Cochrane Revised Risk of Bias Tool (RoB 2)

Additional Considerations for Cluster-Randomized Trials

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Revised Cochrane risk of bias tool for randomized trials (RoB 2) Additional considerations for cluster-randomized trials (RoB 2 CRT)

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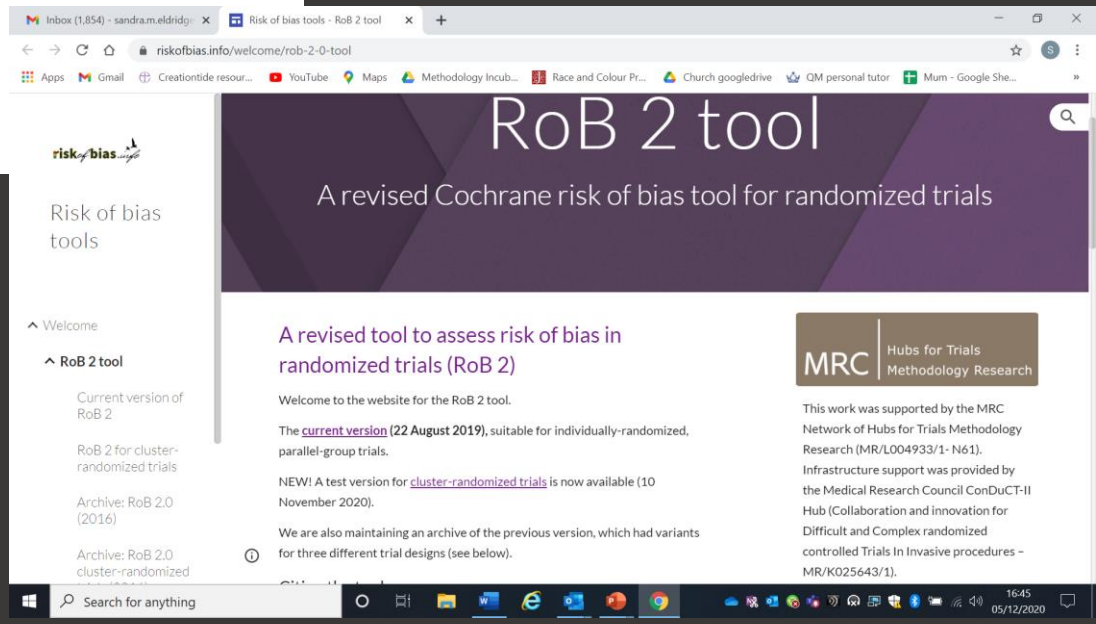
10 November 2020



Six domains

1a Bias arising from the randomization process

1b Bias arising from the identification or recruitment of participants into clusters

NEW

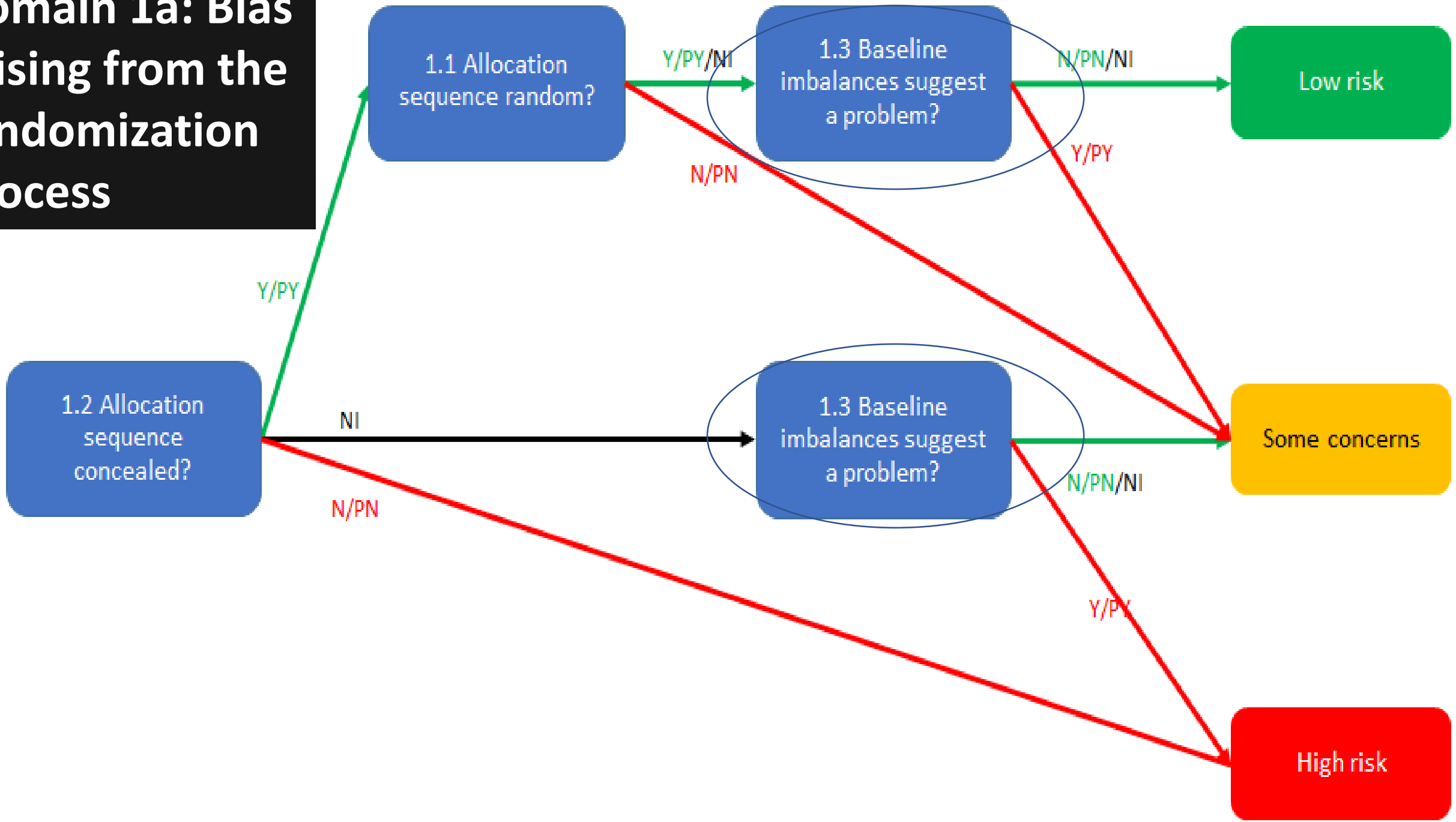
2 Bias due to deviations from intended intervention

3 Bias due to missing outcome data

4 Bias in measurement of the outcome

5 Bias in selection of the reported result

Domain 1a: Bias arising from the randomization process



Baseline imbalances in cluster randomised trials

Randomisation at cluster level

Review baseline imbalances primarily at cluster level

Small numbers of clusters

Chance imbalances more common

Harder to predict how clusters will respond & less chance of subversion

Problems with randomisation less likely

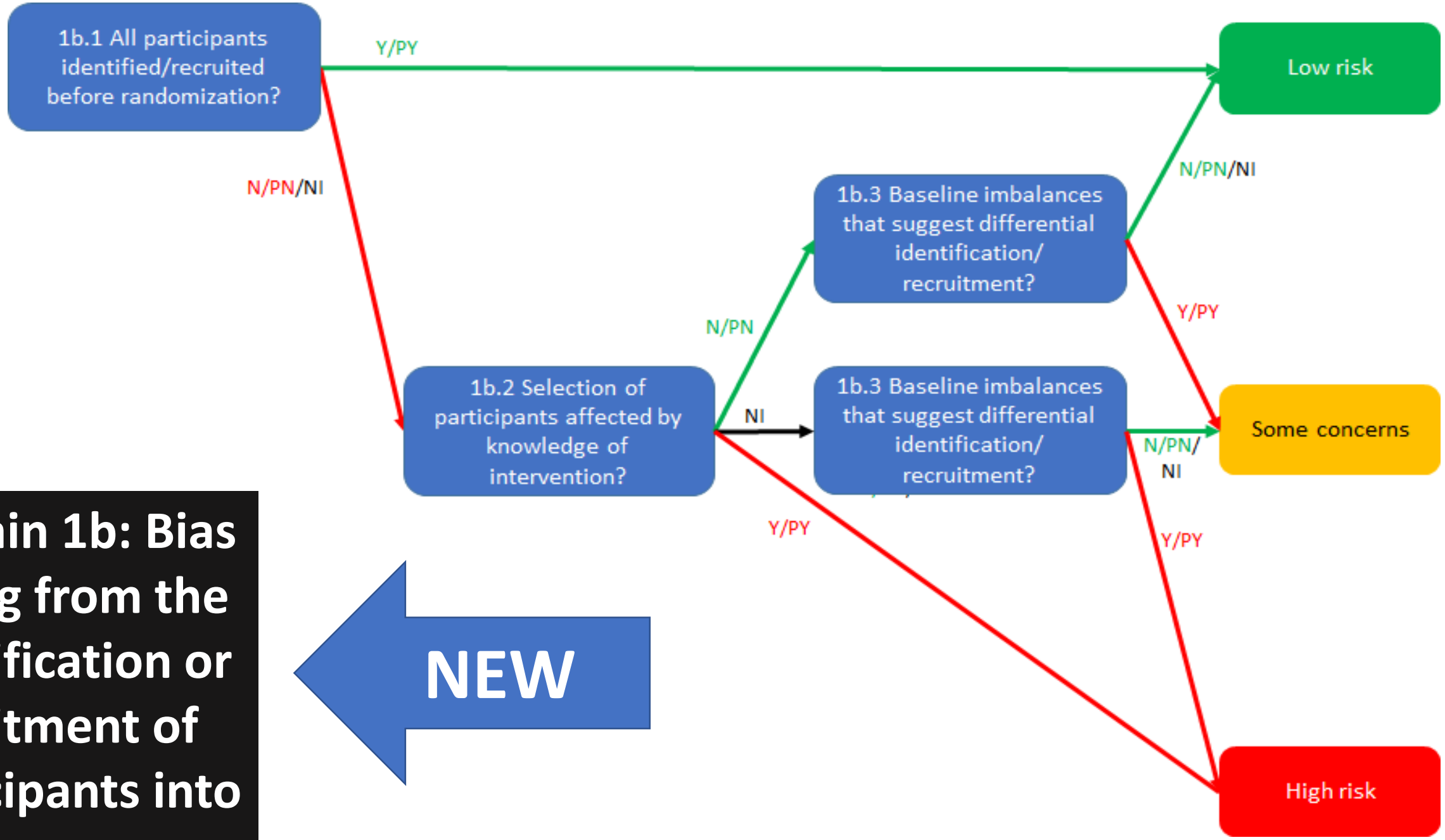
Domain 1b

Another possible reason for imbalance

	All care homes*	Study care homes		
		Total	Intervention	Control
Number	323	78	35	43
Type†				
Nursing	81 (25%)	18 (23%)	9 (26%)	9 (21%)
Residential	242 (75%)	60 (77%)	26 (74%)	34 (79%)
Ownership				
Private	262 (81%)	61 (78%)	28 (80%)	33 (77%)
Voluntary or charity	36 (11%)	16 (21%)	7 (20%)	9 (21%)
Local authority	25 (8%)	1 (1%)	0	1 (2%)
Size				
<32 beds	158	43	20	23
≥32 beds	165	35	15	20
Mean number of beds (SD)	34·89 (19·62)	31·41 (11·49)	31·54 (12·15)	31·30 (11·08)
Median cohort participants per home (IQR)	..	11 (8–15)	11 (7–15)	11 (9–15)

OPERA trial – Underwood et al Lancet 2013

Randomising residential care homes, whole-home activity intervention to reduce depression



Domain 1b: Bias arising from the identification or recruitment of participants into clusters

NEW

Selecting individual participants

Participants = target individuals on whom it has been decided to collect the outcome of interest

Participants may not be recruited

Participants may be clinicians as well as patients

If patients are recruited after randomisation someone involved may know about allocation

Bias may ensue

Recruitment and randomisation

Aim: To improve back pain
Clusters: UK General Practices
Intervention: offer of exercise classes, physiotherapy etc.

Control group:
66 recruited

Intervention group:
165 recruited, suffering from milder back pain

Explanation: participation in the trial very attractive in intervention arm

Cluster 'consent'

Cluster randomisation

Participant consent to randomisation?

Participant consent to data collection, participation

BIAS

e.g. 4KBEAM pilot study

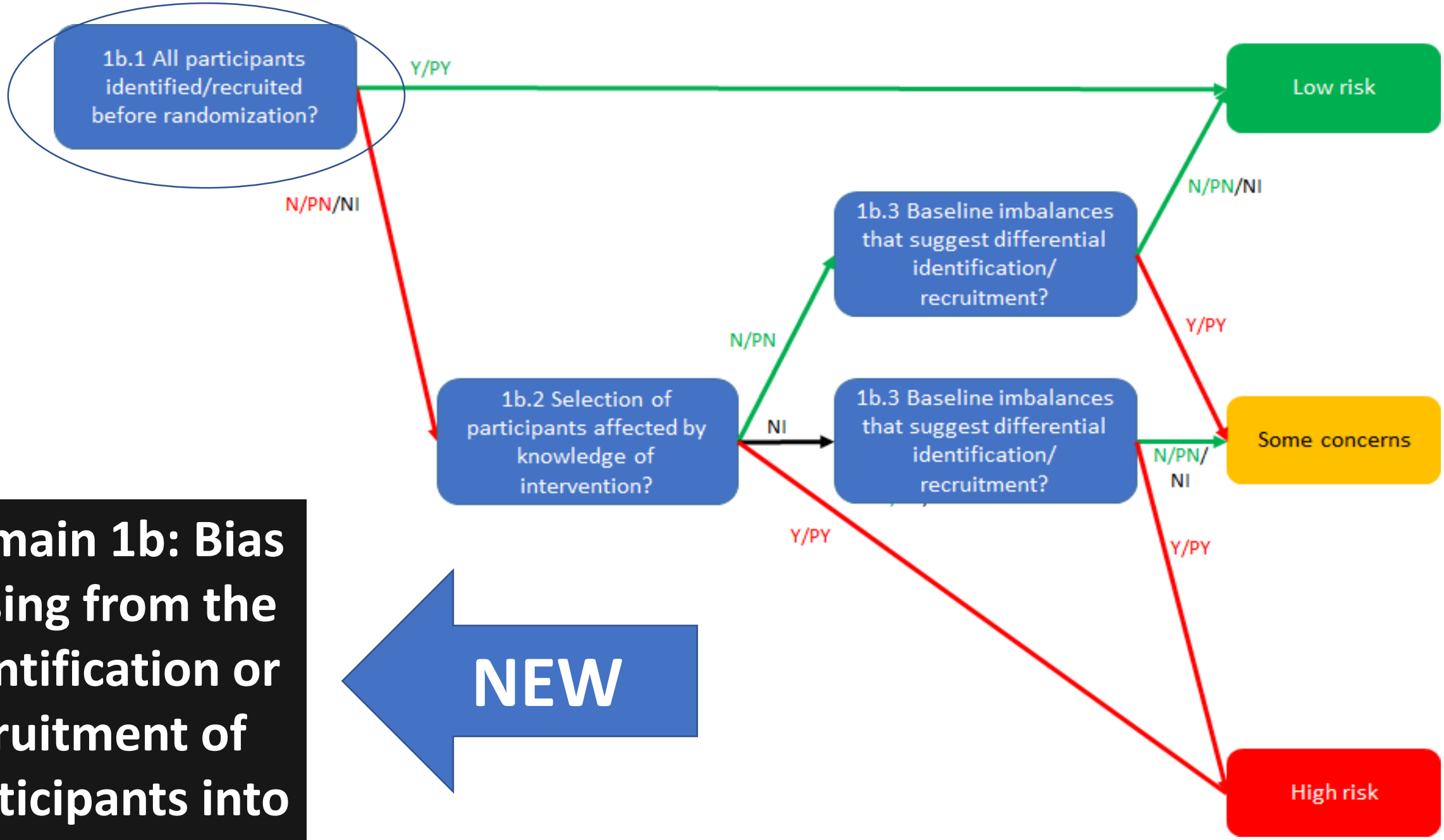
Scenario 1	Scenario 2	Scenario 3	Scenario 4 (identical to 6)	Scenario 5	Scenario 6 (identical to 4)
Cluster randomization	Cluster randomization	Identification of *potential* individual participants	Identification of individual participants	Identification of *potential* individual participants	Identification of individual participants
Identification of *potential* individual participants	Identification of individual participants	Cluster randomization	Cluster randomization	Recruitment of individual participants	Participants not directly recruited
Recruitment of individual participants	Participants not directly recruited	Recruitment of individual participants	Participants not directly recruited	Cluster randomization	Cluster randomization
Potential for identification/recruitment bias although this could be avoided through trial design			No potential for identification/recruitment bias because randomization happens after		

UK BEAM pilot (Farrin et al 2005)

Two further examples in which identification/recruitment bias possible

Scenario 2: Feeding strategies for critically ill patients in intensive care
Clusters: Intensive care unit (ICU) wards
Intervention: Guidelines developed by ICU staff
Outcome: Hospital discharge mortality
Participants not directly recruited but identified by ICU staff (though no evidence of bias)

Scenario 3: Hip protectors for preventing hip fractures
Clusters: Elderly care units within community based health centres
Participants identified prior to randomisation but approached after randomisation
Recruited: 31% in intervention and 9% in control group



Domain 1b: Bias arising from the identification or recruitment of participants into clusters

NEW

Once care homes had agreed to participate, we invited residents to give written, informed consent, or if they lacked capacity to consent, for their next of kin to give written, informed agreement for us to collect data directly from participants, from care-home staff, and from care-home and National Health Service (NHS) records.

891

163

We recruited additional participants for 9 months after randomisation for an end of study cross-sectional analysis, using the same criteria as described previously.

OPERA trial – Underwood et al Lancet 2013

Randomising residential care homes, whole-home activity intervention to reduce depression

Bias assessed separately for different outcomes - OPERA trial as an example

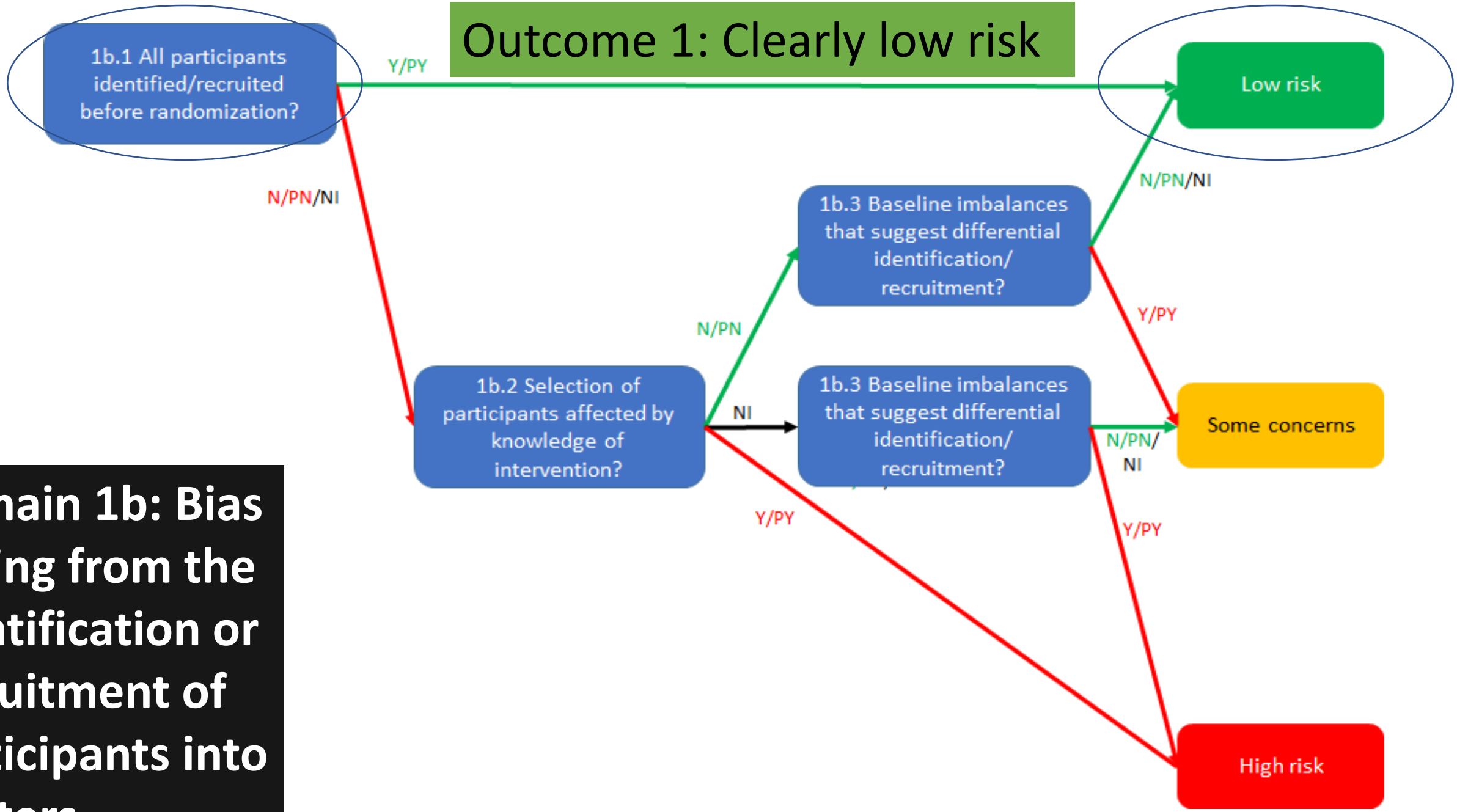
Outcome 1: GDS-15 score at 12 months for those depressed at baseline

Includes only individuals recruited before randomisation

Outcome 2: Being depressed at end of study

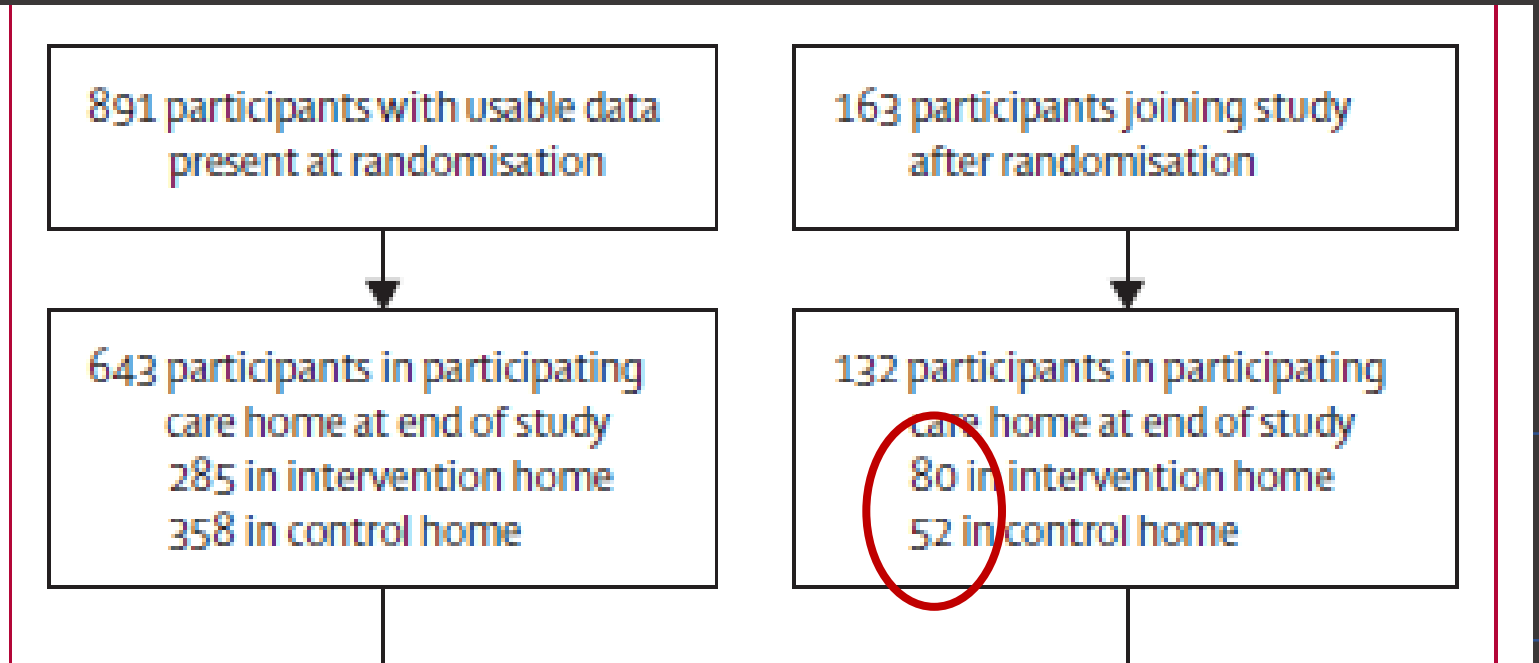
Includes individuals recruited before and after randomisation

Outcome 1: Clearly low risk



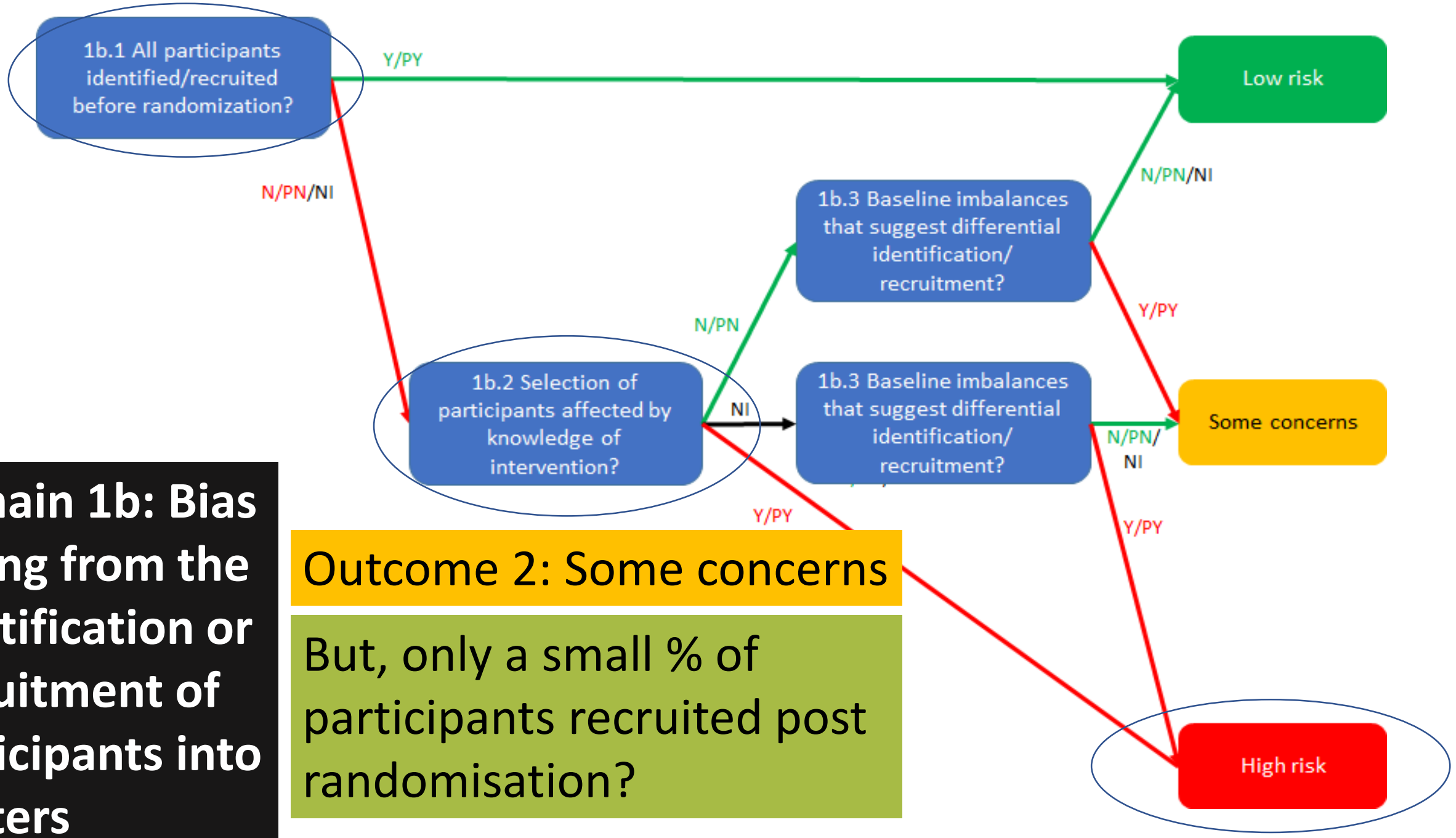
Domain 1b: Bias arising from the identification or recruitment of participants into clusters

The prevalence of depression in all residents at the end of the study is an important analysis to ensure the findings apply to all residents rather than only relatively healthy survivors. In this analysis we recruited more participants in the intervention homes than in the control homes after randomisation. Results were, however, unchanged by excluding the post randomisation participants.



OPERA trial – Underwood et al Lancet 2013

Randomising nursing homes, whole-home activity intervention to reduce depression

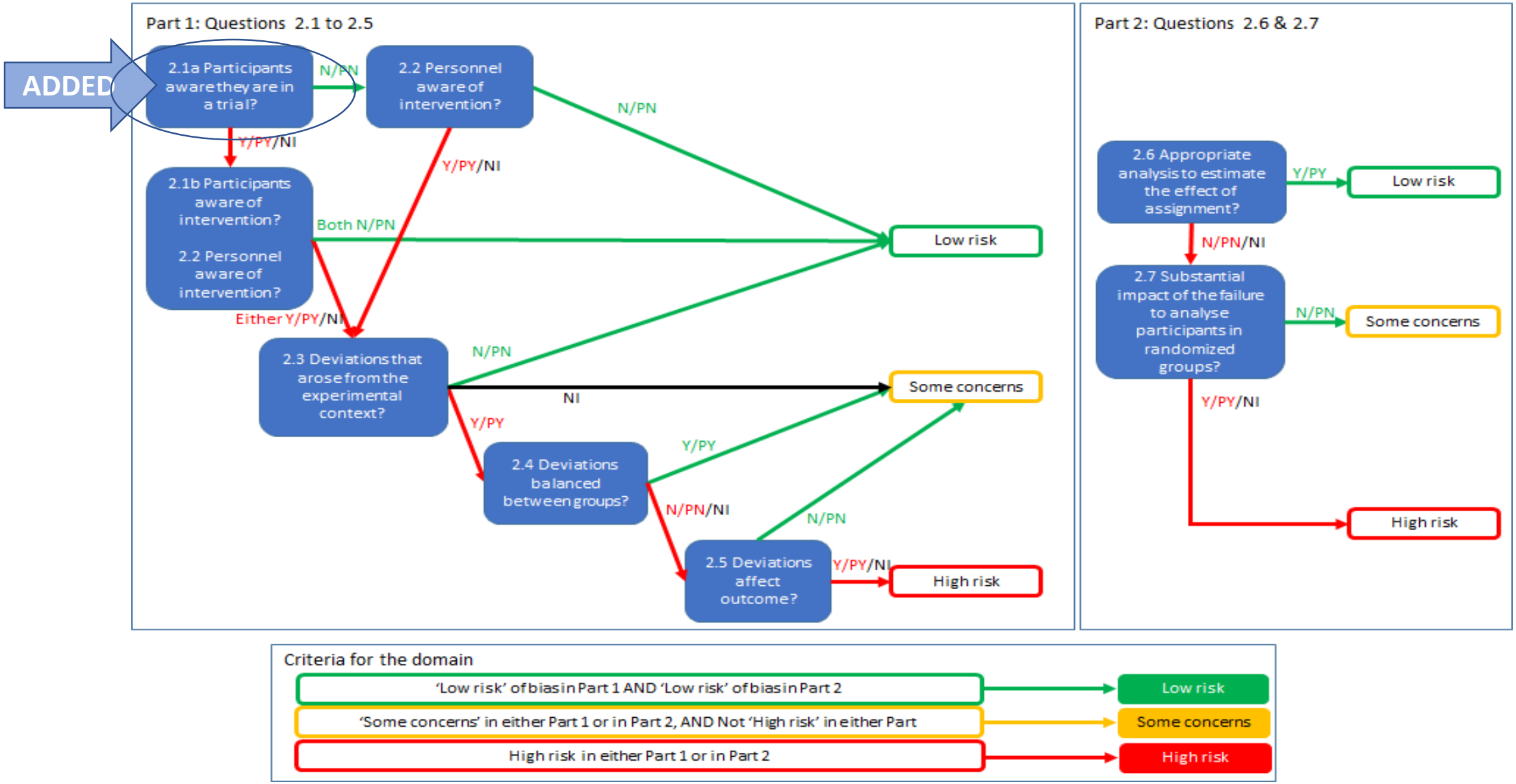


Domain 1b: Bias arising from the identification or recruitment of participants into clusters

Outcome 2: Some concerns

But, only a small % of participants recruited post randomisation?

Domain 2: Bias due to deviations from intended intervention (assignment)



Criteria for the domain

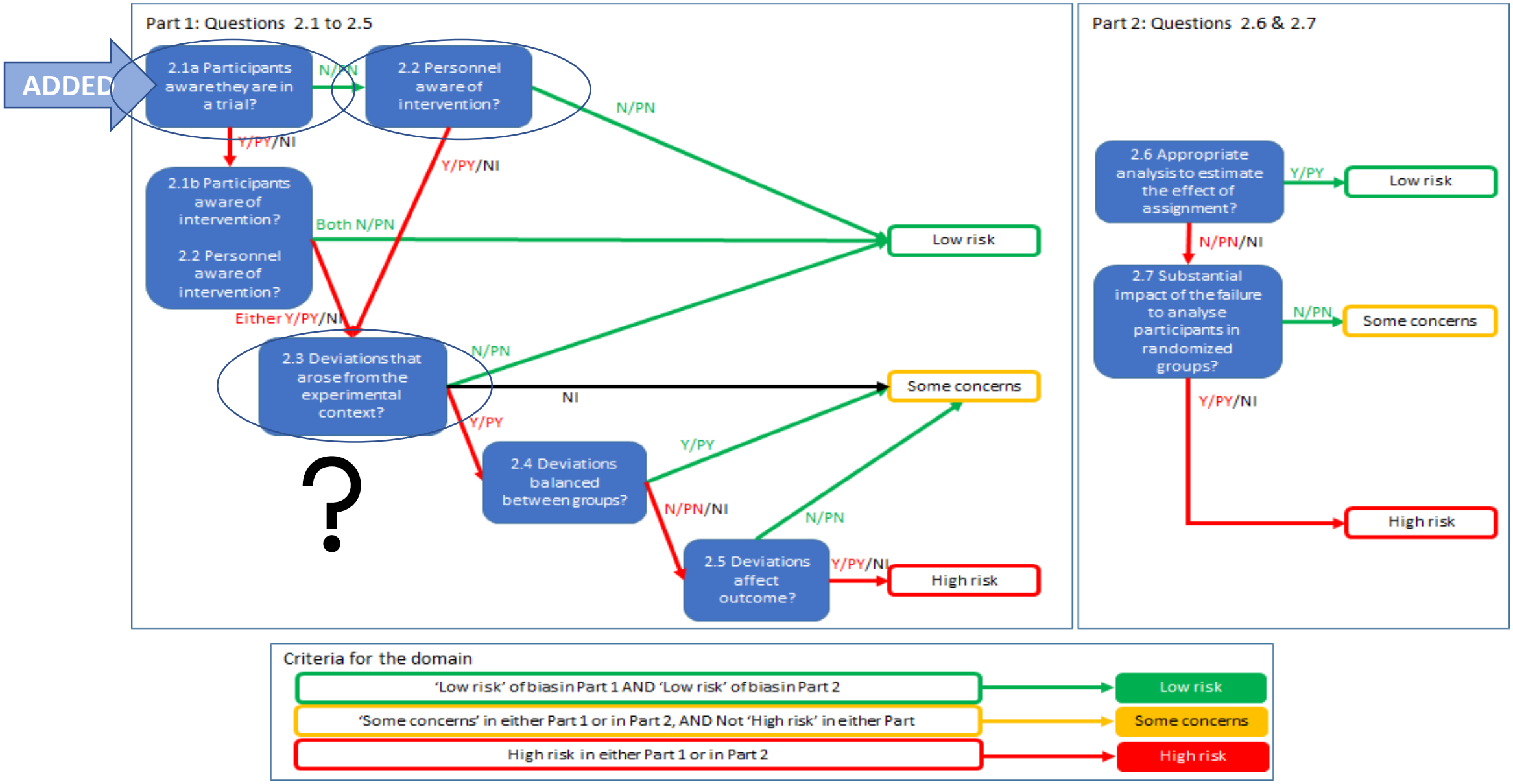
'Low risk' of bias in Part 1 AND 'Low risk' of bias in Part 2	Low risk
'Some concerns' in either Part 1 or in Part 2, AND Not 'High risk' in either Part	Some concerns
High risk in either Part 1 or in Part 2	High risk

IRIS trial, Feder et al, Lancet 2011

Randomising UK general practices, intervention to increase identification of and referral for domestic violence

Because the intervention was targeted at clinicians and administrators and no consent was required for outcome data extraction from medical records, as agreed by the research ethics committee, patients were not aware they were part of a research study.[17]

Domain 2: Bias due to deviations from intended intervention (assignment)



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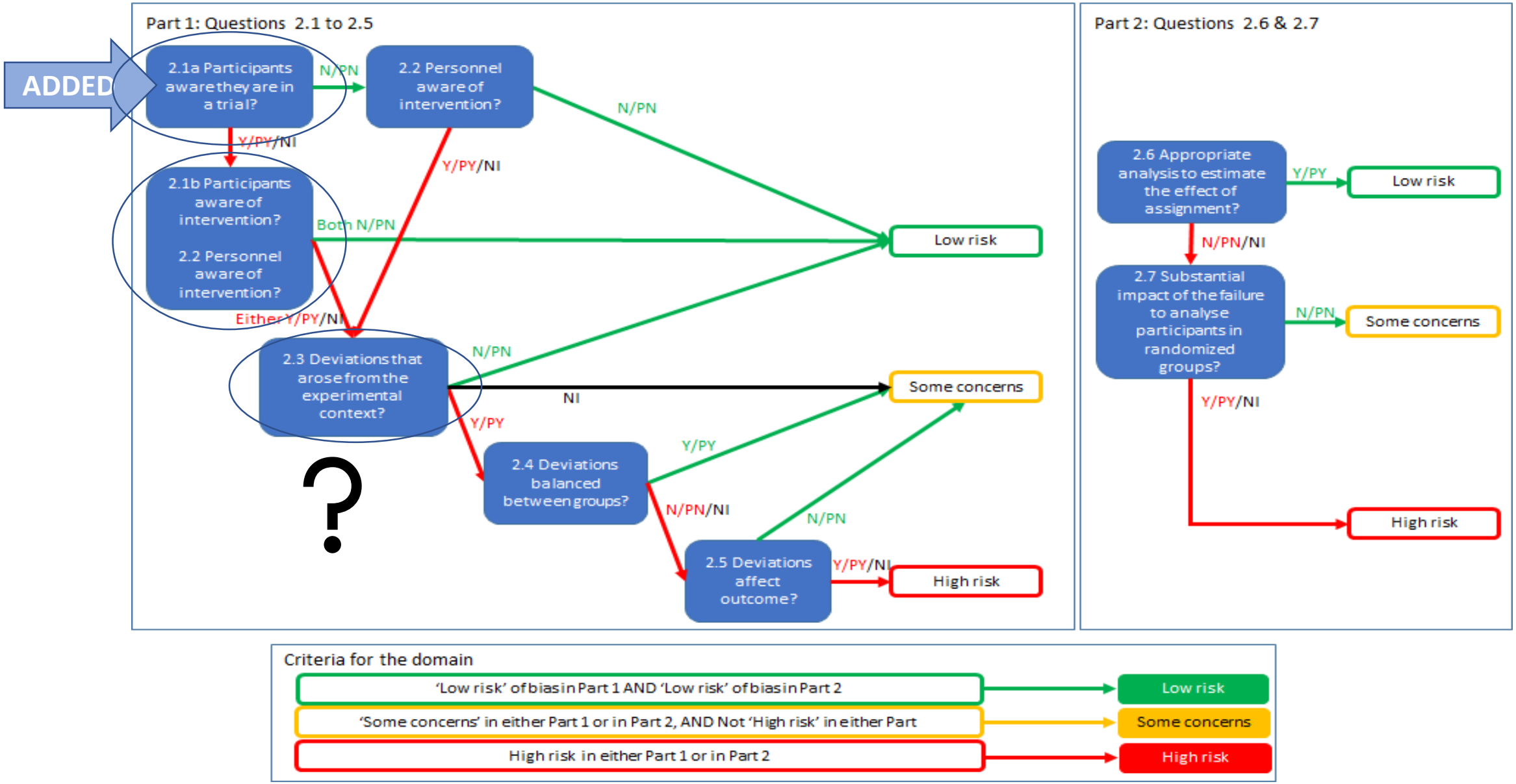
High risk in either Part 1 or in Part 2	High risk

Researchers collecting follow-up data from individual participants, and the participants themselves, were inevitably aware of home randomisation because of the physiotherapists' activities within the home.

OPERA trial – Underwood et al Lancet 2013

Randomising residential care homes, whole-home activity intervention to reduce depression

Domain 2: Bias due to deviations from intended intervention (assignment)



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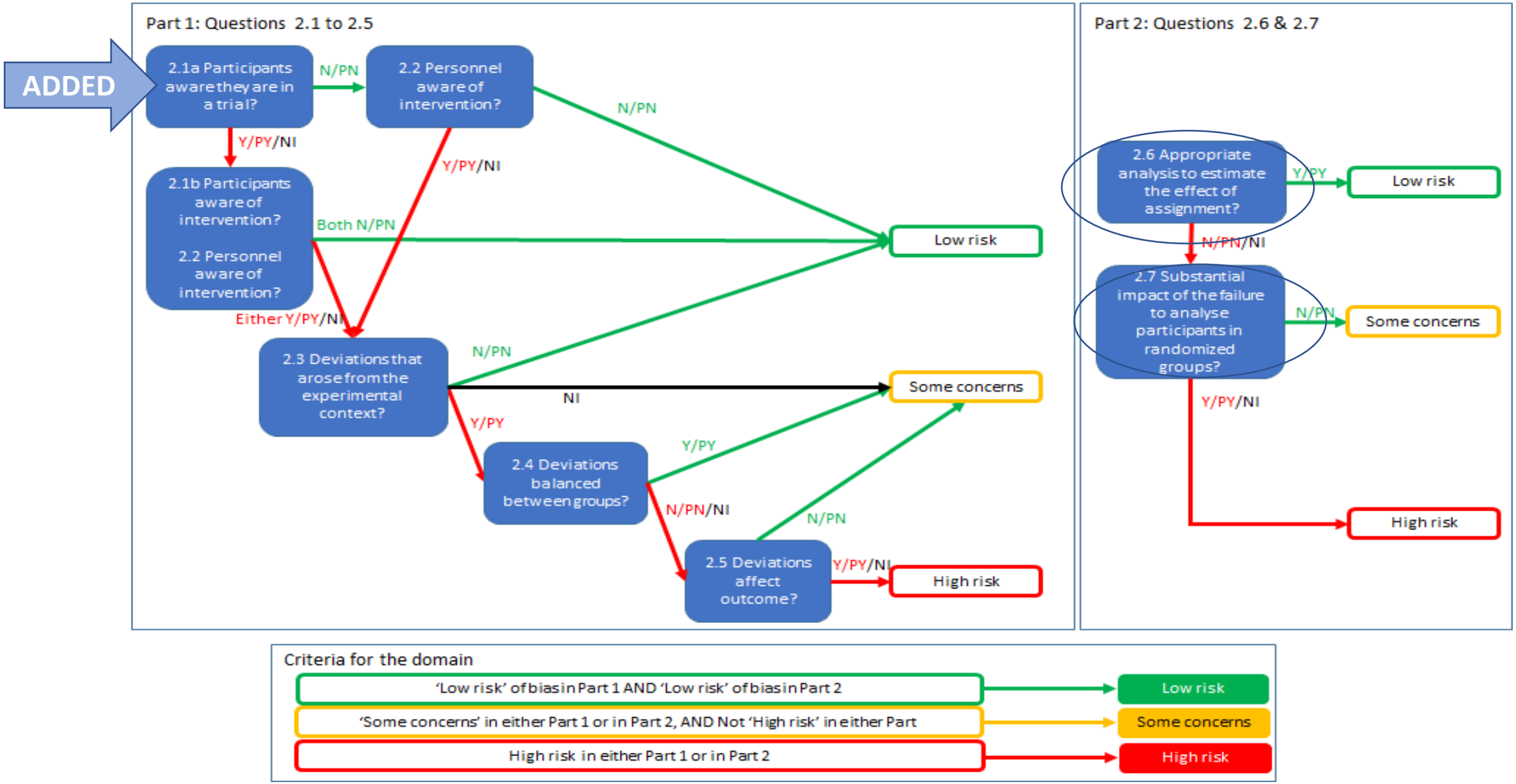

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High risk in either Part 1 or in Part 2	High risk

Intention to treat analyses in cluster randomised trials

Cohort design: Recruit participants at baseline and follow-up

Similar to individually randomised trial, analyse in clusters that they were recruited to

Cross-sectional design: Collect data on cross-section at end of the trial

Can assume that analysing in clusters from which data arose is sufficient in most cases

Repeated cross-sectional design: Collect data on different cross-sections at start and end

Can make similar assumptions as for cross-sectional designs

OPERA was a mixture of cohort and cross-sectional designs

For cohort analyses we included residents in the home from which they were recruited. For cross-sectional analyses we included residents in the home in which they were resident at the end of the study.

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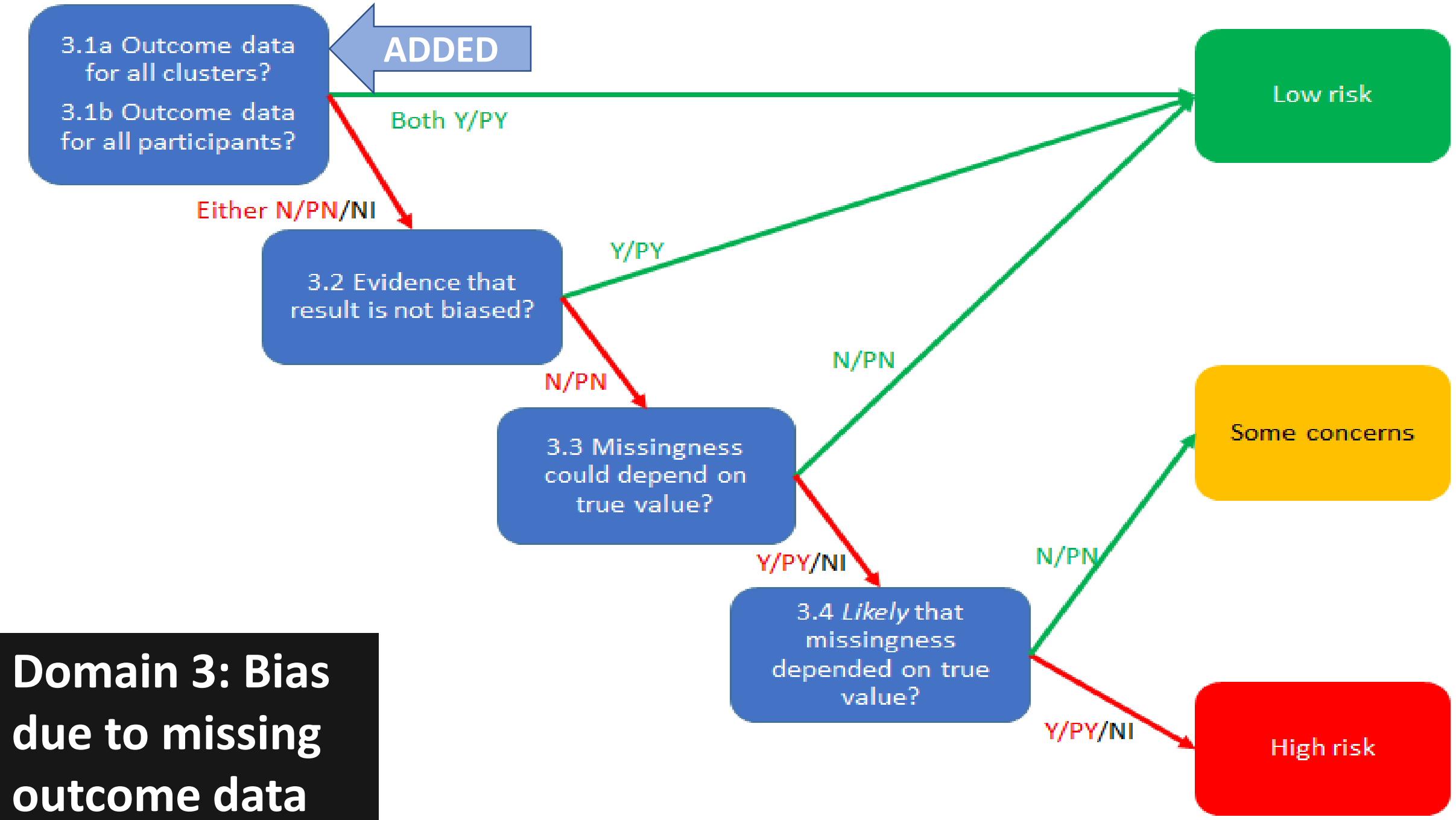


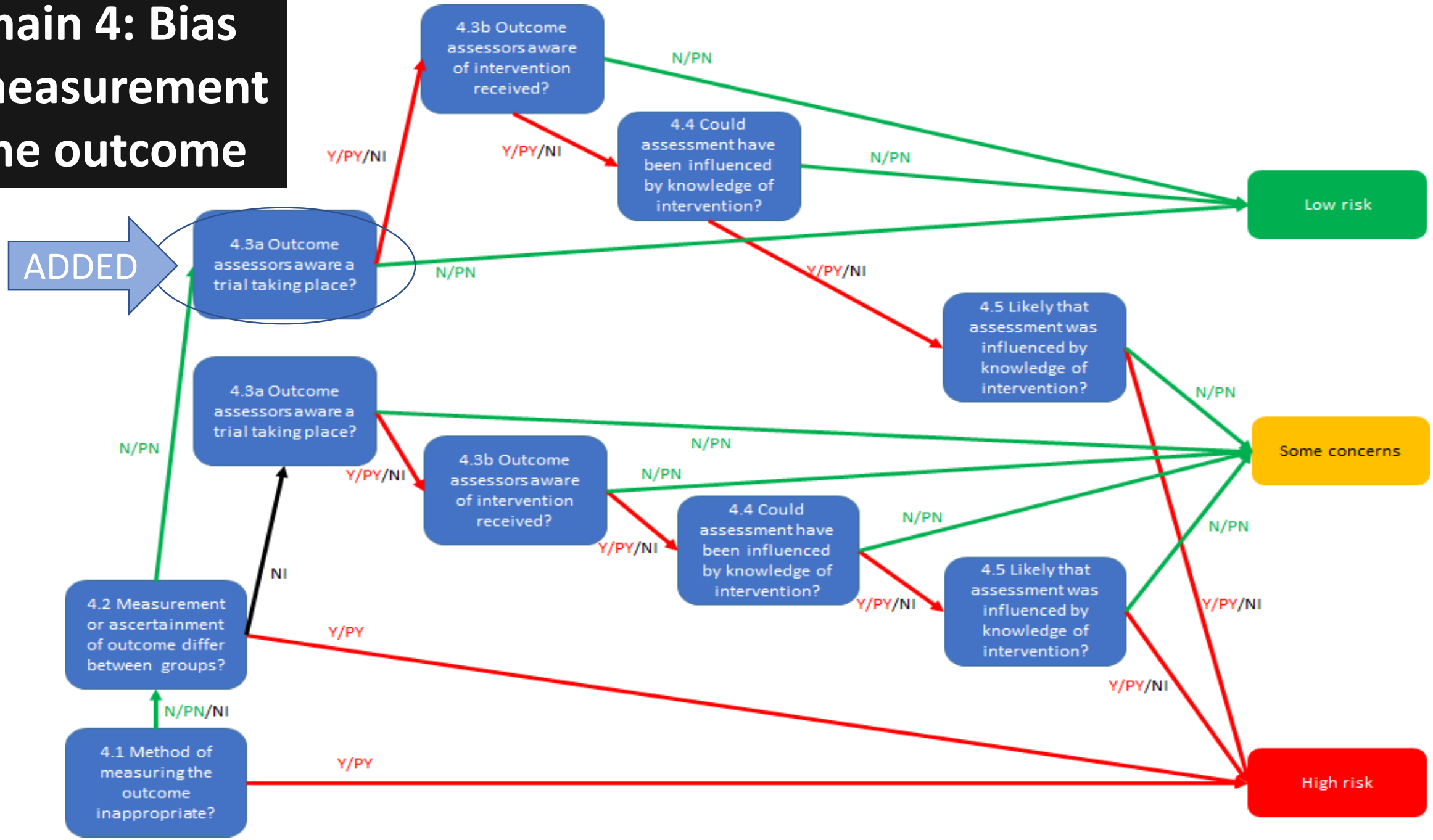
Domain 3: Bias due to missing outcome data

Principles for assessing missingness need to be applied at both individual and cluster level

Missingness related to outcome?

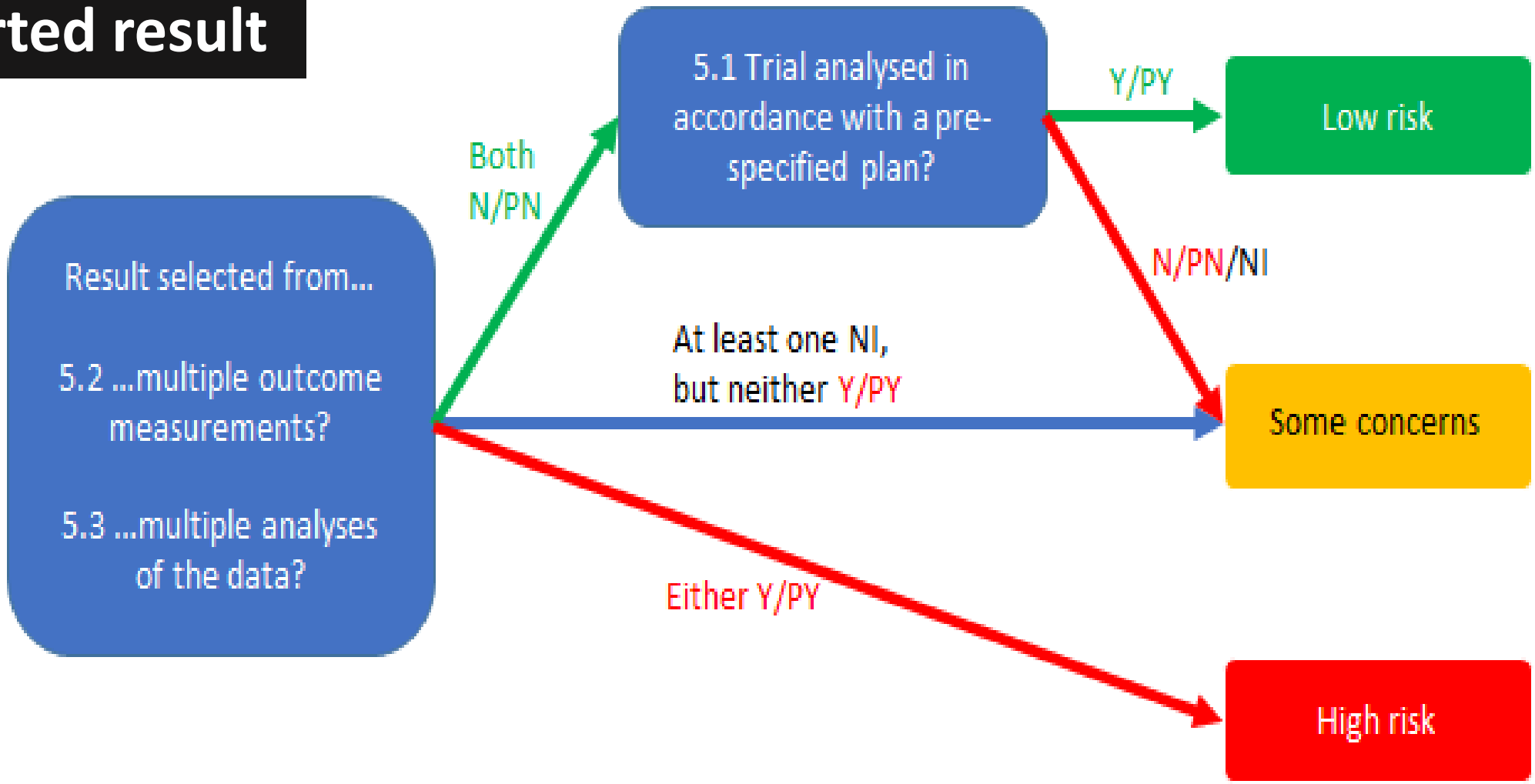
Missingness differential between arms?

Domain 4: Bias in measurement of the outcome



Domain 5: Bias in selection of the reported result

NO CHANGES



Additional Considerations for Cluster-Randomized Trials

1a Bias arising from the randomization process

Unchanged, assessment needs to account for small numbers of clusters and domain 1b

NEW

1b Bias arising from the identification or recruitment of participants into clusters

2 Bias due to deviations from intended intervention

Consider whether participants aware in trial, may be difficult to identify deviations

3 Bias due to missing outcome data

Consider at cluster as well as individual level

4 Bias in measurement of the outcome

Consider whether outcome assessors aware in trial

5 Bias in selection of the reported result

No changes