## Appendix 8: Restrictive population definition, demographics and analysis

The restrictive population was defined as follows:

- 1. Age <40 years
- 2. BMI >18.5 to <30 kg/m<sup>2</sup>
- 3. Non smoker
- 4. No cardiac disease
- 5. No respiratory disease
- 6. No renal disease
- 7. No hepatic disease
- 8. No gastrointestinal disease
- 9. No endocrine disease
- 10. No pre-gestational diabetes
- 11. No hematological disease
- 12. No history of venous thrombo-embolism
- 13. No active malignancy
- 14. No severe maternal conditions (measures were excluded following the time stamp of

diagnosis)

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Applying the "restrictive" population definitions reduced the cohort to 595/1041 women. Delivery information was unavailable for 13 of these women, who were either lost to followup or discontinued participation during the study period. Within this group, 12 women provided data at 12 weeks, 7 at 24 weeks, 6 at 28 weeks and 1 at 32 weeks' gestation, beyond which they no longer participated. Delivery information was available for 582 women within the restrictive cohort, of whom a further 2 withdrew consent during the study period.

**Table A8.1:** Baseline maternal characteristics for restrictive, excluded and total pragmaticpopulations. Values are mean  $\pm$ SD for continuous variables, and number (percentage) for categoricalvalues. BMI= Body Mass Index (kg/m²); GA= Gestational Age. \*defined as Hb <110 g/L, \*</td>unmedicated, \*\*(non-ischaemic non- congenital).

Maternal baseline characteristics	Included in restricted population	Excluded from restricted population	Total N=1041
	N=595	N=446	
Maternal age (years) ±SD	31.5±3.9	31.5±5.9	31.5±4.9
Maternal weight (kg) ±SD	64.3±9.4	73.6±16.6	68.3±13.9
Maternal BMI (kg/m <sup>2</sup> ) ±SD	23.4±3.0	26.9±5.7	24.9±4.7
BMI category - Normal (18.5-24.9 kg/m²) (%)	427 (71.2)	184 (41.3)	611 (58.7)
- Overweight (25.0-29.9 kg/m <sup>2</sup> ) (%)	168 (28.2)	117 (26.2)	285 (27.4)
- Obese (≥30 kg/m²) (%)	0	145 (32.5)	145 (13.9)
GA at first visit (weeks) ±SD	13.1±2.4	13.1±2.4	13.1±2.4
Nulliparous (%)	276 (46.4)	184 (41.3)	460 (44.2)
Ethnicity: - White (%)	511 (85.9)	378 (84.8)	889 (85.4)
- Asian (%)	21 (3.5)	31 (7.0)	52 (5.0)
- African/Caribbean (%)	10 (1.7)	13 (2.9)	23 (2.2)

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- Mixed (%)	11 (1.8)	7 (1.6)	18 (1.7)
- Other (%)	42 (7.1)	17 (3.8)	59 (5.7)
Smoker (%)	0	79 (17.7)	79 (7.6)
Anemia* (%)	3 (0.5)	4 (0.9)	7 (0.7)
Pre-gestational diabetes (%)	0	6 (1.3)	6 (0.6)
Pre-existing hypertension <sup>+</sup> (%)	0	17 (3.8)	17 (1.6)
Cardiac disease <sup>++</sup> (%)	0	12 (2.7)	12 (1.2)
Pre-existing renal disease (%)	0	24 (5.4)	24 (2.3)

In the restrictive group, systolic blood pressure decreased from 12 weeks: median (95% CI) 113 (112 to 114) mmHg to reach its nadir of 112 (111 to 113) mmHg at 18.4 weeks, a change of -1 (-3 to 0) mmHg. Systolic blood pressure then rose progressively from 20 weeks' gestation to a maximum of median (95% CI) 119 (118 to 120) mmHg at 40 weeks, a difference (95% CI) of 7 (5 to 9) mmHg from minimum to maximum systolic BP.

Diastolic blood pressure decreased from 12 weeks: median (95% CI) 70 (69 to 70) mmHg to reach its nadir of 68 (67 to 69) mmHg at 19.5 weeks, a change (95% CI) of -2 (-3 to -1) mmHg. Diastolic blood pressure subsequently increased to a maximum of median (95% CI) 77 (76 to 78) mmHg at 40 weeks, a difference (95% CI) of 9 (8 to 11) mmHg from minimum to maximum diastolic BP.

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**Table A8.2:** Smoothed centiles for systolic blood pressure and diastolic blood pressure (mmHg) for restrictive cohort according to gestational age for 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> centiles (95% CI).

Gestational age (weeks)	Centiles for Systolic Blood Pressure (95% CI)				
	3rd	10th	50th	90th	97th
12	94.9 (93.4 - 96.3)	100.7 (99.8 - 101.7)	113.2 (112.1 - 114.3)	127.1 (125.7 - 128.5)	134.9 (133.1 - 136.7)
14	94.7 (92.8 - 96.7)	100.4 (99.5 - 101.2)	112.6 (111.8 - 113.4)	126.2 (124.7 - 127.8)	133.6 (130.1 - 137.1
16	94.7 (93.5 - 96)	100.1 (99.3 - 101)	112.2 (111.6 - 112.9)	125.7 (124.6 - 126.8)	132.9 (131.2 - 134.5)
18	94.8 (93.8 - 95.8)	100.1 (99.3 - 100.9)	112.1 (111.4 - 112.7)	125.5 (124.5 - 126.5)	132.5 (131 - 133.9)
20	95 (94.1 - 95.9)	100.2 (99.5 - 100.9)	112.1 (111.4 - 112.8)	125.5 (124.5 - 126.5)	132.4 (131 - 133.9)
22	95.3 (93.7 - 96.8)	100.4 (99.6 - 101.3)	112.3 (111.5 - 113.1)	125.7 (124.5 - 126.9)	132.6 (130.2 - 135)
24	95.5 (94.6 - 96.5)	100.7 (99.9 - 101.5)	112.6 (111.8 - 113.3)	125.9 (124.9 - 126.9)	132.8 (131.2 - 134.4)
26	95.8 (94.8 - 96.8)	100.9 (100.1 - 101.8)	112.8 (112.2 - 113.4)	126.2 (125.4 - 127)	133.1 (131.8 - 134.3)
28	96.1 (95.1 - 97.1)	101.2 (100.4 - 102)	113.1 (112.5 - 113.6)	126.5 (125.8 - 127.2)	133.4 (132.3 - 134.4
30	96.4 (95.4 - 97.4)	101.5 (100.7 - 102.3)	113.4 (112.8 - 114)	126.8 (126.1 - 127.6)	133.8 (132.7 - 134.8)
32	96.9 (95.8 - 98)	102 (101.2 - 102.8)	113.9 (113.3 - 114.6)	127.5 (126.6 - 128.3)	134.4 (133.1 - 135.7)
34	97.7 (96.6 - 98.8)	102.8 (102 - 103.6)	114.8 (114.2 - 115.4)	128.4 (127.4 - 129.4)	135.5 (134 - 136.9)
36	98.7 (97.7 - 99.7)	103.9 (103.1 - 104.6)	116 (115.3 - 116.7)	129.8 (128.7 - 130.8)	136.9 (135.4 - 138.3)
38	99.9 (99 - 100.9)	105.1 (104.3 - 106)	117.4 (116.4 - 118.4)	131.4 (130.1 - 132.6)	138.6 (136.9 - 140.2)
40	101.3 (99.7 - 102.9)	106.5 (105.1 - 108)	118.9 (117.6 - 120.3)	133.1 (131.2 - 135)	140.4 (137.8 - 143)

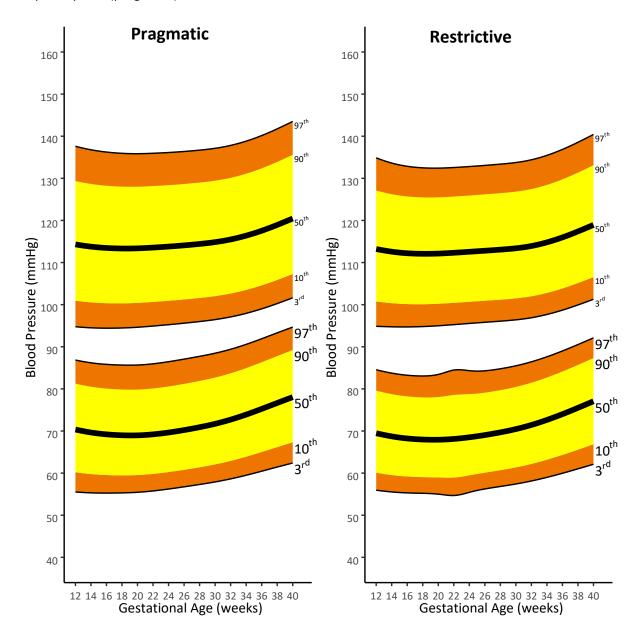
Gestational age (weeks)	Centiles for Diastolic Blood Pressure (95% CI)				
	3rd	10th	50th	90th	97th
12	55.9 (54.8 - 57)	60.1 (59.3 - 60.9)	69.5 (68.7 - 70.2)	79.6 (78.6 - 80.5)	84.5 (83.2 - 85.9)
14	55.5 (54.5 - 56.5)	59.5 (58.8 - 60.3)	68.7 (68.1 - 69.4)	78.8 (77.8 - 79.7)	83.7 (82.4 - 85.1)
16	55.3 (54.4 - 56.2)	59.2 (58.5 - 59.9)	68.2 (67.7 - 68.8)	78.2 (77.3 - 79.1)	83.2 (82.1 - 84.4)
18	55.2 (54.3 - 56.1)	59.1 (58.4 - 59.7)	68 (67.4 - 68.6)	78 (77.1 - 78.8)	83.1 (82 - 84.2)
20	55 (54.1 - 55.9)	59 (58.3 - 59.6)	67.9 (67.4 - 68.5)	78.1 (77.3 - 78.8)	83.4 (82.3 - 84.6)
22	54.7 (51.2 - 58.1)	59 (57.6 - 60.3)	68.1 (67.6 - 68.6)	78.6 (76.9 - 80.2)	84.5 (79.2 - 89.7)
24	55.4 (54.5 - 56.3)	59.5 (58.9 - 60.1)	68.5 (68 - 69.1)	78.8 (78.1 - 79.5)	84.3 (83.2 - 85.5)
26	56.2 (55.4 - 57)	60.1 (59.5 - 60.7)	69 (68.5 - 69.6)	79.1 (78.4 - 79.8)	84.3 (83.3 - 85.3)
28	56.8 (56 - 57.6)	60.7 (60.1 - 61.3)	69.7 (69.1 - 70.2)	79.7 (79 - 80.4)	84.8 (83.8 - 85.7)
30	57.4 (56.6 - 58.3)	61.4 (60.7 - 62)	70.5 (69.9 - 71)	80.5 (79.8 - 81.1)	85.5 (84.5 - 86.4)
32	58.1 (56.7 - 59.6)	62.2 (61.3 - 63.1)	71.4 (70.8 - 72)	81.5 (80.8 - 82.1)	86.4 (85.1 - 87.7)
34	59 (58 - 60)	63.2 (62.5 - 63.9)	72.6 (72.1 - 73.2)	82.7 (82 - 83.4)	87.6 (86.6 - 88.6)
36	60 (59.1 - 60.8)	64.3 (63.7 - 65)	74 (73.4 - 74.6)	84.1 (83.5 - 84.7)	89 (88.2 - 89.8)
38	61 (60.2 - 61.9)	65.6 (64.9 - 66.3)	75.5 (74.7 - 76.3)	85.7 (84.9 - 86.5)	90.5 (89.5 - 91.6)
40	62.1 (60.8 - 63.4)	66.9 (65.8 - 67.9)	77.1 (75.9 - 78.3)	87.3 (85.8 - 88.8)	92.1 (90.4 - 93.9)

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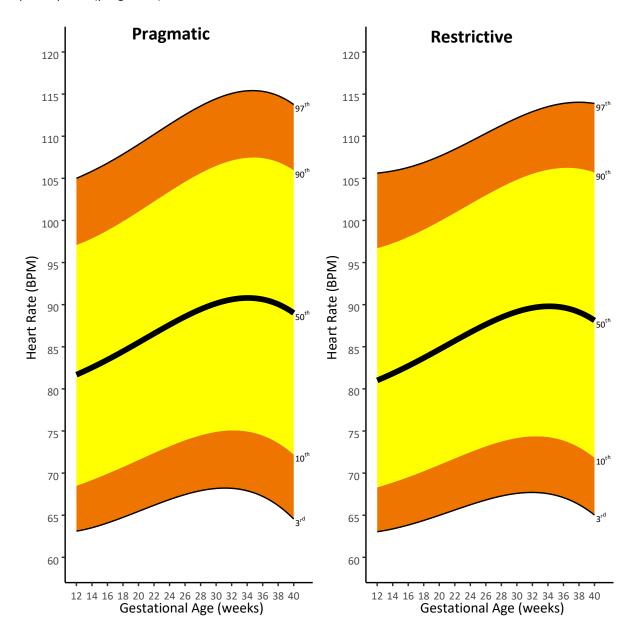
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**Figure A8.1:** Smoothed centiles for blood pressure (mmHg); 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> centiles for all participants (pragmatic) and restrictive cohorts.



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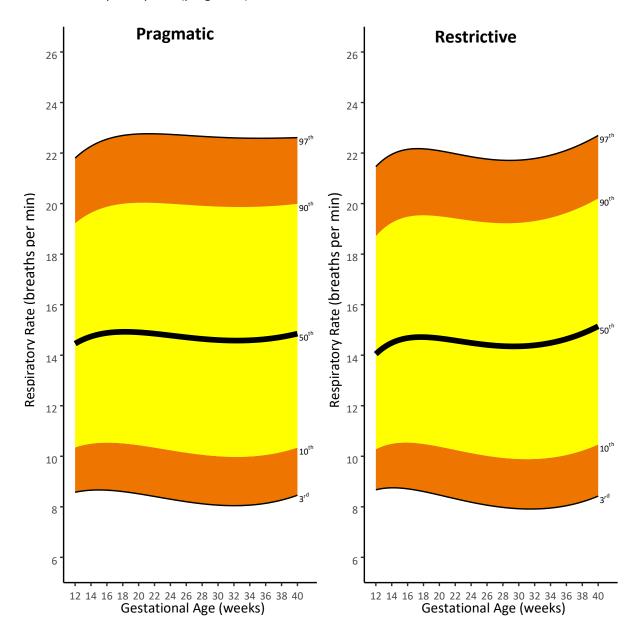


**Figure A8.2:** Smoothed centiles for heart rate (bpm); 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> centiles for all participants (pragmatic) and restrictive cohorts.

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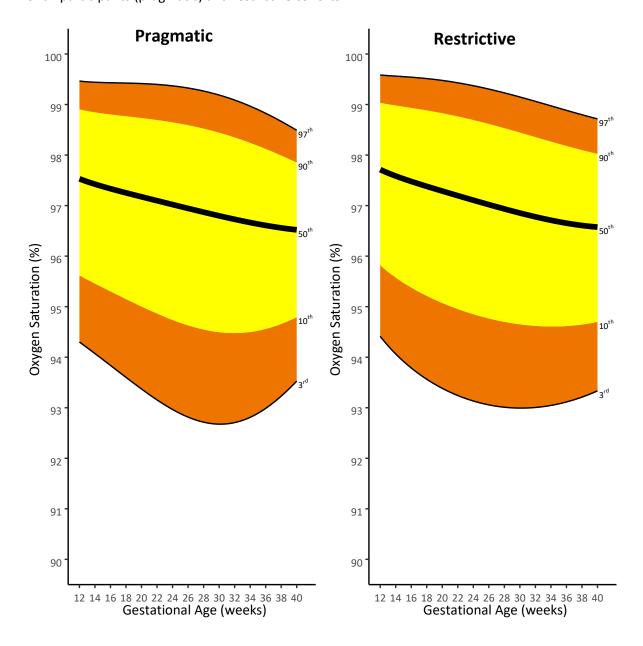
**Figure A8.3:** Smoothed centiles for respiratory rate (breaths per minute); 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> centiles for all participants (pragmatic) and restrictive cohorts.



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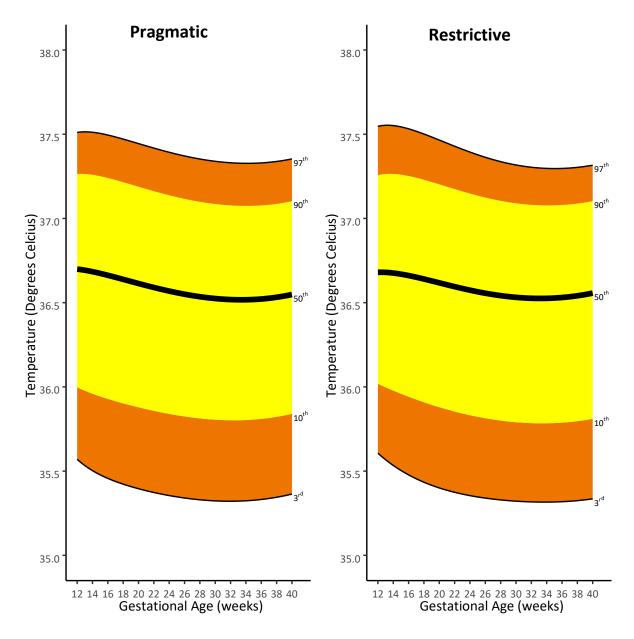
**Figure A8.4:** Smoothed centiles for oxygen saturation SpO<sub>2</sub> (%); 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> centiles for all participants (pragmatic) and restrictive cohorts.



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**Figure A8.5:** Smoothed centiles for temperature (°C) from Genius thermometer device; 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> centiles for all participants (pragmatic) and restrictive cohorts.



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