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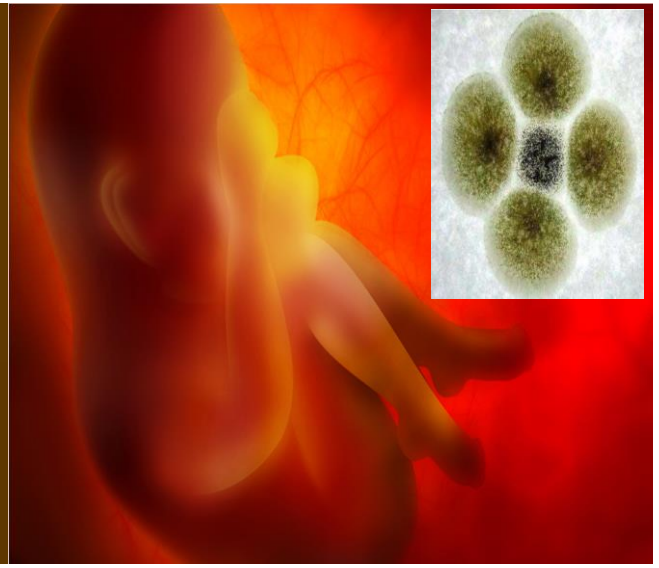
Maternal exposure to multiple mycotoxins and adverse pregnancy outcomes: a prospective cohort study in rural Bangladesh

Biologics | Open access | Published: 17 April 2023 | 97, 1795–1812 (2023)



Presenter: Nicholas Kyei BSc, MD, PhD, MSc, MGCP, MFTM-RCPSG
Affiliations:

CHARITÉ UNIVERSITÄTSMEDIZIN BERLIN
HEIDELBERG UNIVERSITY HOSPITAL
HEIDELBERG INSTITUTE OF GLOBAL HEALTH
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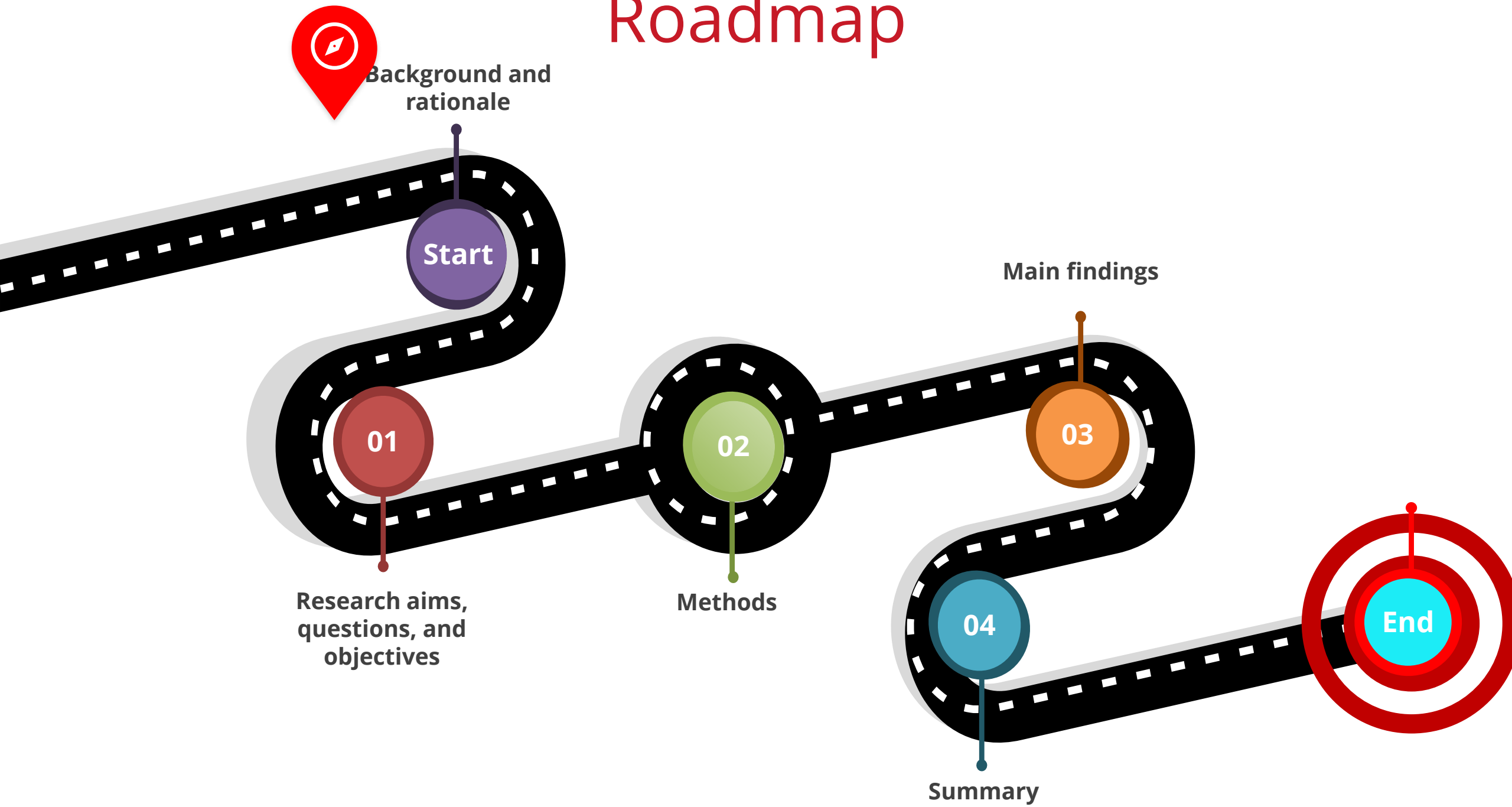
25th September 2024

WCE
WORLD CONGRESS OF EPIDEMIOLOGY 2024

Roadmap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So why this research?

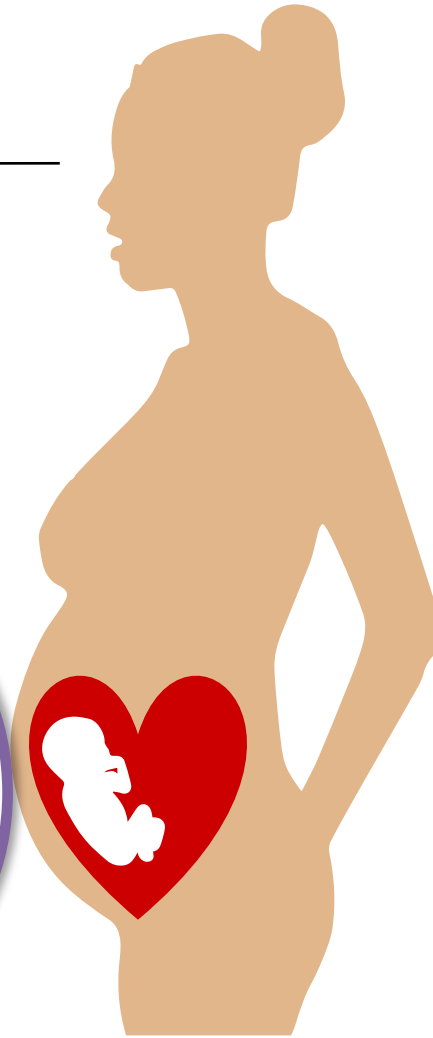
- Adverse Pregnancy Outcomes (APOs) remain a global and local public health concern with long-lasting impacts

Nearly **300,000** maternal deaths in 2020 alone, most in LMICs
(WHO, 2023)

3 million neonatal deaths
2.6 million stillbirths occur each year, nearly 98% in LMICs
(Lawn et al.,2016)

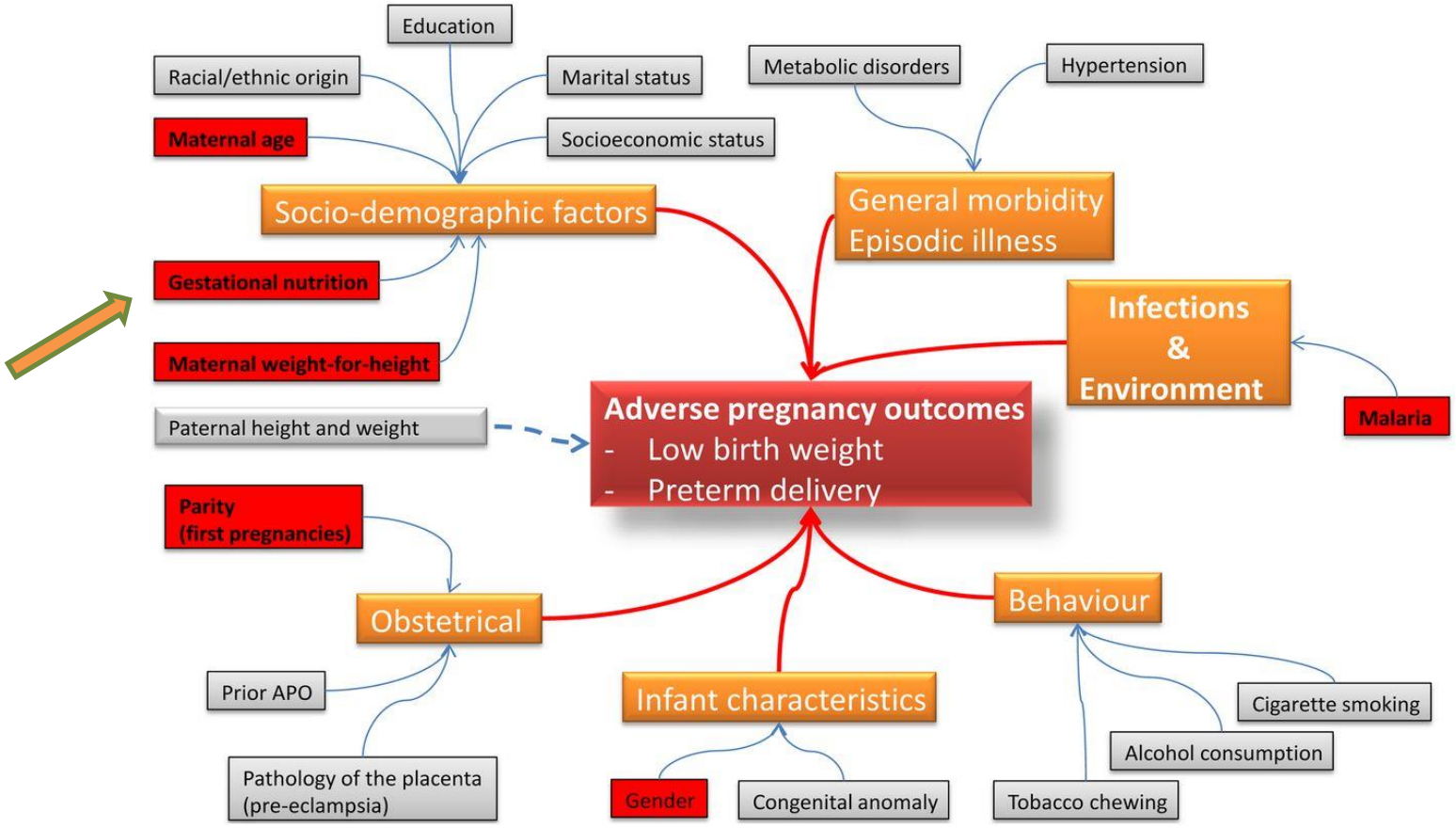
15 million babies born too soon (Preterm birth)
(Blancowe et al., 2012)

About **20 million** babies are born too small (low birth weight)
(Blancowe et al., 2019)



Etiology of APOs: what do we know?

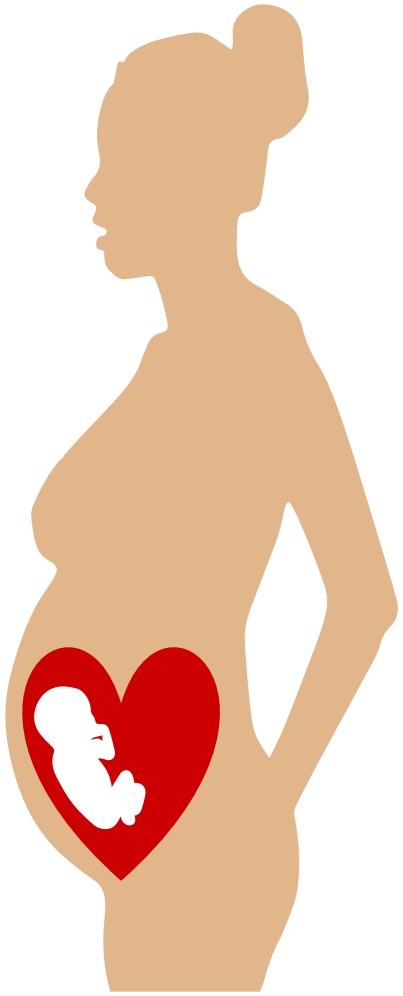
Undisputed impact of maternal nutrition



Conceptual framework of risk factors of adverse pregnancy outcome

Ghyslain Mombo-Ngoma et al. BMJ Open 2016;6:e011783

BMJ Open



"Optimal" Maternal Diet: Different looks shared focus

Food safety

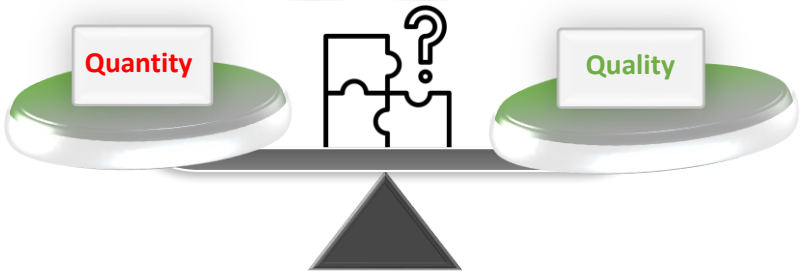
Besides insufficient nutrients, **foods consumed** by expectant mothers, especially in LMIC settings, **may contain hazardous contaminants**

Concentration

Food hygiene and prevention of foodborne diseases (**Microbiology**)

Some attention

Polyaromatic hydrocarbons, heavy metals, and organic pesticides

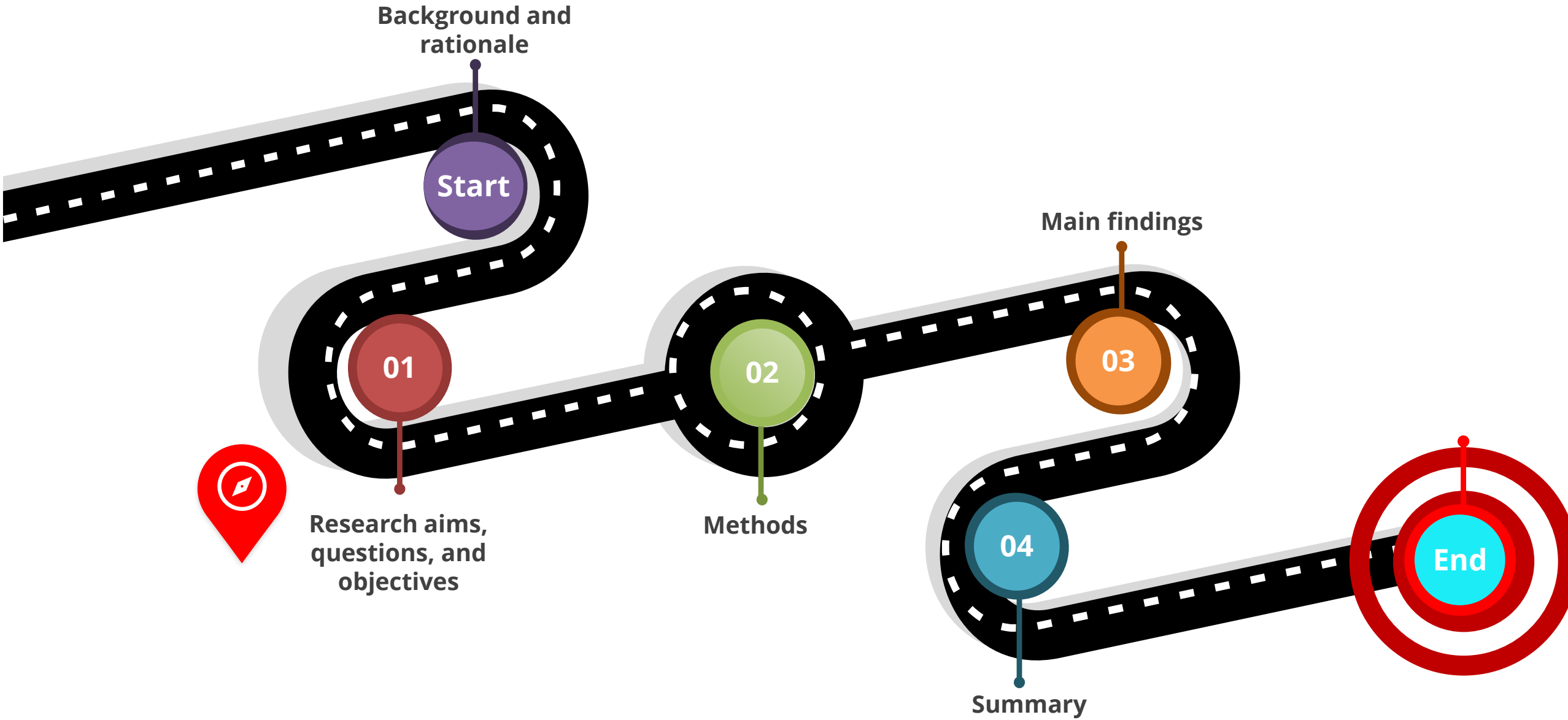


Little attention so far

Natural toxins like **mycotoxins and their impacts on pregnancy outcomes**

Forgotten Element of the "Optimal" Maternal Diet

Roadmap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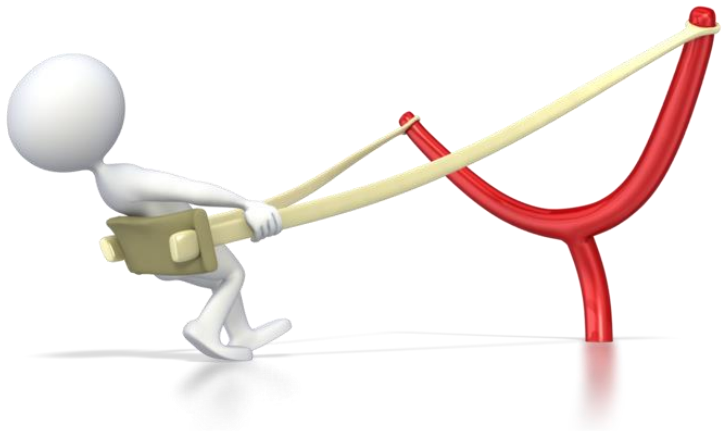
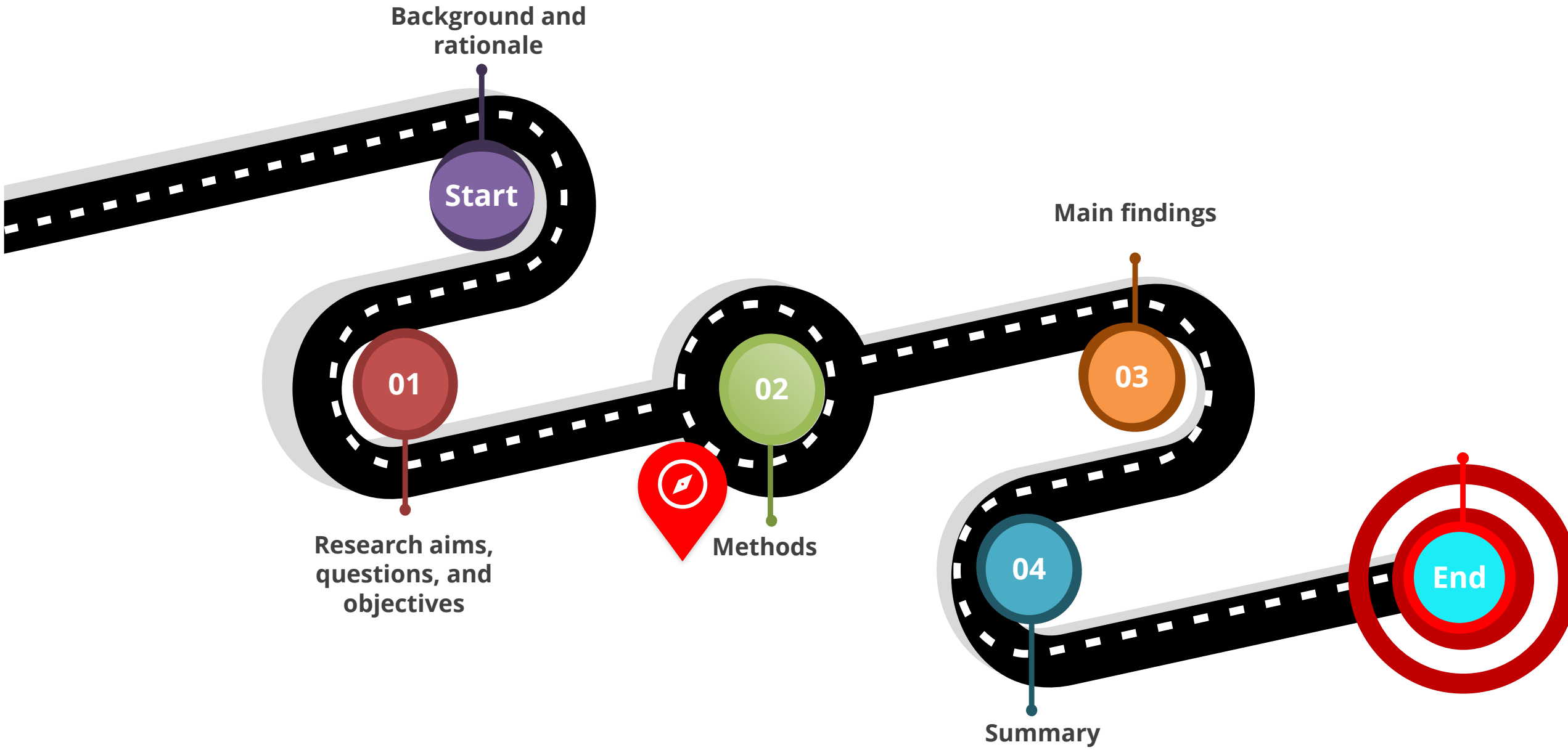
Research aims



1. To quantitatively describe **mycotoxin exposure burden** in pregnant women in rural Bangladesh,
2. identify **critical control points to** minimize dietary mycotoxin exposures, and
3. investigate **potential effects** on adverse pregnancy outcomes

Roadmap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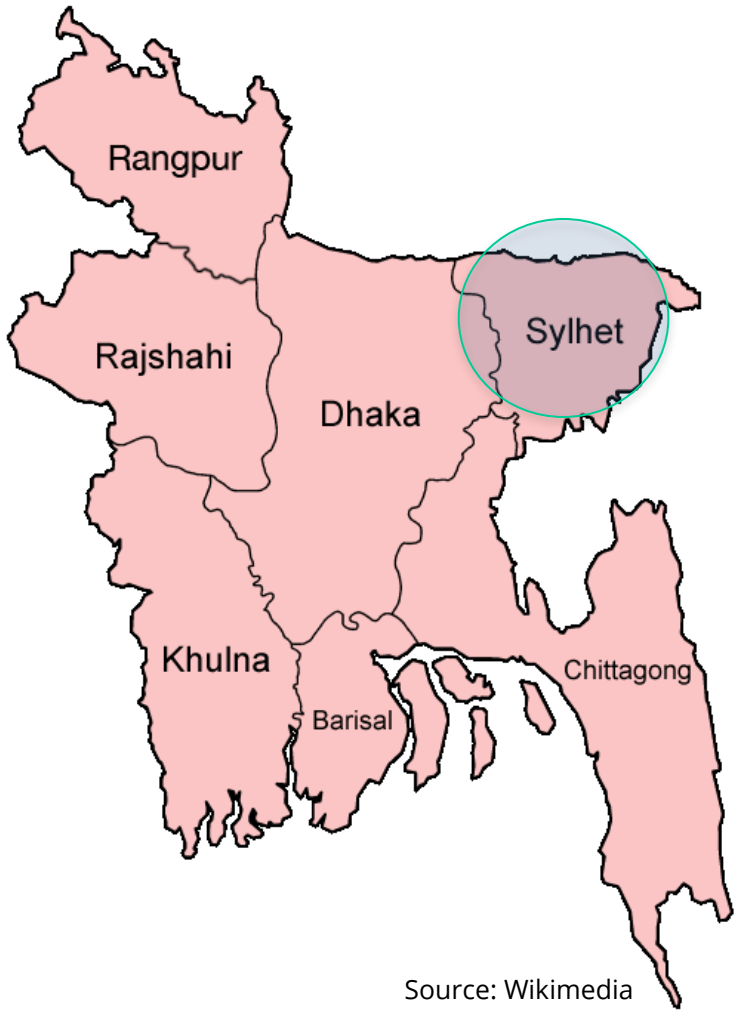
Project context

Source: Wikimedia



Source: Wikimedia

FAARM ফার্ম

FOOD AND AGRICULTURAL APPROACHES TO REDUCING MALNUTRITION

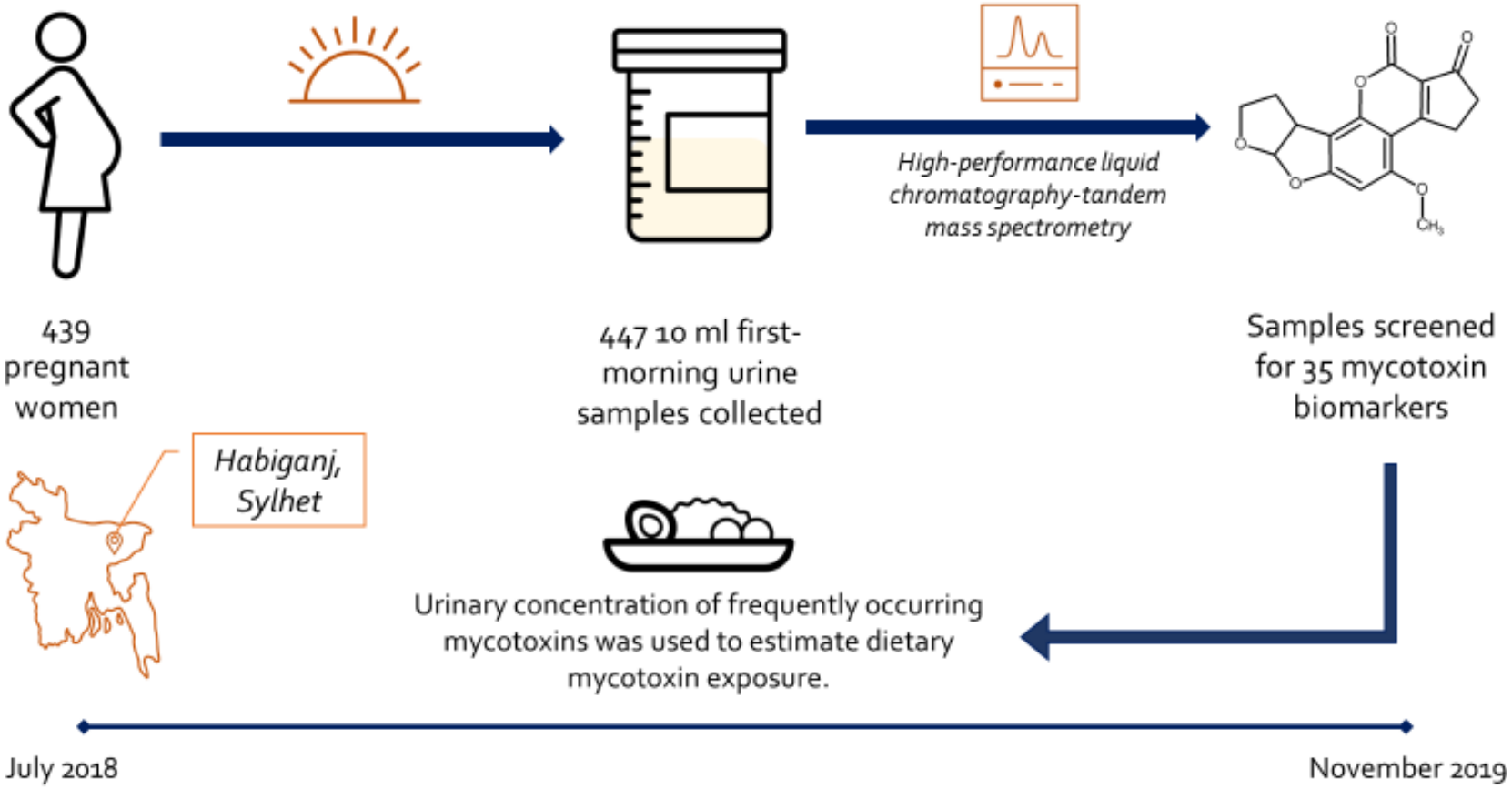
- A cluster-randomized control trial
- In two sub-districts of Habijanj district
- Enrolled 2705 young married women in 96 settlements
- Evaluated the impact of a homestead food production program on undernutrition in young children

What we did…

Objective 1

To describe urinary occurrence and conduct exposure risk assessment of major mycotoxins among pregnant women

Method 1: Add-on cohort study with biomonitoring



- Dietary intake data
- Including data on intake of common local stimulants – betel nut, betel leaf, chewing tobacco

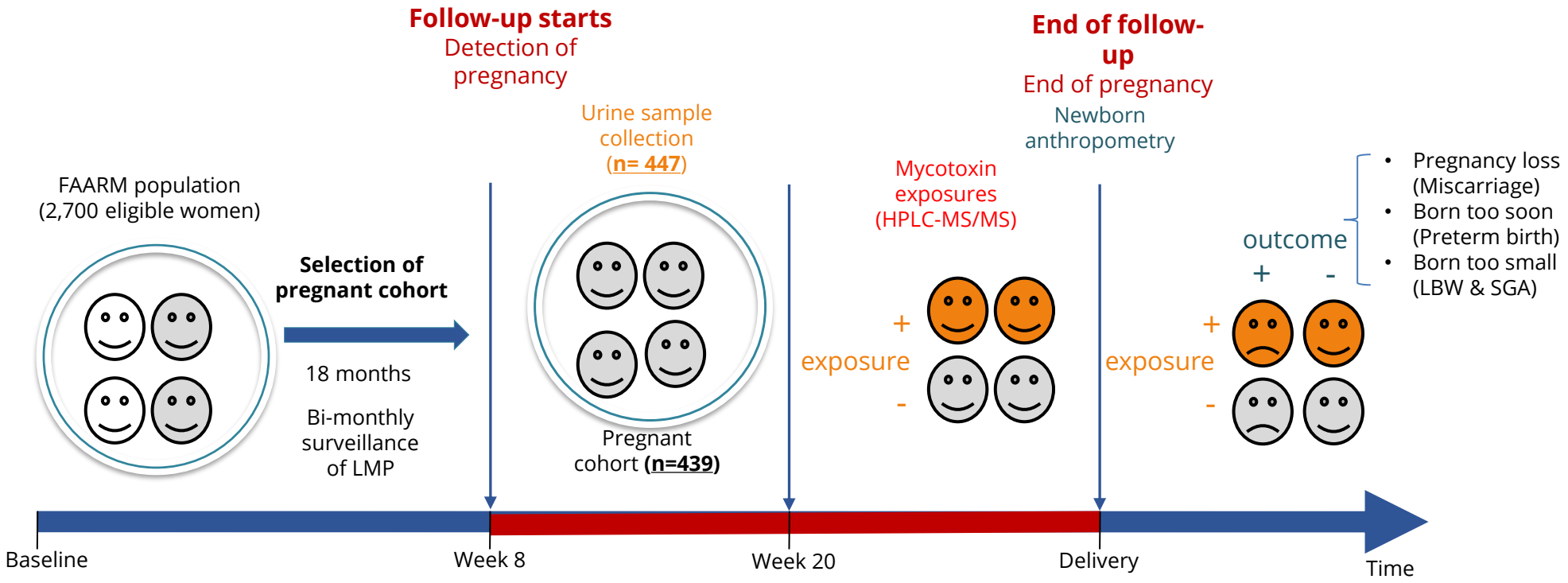
Association analyses

What we did…

Objective 3

To quantify the potential association of maternal exposure to mycotoxins with specific adverse pregnancy outcomes

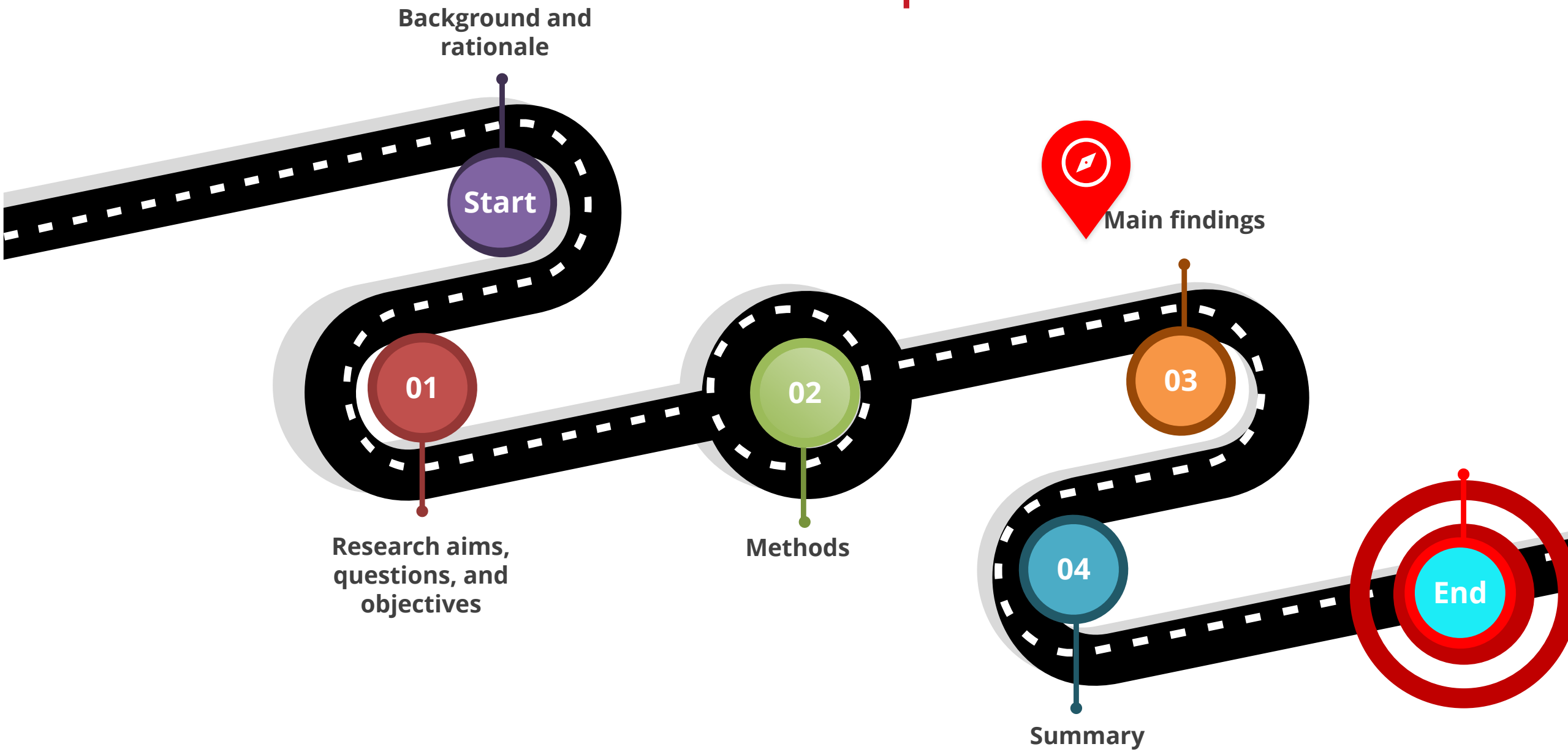
Method 3: Prospective Cohort Study-Based Exposure – Outcome Analysis



Prospective Cohort Design

Prospective assessment of exposures and outcomes

Roadmap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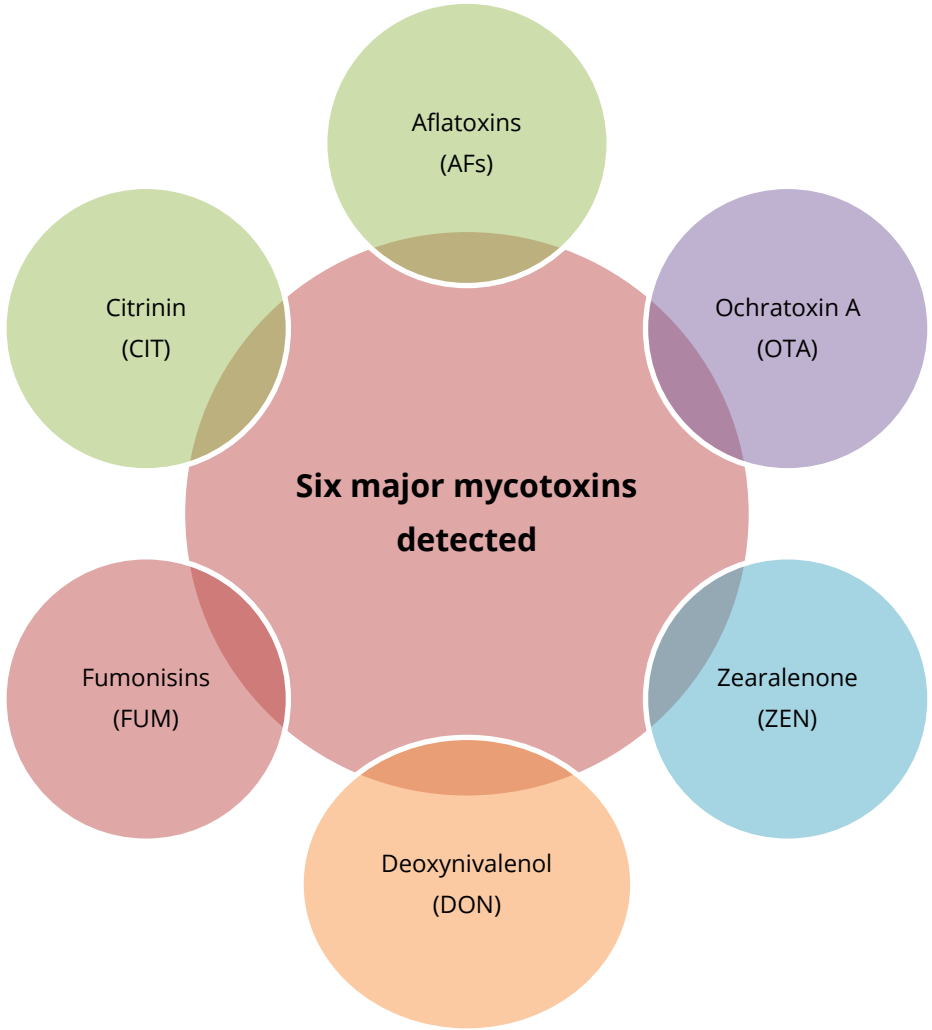
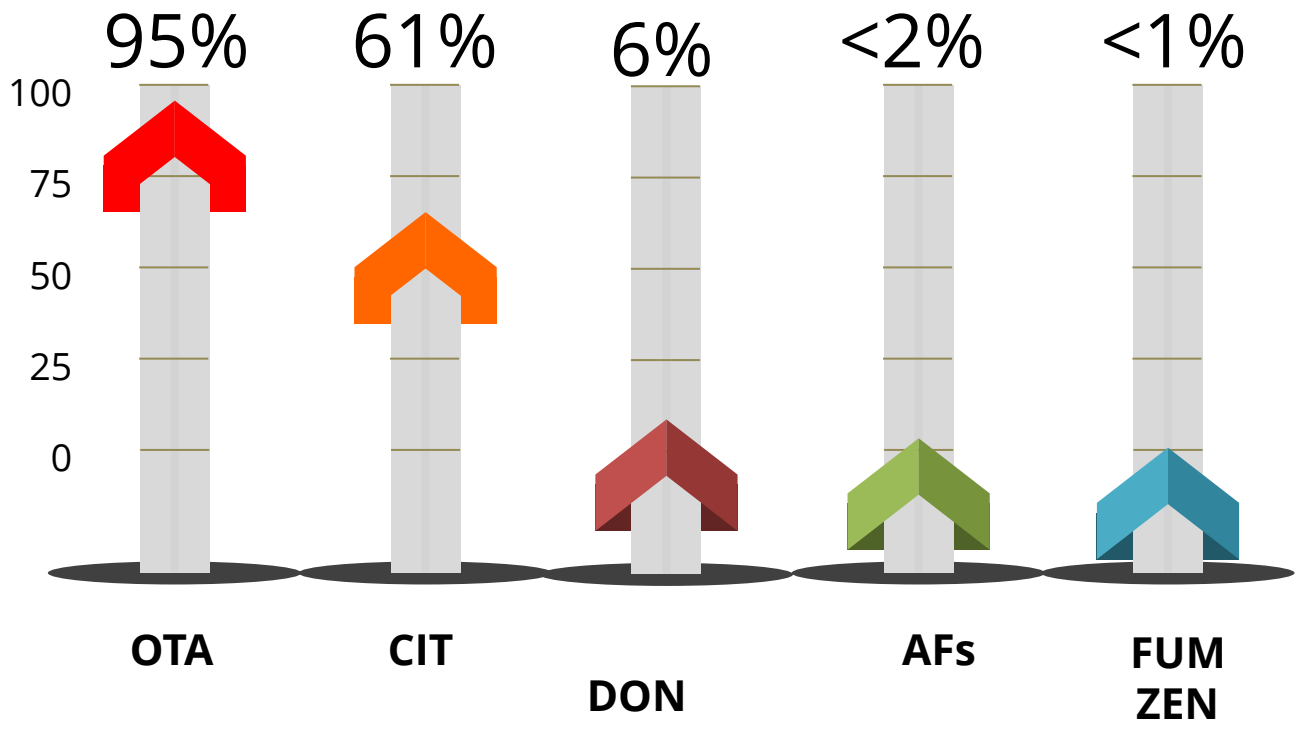
Objective 1: Key findings - Occurrence of mycotoxins in urine



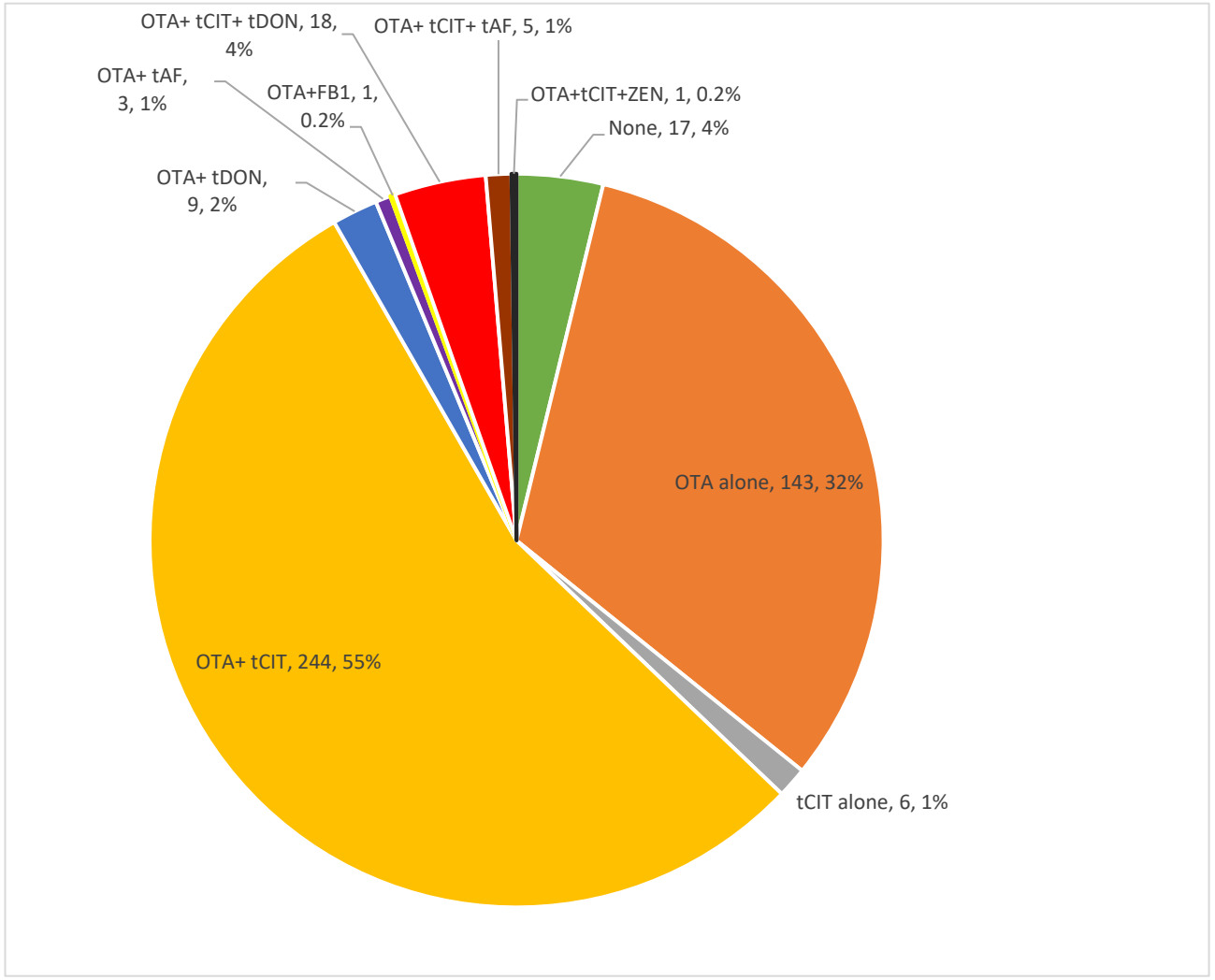


|Positive detection (≥LOD) in urine samples (*n* = 447)|

Kyei et al.,2022; Arch. Toxicol.; 96:2123-2138

Objective 1: key findings - The reality of mycotoxin co-exposure…

Figure 2: Mycotoxin combinations and their occurrence in urine samples of pregnant women in rural Bangladesh (n=447)



Kyei et al. 2022

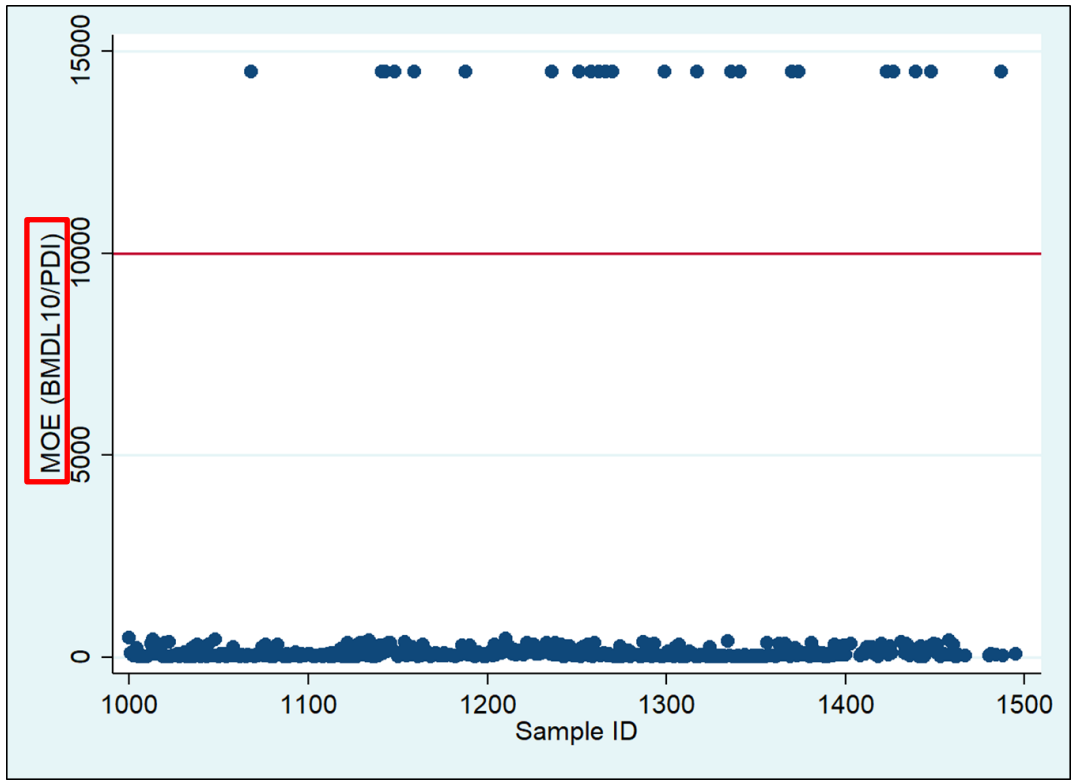
*t*CIT- total CIT (CIT+ HO-CIT); *t*DON- total DON (DON + DON-Glucuronides); *tAF*- total aflatoxins (AFM1+AFB2).

- **Pervasive mycotoxin exposure**; only 17 samples free of all investigated mycotoxins (green)
- Mycotoxins **co-occurrence** found in **281/447 (63%)** urine samples
- Prevailing co-exposure: **Ochratoxin A and Citrinin**

Mycotoxin cocktail

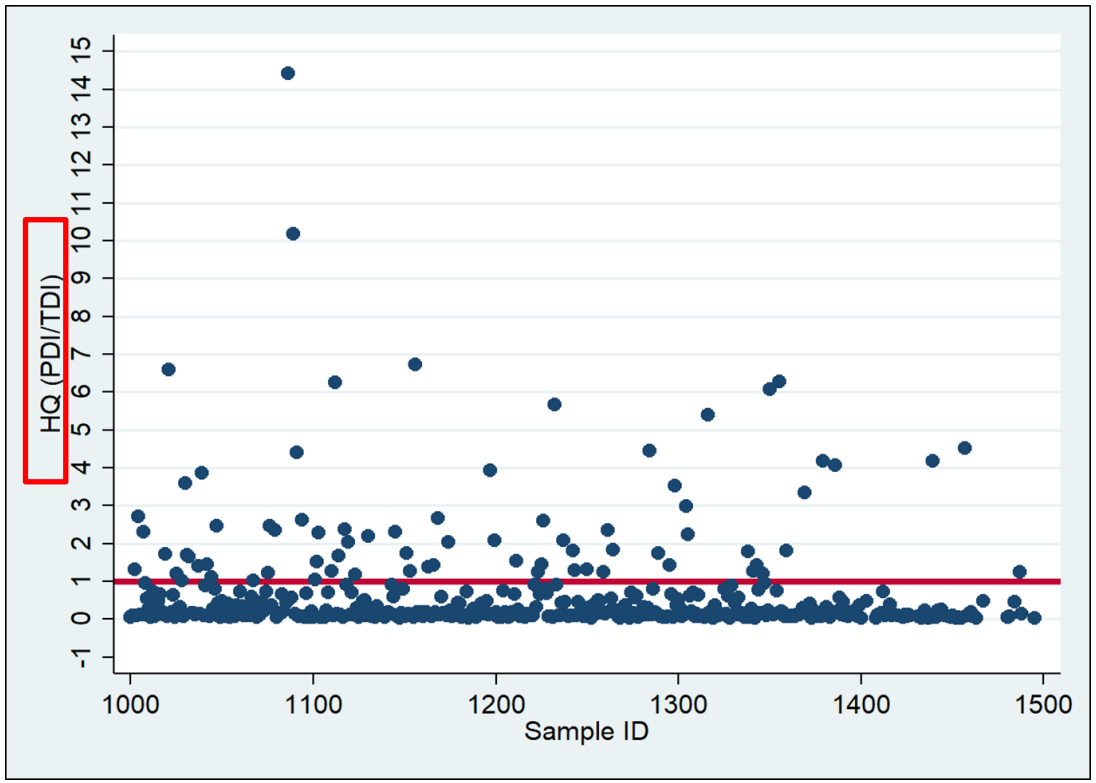
Objective 1: key findings - Dietary mycotoxin health risk assessment

- The Margin of Exposure (MOE) of pregnant women to dietary **ochratoxin A** under the lowest exposure scenario (n=447)



The red line shows a MOE of 10000. If the MOE is <10000, the exposure could be of health concern

- Hazard quotient (HQ) of dietary exposure of pregnant women to **citrinin** (n=447) under a low/moderate exposure scenario



The red line shows a HQ of 1. If the HQ is >1, the exposure could be of health concern.

Kyei et al. 2022

Objective 3: key findings - Health risks for mothers and babies

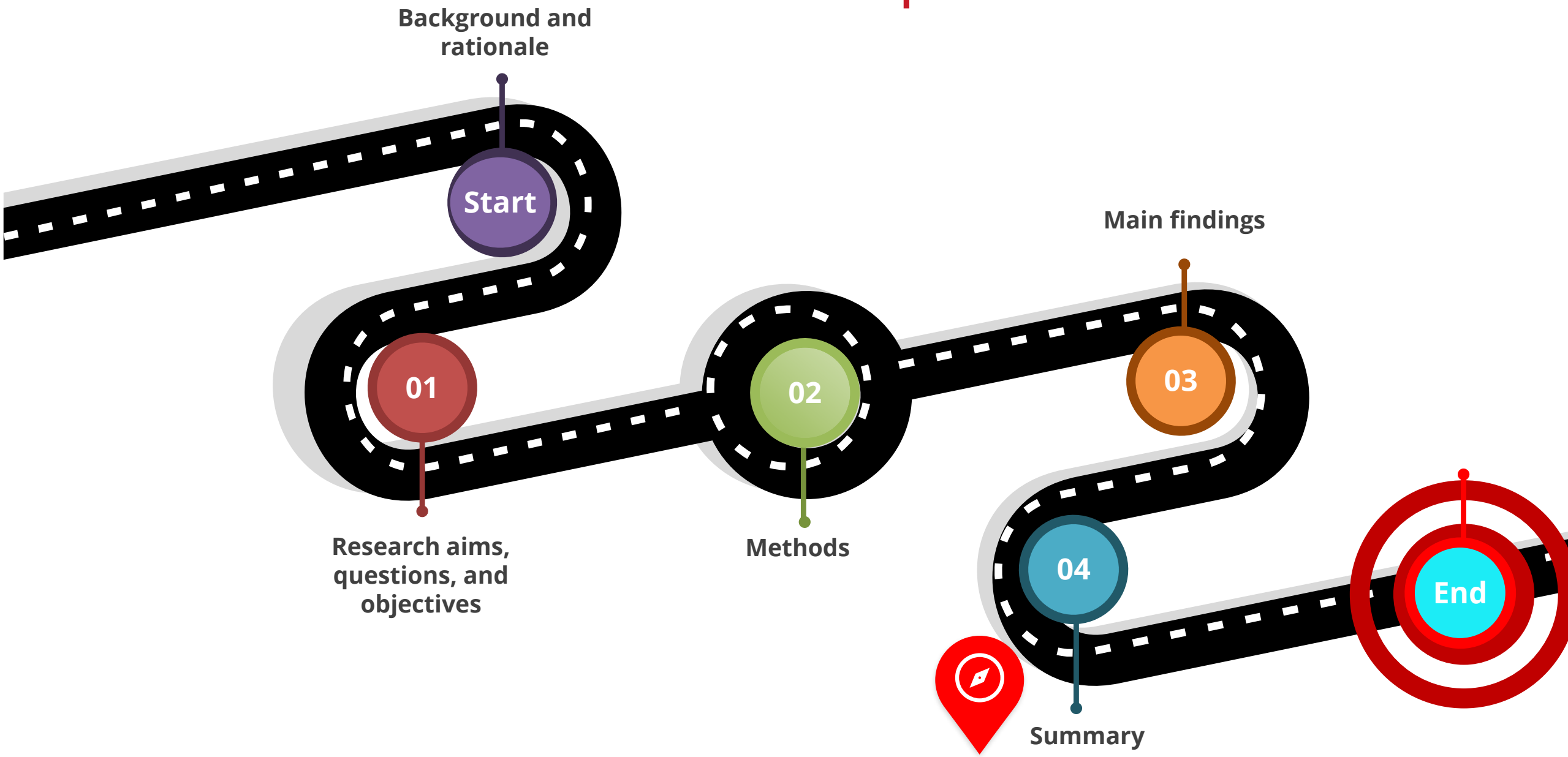
Table 13: Association between adverse birth outcomes and higher maternal dietary intake of ochratoxin A, among pregnant women in rural Habiganj district, Bangladesh

Mycotoxin intake	Pregnancy loss (*N* = 436)	Preterm birth (*N* = 317)	Low birth weight (*N* = 317)	Small for gestational age (*N* = 317)	Small-vulnerable newborn (*N* = 317)
	Adjusted[a] OR (95% CI)	Adjusted[a] OR (95% CI)	Adjusted[b] OR (95% CI)	Adjusted[c] OR (95% CI)	Adjusted[c] OR (95% CI)
PDI of OTA					
Ln (PDI)	0.88 (0.58, 1.35)	0.76 (0.52, 1.11)	1.65 (1.06, 2.55)	1.10 (0.80, 1.51)	1.02 (0.76, 1.38)
Tertiles (ng/kg bw)					
T1 (11–174)	Reference	Reference	Reference	Reference	Reference
T2 (175–400)	1.53 (0.61, 3.81)	0.55 (0.25, 1.24)	1.07 (0.40, 2.91)	0.62 (0.31, 1.26)	0.50 (0.26, 1.0)
T3 (401–3968)	0.93 (0.34, 2.50)	0.65 (0.29, 1.44)	2.64 (0.98, 7.10)	1.30 (0.64, 2.66)	1.08 (0.54, 2.19)
P for trend	0.920	0.331	0.041	0.372	0.684
High PDI of OTA (> 1000 ng/kg/day)					
No	Reference	Reference	Reference	Reference	Reference
Yes (*n* = 26)	0.24 (0.03, 1.95)	1.10 (0.37, 3.23)	4.01 (1.25, 12.81)	2.25 (0.57, 8.87)	1.86 (0.73, 4.70)

Kyei et al. 2023

- ❑ Maternal dietary intake of OTA associated with a dose-dependent increase in the odds of LBW baby
- ❑ Associations between other investigated APO and maternal dietary exposure to OTA, CIT, and DON were inconclusive

Roadmap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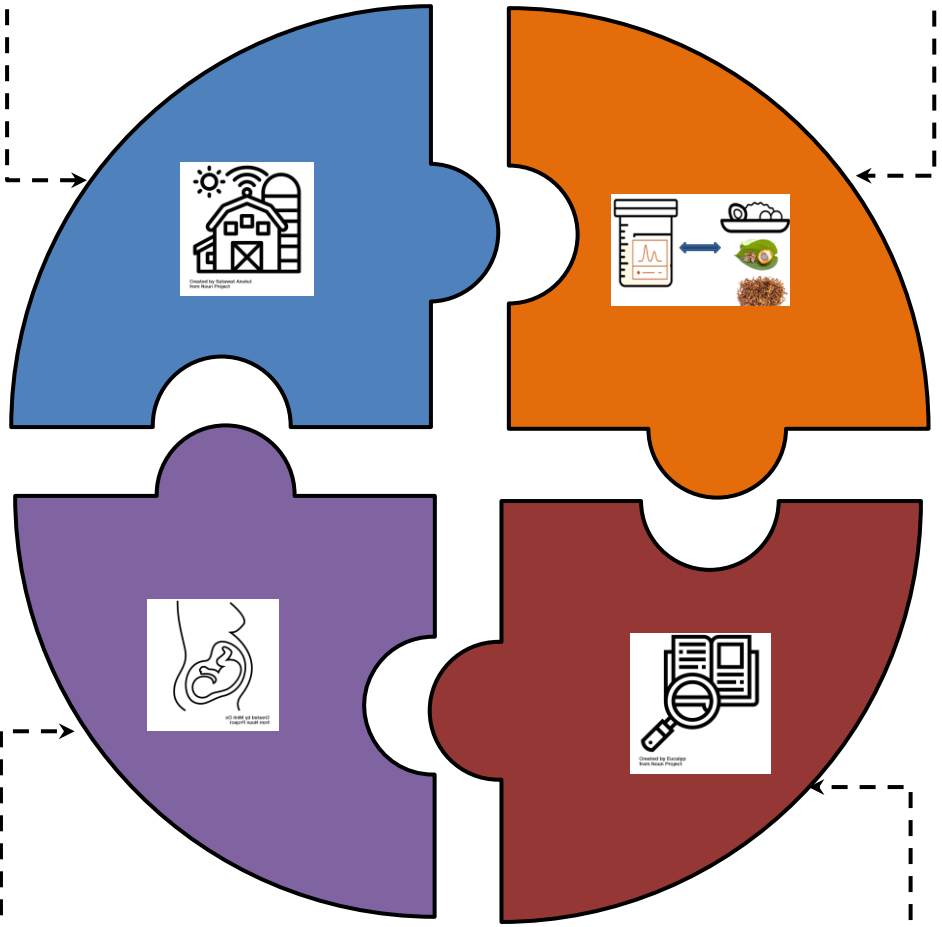
Piecing everything together

1. Pregnant women in rural Bangladesh are exposed to multiple mycotoxins particularly OTA and CIT, often exceeding safety thresholds



2. Local stimulants like betel nut, betel leaf, and chewing tobacco are potential sources of these toxins

3. Evidence of dose-dependent association between maternal ochratoxin A exposure and low birth weight

4. Large uncertainties persist regarding other adverse pregnancy outcomes, requiring further investigations


Source: Nicholas Kyei

Acknowledgments

Collaborators

CHARITÉ UNIVERSITÄTSMEDIZIN BERLIN

HEIDELBERG UNIVERSITY HOSPITAL

Helen Keller INTERNATIONAL

P I K

HEIDELBERG INSTITUTE OF GLOBAL HEALTH

Institut für Lebensmittelchemie

IfADo LEIBNIZ-INSTITUT FÜR ARBEITSFORSCHUNG AN DER TU DORTMUND

FAARM ফার্ম FOOD AND AGRICULTURAL APPROACHES TO REDUCING MALNUTRITION

Hans-Ulrich Humpf

Benedikt Cramer

Nurshad Ali

Giesela Degen

Sabine Gabrysch

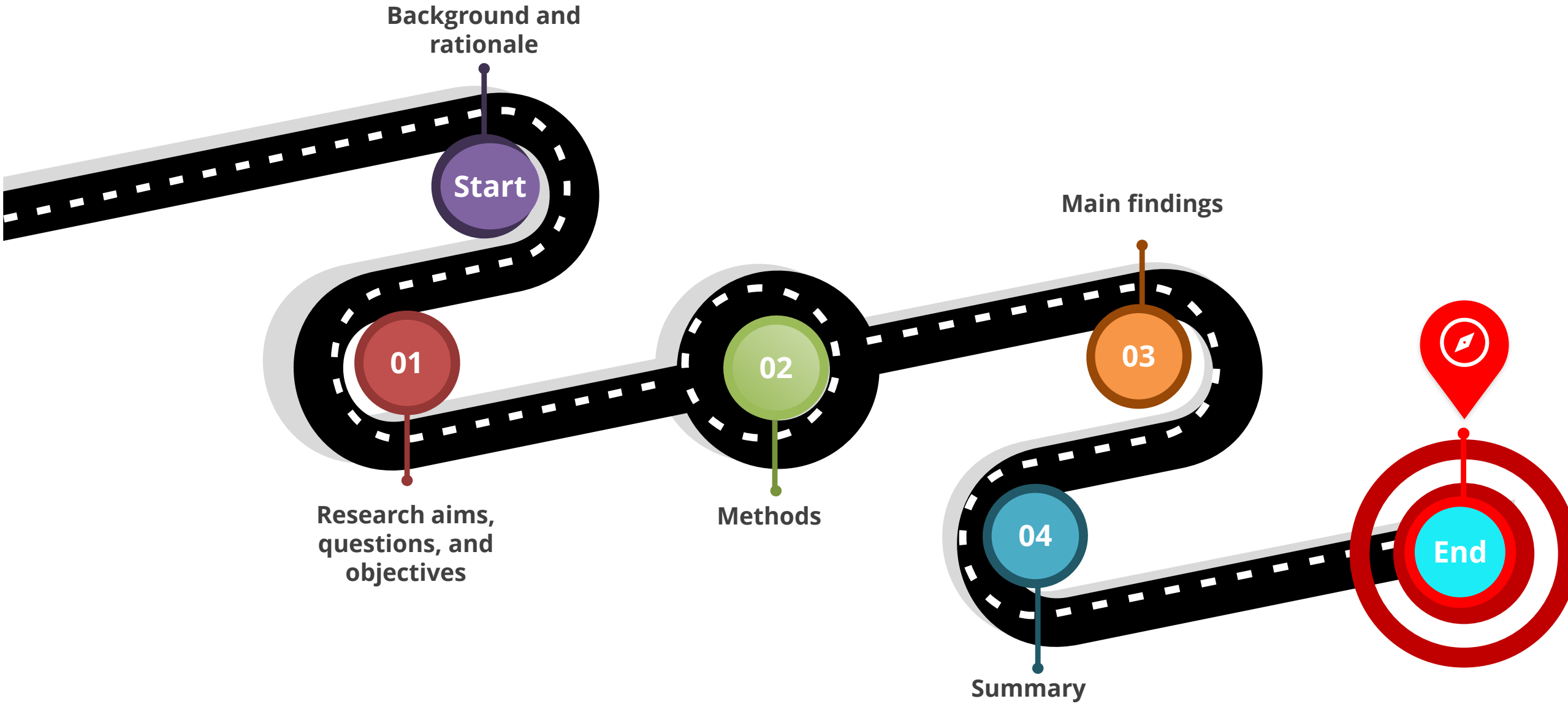
Funding institutions

Bundesministerium für Bildung und Forschung

gnpc Foundation

Impacting Lives

Roadmap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Thank You
Danke / Dankie
Enkosi
Grazie
Gracias
Obrigado
Merci