Vivarium Intervention Effect Size Methodology: Breastfeeding Promotion

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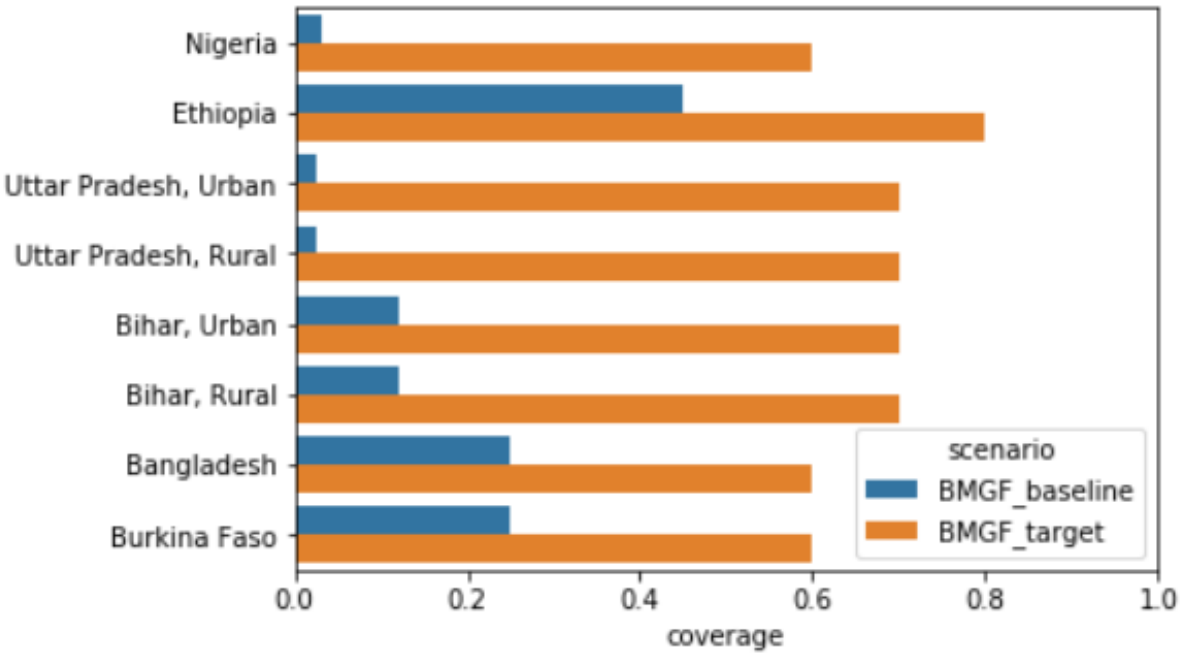
12/10/2018

Outline

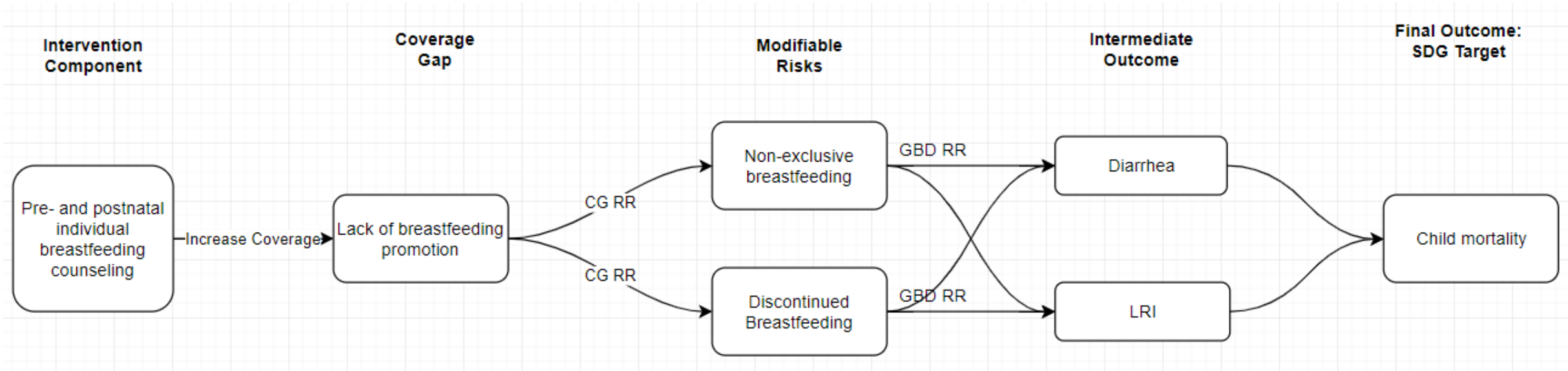
- Breastfeeding Promotion Model & Results
- Breastfeeding Promotion Efficacy Analysis

Breastfeeding Promotion (BFP)

- BMGF interest: If BMGF programs increase BFP coverage from A to B from 2015-2020, how many lives are saved?
  - Intervention protocol isn't clear
  - The best BFP evidence is on individual counseling through multiple pre- and postnatal sessions

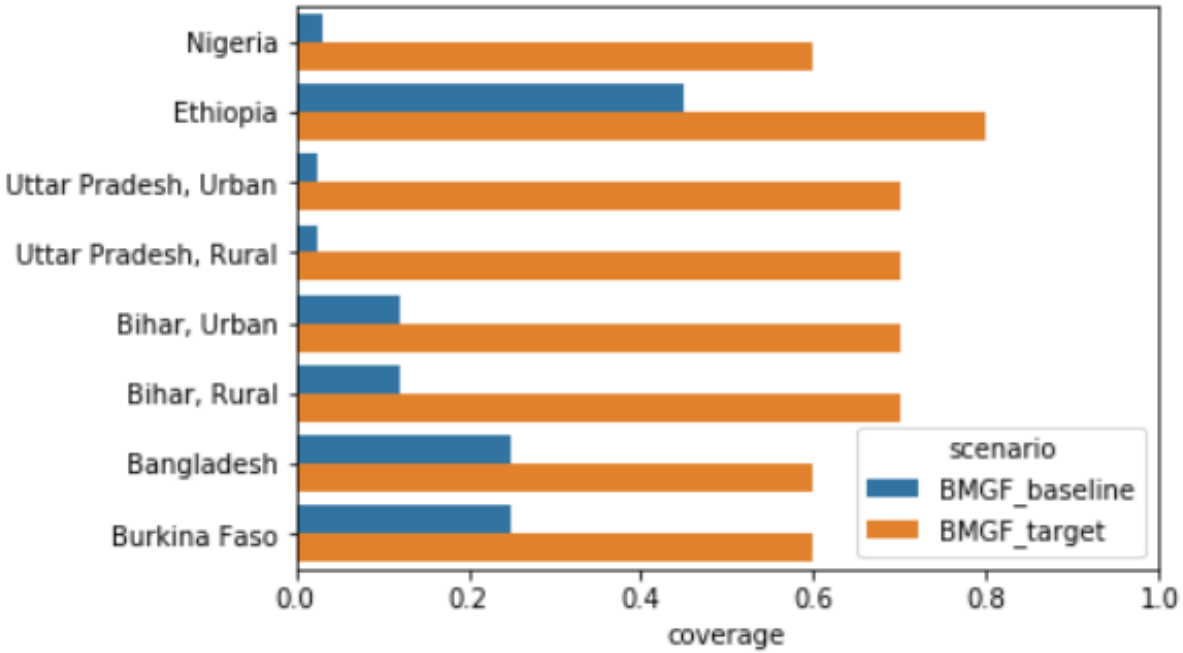


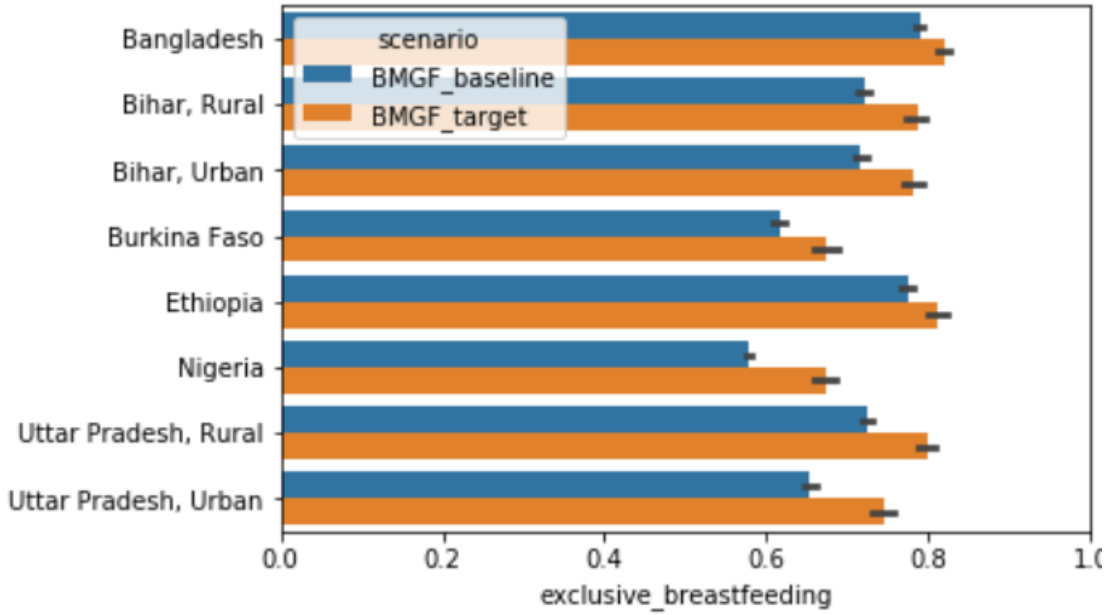
Vivarium Breastfeeding Promotion Model

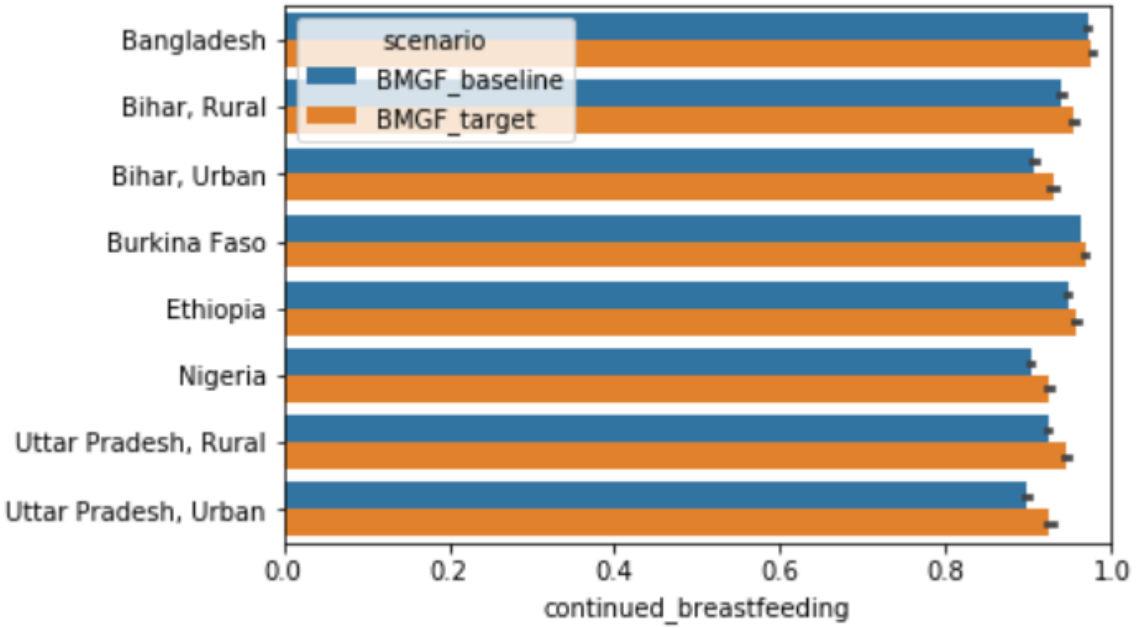


Breastfeeding Promotion Model

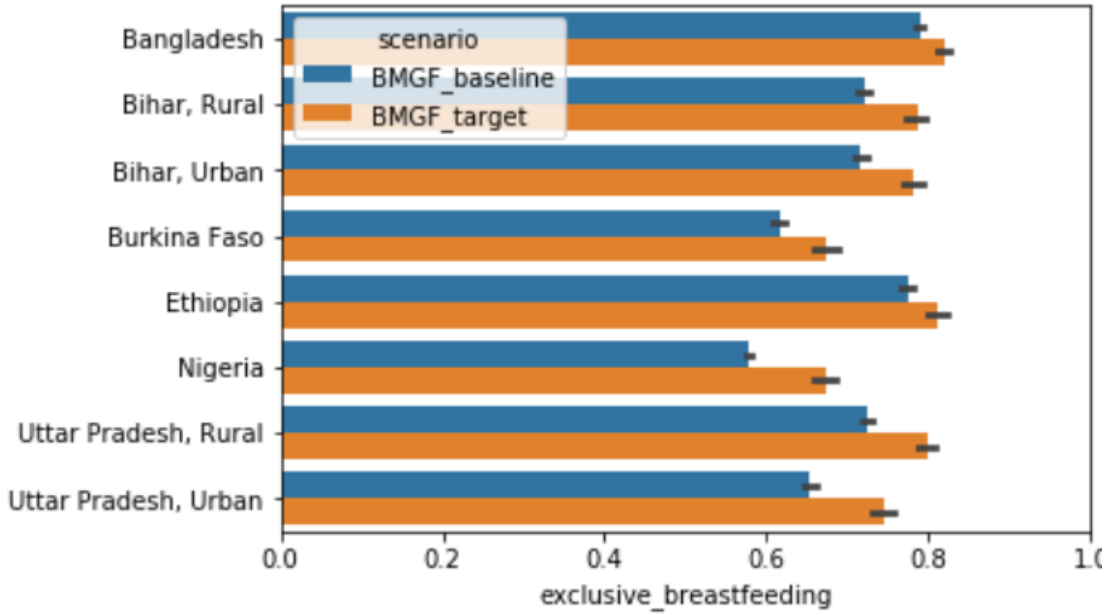
- Open cohort
  - Ages 0-5
  - n=10,000 at start
  - Fertility: crude birth rate
  - 100 draws
- 2015-2020
- Counterfactual analysis: compare 2020 risk exposure and disease rates under two scenarios:
  - Scale-up to BMGF targets
  - Continued baseline coverage

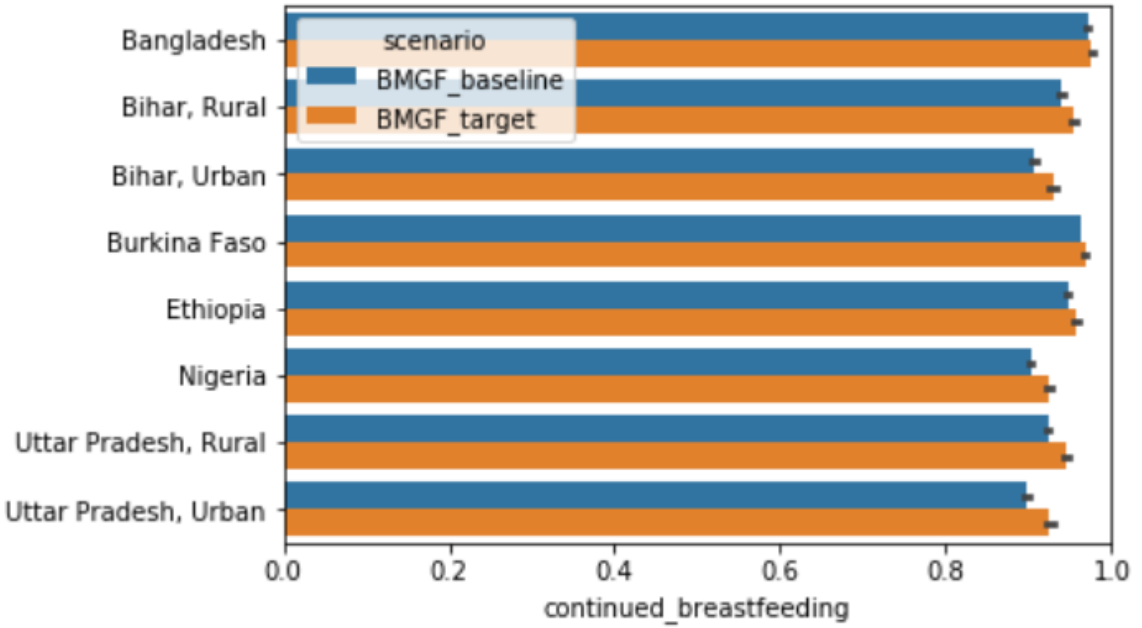




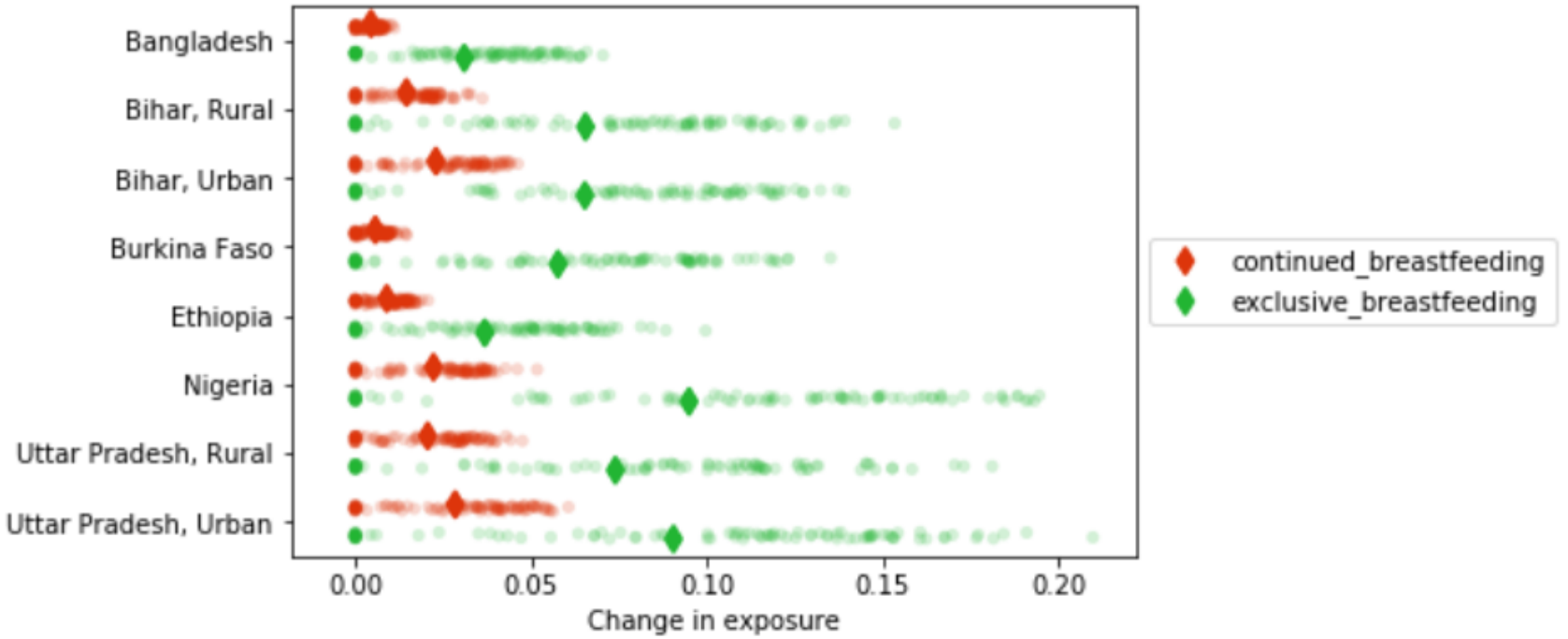


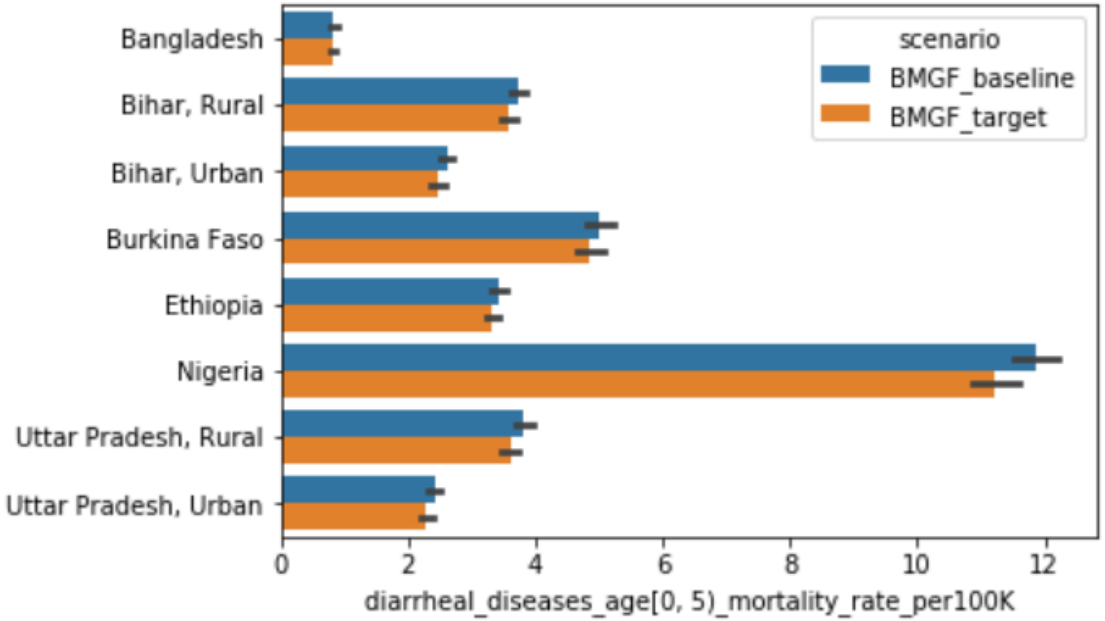
- 2020 population risk exposure in baseline and intervention
- Vivarium's use of common random numbers allows us to assess effect size isolating input uncertainty from stochastic uncertainty

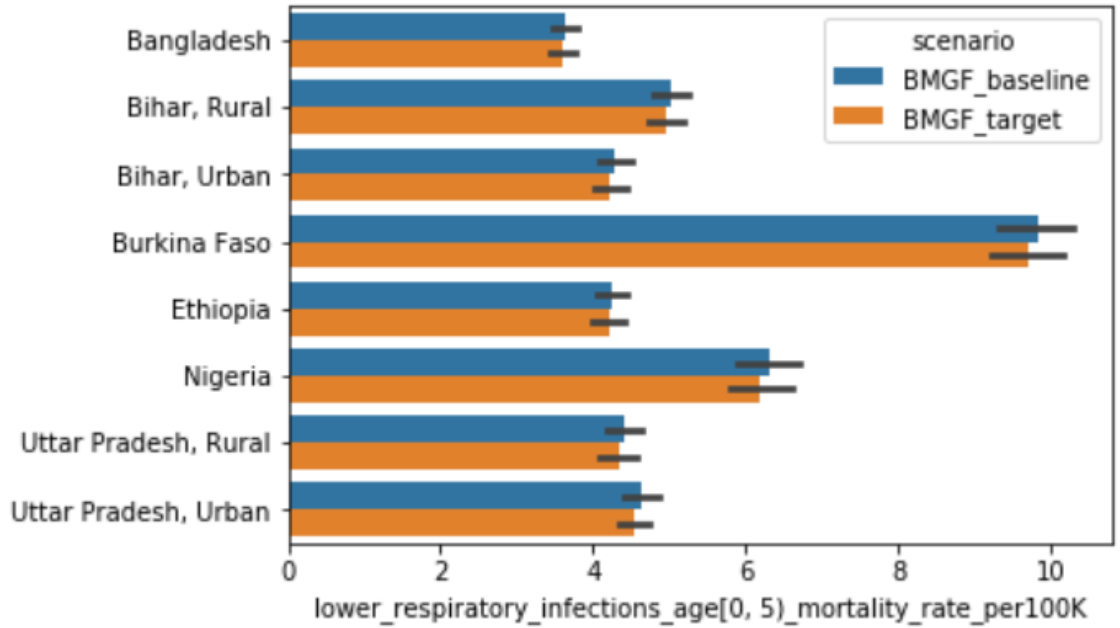




Draw-level comparison




Bangladesh
Bihar, Rural
Bihar, Urban
Burkina Faso
Ethiopia
Nigeria
Uttar Pradesh, Rural
Uttar Pradesh, Urban
scenario
BMGF_baseline
BMGF_target
0
2
4
6
8
10
12
diarrheal_diseases_age[0, 5)_mortality_rate_per100K


Bangladesh
Bihar, Rural
Bihar, Urban
Burkina Faso
Ethiopia
Nigeria
Uttar Pradesh, Rural
Uttar Pradesh, Urban
scenario
BMGF_baseline
BMGF_target
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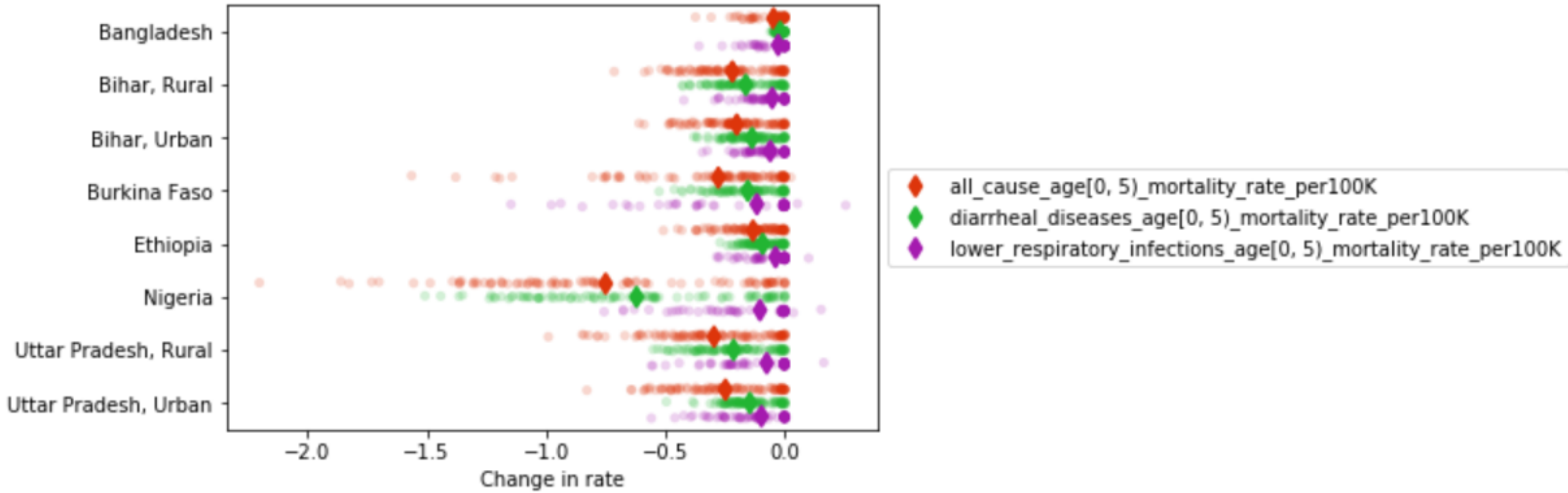
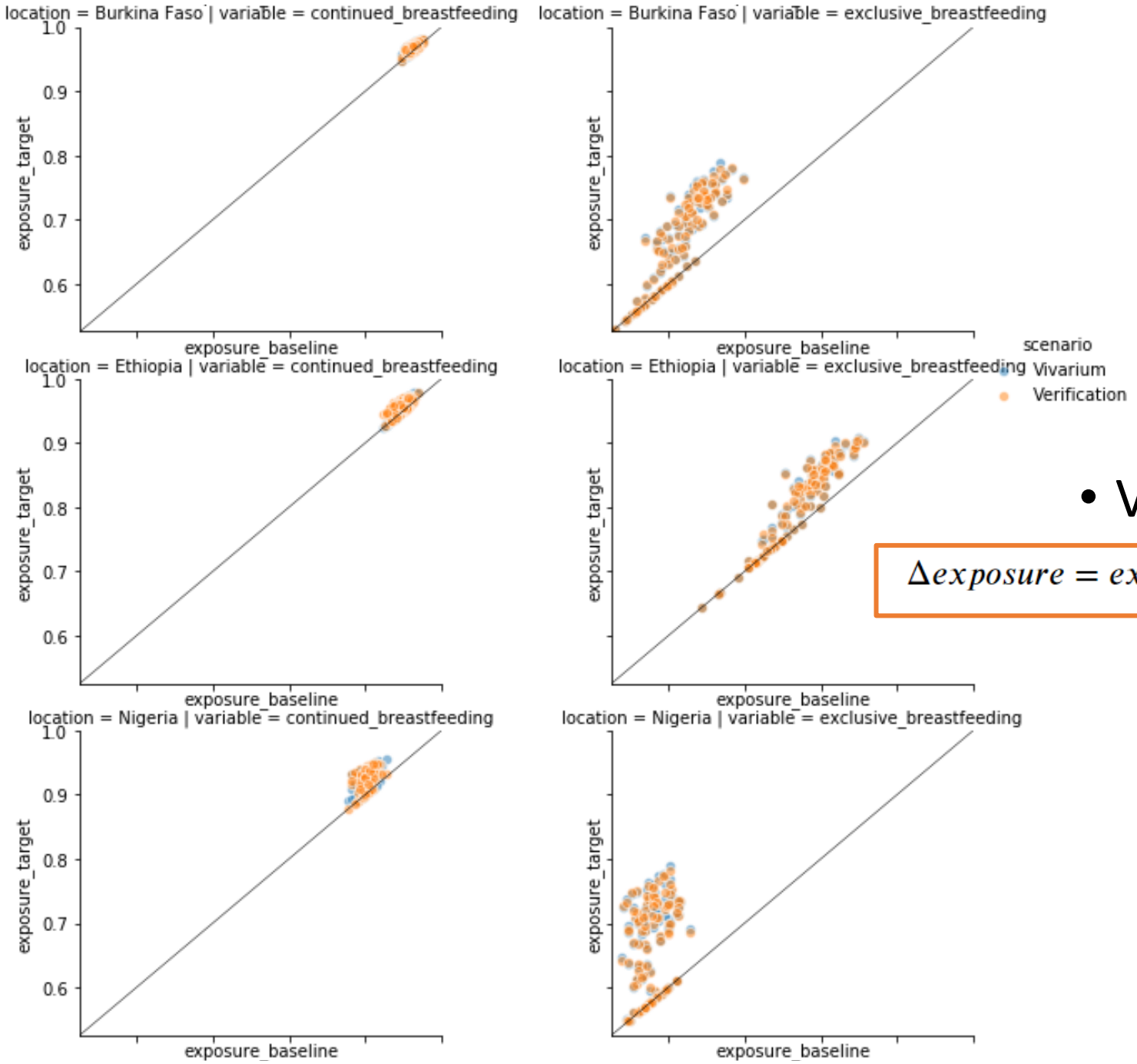
8
10
lower_respiratory_infections_age[0, 5)_mortality_rate_per100K


Bangladesh
Bihar, Rural
Bihar, Urban
Burkina Faso
Ethiopia
Nigeria
Uttar Pradesh, Rural
Uttar Pradesh, Urban
−2.0
−1.5
−1.0
−0.5
0.0
Change in rate
all_cause_age[0, 5)_mortality_rate_per100K
diarrheal_diseases_age[0, 5)_mortality_rate_per100K
lower_respiratory_infections_age[0, 5)_mortality_rate_per100K



- Verification of exposure

$$\Delta exposure = exposure_{baseline} * (1 - PAF) * (RR - 1) * (\Delta coverage)$$

BFP Efficacy Analysis

Primary Source Selection

- Reviewed the 45 sources from Sinha 2017 (LiST meta-analysis) on Breastfeeding Promotion effect on exclusive breastfeeding
- Inclusion criteria: RCTs with ≥ 4 individual counseling visits
- 14 sources fit inclusion criteria and were extracted

Exemplar study

Exclusive breastfeeding promotion by peer counsellors in sub-Saharan Africa (PROMISE-EBF): a cluster-randomised trial

Thorkild Tylleskär, Debra Jackson, Nicolas Meda, Ingunn Marie S Engebretsen, Mickey Chopra, Abdoulaye Hama Diallo, Tanya Doherty, Eva-Charlotte Ekström, Lars T Fadnes, Ameena Goga, Chipepo Kankasa, Jørn I Klungsøyr, Carl Lombard, Victoria Nankabirwa, Jolly K Nankunda, Philippe Van de Perre, David Sanders, Rebecca Shanmugam, Halvor Sommerfelt, Henry Wamani, James K Tumwine, for the PROMISE-EBF Study Group

- Control group: standard of care
- Intervention: One antenatal breastfeeding peer counselling visit and four post-delivery visits by trained peers.
- *All mothers were offered at least five visits, starting with a visit in the third trimester. In Burkina Faso, mothers were scheduled to have home visits during the first week postnatally, and thereafter at weeks 2, 4, 8, 16, and 20. In Uganda and South Africa, home visits were scheduled within the first week and thereafter at weeks 4, 7, and 10.*

The core components of the curriculum included sessions on:

- Your own beliefs about feeding
- Communication and counselling skills
- Composition of breast milk and the importance of breastfeeding
- How milk is produced and released by the breast (frequent feeds increases milk production)
- Helping a mother with positioning herself before she starts breastfeeding
- Attachment of the baby to the breast
- Breast conditions
- Expressing and storing breast milk
- Normal stools and urination
- Practicing exclusive breastfeeding
- Common feeding difficulties (how to handle a crying baby)
- Role plays
- Clinical practice sessions

During each of the visits the peer counsellors undertook the following:

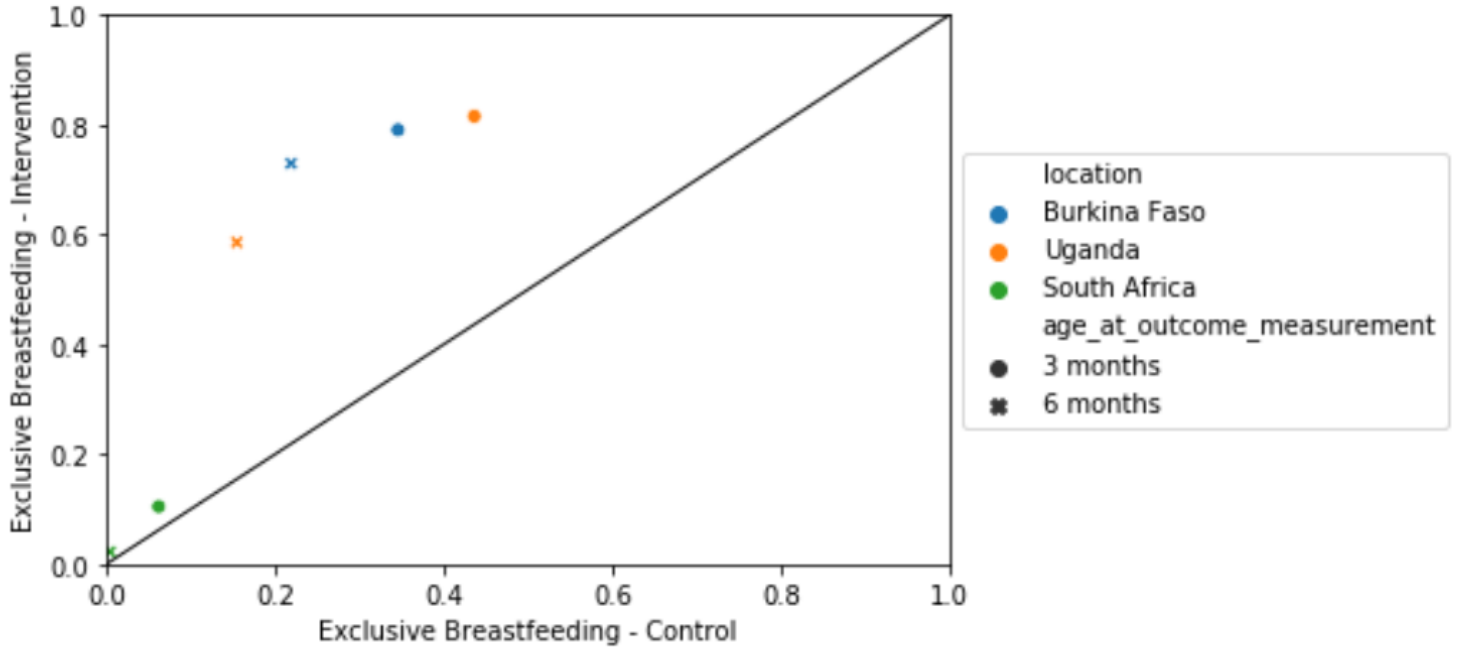
- Provide support, help and counselling to women to optimize their infant feeding practice (as stated in the box above),
- pre-empted and discussed common feeding difficulties
- addressed the mother's/family's feeding concerns/difficulties
- provided basic relevant information on the importance of immunisation and other child health issues
- If the need arises, peer counsellors identified those mothers or children needing urgent referral to the clinic.

The content varied according to the counselling visit. The antenatal visit focused on initiation, colostrum and EBF.

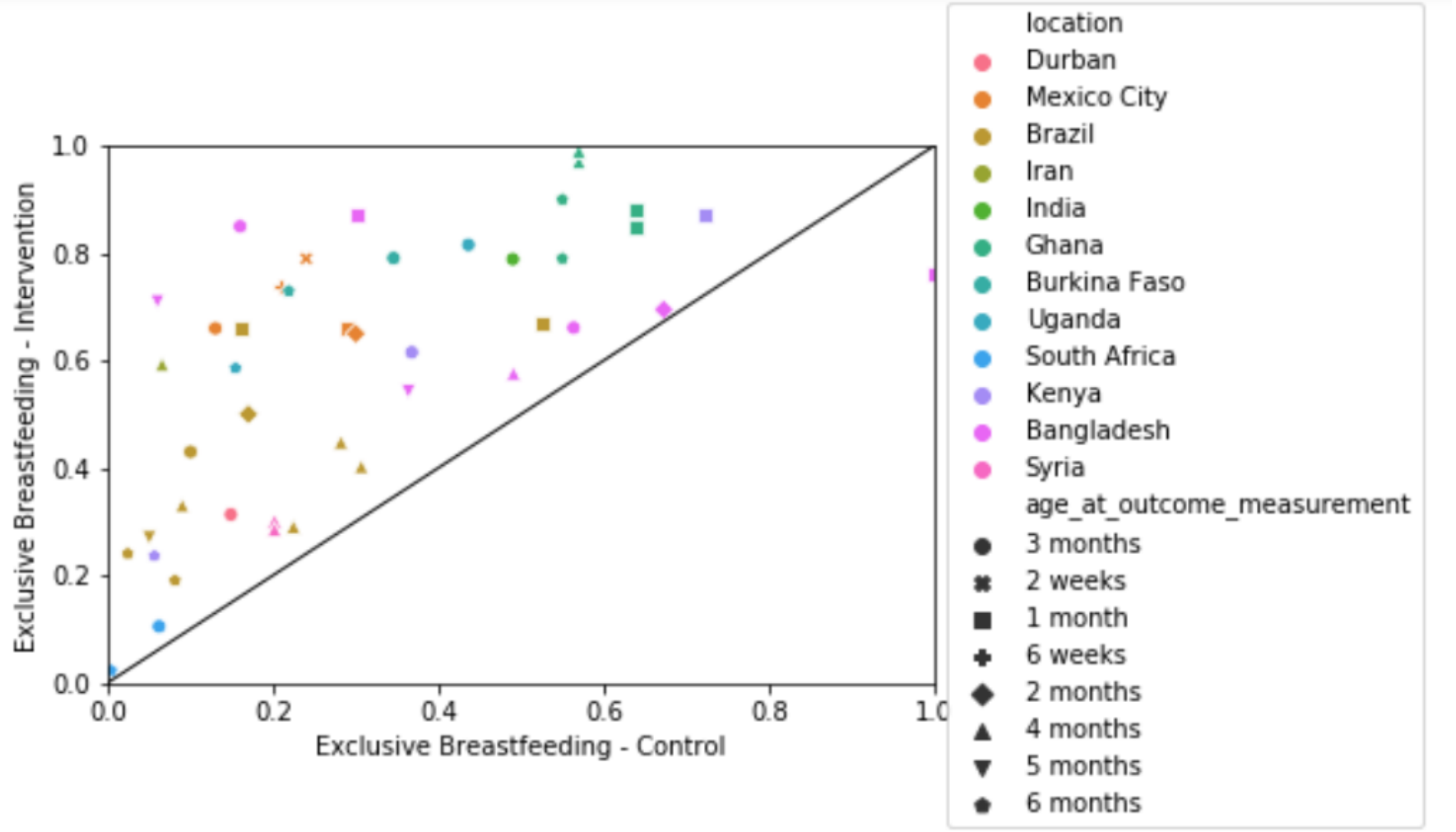
	12 weeks			24 weeks		
	Intervention	Control	Prevalence ratio (95% CI)	Intervention	Control	Prevalence ratio (95% CI)
Burkina Faso						
24-h recall	310/392 (79%)	139/402 (35%)	2·29 (1·33–3·92)	286/392 (73%)	88/402 (22%)	3·33 (1·74–6·38)
7-day recall	300/392 (77%)	94/402 (23%)	3·27 (2·13–5·03)	279/392 (71%)	38/402 (9%)	7·53 (4·42–12·82)
Uganda						
24-h recall	323/396 (82%)	161/369 (44%)	1·89 (1·70–2·11)	232/396 (59%)	57/369 (15%)	3·83 (2·97–4·95)
7-day recall	305/396 (77%)	125/369 (34%)	2·30 (2·00–2·65)	203/396 (51%)	41/369 (11%)	4·66 (3·35–6·49)
South Africa						
24-h recall	56/535 (10%)	30/485 (6%)	1·72 (1·12–2·63)	12/535 (2%)	2/485 (<1%)	5·70 (1·33–24·26)
7-day recall	41/535 (8%)	19/485 (4%)	1·98 (1·30–3·02)	10/535 (2%)	1/485 (<1%)	9·83 (1·40–69·14)

Data are n/N (%), unless otherwise indicated. Data were adjusted for clustering and site. EBF=exclusive breastfeeding.

Table 2: **EBF prevalence at ages 12 weeks and 24 weeks based on 24-h recall and 7-day recall**

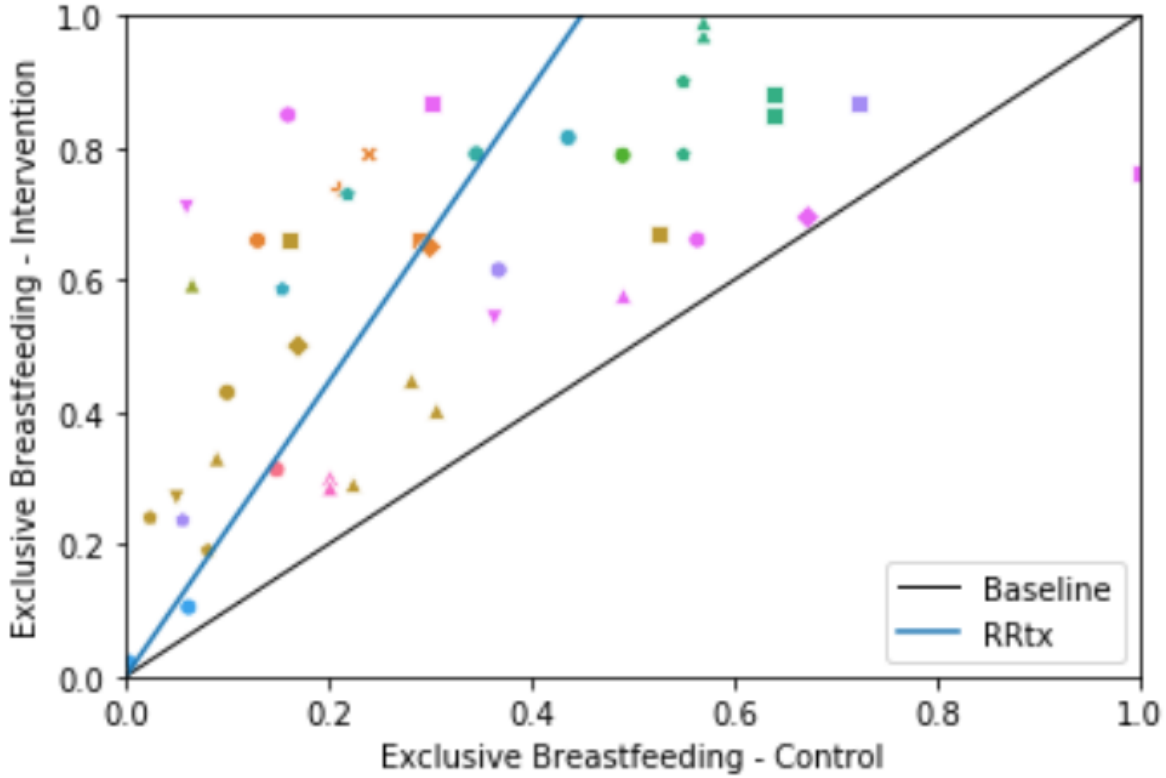


Breastfeeding Promotion RCT data



Treatment Relative Risk

$$RR_{Tx} = \frac{P(EBF|Tx)}{P(EBF|\overline{Tx})}$$



$$P(EBF|Tx) = RR_{Tx} * P(EBF|\overline{Tx})$$

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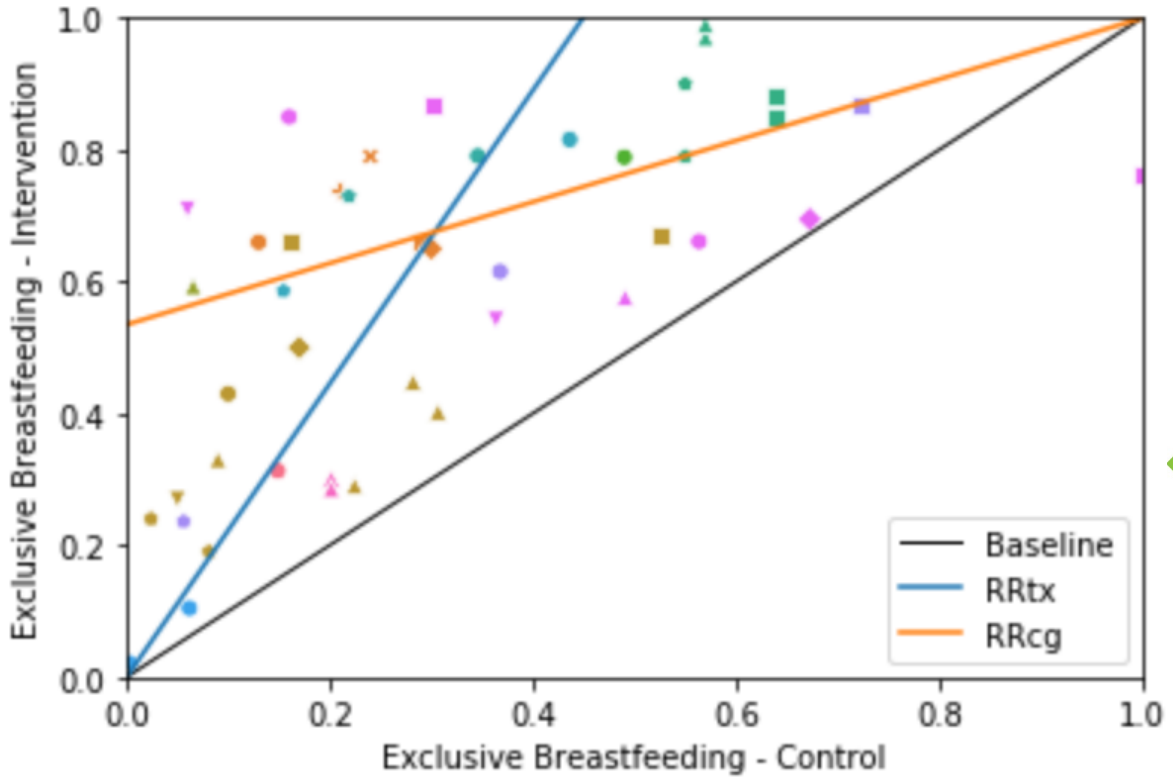
Coverage Gap Relative Risk



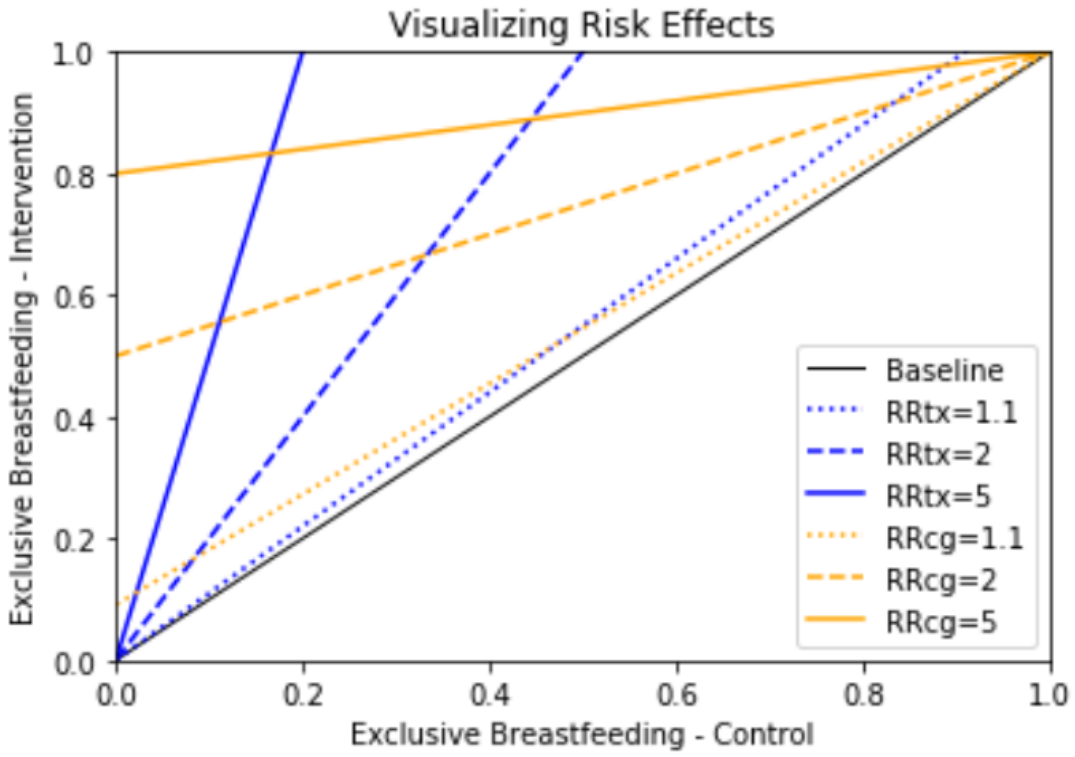
$$RR_{Tx} = \frac{P(EBF|Tx)}{P(EBF|\overline{Tx})}$$

$$P(EBF|Tx) = RR_{Tx} * P(EBF|\overline{Tx})$$

$$RR_{CG} = \frac{P(NEBF|\overline{Tx})}{P(NEBF|Tx)}$$

$$P(EBF|Tx) = 1 - \frac{1-P(EBF|\overline{Tx})}{RR_{CG}}$$

Treatment and Coverage Gap RRs - Logic

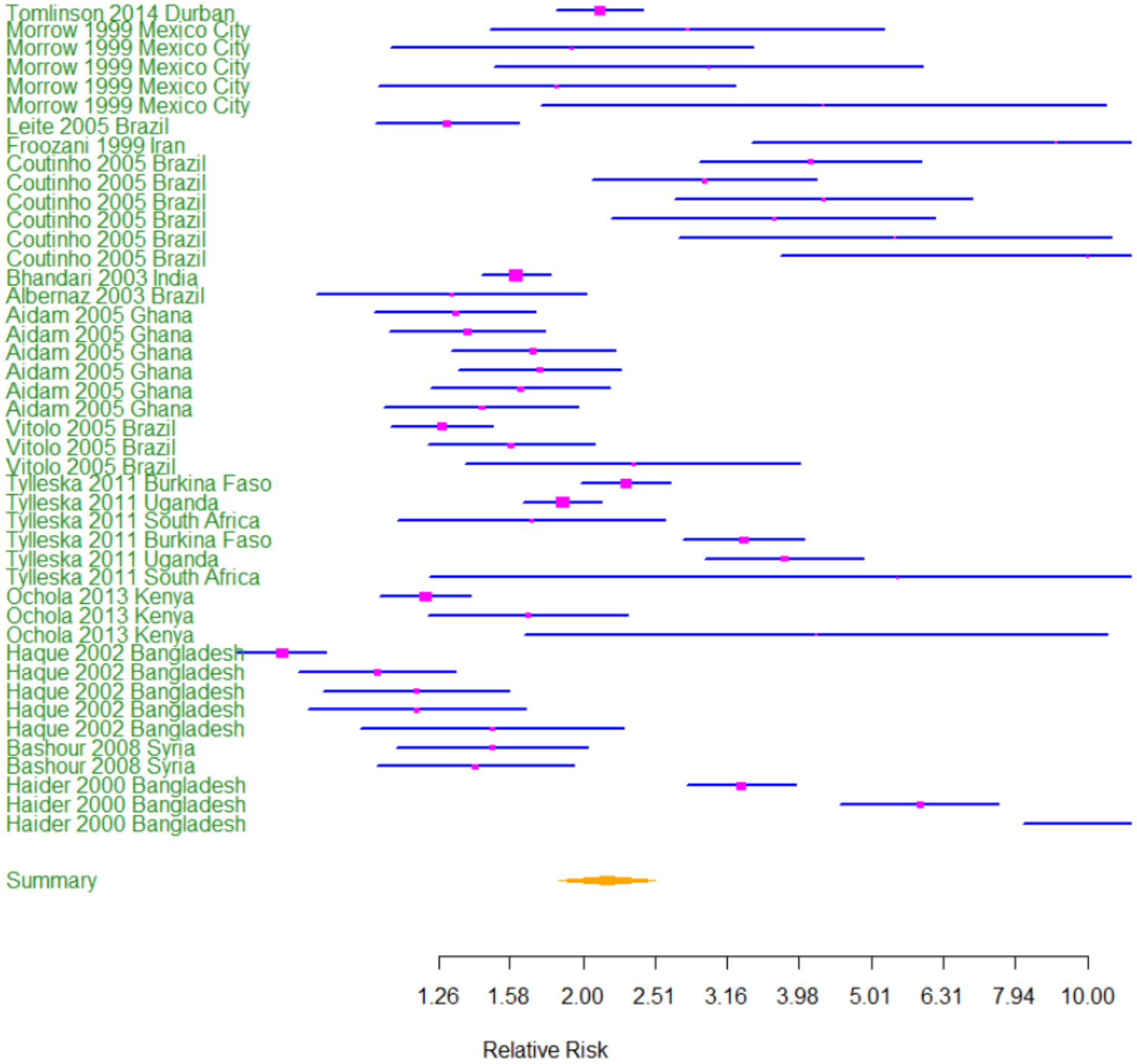


- RR = 2
- Treatment RR: those treated are twice as likely to exclusively breastfeed
- Coverage gap RR: those treated are half as likely to be exposed to non-exclusive breastfeeding risk

Meta-analysis

Random effects meta-analysis

RR 2.12 (1.84-2.51)

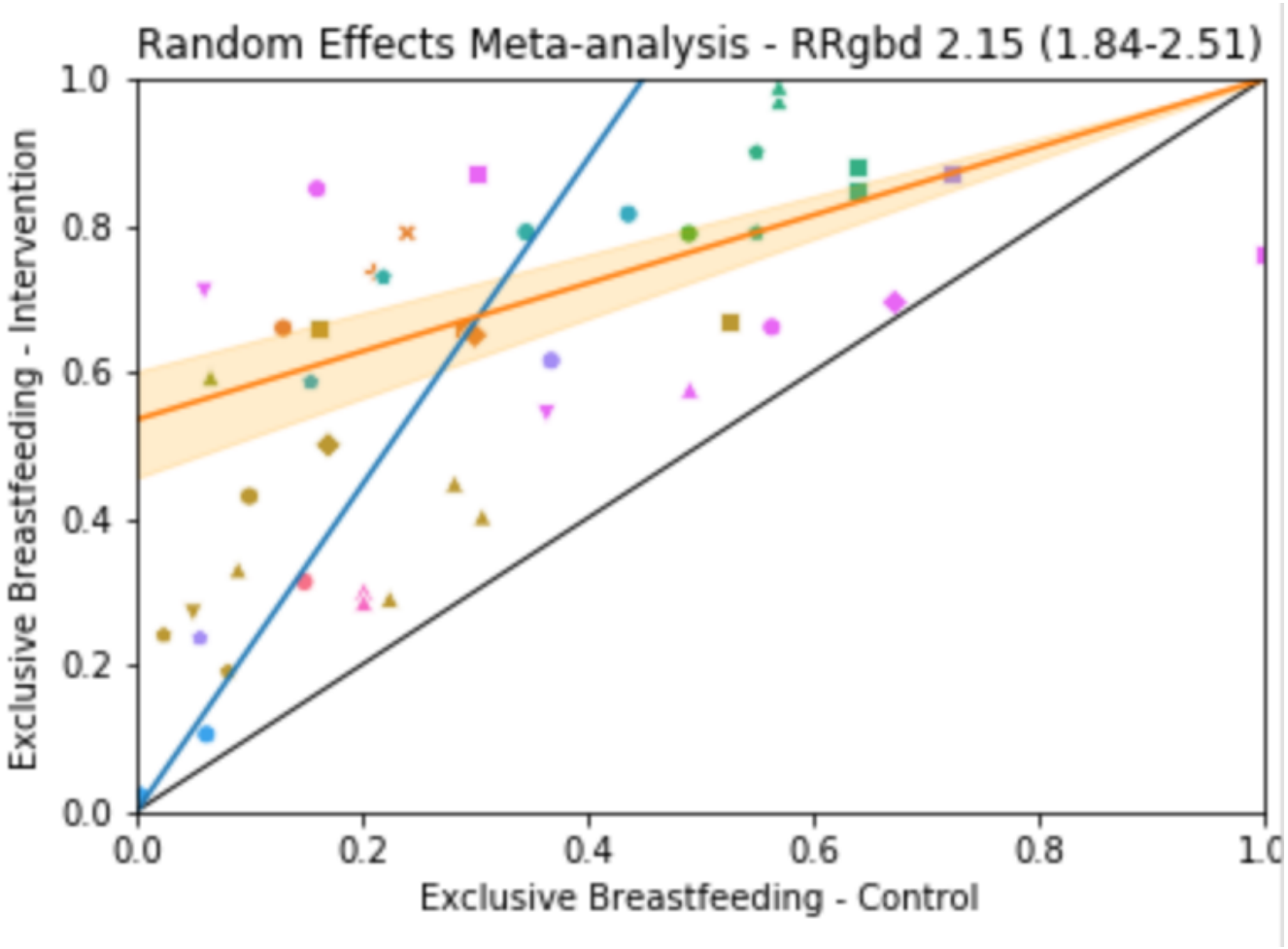


Heterogeneity

- Dimensions
  - Intensity of intervention (e.g. number of visits)
  - Intensity of standard of care
  - Provider type
  - Age at outcome
- Does a meta-regression approach help us answer the BMGF question?

If BMGF programs increase BFP coverage from A to B from 2015-2020, how many lives are saved?

Coverage Gap RR Meta-analysis

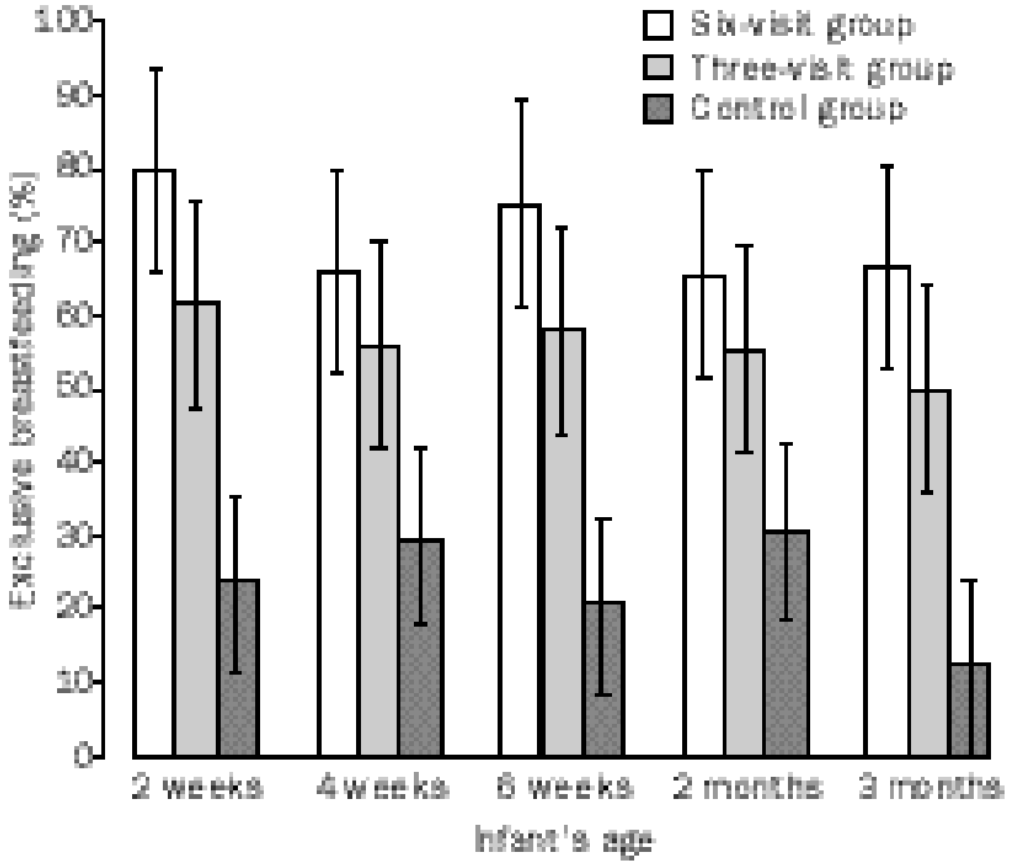


Limitations

- Non-adjustable intervention intensity
- Little to no evidence on individual counseling effect on continued breastfeeding, we're using the same RR as non-exclusive BF
- We don't (yet) have delivery mechanisms, risk correlations, or other model features that highlight the microsimulation approach
- Further discussion needed with BMGF to understand the composition of their programs, and data behind their coverage estimates

Extra Slides

Intervention intensity



Efficacy of home-based peer counselling to promote exclusive breastfeeding: a randomised controlled trial

Ardythe L Morrow, M Lourdes Guerrero, Justine Shults, Juan J Calva, Chessa Lutter, Jane Bravo, Guillermo Ruiz-Palacios, Robert C Morrow, Frances D Butterfoss

- Mother-infant pairs in the intervention groups received either six or three home visits from peer counsellors. In the six-visit group, mothers were visited in mid and late pregnancy, in the first week and weeks 2, 4, and 8 post partum. In the three-visit intervention group, mothers were visited in late pregnancy, in the first week, and week 2 post partum.

Coverage Gaps

- Coverage Gaps are Vivarium's mechanism to make interventions fit within the risk factor framework
- Example:
  - Intervention: breastfeeding promotion
  - Coverage gap: lack of breastfeeding promotion
    - Exposure = 1 – intervention coverage

Treatment and Coverage Gap RRs

- Relative risk: ratio of the probability of an outcome in an exposed group to the probability of an outcome in an unexposed group

$$RR = \frac{P(Outcome|Exposure)}{P(Outcome|\overline{Exposure})}$$

- Treatment RR (generally what's reported by RCTs)
  - Exposure: the treatment
  - Outcome: exclusive breastfeeding

$$RR_{Tx} = \frac{P(EBF|Tx)}{P(EBF|\overline{Tx})}$$

- Coverage gap RR (Vivarium implementation)
  - Exposure: *lack* of the treatment
  - Outcome: non-exclusive breastfeeding

$$RR_{GBD} = \frac{P(NEBF|\overline{Tx})}{P(NEBF|Tx)}$$

Derivation of EBF given RRcg

$$RR_{CG} = \frac{P(NEBF|\overline{Tx})}{P(NEBF|Tx)}$$

$$NEBF_{\overline{Tx}} = RR_{CG} * NEBF_{Tx}$$

$$(1 - EBF_{\overline{Tx}}) = RR_{CG} * (1 - EBF_{Tx})$$

$$(1 - EBF_{Tx}) = \frac{1 - EBF_{\overline{Tx}}}{RR_{CG}}$$

$$EBF_{Tx} = 1 - \frac{1 - EBF_{\overline{Tx}}}{RR_{CG}}$$

INTERVENTION COVERAGE BASELINE AND 2020 TARGETS WERE USED TO MODEL LIVES SAVED

Key

Baseline Coverage → 2020 Coverage

Coverage targets verified in second phase of impact modeling

2016 Intervention Start
2017 Intervention Start
2019 Intervention Start

Coverage: Baseline – 2020 Target

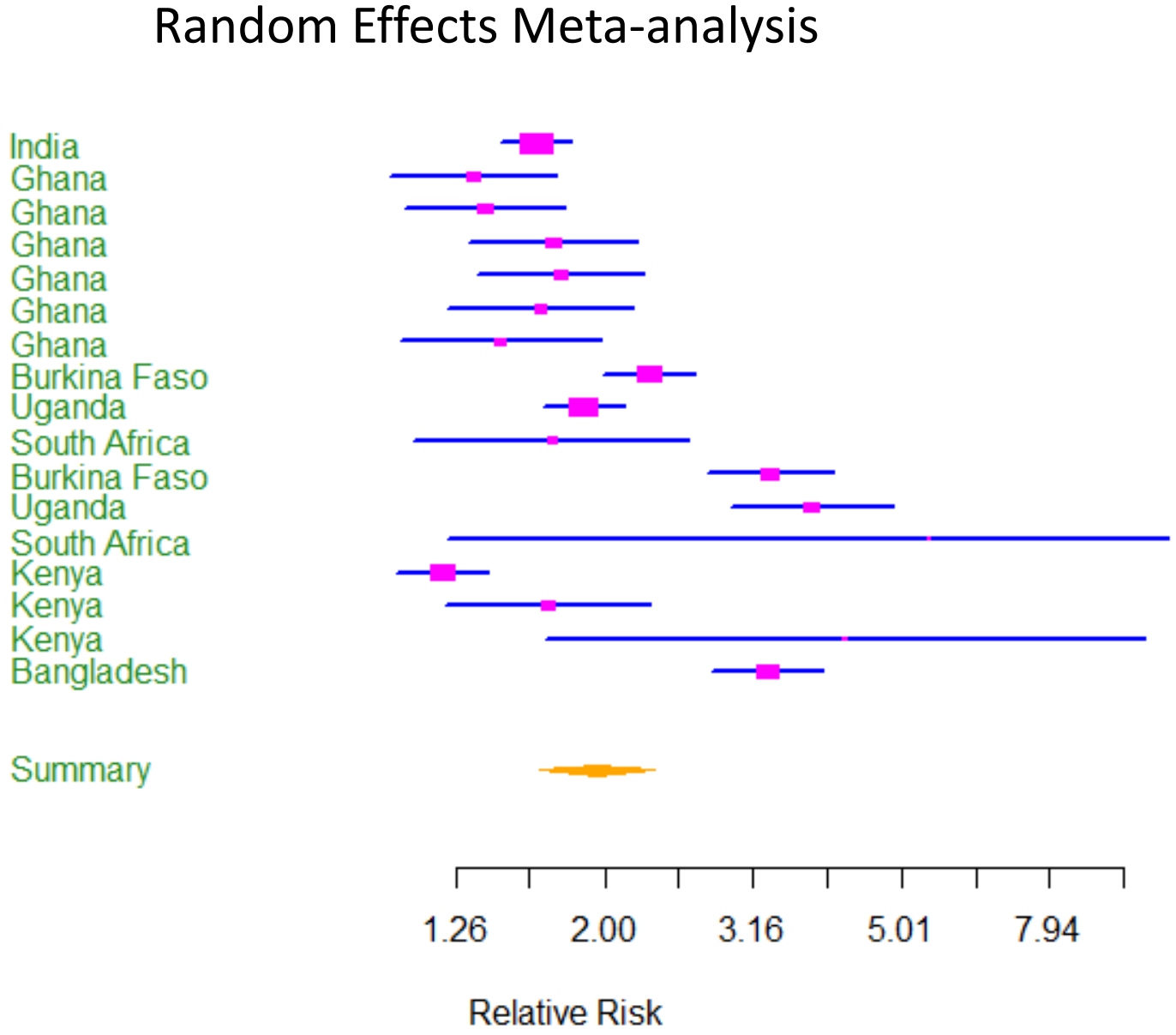
	Coverage Indicator	Nigeria	Ethiopia	Uttar Pradesh	Bihar	Bangladesh	Burkina Faso
Breastfeeding (BF)							
Exclusive BF	*Promotion coverage (home, health, community & work)*	3% (2015) → 60%	45% (2015) → 80%	2.5% (2015) → 70%	12% (2015) → 70%	25% (2015) → 60%	25% (2015) → 60%
Timely Initiation of BF	*Promotion coverage (home, health, & community)*	3% (2015)→ 60%	45% (2015)→ 80%	2.5% (2015) → 70%	16% (2015) → 70%	25% (2015) → 60%	25% (2015) → 60%
Continued BF	*Promotion coverage (home, health, & work)*	3% (2015)→ 60%	45% (2015)→ 80%	2.5% (2015) → 70%	11% (2015) → 70%	25% (2015) → 60%	25% (2015) → 60%
Maternal Nutrition							
Iron & Folic Acid Supplementation	*Supplement consumption rate*	20.5% (2015)→ 50%	0.4% (2015)→ 40%	1.7% (2015)→ 35.0%	3% (2015)→ 35%	28.6% (2015)→50%	50% (2015)→ 70%
Calcium Supplementation	*Supplement consumption rate*	0%	0% (2015)→ 20%	5.0% (2015)→ 10.0%	0% (2015)→ 10%	0% (2015)→ 20%	0% (2015)→ 10%
Balanced Protein Energy Supp. (BPE)	*Supplement consumption rate*	0%	0% (2015)→ 20%	47.0% (2015)→ 60.0%	39% (2015)→ 60%	0% (2015)→ 20%	0% (2015)→ 0%
Multiple Micronutrient Supp.	*Supplement consumption rate*	0%	0%	0%	0%	0%	0%
Vitamin A supplementation							
Coverage of vitamin A supplementation		42% (2015)→ 85%	71% (2015)→ 95%	27% (2015)→ 70%	62% (2015)→ 85%	62% (2015)→ 85%	98% (2015)→ 98%
Complementary Feeding							
Complementary Feeding	*Promotion coverage among food secure/insecure populations*	Insecure: 0% Secure: 3% (2015)→ 60%	Insecure: 0% Secure: 16.2% (2015)→ 80%	Insecure: 10% (2015)→ 25% Secure: 2.5% (2015)→ 70%	Insecure: 8% (2015)→ 50% Secure: 14% (2015)→ 70%	Insecure: 0% Secure: 20.9% (2015)→ 60%	Insecure: 0% Secure: 51.5% (2015)→ 70%
Treatment of SAM							
Treatment of SAM	*% cases identified via MUAC who live in catchment areas and receive services*	16% (2015)→ 30%	100%	1% (2015)→ 20%	1% (2015)→ 20%	0% (2015)→ 10%	2% (2015)→ 20%
Food Fortification *(Proxy: Improvement in Micronutrient Status)*							
Vitamin A	*% pop. shift from current MN status level (e.g., mod→ mild)*	**5%** 2015-2020 (shift from each MN status group / yr)	**5%** 2015-2020 (shift from each MN status group / yr)	**5%** 2015-2020 (shift from each MN status group / yr)	**5%** 2015-2020 (shift from each MN status group / yr)	**5%** 2015-2020 (shift from each MN status group / yr)	**5%** 2015-2020 (shift from each MN status group / yr)
Iron	*% pop. shift from current MN status level (e.g., mod→ mild)*						
Folate	*% pop. shift from current MN status level (e.g., mod→ mild)*						
Zinc	*% pop. shift from current MN status level (e.g., mod→ mild)*						

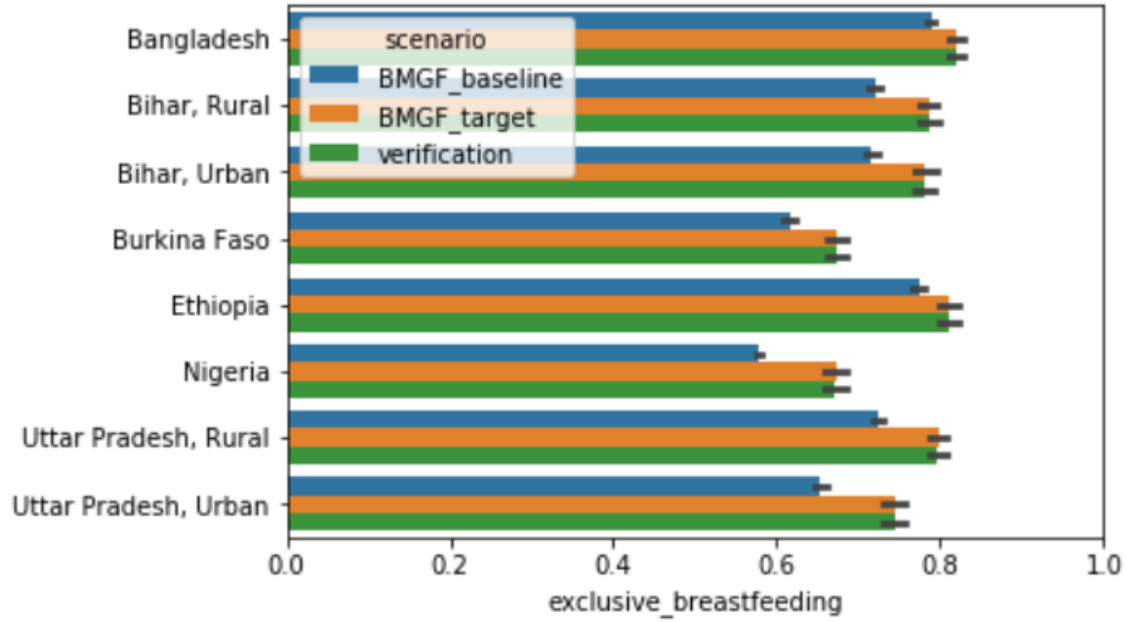
Meta-analysis

Subset to SSA and two important trials in India and Bangladesh

Random effects meta-analysis

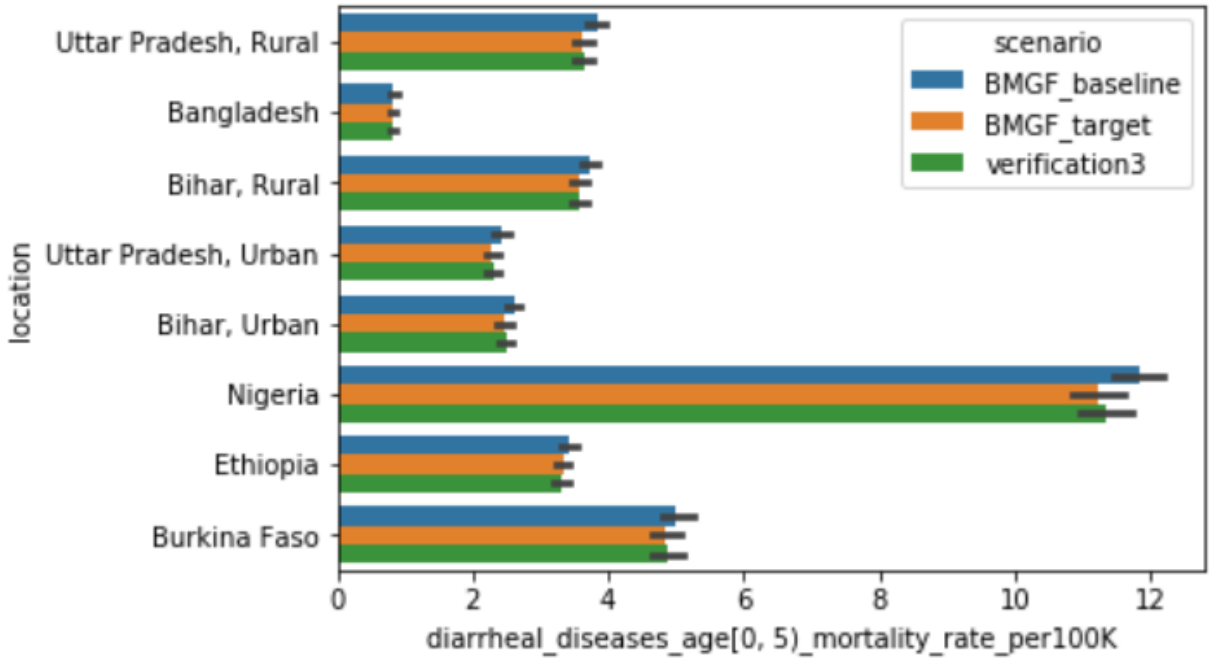
- 1.95 (1.63 – 2.33)



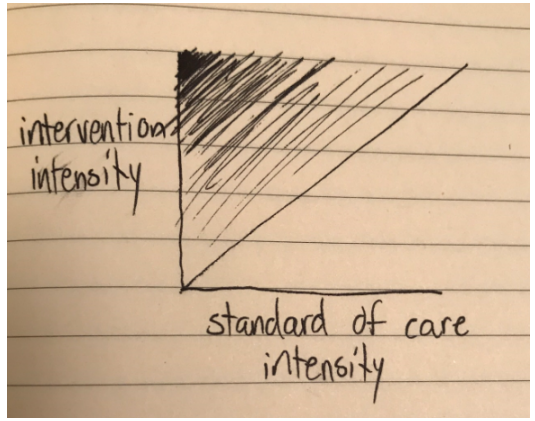


- Verification of exposure using RRcg

$$\Delta exposure = exposure_{baseline} * (1 - PAF) * (RR - 1) * (\Delta coverage)$$



- Verification: using change in exposure and NEBF PAF estimate


intervention intensity
standard of care intensity

Extra Slides: Vivarium Implementation of Coverage Gaps

Coverage Gap Implementation in Vivarium

- Exposure_parameter: the probability that a simulant will be exposed to the risk factor (to be precise, if their propensity is < exposure_parameter, they are exposed to the coverage gap)

- Do you understand why exposure_parameter of exposed to a coverage gap is analogous to the following formulation?

$$P(NEBF|\overline{Tx})$$

Coverage Gap Implementation in Vivarium

- Goal: extrapolate the effect size from study populations to a population of interest

Study population (e.g. RCT)

$$RR_{GBD} = \frac{P(NEBF|\overline{Tx})}{P(NEBF|Tx)}$$

$$P(NEBF|\overline{Tx}) = P(NEBF|Tx) * RR_{GBD}$$

Assumptions

Population of interest (Vivarium)

$$E_i = E * (1 - PAF_{CG}) * (1 + CG_i * (RR_{CG} - 1))$$

E: exposure_parameter (GBD risk factor exposure)
PAF_{CG}: PAF of the coverage gap on the risk factor
CG = Coverage gap exposure (binary)

- Interpretation:
  - Exposure_parameter: the probability that a simulant will be exposed to the risk factor (to be precise, if their propensity is < exposure_parameter, they are exposed to the coverage gap)
  - If RR=2, a simulant is twice as likely to be exposed to the risk factor if they are exposed to the coverage gap.

Coverage Gap Implementation in Vivarium

- Goal: extrapolate the effect size from study populations to a population of interest

Study population (e.g. RCT)

$$RR_{GBD} = \frac{P(NEBF|\overline{Tx})}{P(NEBF|Tx)}$$

$$P(NEBF|\overline{Tx}) = P(NEBF|Tx) * RR_{GBD}$$

Conditional probability of exposure in treatment group of the study population

Assumptions

Population of interest (Vivarium)

Probability of exposure in counterfactual population with no coverage gap exposure

Note that if CGi = 1, this expression reduces to RRcg

$$E_i = E * (1 - PAF_{CG}) * (1 + CG_i * (RR_{CG} - 1))$$

E: exposure_parameter (GBD risk factor exposure)

PAF_{CG}: PAF of the coverage gap on the risk factor

CG = Coverage gap exposure (binary)

- Interpretation:
  - Exposure_parameter: the probability that a simulant will be exposed to the risk factor (to be precise, if their propensity is < exposure_parameter, they are exposed to the coverage gap)
  - If RR=2, a simulant is twice as likely to be exposed to the risk factor if they are exposed to the coverage gap.

Caveats

- Assumes RR_tmrel = 1 (I'm not sure when this is violated)
- As stated in the previous slide, the following extrapolation has several assumptions about how the population of interest matches the study population (e.g. from the RCT), including that there's **no correlation** between risk exposure and treatment propensity

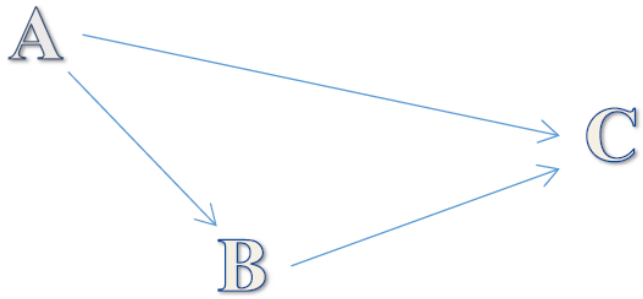
$$E * (1 - PAF) = P(NEBF|Tx)$$

- I don't fully understand the implications of correlation.
- I don't fully understand how this approach compares to mediation (see later slide for details)

Implications of using coverage gap RRs

- Treatment effect in the literature (and meta-analyses) report RRtx, NOT coverage gap RR.
- If the outcome is a disease rate or risk (e.g. preterm birth or nutritional deficiency), you can convert using 1/RRtx
- If the outcome is the lack of the risk (e.g. exclusive breastfeeding), we will likely need to use primary data
- This is much more involved than it seems, as there is extreme heterogeneity in study design, etc. The numbers to extract are not always clear. It's basically as much work as doing the whole meta-analysis over again minus the title/abstract screen.
- I think it **is** possible to implement coverage gaps to properly use RRtx (basically, by reversing the direction of exposure_parameters), but I think the earlier plot shows the fallacy of RRtx for dichotomous outcomes.

Disclaimer: these claims are my current understanding but are NOT verified with GBD experts



Meditation on Mediation

- What is risk factor mediation?
  - *If part of the effect of A is through B, a mediator, we do not adjust the effect of A for B. For example, we do not adjust the RR of BMI for cholesterol as cholesterol lies in the biological pathway between BMI and cardiovascular outcomes* (GBD 2016 RF appendix)
- (The only mediation of GBD risk factors is the metabolic RFs which are not relevant to CONIC)
- Mediation is a tool for **descriptive epidemiology** to handle causal relationships **without fully describing the causal relationship**. For example, while sugar sweetened beverages (SSB) are fully mediated through BMI, that doesn't say what the effect of SSB is on BMI.
  - Mediation as a way to aggregate PAFs up the risk hierarchy (ie, you can't just add the PAFs of SSB and BMI)
- The coverage gap framework can be thought of as handling mediation **by explicitly describing the causal relationship**, which is **necessary for simulation modelling.**
- Other considerations for mediation:
  - To use a mediation approach, you would treat lack of BFP as a risk factor. That means you'd need the effect of BFP on the final outcome (e.g. diarrhea and LRI incidence), which would be rather hard to come by (and would likely not pass GBD causal criteria).
  - While mediation has the benefit of already being in the GBD framework ("coverage gaps" affecting risks is a novel concept), I think Vivarium needs the causal relationship not provided by mediation

OLD SLIDES TO DELETE

Coverage Gaps

- Coverage Gaps are Vivarium's mechanism to make interventions fit within the risk factor framework
- Example:
  - Intervention: breastfeeding promotion
  - Coverage gap: lack of breastfeeding promotion
    - Exposure = 1 – intervention coverage

Treatment and Coverage Gap RRs

- Relative risk: ratio of the probability of an outcome in an exposed group to the probability of an outcome in an unexposed group

$$RR = \frac{P(Outcome|Exposure)}{P(Outcome|\overline{Exposure})}$$

- *We must be very precise with defining outcome & exposure*

Treatment and Coverage Gap RRs

- Relative risk: ratio of the probability of an outcome in an exposed group to the probability of an outcome in an unexposed group

$$RR = \frac{P(Outcome|Exposure)}{P(Outcome|\overline{Exposure})}$$

- Treatment RR (generally what's reported by RCTs)
  - Exposure: the treatment
  - Outcome: desired behavior (ie, *lack* of risk)
- Coverage gap RR (Vivarium implementation)
  - Exposure: *lack* of the treatment
  - Outcome: the GBD risk factor

Treatment and Coverage Gap RRs

- Relative risk: ratio of the probability of an outcome in an exposed group to the probability of an outcome in an unexposed group

$$RR = \frac{P(Outcome|Exposure)}{P(Outcome|\overline{Exposure})}$$

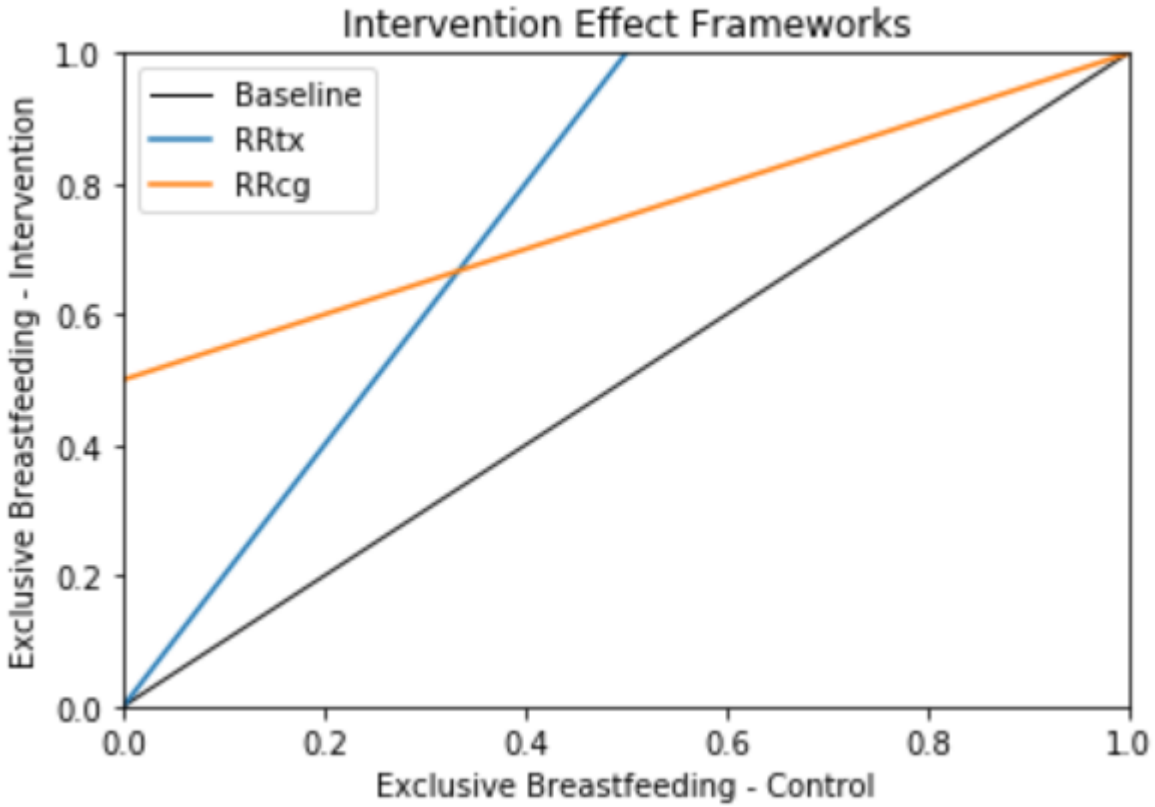
- Treatment RR (generally what's reported by RCTs)
  - Exposure: the treatment
  - Outcome: desired behavior (ie, *lack* of risk)

$$RR_{Tx} = \frac{P(EBF|Tx)}{P(EBF|\overline{Tx})}$$

- Coverage gap RR (Vivarium implementation)
  - Exposure: *lack* of the treatment
  - Outcome: the GBD risk factor

$$RR_{GBD} = \frac{P(NEBF|\overline{Tx})}{P(NEBF|Tx)}$$

Treatment and Coverage Gap RRs - Logic



- RR = 2
- Treatment RR: those treated are twice as likely to exclusively breastfeed
- Coverage gap RR: those treated are half as likely to be exposed to non-exclusive breastfeeding risk

Treatment RR

- Exposure: the treatment
- Outcome: desired behavior (ie, *lack* of risk)

Coverage gap RR

- Exposure: *lack* of the treatment
- Outcome: the risk factor

So how do we estimate Coverage Gap RR?

- First, we look at published meta-analyses for the intervention

- Key insight: Across interventions, the outcome reported in Relative Risk estimation is different

Treatment and Coverage Gap RRs – 3 situations

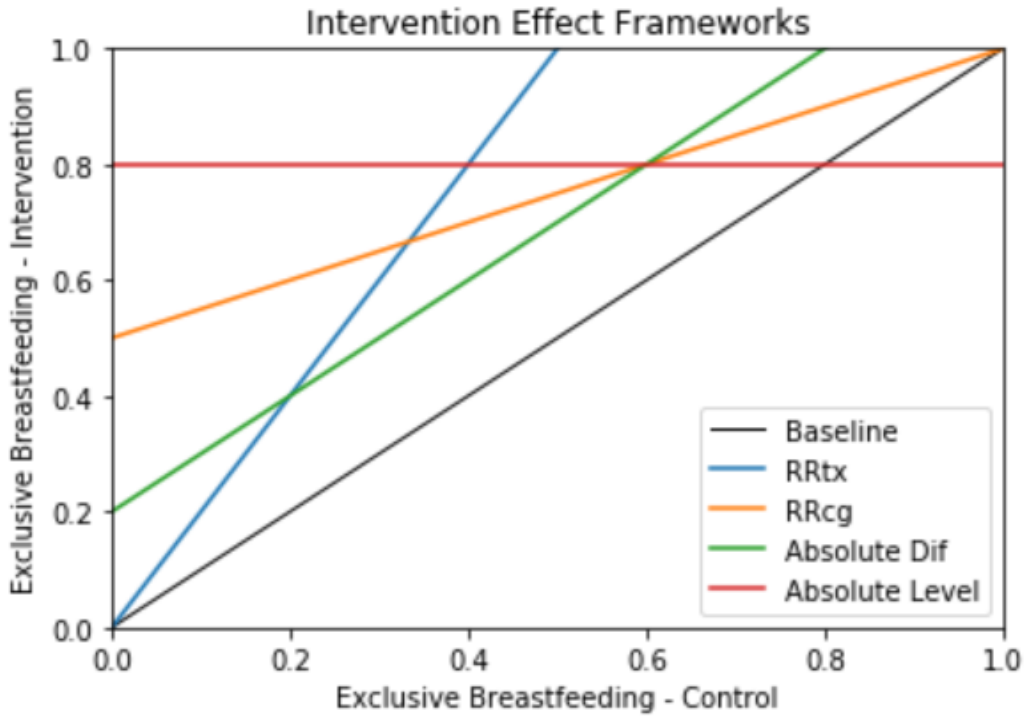
Situation	Outcome is a rate	Outcome is the risk exposure	Outcome is absence of risk
Example	Rotavirus vaccination & diarrhea incidence	Iron supplementation & preterm birth	Breastfeeding promotion & exclusive breastfeeding

Treatment and Coverage Gap RRs – 3 situations

Situation	Outcome is a rate	Outcome is the risk exposure	Outcome is absence of risk
Example	Rotavirus vaccination & diarrhea incidence	Iron supplementation & preterm birth	Breastfeeding promotion & exclusive breastfeeding
RRtx formulation	$RR_{Tx} = \frac{P(diarrhea|Tx)}{P(diarrhea|\overline{Tx})}$	$RR_{Tx} = \frac{P(preterm|Tx)}{P(preterm|\overline{Tx})}$	$RR_{Tx} = \frac{P(EBF|Tx)}{P(EBF|\overline{Tx})}$
RRcg formulation	$RR_{CG} = \frac{P(diarrhea|\overline{Tx})}{P(diarrhea|Tx)}$	$RR_{CG} = \frac{P(preterm|\overline{Tx})}{P(preterm|Tx)}$	$RR_{CG} = \frac{P(\overline{EBF}|\overline{Tx})}{P(\overline{EBF}|Tx)}$
Conversion	$RR_{CG} = 1/RR_{Tx}$	$RR_{CG} = 1/RR_{Tx}$	No summary measure conversion

Breastfeeding Promotion Efficacy Data

- As the treatment efficacy RR summary measure cannot be converted to coverage gap RR, we need to extract primary sources
- This data may elucidate the proper risk effect framework



Primary Source Selection

- Reviewed the 45 sources from Sinha 2017 (LiST meta-analysis) on Breastfeeding Promotion effect on exclusive breastfeeding
- Inclusion criteria: RCTs with multiple visits of individual counseling
- 14 sources fit inclusion criteria and were extracted

Data extraction

$$RR = \frac{P(Outcome|Exposure)}{P(Outcome|\overline{Exposure})}$$

*	*EBF*	*NEBF*
Tx	a	b
$\overline{Tx}$	c	d

$$RR_{Tx} = \frac{P(EBF|Tx)}{P(EBF|\overline{Tx})}$$

$$RR_{Tx} = \frac{a/(a+b)}{c/(c+d)}$$

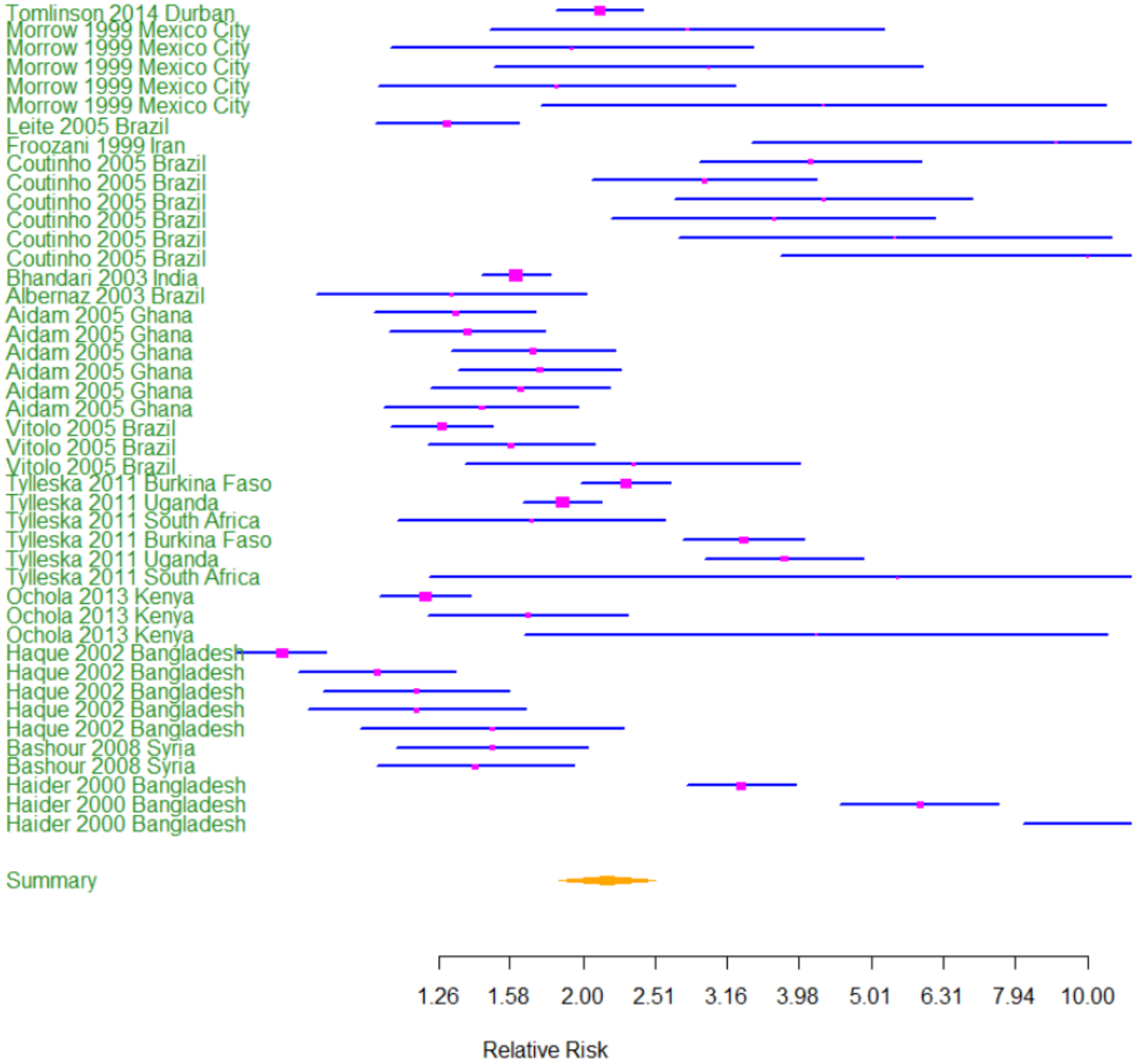
$$RR_{CG} = \frac{P(NEBF|\overline{Tx})}{P(NEBF|Tx)}$$

$$RR_{CG} = \frac{d/(c+d)}{b/(a+b)}$$

Meta-analysis

Random effects meta-analysis

RR 2.12 (1.84-2.51)

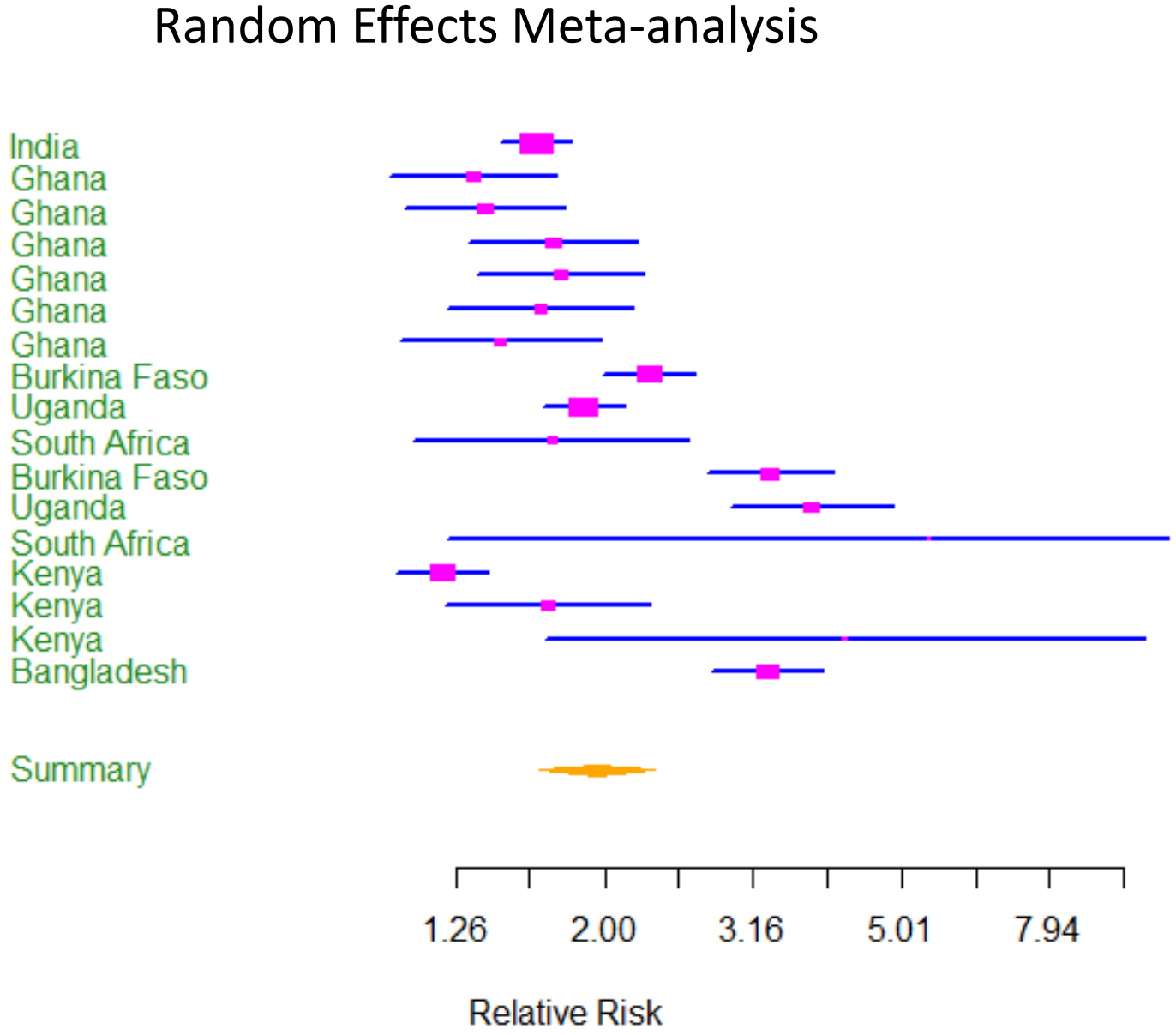


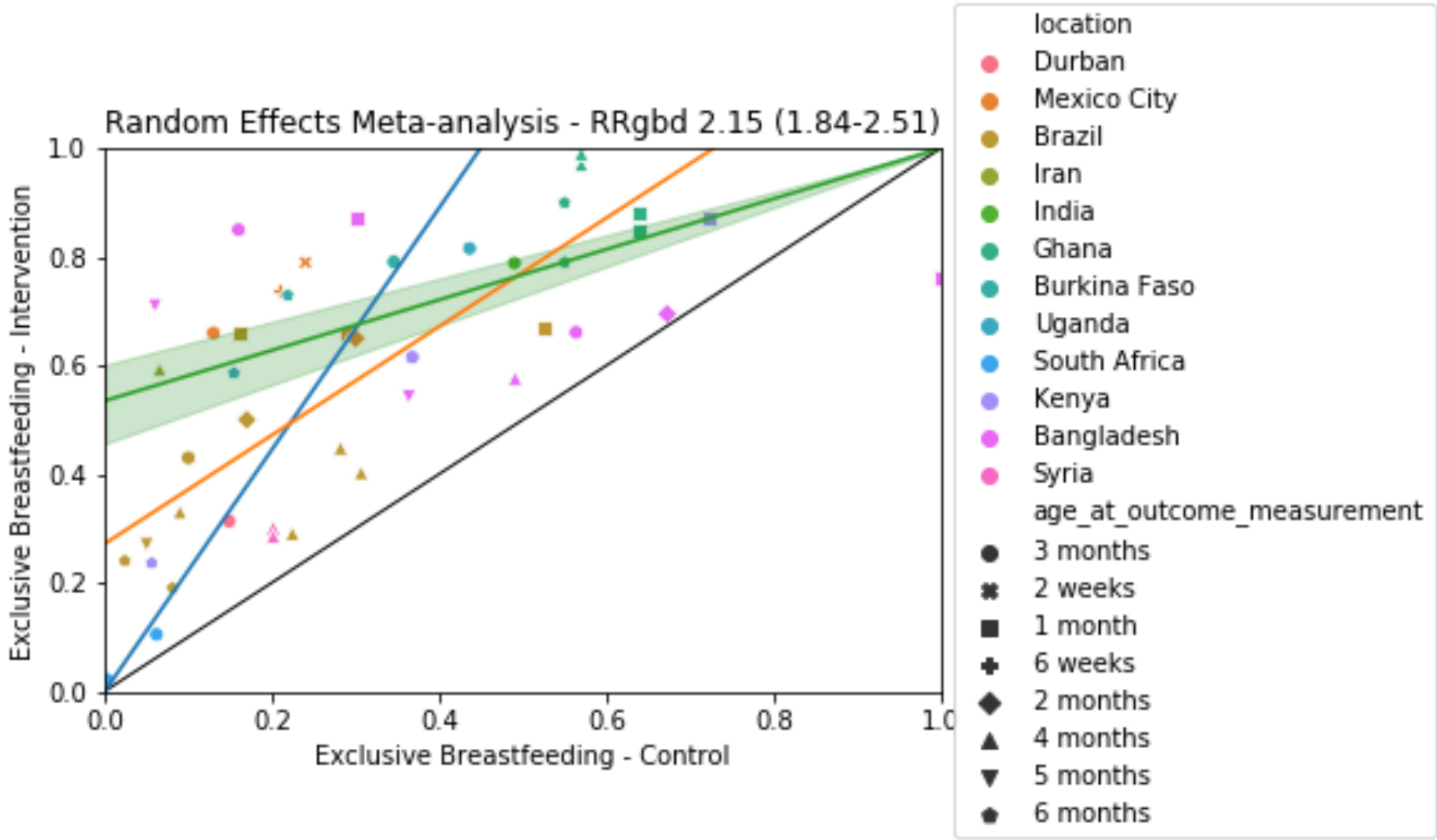
Meta-analysis

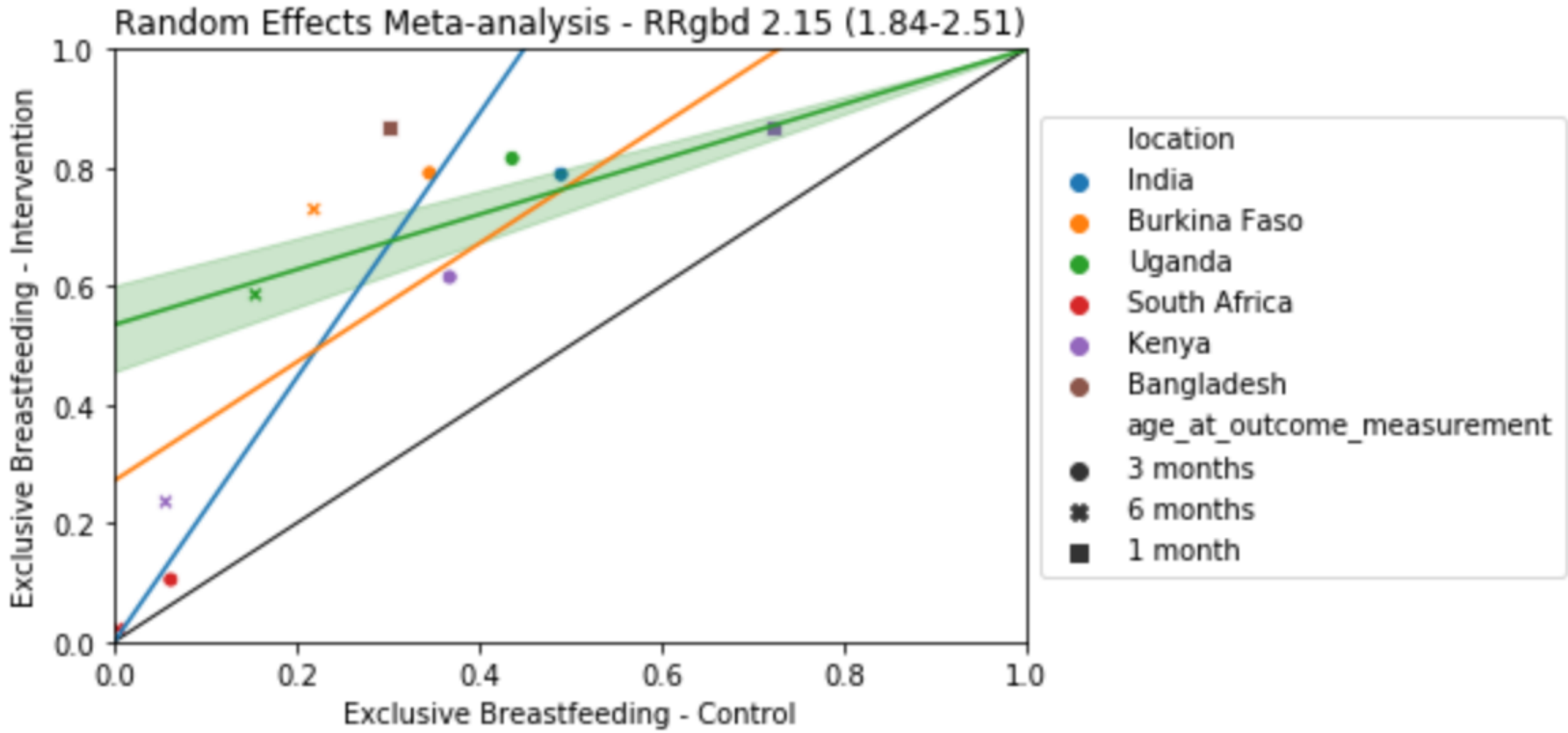
Subset to SSA and two important trials in India and Bangladesh

Random effects meta-analysis

- 1.95 (1.63 – 2.33)

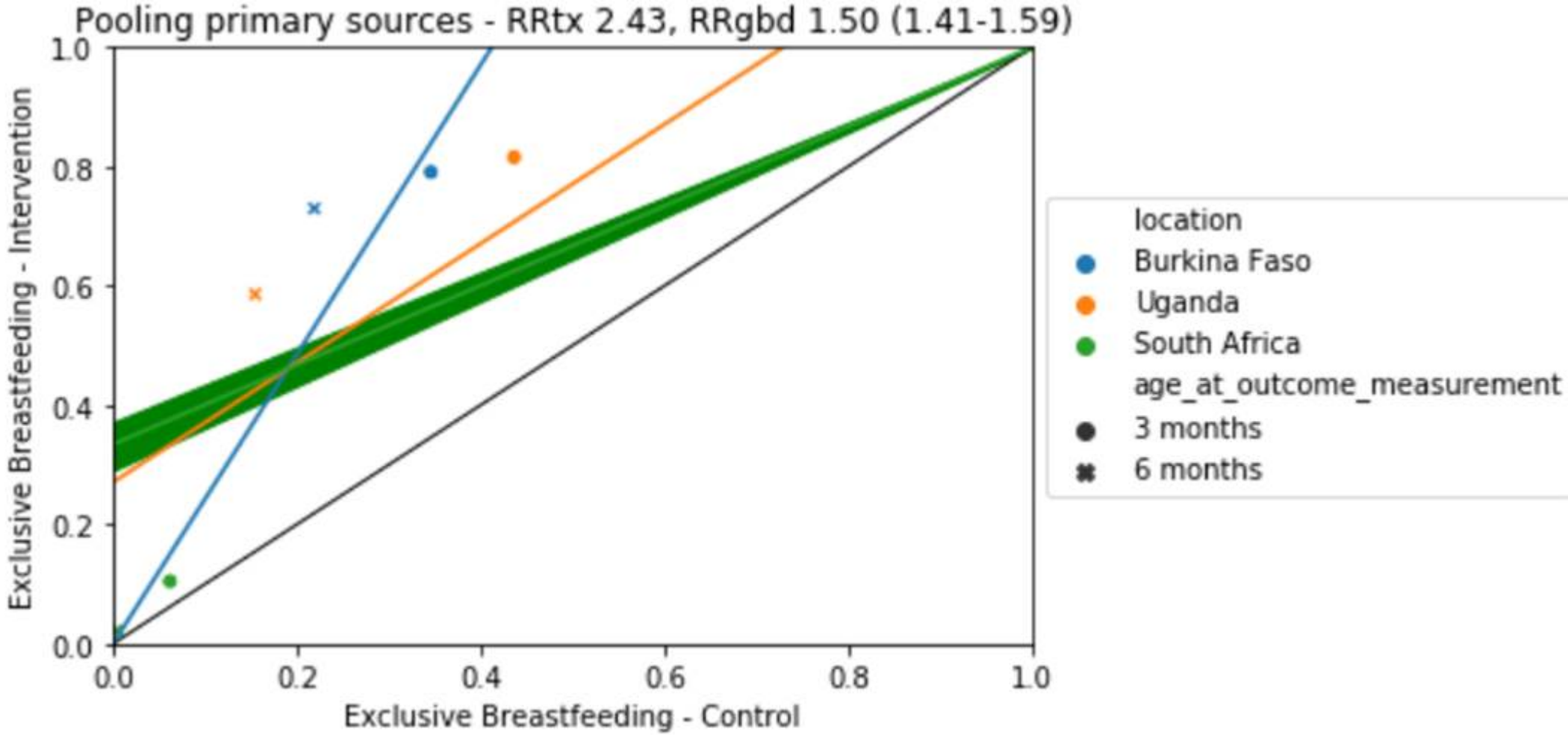


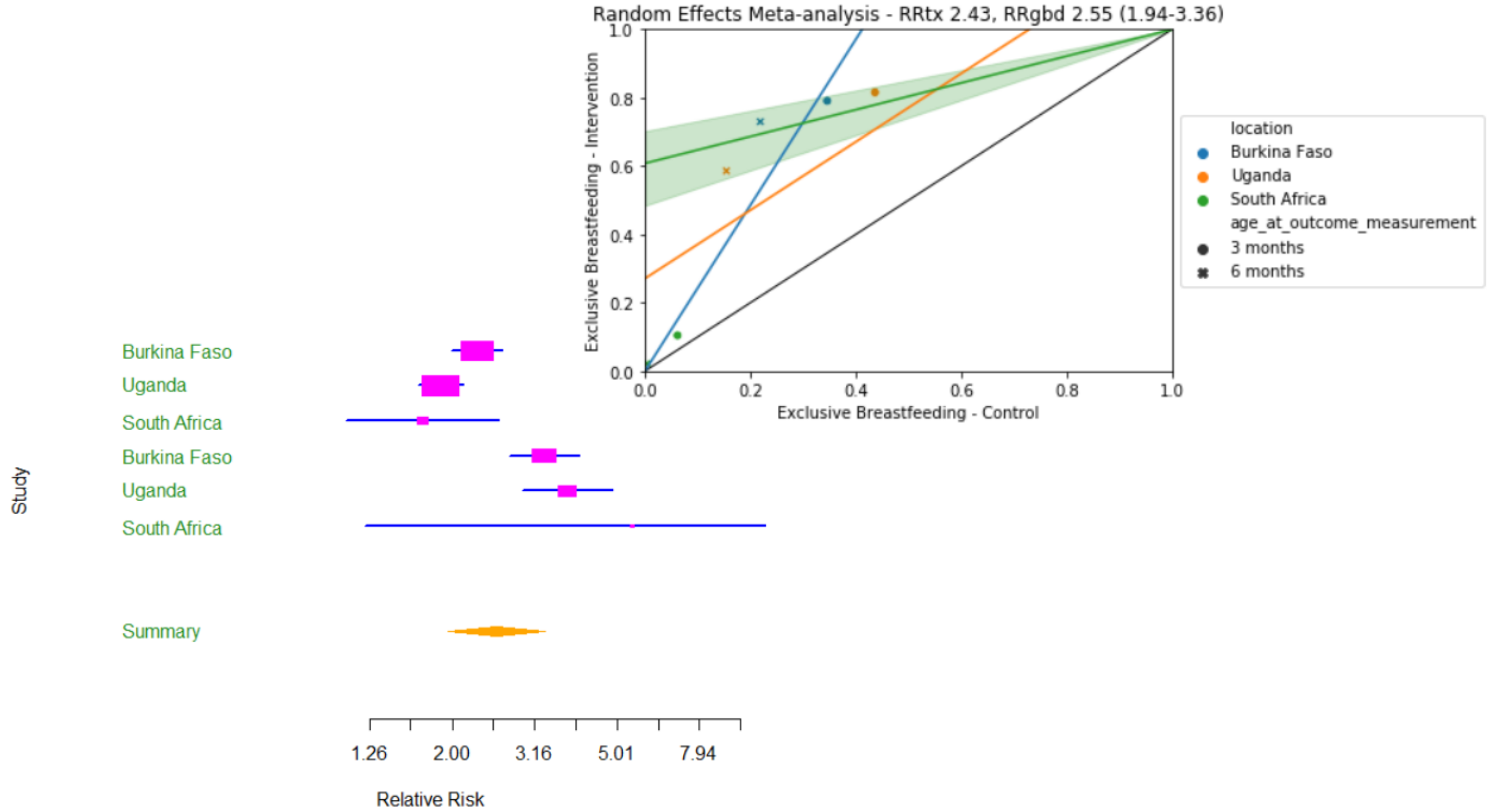

Random Effects Meta-analysis - RRgbd 2.15 (1.84-2.51)
Exclusive Breastfeeding - Intervention
Exclusive Breastfeeding - Control
0.0
0.2
0.4
0.6
0.8
1.0
location
Durban
Mexico City
Brazil
Iran
India
Ghana
Burkina Faso
Uganda
South Africa
Kenya
Bangladesh
Syria
age_at_outcome_measurement
3 months
2 weeks
1 month
6 weeks
2 months
4 months
5 months
6 months

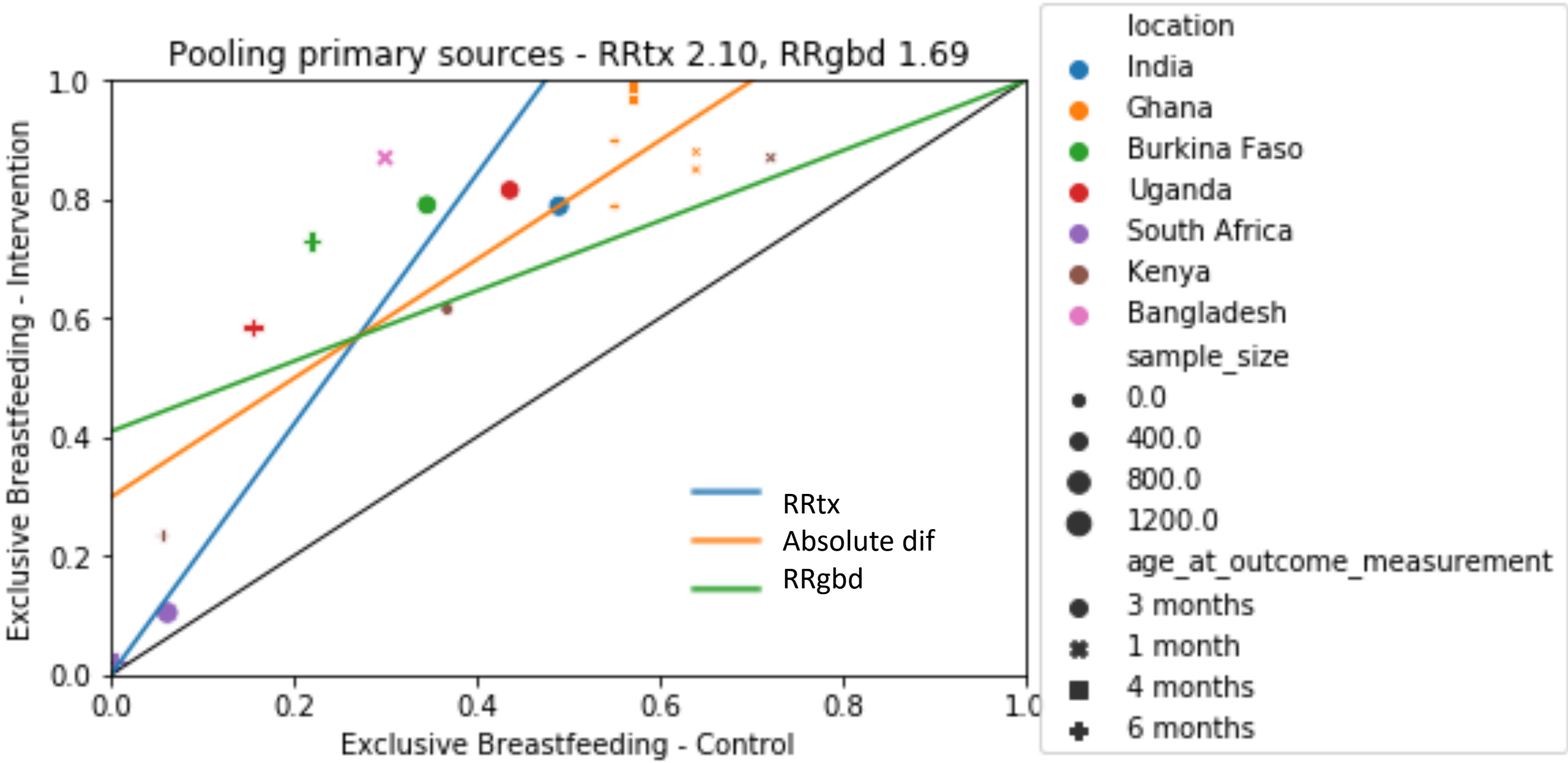

Random Effects Meta-analysis - RRgbd 2.15 (1.84-2.51)
Exclusive Breastfeeding - Intervention
Exclusive Breastfeeding - Control
0.0
0.2
0.4
0.6
0.8
1.0
location
India
Burkina Faso
Uganda
South Africa
Kenya
Bangladesh
age_at_outcome_measurement
3 months
6 months
1 month

Limitations

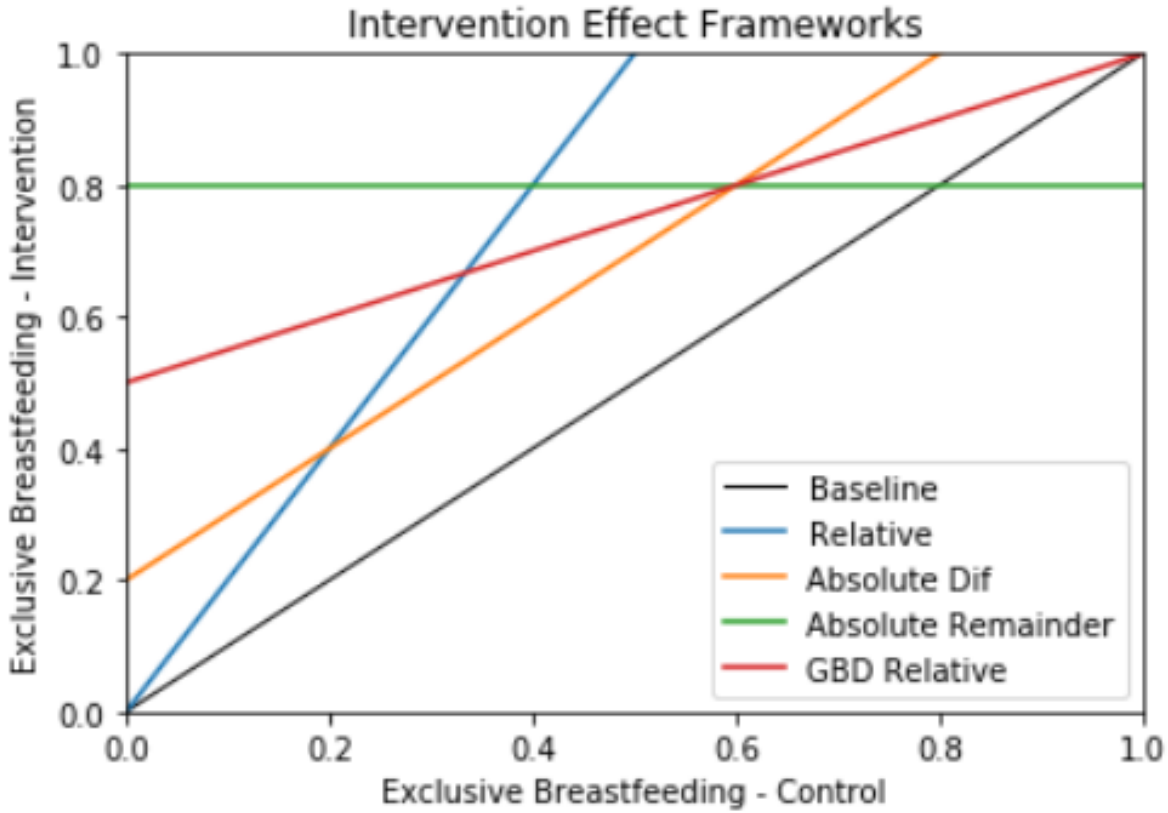
- Cannot really get important subgroups (healthcare worker vs peer, home vs facility, age at outcome) if we want this level of study design consistency
- These studies only report non-exclusive breastfeeding. There are <10 citations for discontinued breastfeeding, and they don’t match our intervention (individual BF counseling)
  - For now, we will use the non-exclusive BF RR
  - Discontinued BF PAF is 5-10X smaller than non-exclusive BF

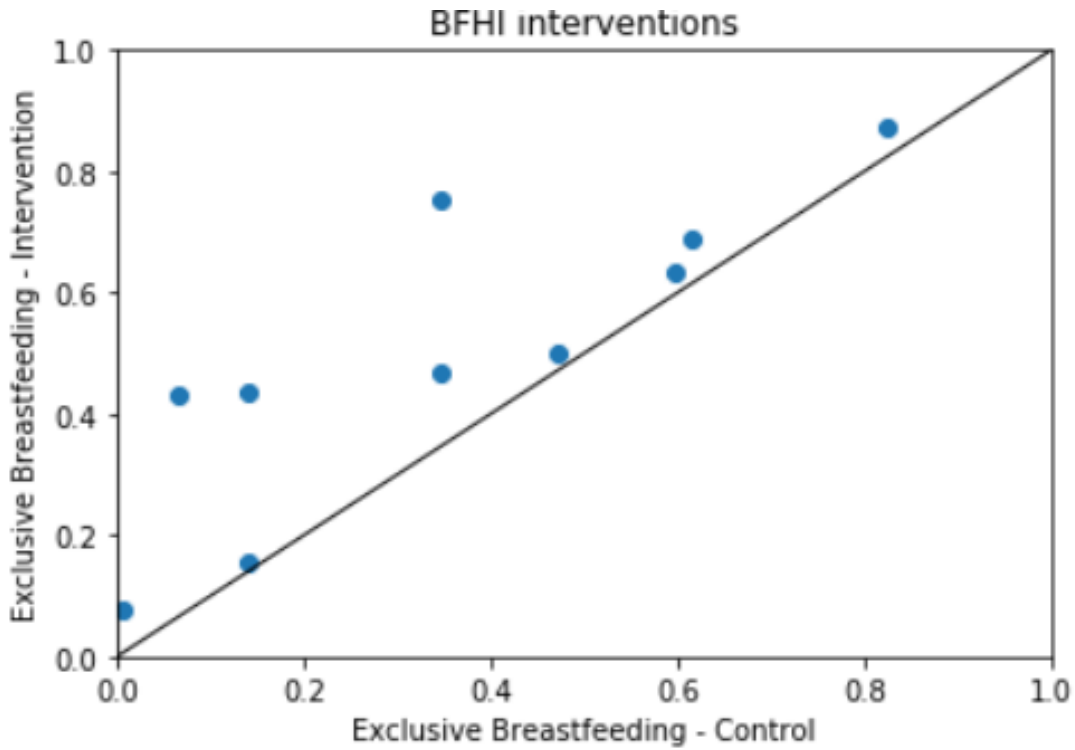

Pooling primary sources - RRtx 2.43, RRgbd 1.50 (1.41-1.59)
Exclusive Breastfeeding - Intervention
Exclusive Breastfeeding - Control
0.0
0.2
0.4
0.6
0.8
1.0
location
Burkina Faso
Uganda
South Africa
age_at_outcome_measurement
3 months
6 months


Random Effects Meta-analysis - RRtx 2.43, RRgbd 2.55 (1.94-3.36)
Exclusive Breastfeeding - Intervention
Exclusive Breastfeeding - Control
0.0
0.2
0.4
0.6
0.8
1.0
location
Burkina Faso
Uganda
South Africa
age_at_outcome_measurement
3 months
6 months
Study
Burkina Faso
Uganda
South Africa
Burkina Faso
Uganda
South Africa
Summary
1.26
2.00
3.16
5.01
7.94
Relative Risk


Pooling primary sources - RRtx 2.10, RRgbd 1.69
Exclusive Breastfeeding - Intervention
Exclusive Breastfeeding - Control
0.0
0.2
0.4
0.6
0.8
1.0
RRtx
Absolute dif
RRgbd
location
India
Ghana
Burkina Faso
Uganda
South Africa
Kenya
Bangladesh
sample_size
0.0
400.0
800.0
1200.0
age_at_outcome_measurement
3 months
1 month
4 months
6 months

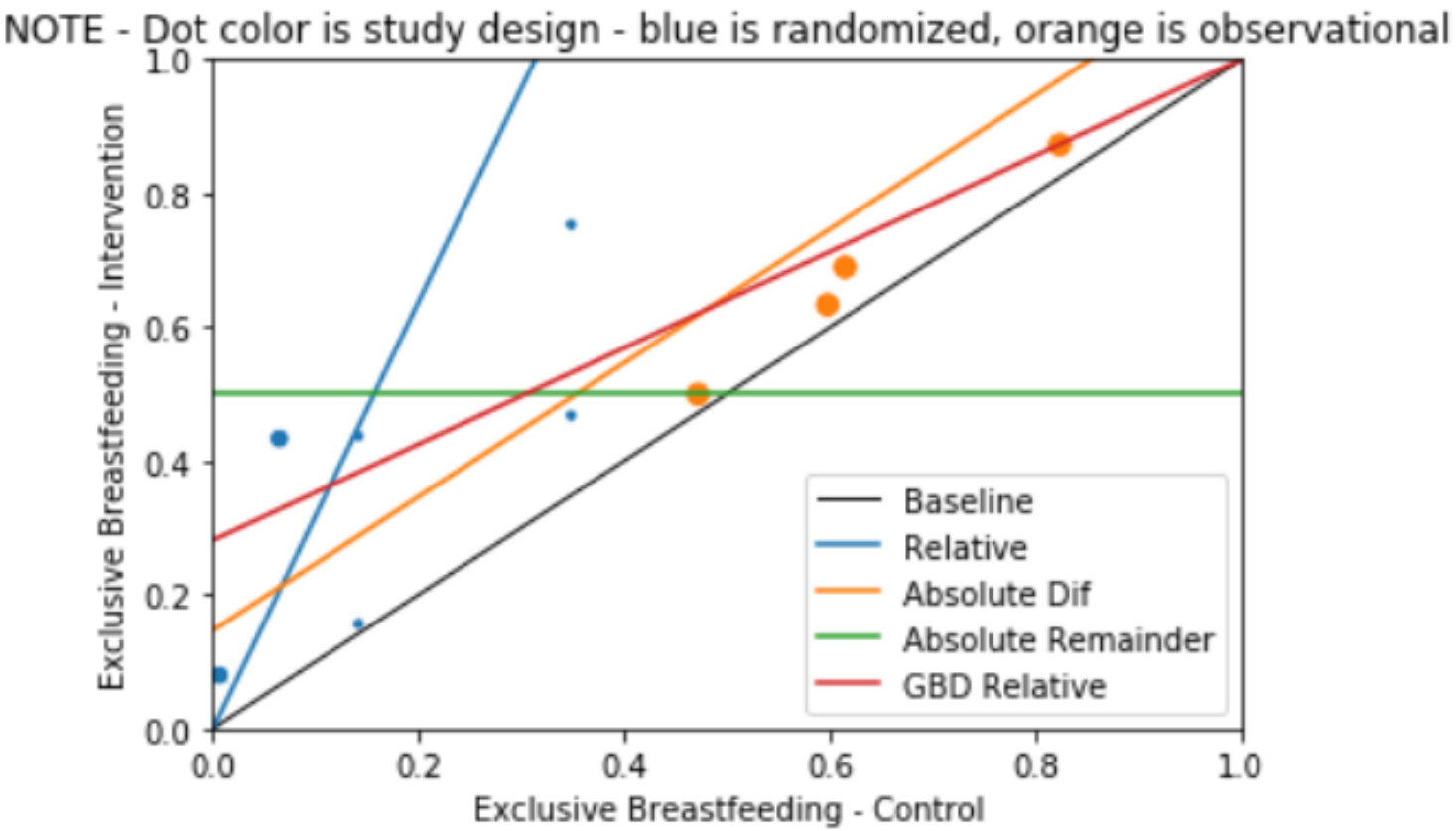
Which risk framework is appropriate?





- We need to be careful how we account for study design heterogeneity!

Baby Friendly Hospital Initiative Efficacy



- BFHI sources (**n=3**) from Sinha 2017
- Simple mean, NOT proper meta-analysis
- **Dot size is sample size**
- **Dot color is study design**
- A meta-analysis would weight on sample size but not study design

- There are many more studies for BFP counseling, if we are to do that

Intervention Protocol

- Often, BMGF teams have specific protocols they want to estimate impact of, rather than our current approach of estimating baseline coverage.

INTERVENTION COVERAGE BASELINE AND 2020 TARGETS WERE USED TO MODEL LIVES SAVED

Key

Baseline Coverage → 2020 Coverage

Coverage targets verified in second phase of impact modeling

2016 Intervention Start
2017 Intervention Start
2019 Intervention Start

Coverage: Baseline – 2020 Target

	Coverage Indicator	Nigeria	Ethiopia	Uttar Pradesh	Bihar	Bangladesh	Burkina Faso
Breastfeeding (BF)							
Exclusive BF	*Promotion coverage (home, health, community & work)*	3% (2015) → 60%	45% (2015) → 80%	2.5% (2015) → 70%	12% (2015) → 70%	25% (2015) → 60%	25% (2015) → 60%
Timely Initiation of BF	*Promotion coverage (home, health, & community)*	3% (2015)→ 60%	45% (2015)→ 80%	2.5% (2015) → 70%	16% (2015) → 70%	25% (2015) → 60%	25% (2015) → 60%
Continued BF	*Promotion coverage (home, health, & work)*	3% (2015)→ 60%	45% (2015)→ 80%	2.5% (2015) → 70%	11% (2015) → 70%	25% (2015) → 60%	25% (2015) → 60%
Maternal Nutrition							
Iron & Folic Acid Supplementation	*Supplement consumption rate*	20.5% (2015)→ 50%	0.4% (2015)→ 40%	1.7% (2015)→ 35.0%	3% (2015)→ 35%	28.6% (2015)→50%	50% (2015)→ 70%
Calcium Supplementation	*Supplement consumption rate*	0%	0% (2015)→ 20%	5.0% (2015)→ 10.0%	0% (2015)→ 10%	0% (2015)→ 20%	0% (2015)→ 10%
Balanced Protein Energy Supp. (BPE)	*Supplement consumption rate*	0%	0% (2015)→ 20%	47.0% (2015)→ 60.0%	39% (2015)→ 60%	0% (2015)→ 20%	0% (2015)→ 0%
Multiple Micronutrient Supp.	*Supplement consumption rate*	0%	0%	0%	0%	0%	0%
Vitamin A supplementation							
Coverage of vitamin A supplementation		42% (2015)→ 85%	71% (2015)→ 95%	27% (2015)→ 70%	62% (2015)→ 85%	62% (2015)→ 85%	98% (2015)→ 98%
Complementary Feeding							
Complementary Feeding	*Promotion coverage among food secure/insecure populations*	Insecure: 0% Secure: 3% (2015)→ 60%	Insecure: 0% Secure: 16.2% (2015)→ 80%	Insecure: 10% (2015)→ 25% Secure: 2.5% (2015)→ 70%	Insecure: 8% (2015)→ 50% Secure: 14% (2015)→ 70%	Insecure: 0% Secure: 20.9% (2015)→ 60%	Insecure: 0% Secure: 51.5% (2015)→ 70%
Treatment of SAM							
Treatment of SAM	*% cases identified via MUAC who live in catchment areas and receive services*	16% (2015)→ 30%	100%	1% (2015)→ 20%	1% (2015)→ 20%	0% (2015)→ 10%	2% (2015)→ 20%
Food Fortification *(Proxy: Improvement in Micronutrient Status)*							
Vitamin A	*% pop. shift from current MN status level (e.g., mod→ mild)*	**5%** 2015-2020 (shift from each MN status group / yr)	**5%** 2015-2020 (shift from each MN status group / yr)	**5%** 2015-2020 (shift from each MN status group / yr)	**5%** 2015-2020 (shift from each MN status group / yr)	**5%** 2015-2020 (shift from each MN status group / yr)	**5%** 2015-2020 (shift from each MN status group / yr)
Iron	*% pop. shift from current MN status level (e.g., mod→ mild)*						
Folate	*% pop. shift from current MN status level (e.g., mod→ mild)*						
Zinc	*% pop. shift from current MN status level (e.g., mod→ mild)*						

Breastfeeding Promotion in Nigeria

- `MagicWandBFP` manually sets coverage level (to either a specified level, or 'baseline')
  - Allows comparison to either our estimates for baseline coverage, or an arbitrary counterfactual

- `FinalExposureObserver` records exposure of ***categorical risks*** for ***specified categories*** for ***specified age groups*** in the ***final population table***
- Be careful!!!
  - Remember re-binning!
  - Exposures for ages outside the age range are inconsistent!

```
sim.get_value('non_exclusive_breastfeeding.exposure')(pop.query('age < 0.5').index).value_counts(normalize=True)
```

```
cat2    0.535714
cat1    0.464286
Name: non_exclusive_breastfeeding_exposure, dtype: float64
```

```
sim.get_value('non_exclusive_breastfeeding.exposure')(pop.query('age > 1').index).value_counts(normalize=True)
```

```
cat2    1.0
Name: non_exclusive_breastfeeding_exposure, dtype: float64
```

Interventions

- To match the effect size and coverage of breastfeeding promotion, it was proposed we could either
  - Have a “step-down” of the trial efficacy to match the standard-of-care BFP
  - Crosswalk “coverage” to “effective coverage”, e.g. some proportion of ANC4/8
- I propose we avoid that rabbit hole, and make simplifying assumptions for two (or more) interventions that match the meta-analysis effect sizes
  - Intensive interventions (e.g. 1:1 counseling, support groups) that are not standard of case – assume 0 coverage (sensitivity: use some fraction of ANC4/8)
  - Baby-friendly hospital initiative (BFHI) – the WHO has reported coverage (% of births in these facilities) that seem plausible, we could scale up to in-facility birth proportion

Table 5 Effect of nature of interventions on breastfeeding outcomes according to settings

	Early Initiation of BF		Exclusive BF		Continued BF	
Nature of Interventions	No. of estimates	RR (95% CI)	No. of estimates	RR (95% CI)	No. of estimates	RR (95% CI)
1. Health systems and services						
Baby friendly support	10	1.20 (1.11; 1.28)	15	1.49 (1.33; 1.68)	3	1.26 (0.96; 1.64)
Counseling or education	10	1.12 (1.05; 1.19)	28	1.66 (1.43; 1.92)	5	1.15 (0.99; 1.35)
Special training of health staff	3	1.09 (1.01; 1.18)	5	1.36 (1.14; 1.63)	–	
2. Home and family environment						
Counseling or Education	5	1.74 (0.97; 3.12)	38	1.58 (1.39; 1.80)	1	1.22 (1.01; 1.47)
Family or Social Support	–	–	5	0.95 (0.87; 1.02)	1	1.69 (0.95; 2.99)
3. Community environment						
Group counseling or education	4	1.65 (1.38; 1.97)	1	1.61 (0.95; 2.71)	–	
Integrated mass media, counseling and community mobilization approach	1	5.33 (2.33;12.19)	5	1.17 (1.01; 1.36)	–	
4. Work environment						
Maternal leave policy	–		2	1.52 (1.03; 2.23)	–	
Workplace support	–		2	1.08 (0.74; 1.60)	–	
Employment status	–		–		1	3.33 (1.43; 10.0)
5. Policy environment						
WIC federal program (US)	–		–	–	–	–
Breast milk substitutes	–		–	–	–	–

*Studies for which RR could not be calculated are not mentioned.

BFHI coverage

Figure 2. Percent of births in facilities designated as Baby-friendly, by country.