# Evaluating the effectiveness of Hepatitis B immunoglobulin and vaccination in preventing mother-to-child transmission of hepatitis B virus, in the context of C4 genotype: a retrospective cohort study in Australia's Northern Territory.

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# Disclosures

- I have no relevant disclosures to declare

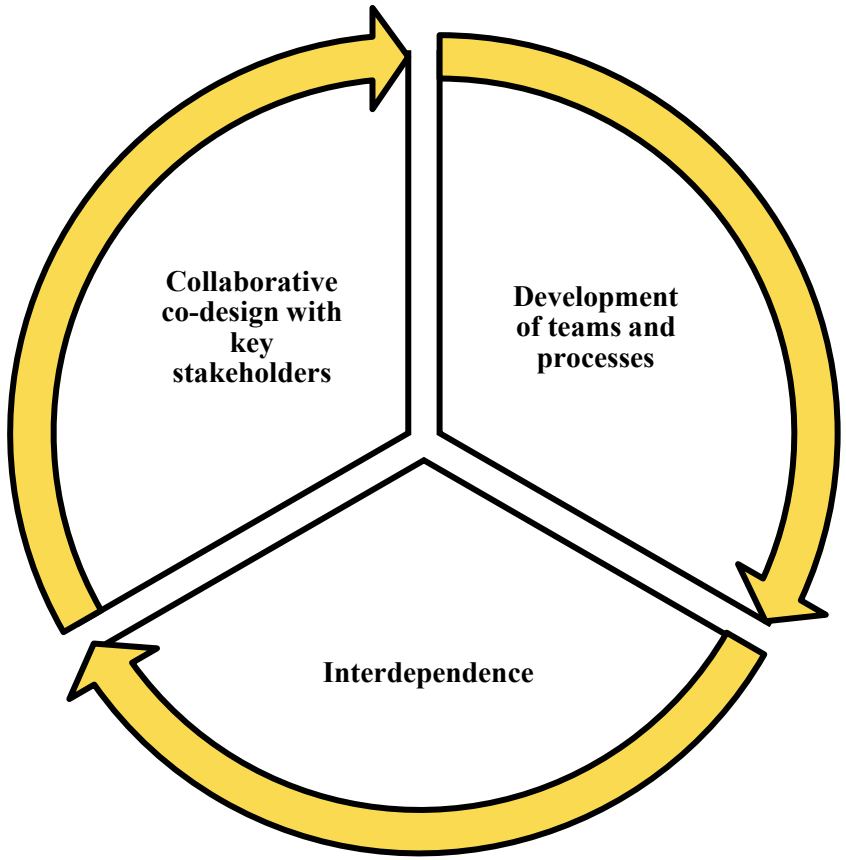
# Acknowledgements

*I wish to begin today by acknowledging that we meet on the beautiful lands of the Kuarna people, to pay my respect to Elders past and present & acknowledge that sovereignty was never ceded. I also wish to acknowledge that much of this work was undertaken on the lands of the Larrakia people. I thank the Aboriginal and Torres Strait Islander people living with hepatitis B who have generously participated in this research.*

# Hepatitis B in the Northern Territory

- Highest prevalence of chronic hepatitis B (CHB) in Australia – 1.73% compared to 0.78%
- Aboriginal and Torres Strait Islander people are disproportionately affected – 6% overall prevalence
- Unique subgenotype C4 identified – associated with faster progression to cirrhosis and liver cancer

# Hep B PAST Program model




**Step 1:** Foundation step.

- HBV status allocation and linkage to care
- Care plans and clinical recalls in place
- Creation of "Hep B Hub" clinical facilitation tool
- Active, continuous quality improvement cycles

**Step 2:** Capacity building the health workforce

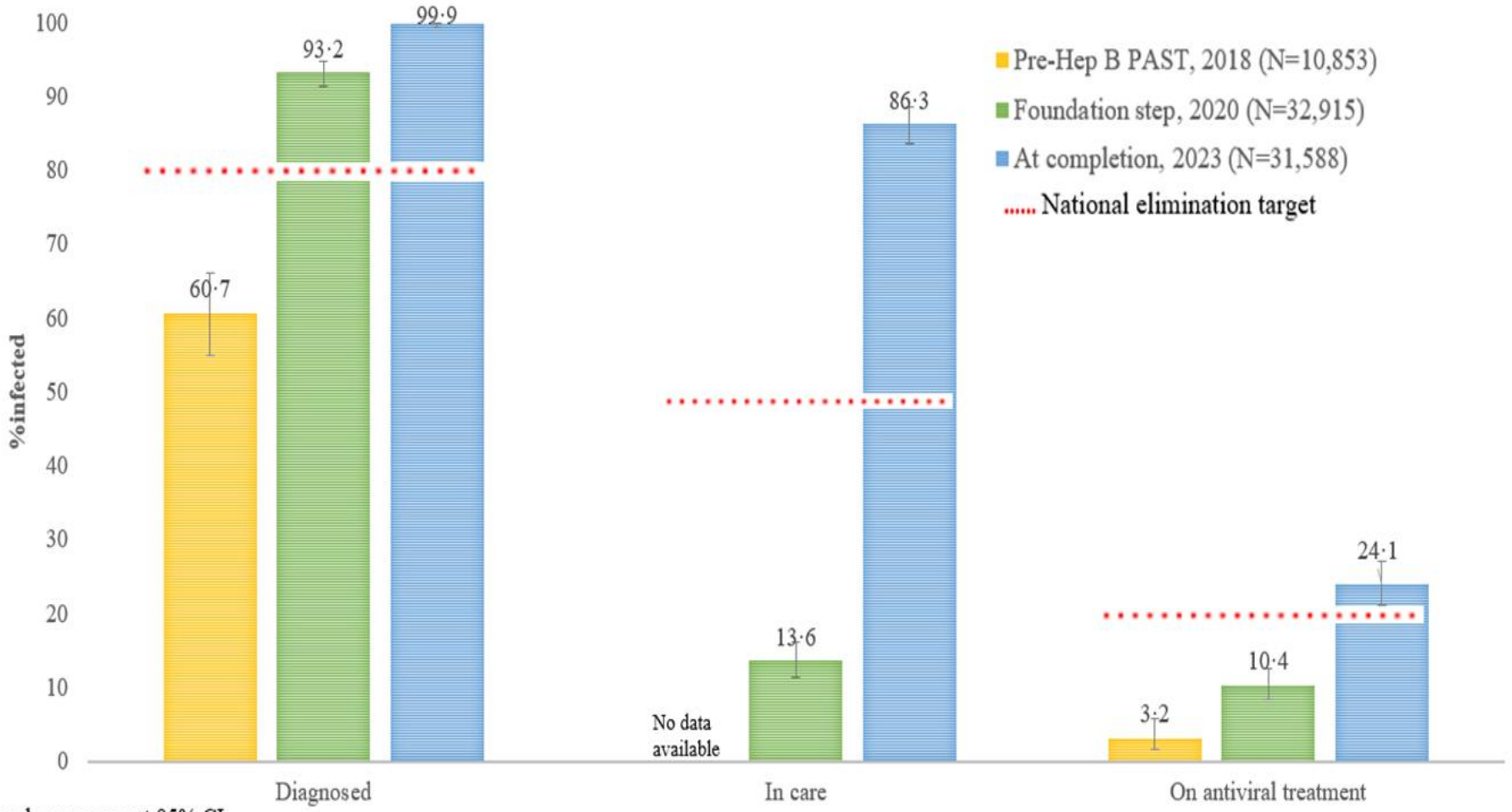
- Clinical care teams in place
- Culturally safe "Managing hepatitis B" training provided
- Ongoing education, support and mentoring
- Active central coordination of care

**Step 3:** Supported transition to PHC

- Delivering care in the community supported by specialist outreach service
- Provide education in a person's first language

Hosking K et al. *Lancet Regional Health*, 2024

# Does it work?




Error bars represent 95% CI

Note: There is no data in Pre-Hep B PAST "in care" as it was not possible to measure this variable before the creation of the "Hep B Hub"

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# Does it work?

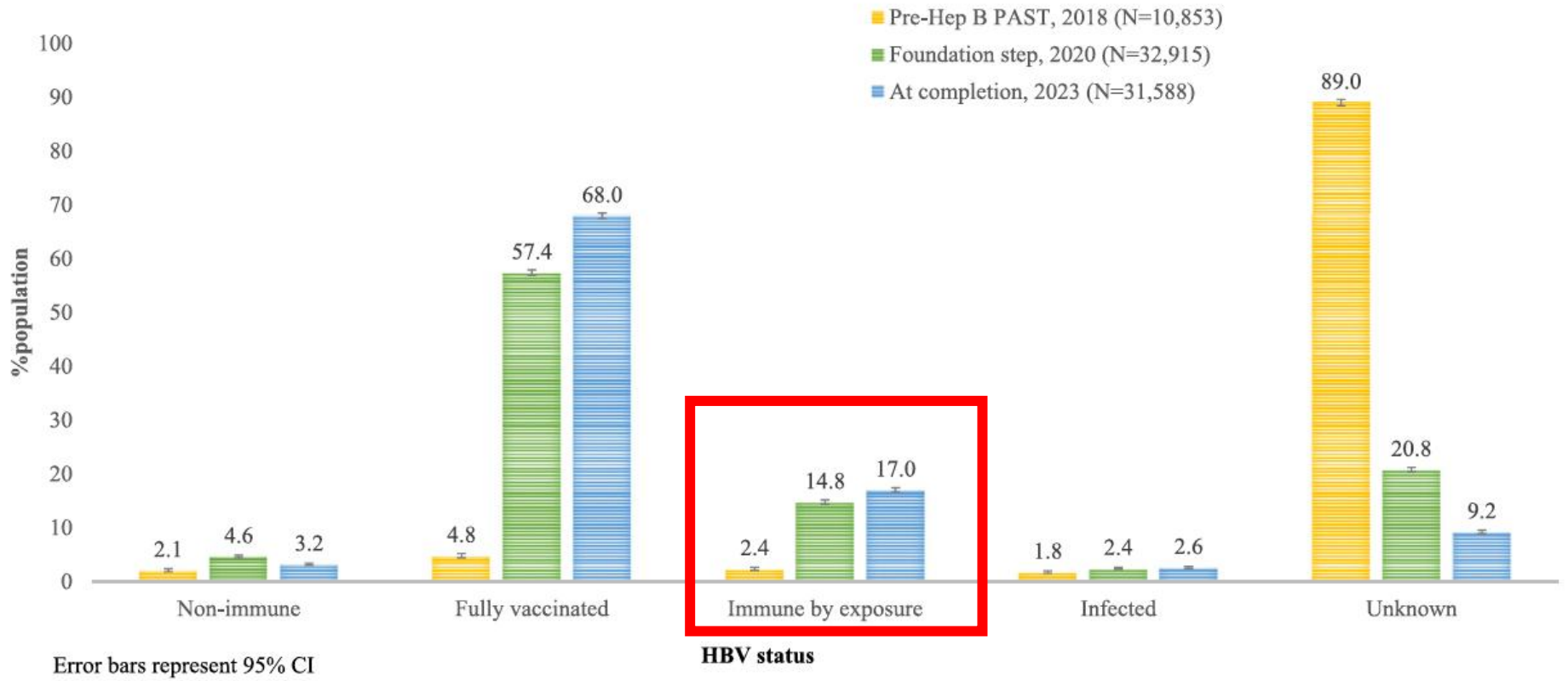


*Fig. 4:* Documented HBV status of the study population, comparing time points 1. Pre–Hep B PAST (2018), 2. Foundation step (2020), and 3. Completion of Hep B PAST (2023).

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# Hepatitis B vaccine in the context of C4 genotype

- Serotype mismatch between hepatitis B vaccine (genotype A, serotype *adw2)* and circulating subgenotype (genotype C4, serotype *ayw3)*
- The hepatitis B vaccine shows good efficacy at preventing infection
- May be suboptimal in protecting against hepatitis B core antibody positivity

# Hepatitis B in birthing parents in the NT

- As part of the Hep B PAST program, manual review of records identified incomplete documentation regarding administration of hepatitis B immunoglobulin (HBIG) in terms of administration, timing and indication

1. Are babies born to Aboriginal and Torres Strait Islander parents in the NT receiving recommended interventions to prevent acquisition of hepatitis B?
2. Do we know the serological status of the babies born?

# Global hepatitis B transmission

HBeAg positivity

High viral load >$10^6$ IU/mL

Mutations e.g. pre-S / S mutations

Lack of birth immunoprophylaxis

Filippo-Villa D, Navas M. *Microorganisms*, 2023.

# PREGNANCY

Screening during pregnancy

↓

Antiviral therapy from 28 weeks if viral load >=200,000 IU/mL

## Preventing vertical transmission of hepatitis B

*Retrospective study of babies born to Aboriginal and Torres Strait Islander people living with chronic hepatitis B, 2010-2023 in the context of C4 genotype*

# NEONATE

Hepatitis B immunoglobulin
Birth dose of hepatitis B vaccine

Within 48 hours
Within 7 days of birth

HBV vaccine – 2 months

Minimum interval 6 weeks

HBV vaccine – 4 months

Minimum interval 1 month

HBV vaccine – 6 months

Minimum interval 2 months

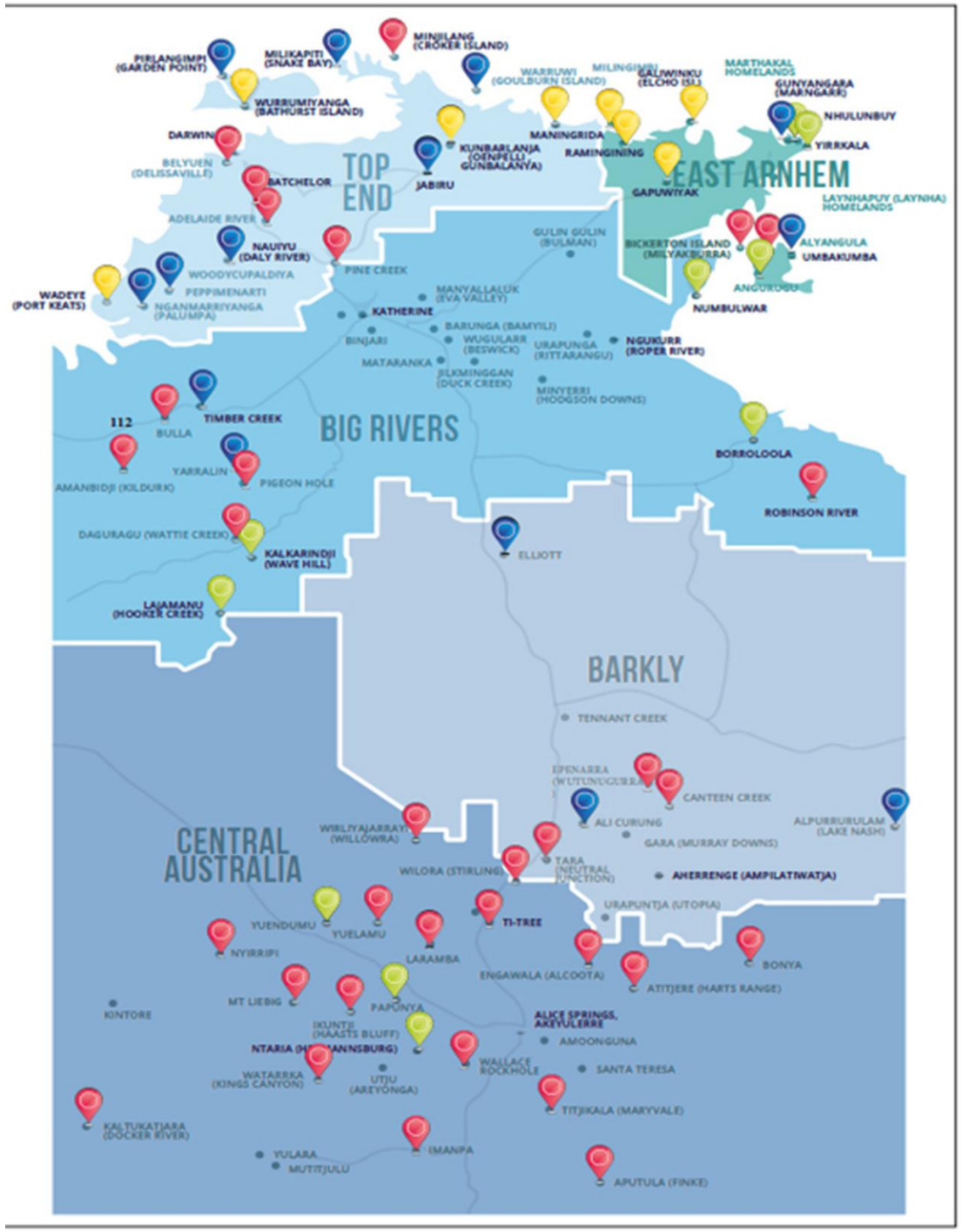
Min 4 months

HBV vaccine – 12 months

If born at <32 weeks' gestation or <2000g

# Outcomes of interest:

- Do Aboriginal and Torres Strait Islander neonates in the Northern Territory receive the recommended number of doses of HBIG and hepatitis B vaccine *on time*?
- Do Aboriginal and Torres Strait Islander children receive appropriate serological follow up?
- How many Aboriginal and Torres Strait Islander children acquire chronic hepatitis B infection (HBsAg positive) or are exposed to the virus (HBsAg negative, HBcAb positive)?




Retrospective cohort study, 2010-2023

Data extracted from medical records of those who had received HBIG including those in the ‘Hep B Hub’

- Electronic register and care facilitation tool from participating communities in the Northern Territory

- Identified birthing parent and siblings
- Extracted:
  - Doses of HBIG and vaccine administered
  - Serological follow up
  - Serological outcomes

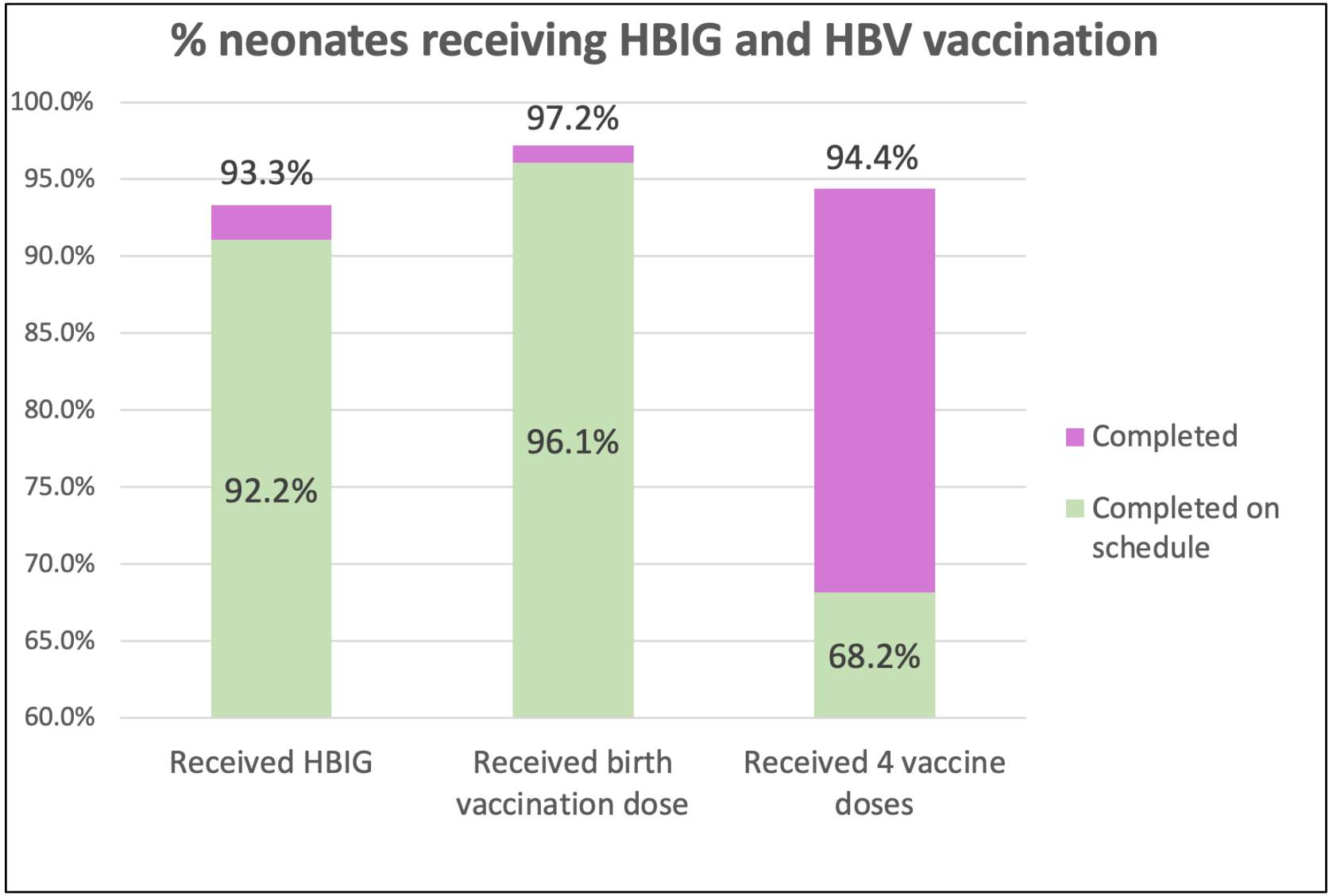
Hosking K et al. *Lancet Regional Health*, 2024

# Results

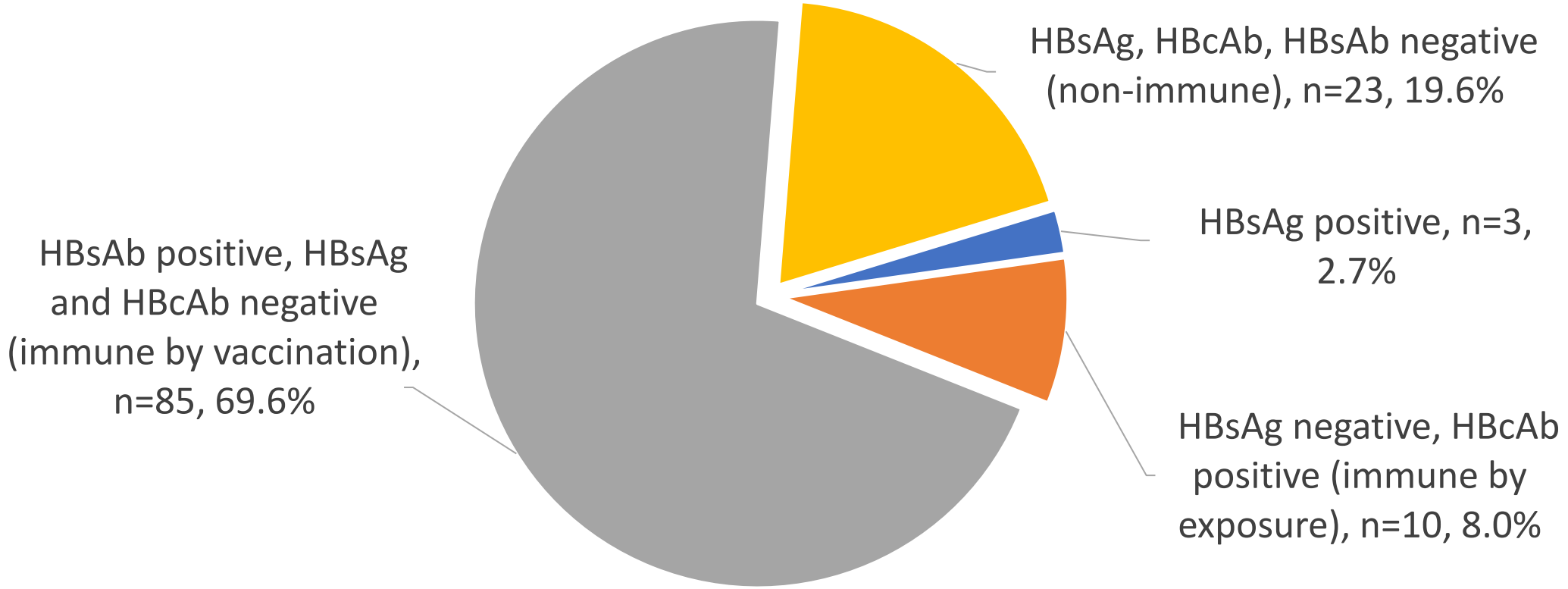
**Demographic data of Aboriginal and Torres Strait Islander people whose infants received Hepatitis B immunoglobulin in the Northern Territory, 2010-2023, n=184**

| Demographic variable (n=184) | |
|---|---|
| Maternal serostatus (n, %) | |
| Hepatitis B sAg positive (overall) | 178 (96.7) |
| Hepatitis B sAg positive, eAg positive | 68 (37.0) |
| Hepatitis B sAg positive, eAg negative | 86 (46.7) |
| Hepatitis B sAg positive, eAg status unknown | 24 (13.0) |
| Hepatitis B sAg negative, cAb positive | 6 (3.3) |
| Maternal viral load (IU/mL; median, range) | 213 (0-2.06x$10^8$) |
| Pregnant people who received antiviral therapy in pregnancy (n, %) | 35 (19.6) |
| Proportion of very preterm births <32 weeks (n, %) | 4 (9.5) |
| Proportion low birth weight <2000g (n, %)[b] | 5 (11.9) |

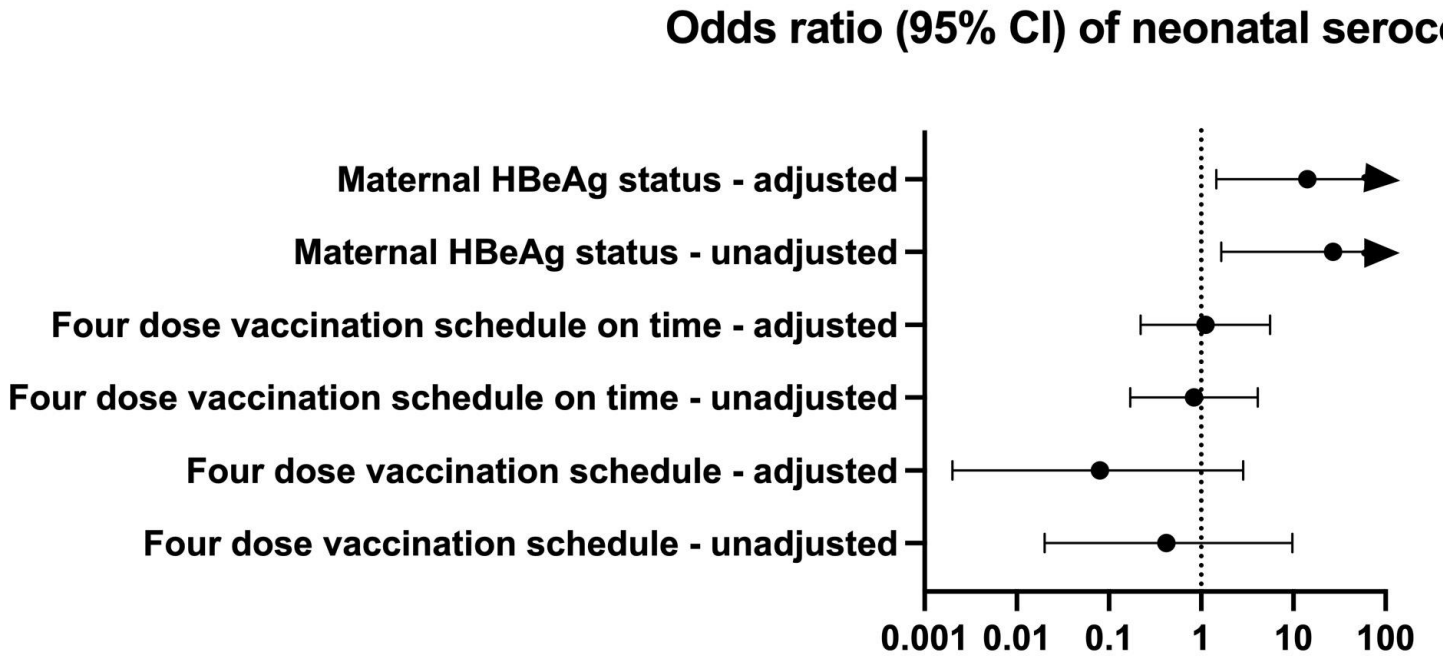
# Proportion of neonates receiving HBIG and hepatitis B vaccination in total, and on schedule, 2010-2023; n=179



# Hepatitis B serological status of neonates, n=121



# Predictors of neonatal seroconversion due to exposure to maternal Hepatitis B among Aboriginal and Torres Strait Island people in the Northern Territory, 2010-2023; n=121




| | OR (95% CI) | p-value |
|---|---|---|
| Maternal HBeAg status - adjusted | 14.2 (1.46, 137.8) | 0.02 |
| Maternal HBeAg status - unadjusted | 27.1 (1.65, 455.4) | 0.02 |
| Four dose vaccination schedule on time - adjusted | 1.12 (0.22, 5.60) | 0.90 |
| Four dose vaccination schedule on time - unadjusted | 0.84 (0.17, 4.12) | 0.82 |
| Four dose vaccination schedule - adjusted | 0.08 (0.002, 2.86) | 0.17 |
| Four dose vaccination schedule - unadjusted | 0.42 (0.02, 9.80) | 0.59 |

HBeAg status **strongest predictor** of neonatal seroconversion due to maternal hepatitis B exposure

# Understanding the drivers of transmission

- 3 cases of transmission of chronic hepatitis B
  - HBeAg positive – key driver of transmission
  - High viral load
  - Lack of antiviral therapy
  - All received HBIG and 4 doses of hepatitis B vaccine on schedule

- 10 cases of hepatitis B core positivity
  - 9 cases HBeAg positive; 8 had viral load >200,000 IU/ML
  - Five received antiviral therapy
  - All received HBIG
  - All received 4 doses of hepatitis B vaccine - 6 ‘on schedule’

# Key Findings

- Overall high degrees of adherence to recommendations including administration of HBIG and 4 dose vaccination schedule
- Doses that were not ‘on schedule’ were often when dose interval was too short
  - Some flexibility required in remote settings

- However, **transmission is continuing in the NT**

# Key Findings

- Need to address health system factors:
  - Access to culturally safe healthcare
  - Specialist outreach support for remote primary care centres

- Does the current vaccine provide adequate protection against acquisition of hepatitis B in the context of C4 genotype?


With thanks to the Aboriginal and Torres Strait Islander mothers living with hepatitis B and their babies in the NT