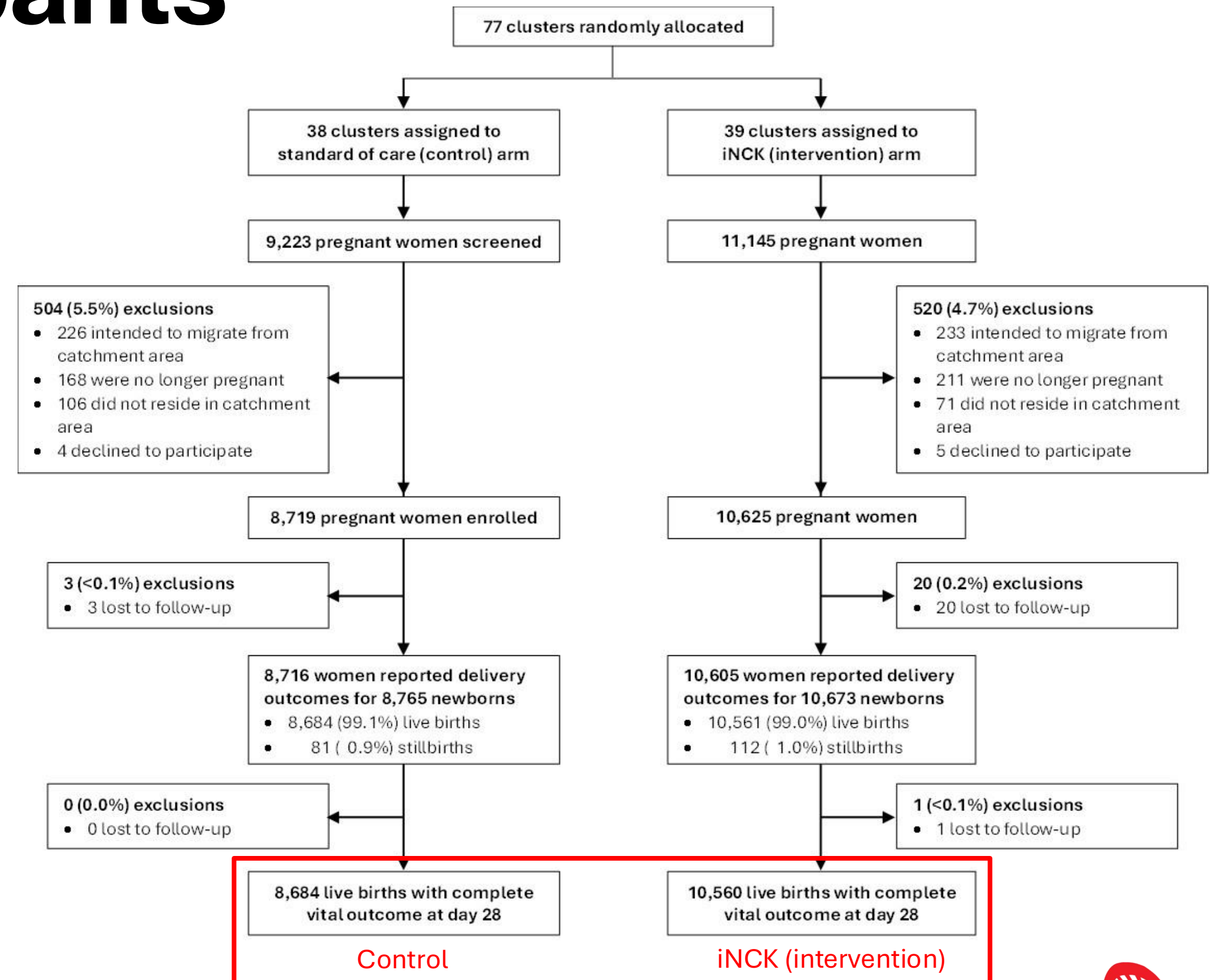
Multivariable robust Poisson regression with generalized estimating equations to estimate the effect of the iNCK on primary and secondary outcomes, adjusting for reproductive, child, and cluster characteristics.

**Findings may be subject to minor changes given ongoing data reconciliation.*

Results – Participants

19,344 women enrolled

- Median age 28 years
- Median 8 years of school
- Median household income = 142 USD/month
- 70% delivered at health facilities
- 24% delivered their first child





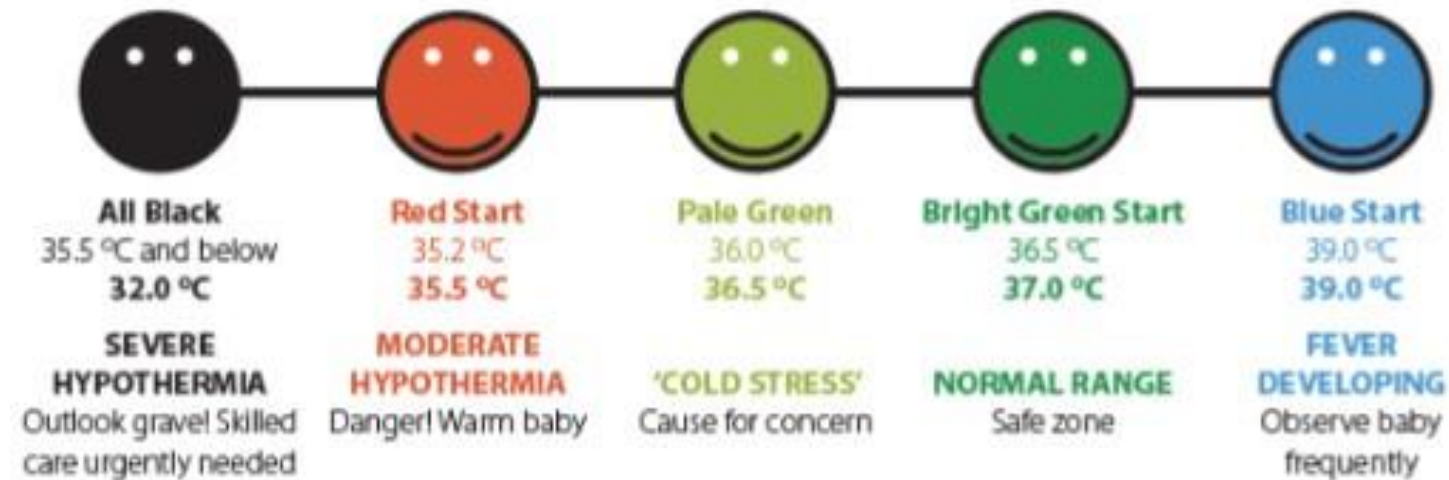
Uptake & Acceptance

Among iNCK arm participants...

- 99.7% used the clean birth kit
- 99.5% used chlorhexidine – **97% on day 1**
- 99.5% used sunflower oil – **94% on day 1**
- 95% used ThermoSpot – **92% on day 1**
- 86% took all three misoprostol tablets

ThermoSpot identified neonates with...

- **Cold stress** (n=1372), **hypothermia** (n=539), and **fever** (n=258)



ThermoSpot indications (*Maternova*)

<https://www.engineeringforchange.org/solutions/product/thermospot/>

Misoprostol...

- Was never incorrectly used prior to delivery
- Caused mild side effects in 5% of users

99.9% of iNCK arm participants thought the iNCK was safe and easy to use.

Effect of the iNCK on Secondary Outcomes

Omphalitis, Postpartum Hemorrhage, and LHW-Measured Birthweight

Omphalitis

- Control: 1681 cases / 8185 newborns (20.5%)
- iNCK: 431 cases / 9919 newborns (4.4%)
- aRR = 0.20, 95% CI 0.12–0.36, $p < 0.001$

↓80% in
iNCK clusters

Postpartum haemorrhage

- Control : 586 cases / 7605 women (7.7%)
- iNCK: 370 cases / 9231 women (4.0%)
- aRR = 0.43, 95% CI 0.20–0.92, $p = 0.026$

↓57% in
iNCK clusters

LHW-measured birthweight

- Control : 1211 weighed / 8144 newborns (14.9%)
- iNCK: 4108 weighed / 9974 newborns (41.2%)
- aRR = 2.86, 95% CI 2.20–3.71, $p < 0.001$

↑186% in iNCK
clusters

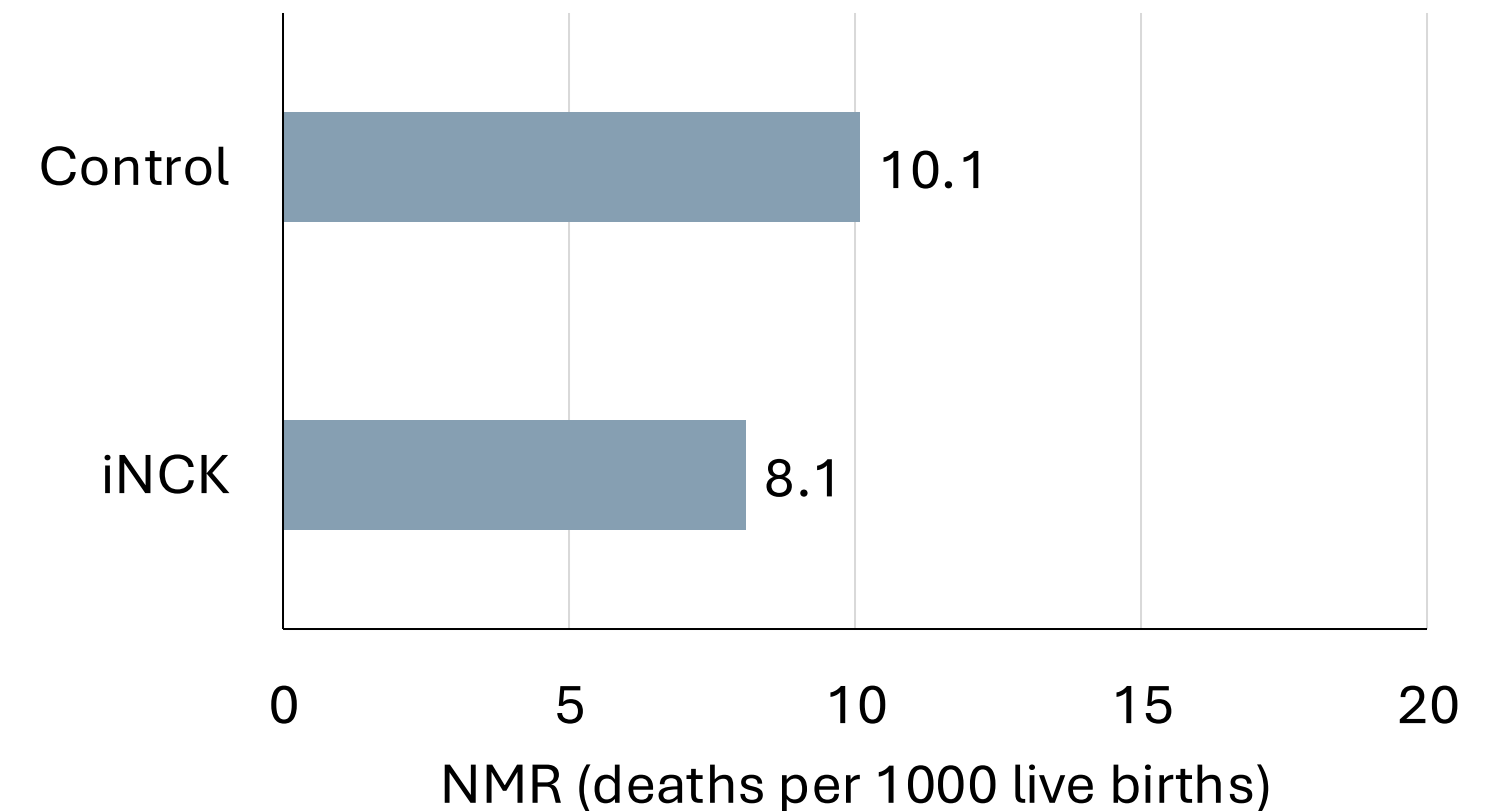
Results – Neonatal Mortality

Control arm: 88 deaths from 8,682 live births

- NMR 10.1 deaths per 1000 live births

iNCK arm: 86 deaths from 10,555 live births

- NMR 8.1 deaths per 1000 live births



Risk of neonatal mortality was 8–23% lower in iNCK vs. control clusters

- Unadjusted RR 0.77, 95% CI 0.52–1.112, p=0.172
- Adjusted RR 0.92, 95% CI 0.67–1.27, p=0.611
 - Adjusting for ANC, district, sex, time, baseline NMR, and baseline % of facility deliveries

*Is lower than expected mortality causing model instability?

Results – Neonatal Mortality

Substantial heterogeneity of effect by district:

District	Control		iNCK		aRR (95% CI)
	Deaths / Live births	NMR	Deaths / Live births	NMR	
Astore	4 / 945	4.2	14 / 1598	8.8	2.16 (0.36–12.79)
Diamer	6 / 755	7.9	12 / 1476	8.1	2.77 (0.52–14.73)
Ghanche	14 / 1763	7.9	13 / 2402	5.4	0.69 (0.38–1.26)
Kharmang	25 / 946	26.4	11 / 702	15.7	0.69 (0.27–1.73)
Nagar	12 / 1347	8.9	7 / 497	14.1	1.29 (0.25–6.68)
Shigar	2 / 809	2.5	13 / 1915	6.8	2.24 (0.65–7.72)
Skardu	26 / 2119	12.3	13 / 1969	6.6	0.44 (0.25–0.78)

Excluding district, neonatal mortality was 24% lower in iNCK vs. control clusters

- aRR 0.76, 95% CI 0.52–1.11, p=0.151
 - Adjusting for ANC, sex, time, baseline NMR, and baseline % of facility deliveries

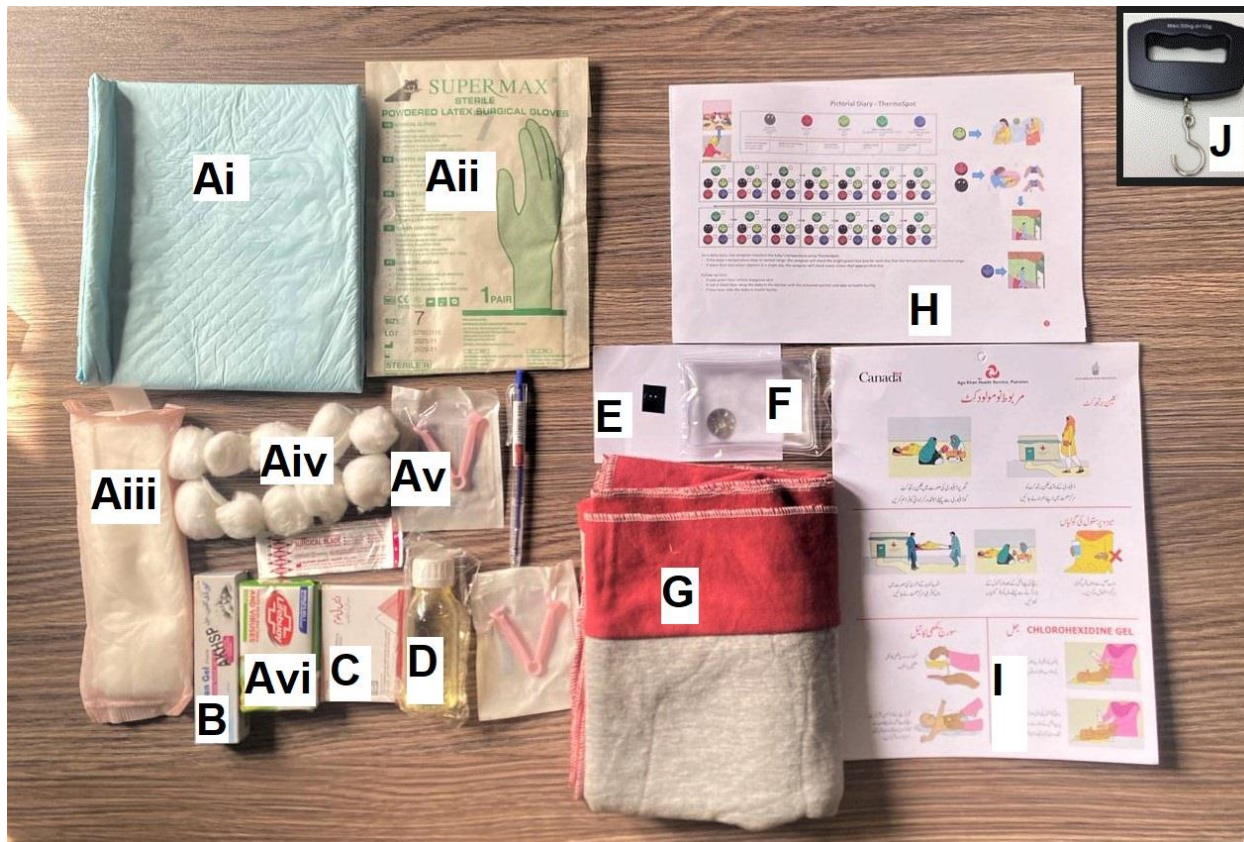
Limitations

- **NMR in both arms was rarer than expected:**
 - NMR may truly be lower than prior estimates
 - NMR may be lower in areas covered by the LHW programme
 - Our study may not have reached the most remote populations
- **Imbalance in participants between arms:**
 - Randomisation did not account for cluster birth rates
 - Potential for lower LHW engagement in control clusters?



Implications & Impact

- The iNCK might reduce neonatal mortality, did prevent omphalitis and postpartum hemorrhage, and improved newborn birthweight measurements
- Delivery of the iNCK by LHWs achieved high uptake, knowledge, and acceptance of iNCK components
- The iNCK platform may be useful for delivery of other MCH interventions, and in humanitarian settings
- Ongoing cost-effectiveness analysis and partnerships to scale-up iNCK programme in Pakistan



Acknowledgements

Research Team



- Dr. Shaun Morris (co-PI)
- Dr. Lisa Pell (co-PI)
- Dr. Zulfiqar Bhutta
- Dr. Diego Bassani
- Dr. Adria Rose
- Dr. Rachel Spitzer



THE AGA KHAN UNIVERSITY

- Dr. Sajid Soofi
- Imran Chauhadry
- Karim Muhammad



Aga Khan Health Services

- Muhammad Yasin
- Falak Madhani
- Shariq Paracha
- Dr. Sher Hafiz Khan
- Nazia Jabeen
- Faisal Ali
- Masood Ali Khan
- Dr. Sifat Wali

- Dr. Monica Taljaard
(University of Ottawa)

Funders



Grand Challenges Canada®
Grands Défis Canada



AGA KHAN FOUNDATION
CANADA

Partners

Lady Health Worker Programme
Gilgit-Baltistan Department of Health
(Dr. Saleem-Ud-Din and Dr. Syed Sadiq Shah)
Aga Khan Foundation, Pakistan

**All participants, data collectors,
supervisors, and drivers**

An integrated newborn care kit to save newborn lives and improve health outcomes in Gilgit-Baltistan, Pakistan: An open-label cluster-randomised controlled trial

Daniel S. Farrar for the GB iNCK Study Team
daniel.farrar@sickkids.ca, shaun.morris@sickkids.ca

