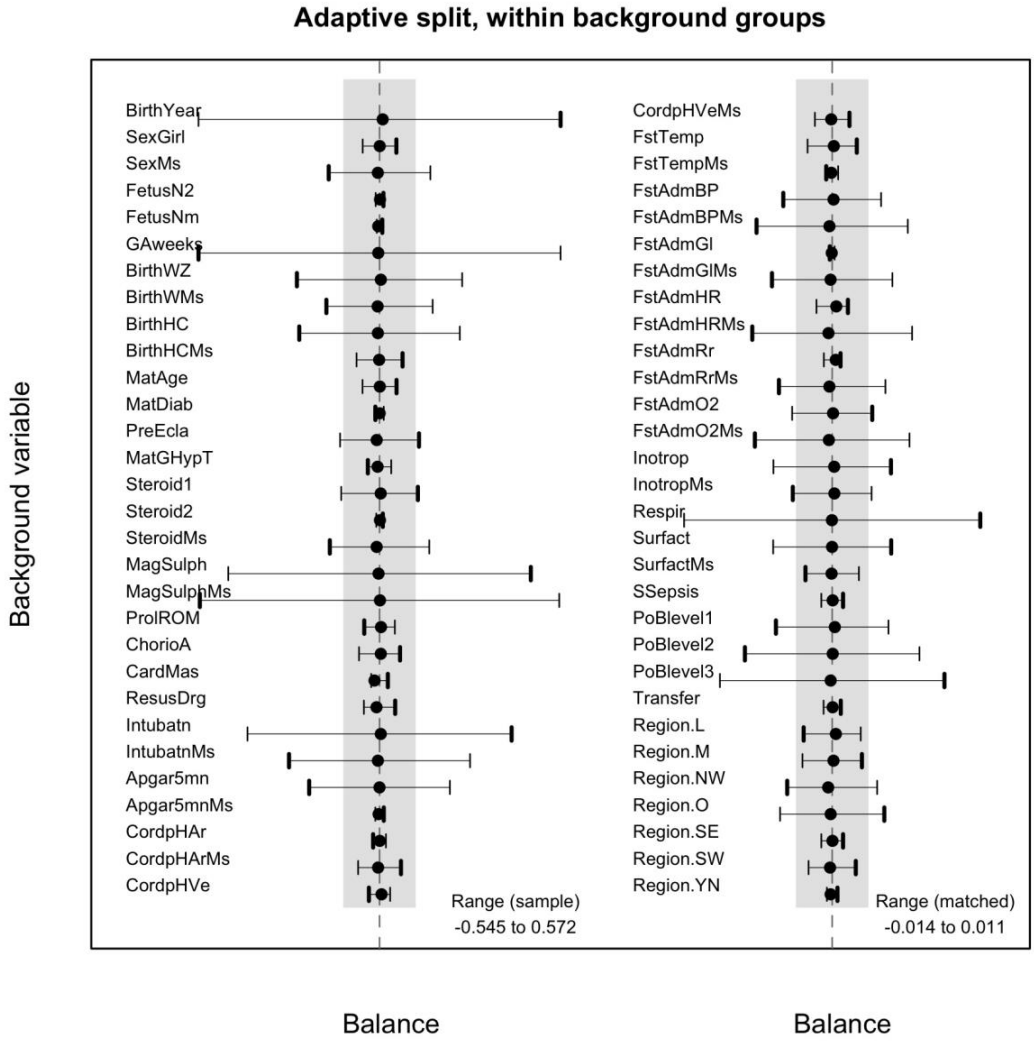
Supplementary eFigure 1: Balance plot for the matched treatment groups used for primary analysis



The thin horizontal segments are drawn between the imbalance (the scaled difference of the means or rates for the two treatment groups) in the entire cohort and its negative. The black disc is placed at the imbalance evaluated for the matched subgroups. The grey strip covers the region of acceptable imbalances, (-0.1, 0.1). The figures at the bottom are the range of imbalances for the entire sample (in the middle) and for the matched subgroups (at the right-hand margin). The average absolute balance is 0.134 for the entire sample and 0.0044 for the matched groups.

Abbreviations

For all categories the suffix Ms denotes missing data.

FetusN2: more than one fetus. FetusNm: number of fetusus not known (missing) GAweeks: Gestational age in weeks. BirthWZ: birth weight z-score. BirthW: birth weight. BirthHC: Birth head circumference. MatAge: maternal age. MatDiab: Maternal diabetes mellitus. PreEcla: maternal pre-eclampsia. MatGHypT: maternal gestational hypertension. Steroid1: complete course of antenatal steroids. Steroid2: incomplete course of antenatal steroids. MagSulph: maternal receipt of magnesium sulphate. ProlROM: maternal prolonged rupture of membranes. ChorioA: maternal chorioamnionitis. CardMas: chest compressions administered during resuscitation after birth. ResusDrg: emergency resuscitation drugs administered during resuscitation after birth. Intubatn: intubation during resuscitation after birth. Apgar5mn: Apgar score at 5 minutes. CordpHAr:: cord arterial pH. CordpHve: cord venous pH. FstTemp: temperature on admission to NICU. fstAdmBP: mean blood pressure on admission to NICU.FstAdmGl: blood glucose level on admission to NICU. FstAdmHR: heart rate on admission to NICU. FstAdmRr: respiratory rate on admission to NICU. FstAdm02: oxygen saturation on admission to NICU. Inotrop: receipt of inotropes on first postnatal day. Respir: mechanical ventilation on first postnatal day. Surfact: receipt of surfactant on first postnatal day. SSepsis: suspected sepsis on first postnatal day. PoBlevel1: place of birth in a level 1 neonatal unit. POBlev2: place of birth in a level 2 neonatal unit. POBlev3: place of birth in a level 3 neonatal unit. Transfer: infant underwent transfer between neonatal units on first postnatal day. Region.L: place of birth in London region. Region.M: place of birth in the Midlands. Region.NW: place of birth in North West England. Region.O: place of birth in other region (home, in transit, not NHS, not known). Region.SE: place of birth in South East England. Region.SW: place of birth in South West England. Region.YN: place of birth in Yorkshire and North. (Reference category Region was East of England).

Supplementary eTable 1

Exclusion criteria: list of major congenital gastrointestinal malformations

Clevermed code	ICD-10 code	Diagnosis
10741	Q39.0	Oesophageal atresia without distal fistula
16195	Q39.0	Atresia of oesophagus without fistula
10740	Q39.1	Oesophageal atresia with distal tracheo-oesophageal fistula
16196	Q39.1	Atresia of oesophagus with tracheo-oesophageal fistula (TOF)
16197	Q39.2	Congenital tracheo-oesophageal fistula without atresia (TOF)
10273	Q39.3	Congenital stenosis of the oesophagus
16198	Q39.3	Congenital stenosis and stricture of oesophagus
16199	Q39.4	Oesophageal web
10358	Q41.0	Duodenal atresia / stenosis / web (specify)
16212	Q41.0	Congenital absence, atresia and stenosis of duodenum
16213	Q41.0DA	Duodenal atresia / stenosis
10605	Q41.1	Jejunal atresia / stenosis (specify)
16214	Q41.1JA	Jejunal atresia / stenosis
10541	Q41.2	Ileal atresia / stenosis (specify)
16215	Q41.2	Congenital absence, atresia and stenosis of ileum
16216	Q41.2IA	Ileal atresia / stenosis
16217	Q41.X	Congenital absence, atresia and stenosis of small intestine
16218	Q42.0	Congenital absence, atresia and stenosis of rectum with fistula
10496	Q42.00	High anorectal anomaly with rectourethral fistula
10497	Q42.01	High anorectal anomaly with rectovesical fistula
10498	Q42.02	High anorectal anomaly with rectovulval fistula
10495	Q42.03	High anorectal anomaly with rectocutaneous fistula
10494	Q42.04	High anorectal anomaly with rectocloacal fistula
10493	Q42.08	High anorectal anomaly with fistula (specify)
10499	Q42.1	High anorectal anomaly without fistula
16219	Q42.1	Congenital absence, atresia and stenosis of rectum without fistula
16220	Q42.2	Congenital absence, atresia and stenosis of anus with fistula
10636	Q42.20	Low anorectal anomaly with anocutaneous fistula
10637	Q42.21	Low anorectal anomaly with anovestibular fistula
10638	Q42.28	Low anorectal anomaly with fistula (other specify)
10639	Q42.3	Low anorectal anomaly without fistula
16221	Q42.3	Congenital absence, atresia and stenosis of anus without fistula
10240	Q42.31	Congenital anal stenosis

16222	Q42.8	Congenital absence, atresia and stenosis of anus of other parts of large intestine
16223	Q429	Congenital absence, atresia and stenosis of anus of large intestine, part unspecified
16224	Q42X	Congenital absence, atresia and stenosis of large intestine
16235	Q43.7	Persistent cloaca

Exclusion criteria: list of life-limiting conditions or conditions requiring surgery in the neonatal period

Clevermed code	ICD-10 code	Diagnosis
15890	Q00.0	Anencephaly
15891	Q00.1	Craniorachischisis
15892	Q00.2	Iniencephaly
15893	Q00.X	Anencephaly and similar malformations
15894	Q01.0	Frontal encephalocele
15895	Q01.1	Nasofrontal encephalocele
15896	Q01.2	Occipital encephalocele
15897	Q01.8	Encephalocele of other sites
15898	Q01.9	Encephalocele (unknown or unspecified cause)
15899	Q01.X	Encephalocele
15918	Q04.2	Holoprosencephaly
15926	Q05.0	Cervical spina bifida with hydrocephalus
15927	Q05.1	Thoracic spina bifida with hydrocephalus
15928	Q05.2	Lumbar spina bifida with hydrocephalus
15929	Q05.3	Sacral spina bifida with hydrocephalus
15930	Q05.4	(unknown or unspecified cause) spina bifida with hydrocephalus
15931	Q05.5	Cervical spina bifida without hydrocephalus
15932	Q05.6	Thoracic spina bifida without hydrocephalus
15933	Q05.7	Lumbar spina bifida without hydrocephalus
15934	Q05.8	Sacral spina bifida without hydrocephalus
15935	Q05.9	Spina bifida (unknown or unspecified cause)
10986	Q05.9a	Spina bifida
10704	Q05.9b	Myelomeningocele (specify site)
15936	Q05.X	Spina bifida
16024	Q20.0	Common arterial trunk (Truncus malformation)
10356	Q20.1	Double outlet right ventricle (DORV)
16025	Q20.1	Double outlet right ventricle (DORV)
16026	Q20.2	Double outlet left ventricle (DOLV)
11070	Q20.3	Transposition of the great vessels (TGA)
16027	Q20.3	Transposition great arteries (TGA)
16028	Q20.4	Double inlet ventricle (DILV)
16029	Q20.5	Discordant atrioventricular connection
16030	Q20.6	Isomerism of atrial appendages
16031	Q20.8	Other cong malforms of cardiac chambers and connections
16032	Q20.9	Cong malforms of cardiac chambers and connections unspec
16033	Q20.X	Congenital malformations of cardiac chambers and connections
16035	Q20.91	Atrium single

16036	Q20.92	Ventricle single
10097	Q21.2	Atrio-ventricular septal defect (AVSD)
16039	Q21.2	Atrioventricular septal defect (AVSD)
11043	Q21.3	Tetralogy of Fallot
16040	Q21.3	Tetralogy of Fallot
16045	Q22.0	Pulmonary valve atresia
16046	Q22.1	Congenital pulmonary valve stenosis
16047	Q22.2	Congenital pulmonary valve insufficiency
16048	Q22.3	Other congenital malformations of pulmonary valve
16049	Q22.4	Congenital tricuspid atresia / stenosis
16050	Q22.5	Ebstein's anomaly
16051	Q22.6	Hypoplastic right heart syndrome
16052	Q22.8	Other congenital malformations of tricuspid valve
16053	Q22.9	Congenital malformation of tricuspid valve (unknown or unspecified cause)
16054	Q22.X	Congenital malformations of pulmonary and tricuspid valves
16055	Q23.0	Congenital stenosis of aortic valve (AS)
16056	Q23.1	Congenital insufficiency of aortic valve
16057	Q23.2	Congenital mitral stenosis (MS)
16058	Q23.3	Mitral atresia
16059	Q23.4	Hypoplastic left heart syndrome (HLH)
16060	Q23.8	Other congenital malformations of aortic and mitral valves
16061	Q23.9	Congenital malformation of aortic and mitral valves unspec
16062	Q23.X	Congenital malformations of aortic and mitral valves
16079	Q25.1	Coarctation of aorta
10227	Q25.19	Coarctation of the aorta
16080	Q25.2	Hypoplasia of aortic arch
16081	Q25.3	Stenosis of aorta (AS)
16082	Q25.4	Malformation of aorta
16083	Q25.5	Atresia of pulmonary artery
16084	Q25.6	Stenosis of pulmonary artery (PS)
16086	Q25.8	Other congenital malformations of great arteries
16087	Q25.8	Transposition of the great vessels (TGA)
11057	Q26.2	Total anomylous pulmonary venous drainage (TAPVD)
16092	Q26.2	Total anomalous pulmonary venous connection (TAPVD)
16154	Q33.6	Hypoplasia and dysplasia of lung
16241	Q44.2	Atresia of bile ducts
10123	Q60.1	Bilateral renal agenesis
16318	Q60.1B	Renal agenesis, bilateral
16324	Q60.6	Potter's syndrome
16327	Q61.1	Polycystic kidney, infantile type
10100	Q61.1a	Autosomal recessive polycystic kidney - infantile

10367	Q64.1	Ectopia vesicae
16356	Q64.1	Exstrophy of urinary bladder
10854	Q64.2	Posterior urethral valves (PUV)
16357	Q64.2	Congenital posterior urethral valves (PUV)
16360	Q64.5	Congenital absence of bladder and urethra
10008	Q64.5a	Absence of bladder
10236	Q64.5b	Congenital absence of urethra
16475	Q77.1	Thanatophoric short stature
10246	Q79.0	Congenital diaphragmatic hernia
10490	Q79.0	Hernia into the cord
16495	Q79.0	Congenital diaphragmatic hernia
16496	Q79.1A	Aplasia of diaphragm
16497	Q79.1E	Eventration of diaphragm
16498	Q79.2	Exomphalos
10395	Q79.2	Exomphalos
16499	Q79.3	Gastroschisis
16589	Q90.0	Trisomy 21, meiotic nondisjunction
16590	Q90.1	Trisomy 21, mosaicism (mitotic nondisjunction)
16591	Q90.2	Trisomy 21, translocation
16592	Q90.9	Down's syndrome (unknown or unspecified cause)
16593	Q90.X	Down's syndrome
16594	Q91.0	Trisomy 18, meiotic nondisjunction
16595	Q91.1	Trisomy 18, mosaicism (mitotic nondisjunction)
16596	Q91.2	Trisomy 18, translocation
16597	Q91.3	Edwards' syndrome (unknown or unspecified cause)
16598	Q91.4	Trisomy 13, meiotic nondisjunction
16599	Q91.5	Trisomy 13, mosaicism (mitotic nondisjunction)
16600	Q91.6	Trisomy 13, translocation
16601	Q91.7	Patau's syndrome (unknown or unspecified cause)
16602	Q91.X	Edwards' syndrome and Patau's syndrome

Supplementary eTable 2

Deaths by days from birth: numbers, percentages and cumulative percentages from birth

	Early (N)	Early (%)	Early (% cum)	Late (N)	Late (%)	Late (% cum)
Day 1	271	0.6	0.6	89	0.4	0.4
Day 2	367	0.8	1.5	650	3	3.4
Day 3	360	0.8	2.3	217	1	4.4
Day 4	226	0.5	2.8	103	0.5	4.9
Day 5	188	0.4	3.3	63	0.3	5.2
Day 6	156	0.4	3.6	74	0.3	5.5
Day 7	172	0.4	4	49	0.2	5.8
Days 8-28	1577	3.6	7.6	415	1.9	7.7
Days 28+	1117	2.6	10.2	349	1.6	9.3
Survived	38975	89.8		19541	90.7	

Cum: cumulative

Supplementary eTable 3

Numbers of babies in groups based on three principal background variables

Numbers of babies	2008 - 2011		2012-2015		2016- 2019	
	Early	Late	Early	Late	Early	Late
Total babies	9782	10,017	15,977	6740	17,677	4840
GA 23-25	2180	1275	3513	671	3773	444
GA 26-27	2963	1825	4245	867	4426	534
GA 28-30	4639	6917	8219	5202	9478	3862
Multiple birth						
Singleton	7195	7571	11,867	5029	13,255	3591
Twin	2332	2212	3705	1555	4067	1159
2+ fetuses	255	234	405	156	355	90