



HPTN 084: Managing Pregnancy and Infants on Study

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- Pregnancy and infant sub-study purpose
- Operational targets
 - Mother/infant visit schedules
 - Primary care MNCH services
 - Delivery planning
 - Sample collection
- Infant physical exams
- Infant blood collection

Confirmatory test same day

Pregnant and post-partum participants **with prior or current exposure to CAB** during pregnancy:

- To estimate the **incidence of pregnancy** among participants during the OL period
- To evaluate **safety and infant outcomes** among pregnant participants
- To evaluate the **PK of CAB LA** among pregnant participants, combining blinded, unblinded and OL periods
- To evaluate **concentration in breastmilk and infants** among women who receive CAB LA injections during pregnancy and/or the early post-partum period.

Operational Target 1

Study visit schedules for mothers and infants are coordinated

- Reduce participant burden (promote retention)

Time on <u>Pregnancy and Infant Sub-study</u>	Delivery	Week 2, pp	Week 4, pp	Week 8, pp	Week 16, pp	Week 24, pp	Week 32, pp	Week 40, pp	Week 48, pp
Infant									
Pregnancy outcome assessment including abbreviated infant examination ¹²				X					X
Infant feeding history				X	X	X			
Cord blood collection ¹⁷	X								
Infant blood collection ¹⁷	X	X	X	X	X	X	X	X	X
Infant AE assessment ¹⁸	X	X	X	X	X	X			
Infant HIV testing, if the mother has one or more reactive/positive HIV test results ¹³	X	X	X	X	X	X	X	X	X
Cord blood storage ^{9,14}	X								
Dried blood spot storage ^{9, 16}	X	X	X	X	X	X	X	X	X
Infant plasma storage ^{9,14}	X	X	X	X	X	X	X	X	X

Operational Target 2

Routine MNCH services are provided by collaborating specialists

- Assure access to high quality standard of care services
- Facilitate access to specialist care and treatment, when needed
- Assure access to non-study source records

5.14 The site IoR or designee will refer pregnant participants to all applicable pregnancy-related services and will be provided a letter to obstetric services detailing participation in the trial; however, sites will not be responsible for paying for pregnancy-related care. The site IoR or designee will counsel any participants who become pregnant regarding possible risks to the fetus according to site-specific SOPs.

Time on <u>Pregnancy and Infant Sub-study</u>	Delivery	Week 2, pp	Week 4, pp	Week 8, pp	Week 16, pp	Week 24, pp	Week 32, pp	Week 40, pp	Week 48, pp
Infant									
Pregnancy outcome assessment including abbreviated infant examination ¹²				X					X
Infant feeding history				X	X	X			
Cord blood collection ¹⁷	X								
Infant blood collection ¹⁷	X	X	X	X	X	X	X	X	X
Infant AE assessment ¹⁸	X	X	X	X	X	X			
Infant HIV testing, if the mother has one or more reactive/positive HIV test results ¹³	X	X	X	X	X	X	X	X	X
Cord blood storage ^{9,14}	X								
Dried blood spot storage ^{9, 16}	X	X	X	X	X	X	X	X	X
Infant plasma storage ^{9,14}	X	X	X	X	X	X	X	X	X

Operational Target 3

Pregnancy outcome recorded

- Assure awareness of pregnancy outcome
- Avoid missing data from labour and delivery non-study source

Time on <u>Pregnancy</u> and Infant Sub-study	Delivery	Week 2, pp	Week 4, pp	Week 8, pp	Week 16, pp	Week 24, pp	Week 32, pp	Week 40, pp	Week 48, pp
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Cord blood storage ^{9,14}	X								
Dried blood spot storage ^{9, 16}	X	X	X	X	X	X	X	X	X
Infant plasma storage ^{9,14}	X	X	X	X	X	X	X	X	X

Operational Target 4

- Avoid missed tests

Cord blood collected & stored

17 Cord blood and infant blood should be collected if feasible. If blood collection is not possible, simply note that in participant files.

14 Stored cord blood and plasma samples will be used for PK analysis and may be used for other assessments, including virology testing. Results from this testing will not be returned to the study sites or participants.

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Infant plasma storage ^{9,14}	X	X	X	X	X	X	X	X	X

Operational Targets

1. Study visit schedules for mothers and infants are coordinated

2. Routine MNCH services are provided by collaborating specialists

3. Pregnancy outcome recorded

4. Cord blood collected & stored

What strategy works for you?

What challenges have you met?

- Affiliated maternity unit:
 - Far from home (transport, visitors)
 - Very busy (assist to get service)
- Delivery often after hours
- Partners against infant blood draws

- Pregnancy and infant sub-study purpose
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- • Infant physical exams
- Infant blood collection

Infant Physical Exams

Week 48, pp
Week 40, pp
Week 32, pp
Week 24, pp
Week 16, pp
Week 8, pp
Week 4, pp
Week 2, pp
Delivery

- Complete newborn exam (birth)
- Follow-up physical exam (wks 2, 4, 8, 16, 24, 32, 40, 48)

Infant Physical Exams

- Prepare
- Look
- Listen
- Chat with mum
- Play
- Touch
- Be opportunistic
- Be quick

- Plan assessments in advance
- Supplies laid out and within reach
- Room warm and well lit
- Mother informed and comfortable
- Assistant attentive
- No interruptions
- Wash your hands

Infant Danger Signs

Assess for the following **danger** signs at each postnatal visit:

- (1) stopped feeding well,
- (2) history of convulsions,
- (3) fast breathing,
- (4) severe chest in-drawing,
- (5) no spontaneous movement,
- (6) temperature $>37.5^{\circ}\text{C}$,
- (7) temperature $<35.5^{\circ}\text{C}$
- (8) any jaundice in first 24 hours of life, or yellow palms and soles at any age

Newborn Step-wise Surface Exam

- Physical appearance
- Length
- Weight
- Skin
- Head (including fontanelles and circumference)
- Face (including mouth)
- Neck
- Chest
- Abdomen and anus
- Hips and genitalia
- Arms, legs, fingers, and toes
- Spine
- Auscultation of chest
- Neurologic assessment

<https://vimeo.com/230041447>

Video Guide to a Stepwise Surface Examination of Newborns

TDR, the Special Programme for Research and Training in Tropical Diseases

who.int/tdr/publications/videos/stepwise-surface-examination-newborns/en/

December 2012

~30 minutes

Global Birth Defects App for the assessment and classification of birth defects

<https://globalbirthdefects.tghn.org/download-birth-defects-surveillance-app/>

General Appearance and Vitals

- Warm, responsive, alert / active / listless / limp
- Well perfused peripheries / dusky / shut down
- Colour pink / plethoric / jaundiced / bruised
- Feeding well / weak suckle / unable to feed (prostrate)
- Cry vigorous / weak / hoarse / funny pitch
- Vital signs (count resp rate over 1 minute)
- Head size and shape, caput, haematoma, sutures, fontanelles
- Abnormal features / dysmorphism
- Posture, tone and movement (flexed limbs, ventral suspension, pull to sit, symmetry)

Newborn Skin

- Jaundice
- Common newborn rashes
 - Heat rash / Milia / Erythema toxicum / Cradle cap
- Birth mark/ blue spot



- Cornea for cloudiness (sign of congenital cataracts).
- Conjunctiva for erythema, exudate, orbital oedema, subconjunctival haemorrhage, jaundice of sclera.
- Pupil size, shape, equality and reactivity to light (PERRL: pupil, equal, round, reactive to light).

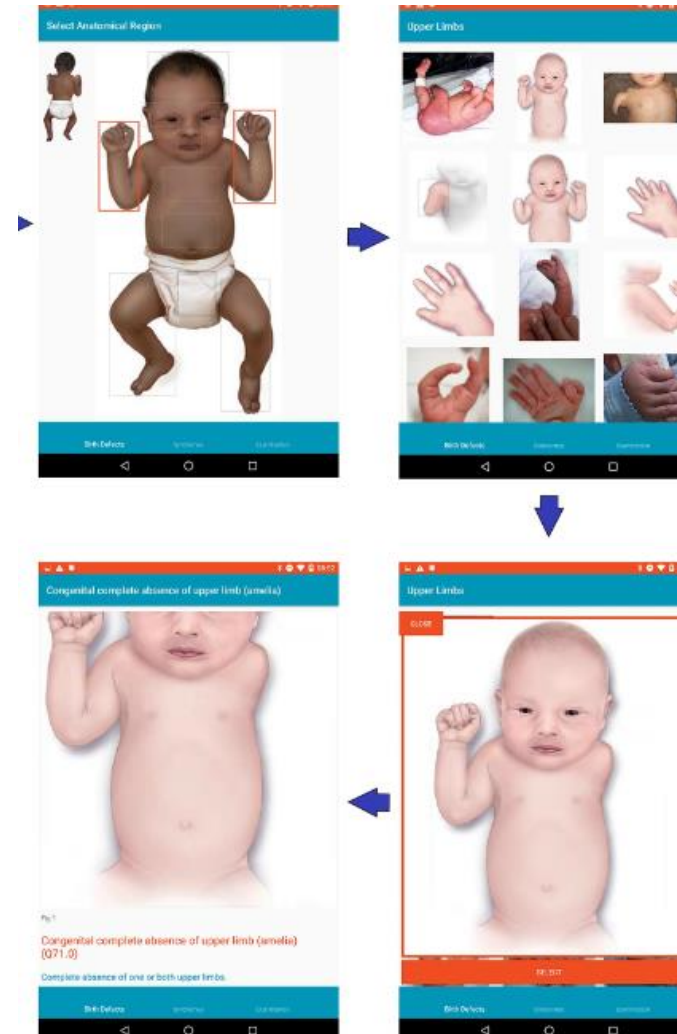
- Defects such as cleft lip and palate
- Oral thrush
- Tongue size
- Gum cysts
- Suckling blister



- Abdominal distension, masses, obvious malformations
 - Eg Omphalocele/Gastroschisis.
- Umbilical cord:
 - Count the vessels (one big vein and two arteries).
 - Check for effective clamping, no bleeding
 - Check for pus discharge and for skin redness around umbilicus.
- Anus patent (passed meconium?)

Limbs and Extremities

- Fingers and toes
 - Extra digits
 - Talipes equinovarus
 - Deformities



- Pupil reflexes normal, able to breastfeed ok, facial symmetry when crying
- Primitive reflexes
 - Rooting Reflex
 - Sucking Reflex
 - Palmar Grasp Reflex
 - Moro Reflex
 - Stepping Reflex

Gestational Age

- Modified Ballard Score
 - Physical maturity

Physical Maturity




































Skin	Sticky, friable, transparent	Gelatinous, red, translucent	Smooth, pink; visible veins	Superficial peeling and/or rash; few veins	Cracking, pale areas; rare veins	Parchment, deep cracking; no vessels	Leathery, cracked wrinkled
Lanugo	None	Sparse	Abundant	Thinning	Bald areas	Mostly bald	Maturity Rating
Plantar surface	Heel-toe 40-50 mm: -1 <40 mm: -2	>50 mm, no crease	Faint red marks	Anterior transverse crease only	Creases anterior 2/3	Creases over entire sole	
Breast	Imperceptible	Barely perceptible	Flat areola, no bud	Stippled areola, 1-2 mm bud	Raised areola, 3-4 mm bud	Full areola, 5-10 mm bud	Score
Eye/Ear	Lids fused loosely: -1 tightly: -2	Lids open; pinna flat; stays folded	Slightly curved pinna; soft; slow recoil	Well curved pinna; soft but ready recoil	Formed and firm, instant recoil	Thick cartilage, ear stiff	Weeks
Genitals (male)	Scrotum flat, smooth	Scrotum empty, faint rugae	Testes in upper canal, rare rugae	Testes descending, few rugae	Testes down, good rugae	Testes pendulous, deep rugae	
Genitals (female)	Clitoris prominent, labia flat	Clitoris prominent, small labia minora	Clitoris prominent, enlarging minora	Majora and minora equally prominent	Majora large, minora small	Majora cover clitoris and minora	
							-10
							-5
							0
							5
							10
							15
							20
							25
							30
							35
							40
							45
							50

<https://epomedicine.com/clinical-medicine/new-ballard-score-how-to-use-it-correctly/>

Gestational Age

- Modified Ballard Score
 - Neuromuscular maturity

Neuromuscular Maturity

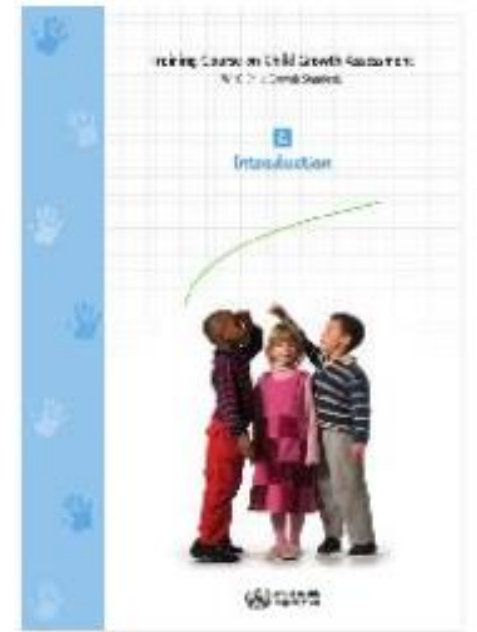
Score	-1	0	1	2	3	4	5
Posture							
Square window (wrist)	 >90°	 90°	 60°	 45°	 30°	 0°	
Arm recoil		 180°	 140°–180°	 110°–140°	 90°–110°	 <90°	
Popliteal angle	 180°	 160°	 140°	 120°	 100°	 90°	 <90°
Scarf sign							
Heel to ear							

Complete Examination of the Newborn.
Effective Perinatal Care
Geneva: World Health Organization

https://www.euro.who.int/__data/assets/pdf_file/0006/146814/EPC_FAC_guide_pt2_mod_1N_7N.pdf

World Health Organization.
Training Course on Child Growth Assessment.
Geneva, WHO, 2008.

https://apps.who.int/iris/bitstream/handle/10665/43601/9789241595070_B_eng.pdf?sequence=2&isAllowed=y

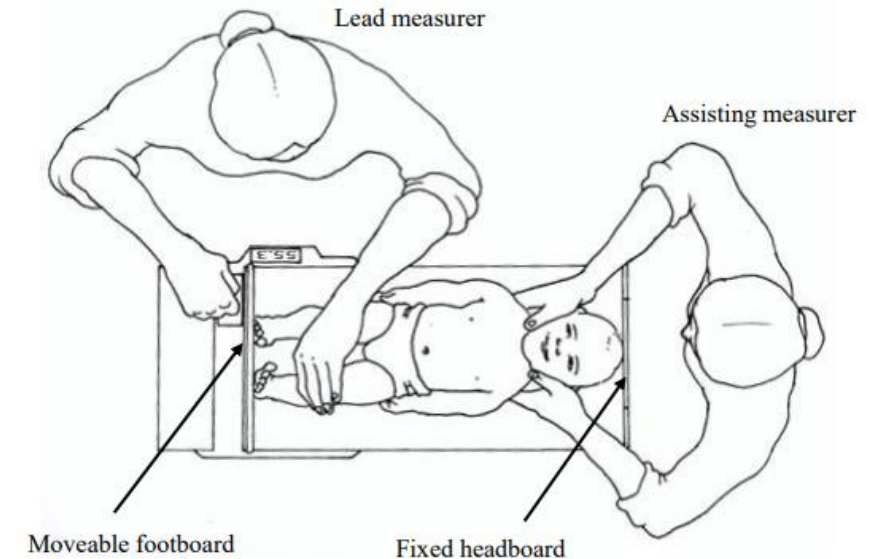
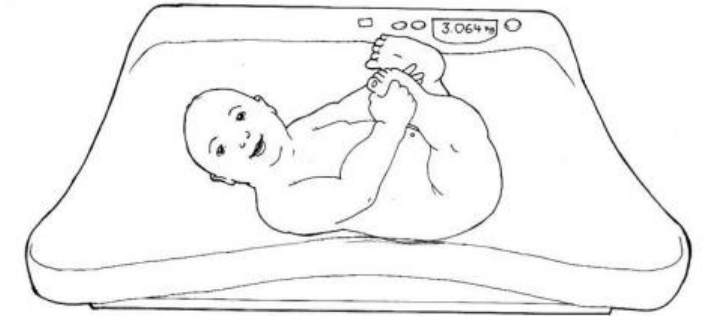


Infant Growth Assessment

- Child Growth Assessment = *STANDARDIZE*

- Undress
 - Length board
 - ~Tape
- Weight
 - Scale calibrated >2x/wk
 - 5-10g precision
- Head circumference
- Feed
- Bleed

INTERGROWTH-21st Anthropometry Manual



Infant Anthropometry Checklist

Weight:

1. Turn scale on
2. Tare if necessary
3. Place baby on scale
4. Press HOLD
5. Remove baby
6. Record to the nearest gram.

Length:

1. Position head
2. Top of head (vertex) touching headboard
3. Body straight
4. Legs straight
5. Footboard to touch heel(s)
6. Read to last completed unit (mm)

Head circumference:

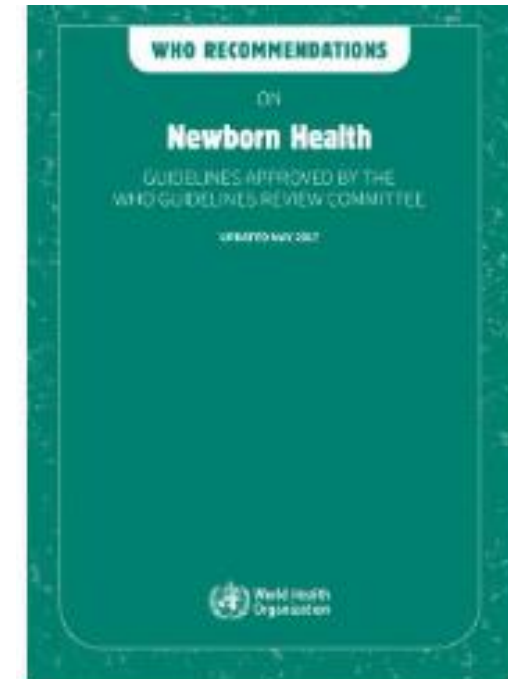
1. Position head
2. Anchor tape just above eyebrows
3. Palpate most posterior part of head
4. Pass tape around head
5. Cross-over tape ends
6. Hold tape against front and back of head
7. Pull tight
8. Read to last completed unit (mm)

WHO recommendations on newborn health:
guidelines approved by the WHO Guidelines
Review Committee.

Geneva: World Health Organization; 2017
(WHO/MCA/17.07).


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<https://www.who.int/publications/i/item/WHO-MCA-17.07>



Infant Blood Sample Collection

- Closed system
- Small gauge butterfly needle with extension
- Small volume tube and low vacuum
- Immobilise and assistant
- Warm up
- Vein finder
- Tourniquet vs flexed wrist



***What
strategy
works for
you?***

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- National Institutes of Mental Health

Pharmaceutical support

- Gilead Sciences

HIV Prevention Trials Network

- Leadership and Operations Centre, FHI360
- Laboratory Centre (Johns Hopkins)
- Statistical Center for HIV/AIDS Research and Prevention, Fred Hutchinson Cancer Research Center
- HPTN Leadership

HPTN 084 Study team

- 20 sites in 7 countries in sub-Saharan Africa
- Community advisory boards and partners

... and our study participants!



/HIVptn

UM1AI068619-15 (HPTN Leadership and Operations Center), UM1AI068617-15 (HPTN Statistical and Data Management Center), and UM1AI068613-15 (HPTN Laboratory Center).

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