A report by the National Guideline Alliance about twin pregnancy costing

Commissioned by:
The Human Fertilisation and Embryology Authority, The British Fertility Society, The Multiple Births Foundation and Fertility Network UK

Executive summary

Multiple pregnancy is associated with higher risks for the mother and babies compared to singleton pregnancy. There are also significant costs to the NHS and wider public services associated with multiple births. The HFEA, British Fertility Society, Multiple Births Foundation and Fertility Network UK commissioned this report to help establish the increased economic cost to the NHS.

The increased risks to the mother include miscarriage, pregnancy induced hypertension, pre-eclampsia, gestational diabetes and caesarean section with the result being that maternal mortality is 2.5 times greater. Most of the health problems of twins can be explained by their frequent prematurity and their lower gestational weight. About half of twins are born under 37 weeks gestation and 10% before 32 weeks, compared with 1% of singletons; and, as a rough estimate, IVF twins are born with a mean birth weight ranging between 800g and 1000g less[1].

Perinatal mortality is about 7 times higher for twins than singletons, they are 10 times more likely to be admitted to a neonatal unit and those who survive have a 6 times higher risk of cerebral palsy. Overall about 1 in 12 multiple pregnancies end in death or disability for one or more babies.

Multiple pregnancy is widely recognised as associated with IVF. The number of twin pregnancies arising from natural conception is low and relatively stable at 1-2%, but the development of assisted reproduction technologies has resulted in a marked increase in the number of multiples in all countries with assisted conception services. This is largely because of the trend to transfer two or more embryos to the womb during treatment.

The percentage of multiple pregnancies from IVF in the UK has dropped to 11% in 2016 from just over a quarter in 2008. This is largely because of changes in policy and clinical practice in response to an Expert Group Report in 2006[2], the twinning rate has been steadily reducing and many clinics are achieving the target of less than 10% set by the HFEA. However, the decrease needs to be sustained.

The report draws on the latest available data and represents the most comprehensive assessment to date of the true costs of multiple pregnancies in the UK. The report is intended to inform commissioning decisions and ensure there is wider understanding of the issues involved so that public resources are most efficiently used.

The key findings are:

- Multiple pregnancies are, on average, almost three times as expensive as single pregnancies - the mean cost of a singleton pregnancy in the UK over the period of pregnancy, birth, neonatal care and long term disability is estimated to be £4,892. The costs of a mean twin pregnancy over the same period is £13,959.
- Much of the difference in costs between singleton and multiple pregnancies come from the need for emergency caesarean section, post neonatal death, admissions to neo-natal intensive care, and a range of other conditions, like cerebral palsy.

[1] Reference 23 in the ‘One child at a time’ report, October 2006 https://ifqlive.blob.core.windows.net/umbraco-website/1311/one-child-at-a-time-report.pdf
[2] 'One child at a time' report, October 2006: https://ifqlive.blob.core.windows.net/umbraco-website/1311/one-child-at-a-time-report.pdf

- That a reduction of 10% in the twin pregnancy rate from its current level would lead to a saving of £15 million to the NHS, which, though small in the context of NHS spend in this area, is considerably in excess of what NICE regard as a significant resource impact

- It must also be remembered that there are costs to families, not only financial but also emotional and psychological for parents and the children themselves, which can have a long term impact. For all these reasons the aim of all IVF treatment should be the birth of a single healthy child.

This executive summary was written jointly by the HFEA, British Fertility Society, Multiple Births Foundation and Fertility Network UK. We are very grateful to the RCOG's National Guideline Alliance for authoring the following report, upon which this summary was based.

Twin Pregnancy Costing

A comparative analysis of the additional costs to the NHS of twin pregnancy relative to a singleton pregnancy

Authors: Paul Jacklin and Gemma Marceniuk

Background

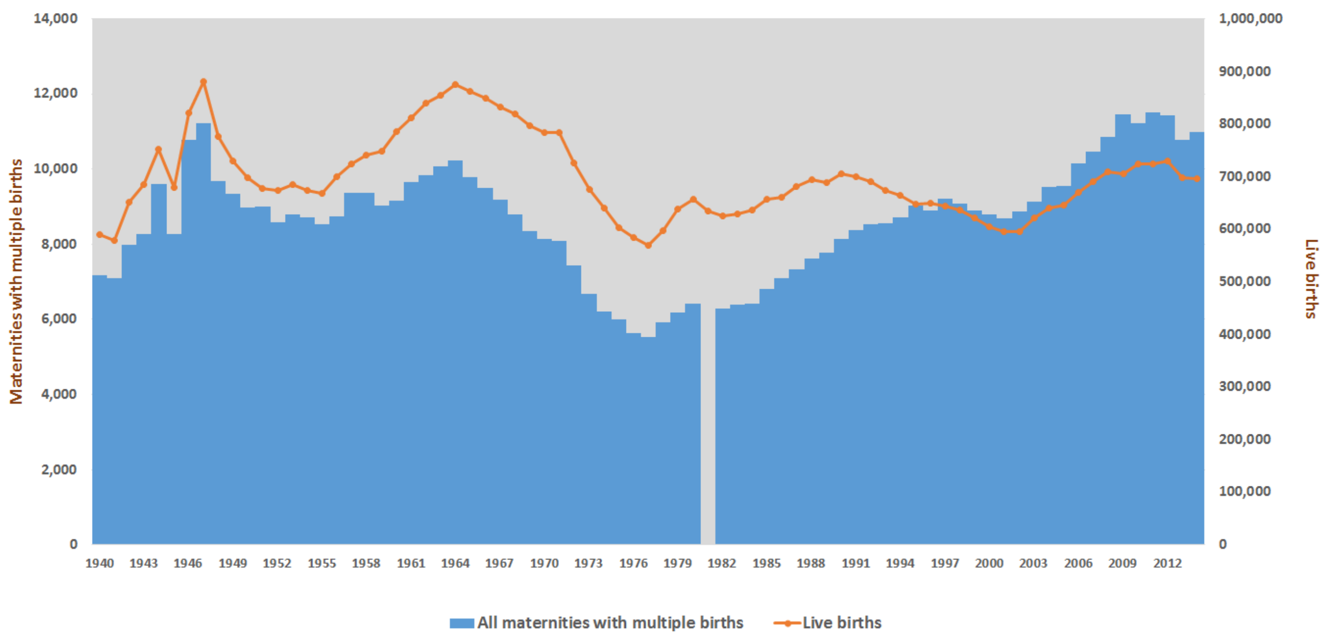
Multiple pregnancy carries additional risks to both the mother and the baby compared to a singleton pregnancy. These risks are summarised in Table 1.

Table 1: Increased risks associated with multiple pregnancy

Increased Risks to mother	Increased Risks to baby
Miscarriage	Premature birth
Pregnancy induced hypertension	Perinatal mortality
Pre-eclampsia	Neonatal care
Caesarean section	Long term health complications
Maternal mortality	

There is of course a possibility of a multiple pregnancy with natural conception, but the introduction of assisted reproduction technologies has increased the rate of multiple births above their natural conception level. Figure 1 below, depicts the temporal relationship between maternities with multiple birth and live births (Birth Characteristics 2014 (ONS, 2015)). This shows that since the early 1980s the number of maternities with multiple birth has increased markedly, whilst the overall live birth rate has remained relatively constant.

Figure 1: Graph to show the number of live births and maternities with multiple pregnancy in England and Wales, 1940-2014



The number of multiple maternities arising from assisted reproduction are potentially amenable to changes in policy and clinical practice. As a result a number of professional bodies are supporting "One at a time" (https://www.hfea.gov.uk/about-us/our-campaign-to-reduce-multiple-births/) a campaign aimed at reducing the risks of multiple pregnancies from fertility treatment. In particular, this campaign seeks to reduce the rate of multiple birth by encouraging a policy of elective single embryo transfer consistent with NICE guidance on the assessment and treatment of fertility problems (CG156).

In addition to the additional disease burden associated with multiple pregnancy, there are also important economic consequences with increased costs to the health service. This includes the requirement for added ante-natal care monitoring according to national guidelines, as well as the "downstream" costs associated with adverse clinical outcomes.

This report compares the costs of a twin conception relative to the costs of a singleton conception. It is accompanied by a Microsoft Excel® costing tool.

The costing was broadly split into the following phases:

i. Ante-natal care

ii. Birth

iii. Neonatal care

iv. Long term costs (associated with prematurity)

Methods

Perspective of the analysis

Whilst recognising that multiple pregnancy imposes wider costs on society, this analysis was undertaken from the perspective of the NHS and Personal Social Services, which aligns with the NICE Reference Case (Developing NICE guidelines: the manual). Costs are based on a price year of 2015-16 reflecting the most recently available NHS Reference costs at the time of writing. Where possible unit costs were obtained from published UK sources, for example Department of Health 2015/16 NHS Reference Costs (DoH, 2016) and the Personal Social Services Research Unit report Unit costs of health and social care 2016 (University of Kent, 2016). Where such costs were not available, then other published sources were used.

Any future costs were discounted at a rate of 3.5%, which is in accordance with the NICE reference case. Results are reported as the cost per conception although an estimated aggregate cost to the NHS is also presented for a given number of singleton and twin conceptions. This allows the cost savings to the NHS of reducing twin conception to be estimated.

Population

The model population includes the mother and baby/babies and starts with conceptions surviving to six weeks gestational age, but excluding any conceptions leading to termination of pregnancy.

Time horizon

The time horizon for the model differs for the mother and baby. For the mother the time period is restricted to pregnancy and birth. The analysis does not include any long term morbidity that might arise as a complication from the mode of birth such as urinary incontinence.

Whilst a detailed life-time horizon is not feasible for babies, the analysis does include the costing of some life-time long term costs relating to adverse birth outcomes.

Model structure

A costing model was developed in Microsoft Excel® using an essentially decision analytic approach. Whilst a twin or singleton conception is not strictly a policy decision, it is something that can be influenced by policy or practice. The decision analytic approach allows a weighted average cost to be calculated by assigning probabilities to various outcomes.

To capture the unfolding of events over time during pregnancy a Markov modelling approach was adopted and is illustrated in Figure 2 and Figure 3. For ease of exposition the structure is displayed separately for gestational ages 6-23 weeks and for gestational ages 24-42 weeks. The Markov model involves the transition of a hypothetical conception into different ‘health states’ over time, divided into equally spaced cycles. In this model, each cycle represented one week of gestational age. Transition between different states occurs at the end of cycles and is determined by transition probabilities derived from the literature, see Table 3, Table 12, Table 15, Table 22 and Table 24.

Figure 2: Schematic of model structure detailing pregnancy pathway from a gestational age of 6-23 weeks

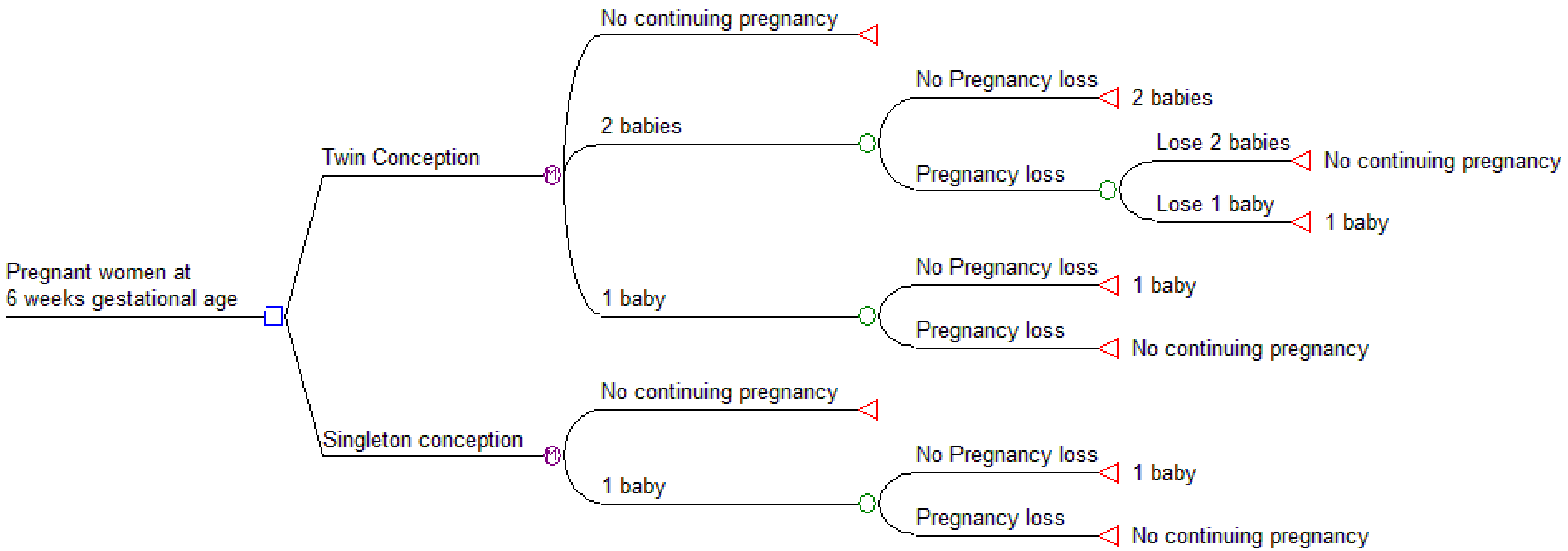
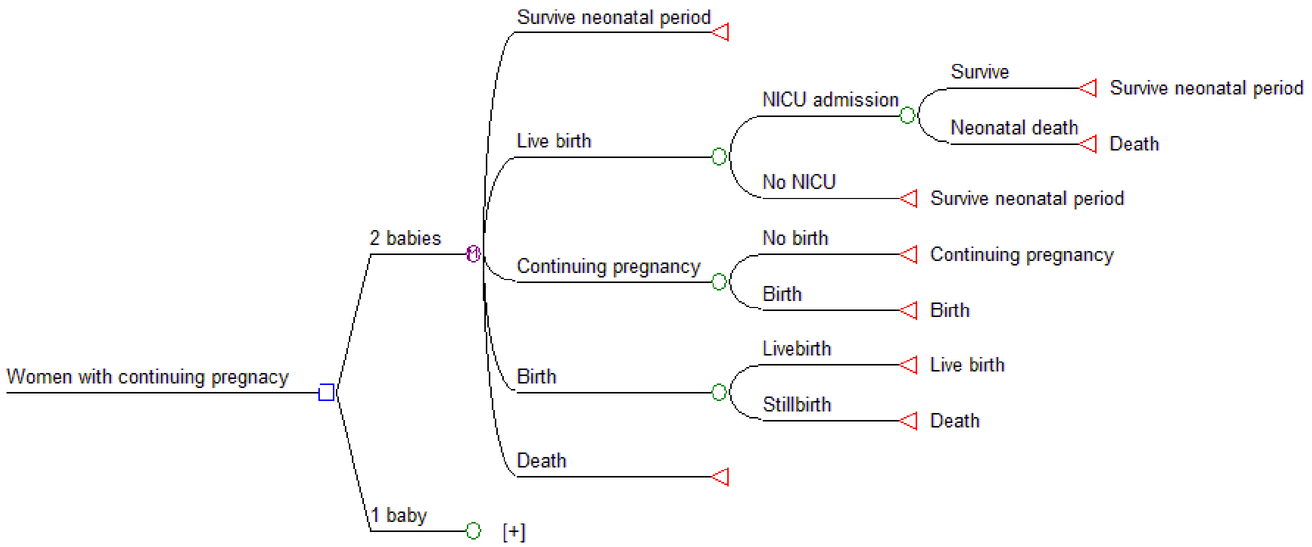


Figure 3: *Schematic of the model structure detailing pregnancy pathway from a gestational age of 24-42 weeks*[a]



The health states shown in Figure 2:

i. Continuing pregnancy with 2 babies (twin conception only)
ii. Continuing pregnancy with 1 baby (twin and singleton conception)
iii. No continuing pregnancy

To simplify the diagram shown in Figure 3, the health states for twin birth represent the various pathways for each twin separately. In other words a twin birth can produce both a live birth and a still birth as outcomes as well as two live births or two still births.

The health states included in Figure 3:

iv. Continuing pregnancy
v. Birth
vi. Live birth
vii. Survive neonatal period
viii. Death

For babies surviving beyond the neonatal period a more basic decision analytic frame was utilised. Figure 4 and Figure 5 illustrate the model structure for assessing "downstream" costs arising from adverse pregnancy

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[a] The '+' in Figure 3 indicates that the pathway is truncated. The pathway for 1 baby is identical to the one shown for 2 babies although the transition probabilities differ

outcomes in the two years after the initial discharge from hospital and from lifelong morbidity. A more simplified approach was also used to assess maternal complications and this is illustrated in Figure 6.

Figure 4: Schematic of model structure used to assess costs incurred by the NHS in the two-years post initial discharge from hospital

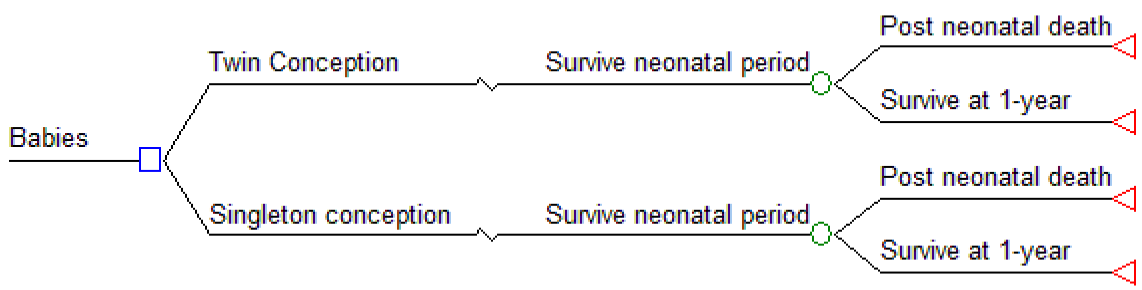


Figure 5: Schematic of model structure used to assess long-terms costs arising from adverse neonatal outcomes and morbidity

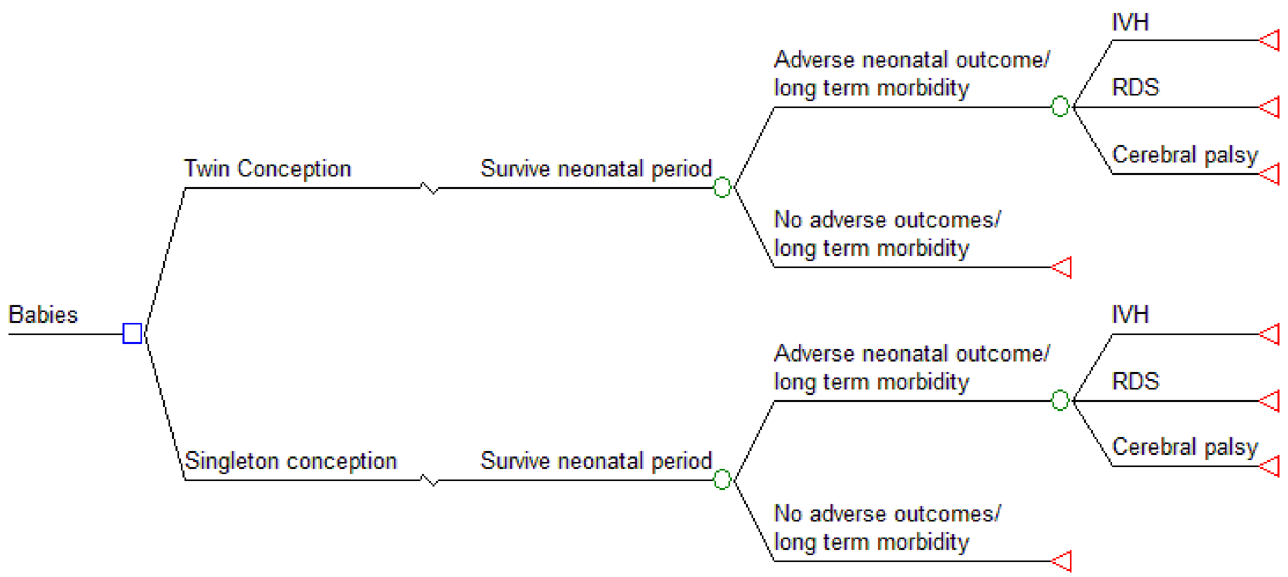
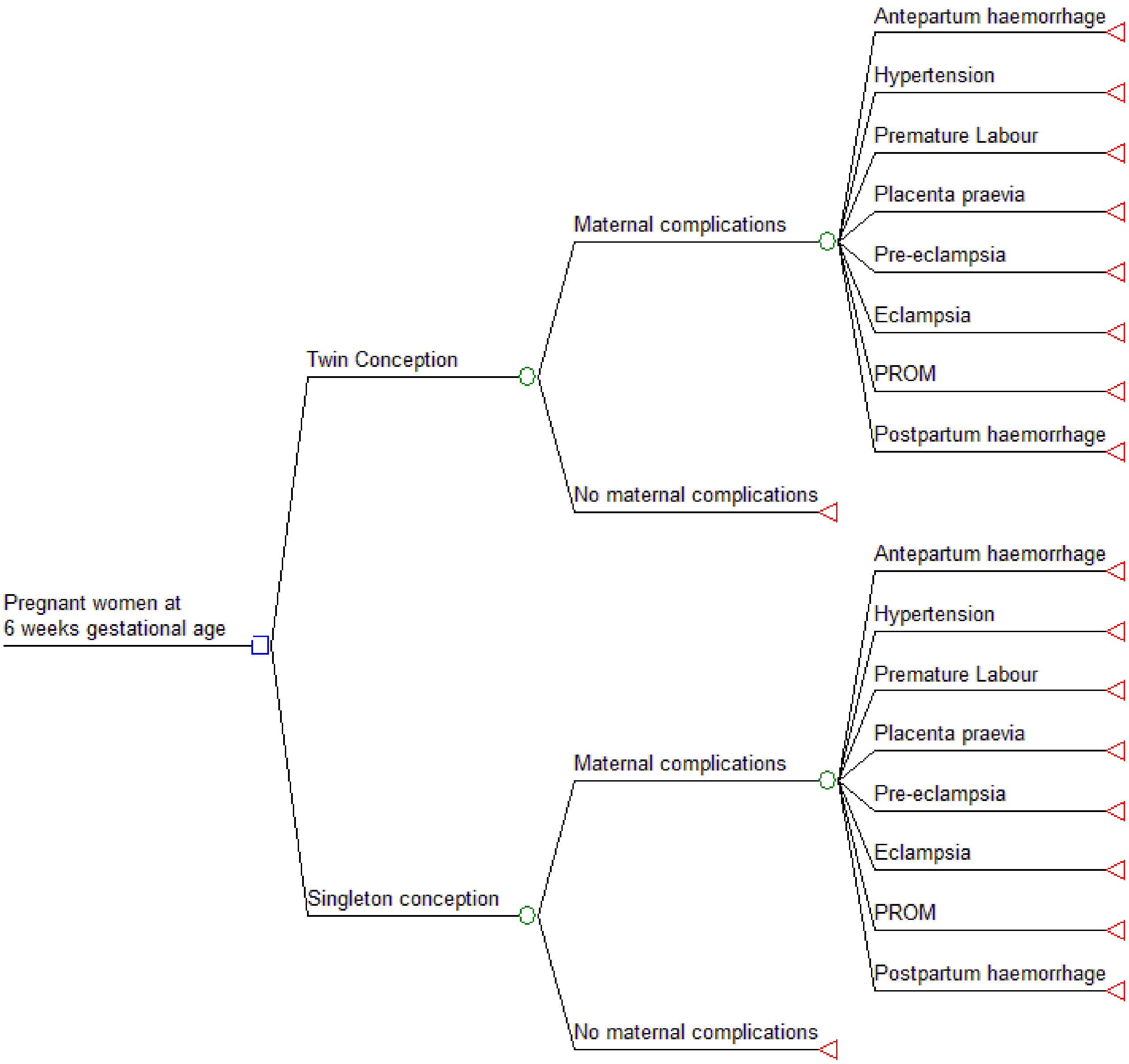


Figure 6: Schematic of model structure used to assess maternal complications



Outcomes and transition probabilities

With the resources available for this analysis it wasn't possible to systematically search the literature for model inputs and probabilities. However, a pragmatic search strategy was used to identify epidemiological data which could inform model inputs.

Ante-natal care

Babies (multiples/singleton) are assumed to receive ante-natal care as per the recommendations in the respective NICE guidance; CG129, CG62. The package of antenatal care for multiple pregnancy and routine healthy singleton was then costed as per NICE recommendations.

However, the schedule of appointments only applies to women with a continuing pregnancy. So in order to estimate the costs of antenatal care it was necessary to estimate the proportion of conceptions that would be continuing pregnancies by gestational age. In the early part of pregnancy this is determined by the proportion of pregnancies affected by miscarriage or early pregnancy loss.

Miscarriage

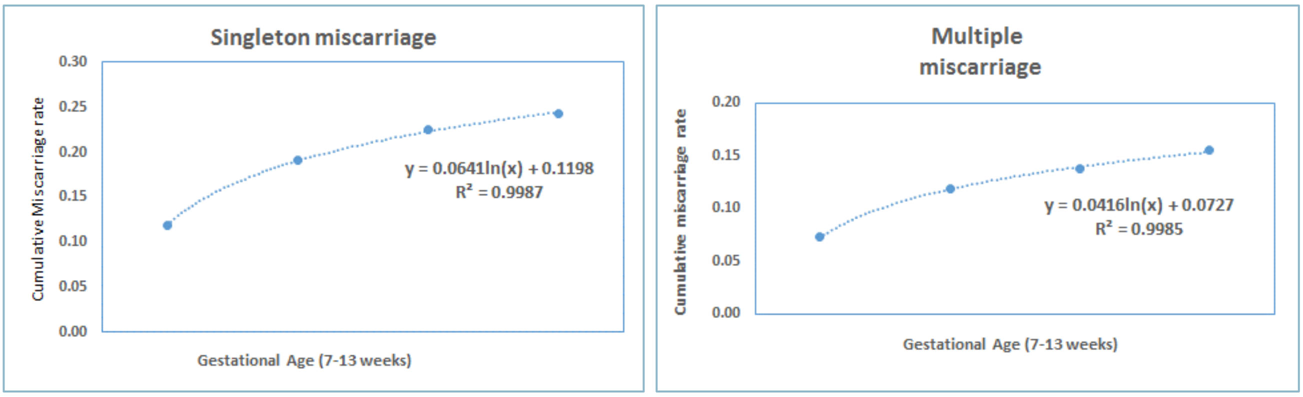
A published paper was used to estimate the risk of miscarriage by gestational age per fetal sac[1]. Whilst this study was undertaken for IVF/ICSI pregnancies, rates of miscarriage are not thought to be higher in these groups (American Society of Reproductive Medicine (2014)). The data taken from this paper indicated spontaneous miscarriage rates as shown in Table 2.

Table 2: Risk of spontaneous miscarriage per fetal sac by gestational age for twin and singleton pregnancies

Gestational age	Singleton (cumulative)	Twin (cumulative)
7 weeks	11.9% (11.9%)	7.3% (7.3%)
9 weeks	8.2% (19.1%)	4.9% (11.8%)
11 weeks	4.2% (22.5%)	2.2% (13.8%)
13 weeks	2.2% (24.2%)	2.0% (15.5%)

The model required a transition probability for each week of gestational age and a trend line was fitted to the data in Table 2 using Microsoft Excel as shown in Figure 7 below.

Figure 7: Fitted trend line and equation for cumulative miscarriage rates per fetal sac between 7-13 weeks



Then the equation for the fitted lines was used to estimate the cumulative miscarriage rates per fetal sac between gestational ages of 7-23 weeks where x in the equation represents the gestational age in weeks.

Table 3: Estimated cumulative miscarriage rates per fetal sac for a singleton and twin pregnancy for gestational age 7-23 weeks

Gestational age	Singleton	Twin
7 weeks	12.0%	7.3%
8 weeks	16.4%	10.2%
9 weeks	19.0%	11.8%
10 weeks	20.9%	13.0%
11 weeks	22.3%	13.9%
12 weeks	23.5%	14.7%
13 weeks	24.5%	15.3%
14 weeks	25.3%	15.9%
15 weeks	26.1%	16.4%
16 weeks	26.7%	16.8%
17 weeks	27.4%	17.2%

18 weeks	27.9%	17.6%
19 weeks	28.4%	17.9%
20 weeks	28.9%	18.2%
21 weeks	29.3%	18.5%
22 weeks	29.8%	18.8%
23 weeks	30.1%	19.1%

The NHS incurs costs as a result of miscarriage. It is estimated that there are approximately 250,000 miscarriages per annum (http://www.miscarriageassociation.org.uk/about-us/media-queries/background-information/). According to NHS Digital there were 38,349 miscarriages that resulted in an NHS Hospital stay in England in 2015-16 (http://content.digital.nhs.uk/catalogue/PUB22384). NHS Reference Costs 2015-16 includes the data shown in Table 4 and Table 5 on threatened or spontaneous miscarriages.

Table 4: NHS Reference Cost 2015-16 data on threatened or spontaneous miscarriage (Currency code MB08A and MB08B)

Setting	With intervention	Number of FCE	Unit Costs	No. Inlier bed days	Average length of stay (days)
Elective inpatient	Yes	26	£2,311	62	2.38
Elective inpatient	No	855	£617	949	1.11
Non-elective long stay	Yes	776	£2,103	2,124	3
Non-elective long stay	No	3,419	£1,727	8,104	2
Non-elective short stay	Yes	48	£898	-	-
Non-elective short stay	No	40,513	£466	-	-
Day Case	Yes	3	£899	-	-
Day case	No	1,731	£439	-	-
Regular day & night admission	No	109	£266	-	-

Table 5: NHS Reference Cost 2015-16 data on excess bed days for threatened or spontaneous miscarriage (Currency code MB08A and MB08B)

Setting	With intervention	Excess bed days	Unit Costs
Elective inpatient	No	36	£442
Non-elective long stay	Yes	235	£429
Non-elective long stay	No	1,806	£502

The total cost of the excess bed days was calculated as:

Excess Bed Days x unit cost

(36 x £442) + (235 x £429) + (1,806 x £502) = **£1,022,720**

The total cost of threatened or spontaneous miscarriage less excess bed days was calculated as:

Number of Finished Consultant Episodes (FCE) x unit cost

(26 x £2,311) + (855 x £617) + (776 x £2,103) + (3,419 x £1,727) + (48 x £898) + (40,513 x £466) + (3 x £899) + (1,731 x £439) + (109 x £266) = **£27,843,760**

Therefore the total cost of miscarriages resulting in a hospital stay was estimated as **£28,866,480.** Table 4, indicates that this is based on 47,480 finished consultant episodes and therefore:

Mean cost per miscarriage admitted for hospital: £28,866,480 ÷ 47,480 = **£608**

Based on a total number of miscarriages estimated at 250,000 it was assumed that approximately 20% of miscarriages would incur this cost. It was also assumed that all women experiencing a miscarriage would have one related GP visit, with a unit cost of £36.

Maternal complications

A twin pregnancy carries additional risks for the mother and the associated morbidity results in "downstream" costs to the NHS. We used the same maternal complications and risks as reported in a previous study[2] although we are aware that this list is not necessarily a definitive list of all maternal complications that have a higher risk in a twin pregnancy. For example, it is reported that a twin pregnancy carries a higher risk of gestational diabetes than a singleton pregnancy.[3] The complications and risk used in the model are given in Table 6.

Table 6: Maternal complications and risks for singleton and twin pregnancies

Maternal complication	Singleton pregnancy risk	Twin pregnancy risk
Antepartum haemorrhage	0.0337	0.0344
Hypertension	0.11	0.17
Premature Labour[b]	-	-
Placenta praevia	0.052	0.064
Pre-eclampsia	0.03	0.13
Eclampsia	0.001	0.011
PROM	0.030	0.075
Post-partum haemorrhage	0.0491	0.1037

PROM - Premature Rupture of Membranes

We followed the approach of this published study[2] by estimating the cost of these complications by the length of stay associated with them. However, we used recently produced data from the Health and Social Care Information Centre to estimate the mean length of stay associated with these maternal complications (content.digital.nhs.uk/catalogue/PUB19124/hosp-epis-stat-admi-diag-2014-15-tab.xlsx), as shown in Table 7.

Table 7: Maternal complication and length of stay

Diagnosis	Admissions	Bed-days	Mean LOS (days)
Ante-partum haemorrhage	30,464	32,692	1.07
Pregnancy induced hypertension	25,317	70,155	2.77
Pre-term labour and delivery	12,568	44,410	3.53
Placenta praevia	6,837	27,607	4.04
Pre-eclampsia	2,127	13,677	6.43
Eclampsia	278	1,136	4.09
PROM	47,180	69,068	1.46
Post-partum haemorrhage	22,162	49,073	2.21

To estimate the cost of a maternal complication requires multiplying the length of stay by the per diem cost of an in-patient hospital stay. This per diem cost was estimated at £417, which is a weighted average of the NHS Reference Cost 2015-16 data reported in Table 8.

[b] The model structure allows the number of premature births to be estimated directly and therefore whilst included as a maternal complication we did not use the study estimates of risk for this outcome

Table 8: Cost of excess bed-day of ante-Natal False Labour, including Premature Rupture of Membranes

Currency code	Excess Bed-days	Average unit cost
NZ17A	1,276	£410
NZ17B	4,827	£419

Antenatal appointments

Figure 8 (below) outlines the schedule of antenatal appointments for multiple pregnancy based on NICE guidelines.

Figure 8: Schedule of Specialist antenatal appointments for multiple pregnancy, CG129

Schedule of specialist antenatal appointments

Type of pregnancy	Weeks 6 to 19													
	6	7	8	9	10	11	12	13	14	15	16	17	18	19
All pregnancy types below													Anomaly scan (18^{+0} to 20^{+6} weeks)**	
Monochorionic diamniotic twins	Booking appt by 10 weeks*					Appt + early scan (approximately 11^{+0} to 13^{+6} weeks)					Appt/scan FFTS		Appt/scan FFTS	
Dichorionic twins											Appt only (no scan)			
Monochorionic & dichorionic triplets (triamniotic)											Appt/scan FFTS		Appt/scan FFTS	
Trichorionic triamniotic triplets											Appt only (no scan)			

Type of pregnancy	Weeks 20 to 29									
	20	21	22	23	24	25	26	27	28	29
All pregnancy types below	Anomaly scan (18^{+0} to 20^{+6} weeks)									
	Monitor for IUGR at each scan from 20 weeks									
Monochorionic diamniotic twins	Appt/scan FFTS		Appt/scan FFTS		Appt/scan FFTS				Appt/scan	
Dichorionic twins	Appt/scan				Appt/scan				Appt/scan	
Monochorionic triamniotic & dichorionic triamniotic triplets	Appt/scan FFTS		Appt/scan FFTS		Appt/scan FFTS		Appt/scan		Appt/scan	
Trichorionic triamniotic triplets	Appt/scan				Appt/scan				Appt/scan	

* See 'Antenatal care' at **www.nice.org.uk/guidance/CG62**
** Consider scheduling anomaly scan slightly later if needed.

Type of pregnancy	Weeks 30 to 37							
	30	31	32	33	34	35	36	37
All pregnancy types below	Monitor for IUGR at each scan from 20 weeks							
Monochorionic diamniotic twins			Appt/scan		Appt/scan		Offer birth If declined: weekly appts + scans	
Dichorionic twins			Appt/scan		Appt only (no scan)		Appt/scan	Offer birth If declined: weekly appts + scans
Monochorionic triamniotic & dichorionic triamniotic triplets	Appt/scan		Appt/scan		Appt/scan	Offer birth If declined: weekly appts + scans		
Trichorionic triamniotic triplets			Appt/scan		Appt/scan	Offer birth If declined: weekly appts + scans		

As Figure 8 shows the appointment schedule is different for monochorionic diamniotic twins than for dichorionic twins and therefore in order to obtain a weighted average of the cost of antenatal twin appointments it was necessary to include the relative proportion of each twin type as a model input, as shown in Table 9.

Table 9: Proportion of twin type

Type	Proportion	Source/notes
Monozygotic proportion	0.33	http://www.multiplebirths.org.uk/media.asp
Monochorionic|monozygotic[c]	0.75	
Dichorionic|monozygotic	0.25	Schulman et al. (2006)[4]
Dyzogotic proportion	0.67	http://www.multiplebirths.org.uk/media.asp
Monochorionic|dizygotic	0.00	
Dichorionic|dyzogotic	1.00	Schulman et al. (2006)[4]

Figure 9 (below) outlines the schedule of antenatal appointments for singleton pregnancy based on NICE guidelines.

Figure 9: Antenatal schedule for single birth adapted from CG62

Weeks 6 to 17											
6	7	8	9	10	11	12	13	14	15	16	17
Booking appt by 10 weeks					First appt & early scan					Appt	

Weeks 18 to 29											
18	19	20	21	22	23	24	25	26	27	28	29
Appt & anomaly scan							Appt if 1st birth			Appt	

Weeks 30 to 37							
30	31	32	33	34	35	36	37
	Appt if 1st birth			Appt		Appt	

Weeks 38 to 42+				
38	39	40	41	42+
Appt		Appt if 1st birth	Offer birth	Offer weekly appts + scans until birth

[c] | denotes a conditional probability, the probability that a pregnancy is monochorionic given that it is monozygotic

The unit cost of antenatal attendances and monitoring procedures undertaken as part of antenatal care are provided in Table 10 and Table 11 respectively. All women undergoing a specialist pregnancy should have at least two of their appointments with the specialist obstetrician according to CG129. It was assumed those specialist appointments occur at a gestational age of 12 and 32 weeks. It was assumed that all pregnancies are in nulliparous women in whom guidelines recommend additional appointments at gestational ages of 25 and 31 weeks.

Table 10: Cost of antenatal HCP attendances

HCP attendance	Cost	Source
Midwife (first specialist booking)	£122	NHSRC 2015/16: Consultant led, WF01C, Non-Admitted Face to Face Attendance, First, 560, Midwifery service
Specialist midwife (follow- up)	£77	NHSRC 2015/16: Consultant led, WF01B, Non-Admitted Face to Face Attendance, Follow-up, 560, Midwifery service
Consultant obstetrician (first)	£161	NHSRC 2015/16: Consultant led, WF01B, Non-Admitted Face to Face Attendance, First, 501, Obstetrics
Consultant obstetrician (follow-up)	£121	NHSRC 2015/16: Consultant led, WF01A, Non-Admitted Face to Face Attendance, Follow-up, 501, Obstetrics
Ante-natal routine observation (non-specialist)	£62	NHSRC 2015/16: Non-consultant-led, Non-Admitted Face to Face Attendance, Follow-up, 560, Midwifery Services

Table 11: Cost of antenatal procedures

Procedure	Cost	Comment	Source
FFTS	£6	Monitored using ultrasound - assumed to require an additional 10% of a non-consultant led attendance resources	NHSRC 2015/16: Non-Consultant led, WF01B, Non-Admitted Face to Face Attendance, Follow-up, 560, Midwifery service £62
IUGR	£12	Monitored with maternal physical examination, but doppler/vascular type studies may be used - assumed to require an additional 20% of a non-consultant led attendance resources	NHSRC 2015/16: Non-Consultant led, WF01B, Non-Admitted Face to Face Attendance, Follow-up, 560, Midwifery service £62
Ultrasound scan	£72	N/A	NHSRC 2015/16: Ante-natal Standard Ultrasound Scan, Outpatient procedure, NZ21Z, 560, Midwifery Services
Anomaly scan	£117	N/A	NHSRC 2015/16: Ante-natal Specialised Ultrasound Scan, Outpatient Procedure, NZ22Z, 560, Midwifery Services

FFTS, feto-fetal transfusion syndrome; IUGR, intrauterine growth restriction

It is assumed that a woman with a twin conception who loses a single fetus in the first 12 weeks of pregnancy will have an antenatal appointment schedule as for a singleton pregnancy. If a single fetus from a twin conception is lost after 12 weeks then they are assumed to continue with an appointment schedule as for a twin pregnancy as they would be in consultant led care by this point.

The costing model takes into account that once a baby has been born, no further antenatal appoints will occur regardless of the gestational age at birth. By estimating the proportion of singleton and twin births delivered at each gestational age, as described below, the model is able to takes into account that the costs of antenatal care will be affected by the fact that prematurity is more common in twin births than it is for singletons.

A Japanese study of multiple births[5] was used to estimate the cumulative frequency of twin births by gestational age. Using UK data (Birth Characteristics 2014 (ONS, 2015)) on maternities with multiple birth the number of twin births was estimated as 21,978[d] and using the Japanese data on cumulative frequency the total number of twins births by gestational age was calculated. The number of singleton births by gestational age was estimated using UK data on births by gestational age and subtracting those births that were twin. These data then allowed the cumulative frequency of singleton births by gestational age to be estimated. Using cumulative frequency the proportion of births by gestational age can be calculated, as summarised in Table 12 below.

Table 12: Cumulative frequency of singleton and twin births by gestational age

Gestational age	Twin birth Cumulative Frequency[5]	Twin births (ONS, 2016)	All births (ONS, 2016)	Singleton births	Singleton birth cumulative frequency	Proportion singleton births	Proportion twin births
24 weeks	0.0023	51	650	599	0.0009	0.0009	0.0023
25 weeks	0.0059	79	730	651	0.0019	0.0010	0.0036
26 weeks	0.0094	75	817	742	0.0030	0.0011	0.0034
27 weeks	0.0144	110	872	762	0.0041	0.0011	0.0050
28 weeks	0.0206	138	1,106	968	0.0055	0.0014	0.0063
29 weeks	0.0271	142	1,218	1,076	0.0071	0.0016	0.0064
30 weeks	0.0363	204	1,592	1,388	0.0092	0.0021	0.0093
31 weeks	0.0480	257	2,095	1,838	0.0119	0.0027	0.0117
32 weeks	0.0670	417	2,850	2,433	0.0156	0.0036	0.0190
33 weeks	0.0941	598	3,947	3,349	0.0205	0.0050	0.0272
34 weeks	0.1365	929	6,963	6,034	0.0295	0.0090	0.0423
35 weeks	0.2053	1,512	10,159	8,647	0.0424	0.0129	0.0688
36 weeks	0.3356	2,864	20,699	17,835	0.0689	0.0265	0.1303
37 weeks	0.5594	4,918	46,701	41,783	0.1311	0.0622	0.2238
38 weeks	0.7817	4,885	93,000	88,115	0.2623	0.1311	0.2223
39 weeks	0.9213	3,070	167,487	164,417	0.5070	0.2447	0.1397
40 weeks	0.9844	1,386	184,930	183,544	0.7801	0.2732	0.0631
41 weeks	0.9988	316	127,334	127,018	0.9692	0.1890	0.0144
42 weeks	1.0000	27	20,729	20,702	1.0000	0.0308	0.0012

[d] The number of maternities with multiple birth in 2014 (in England and Wales) was 10,989. A simplifying assumption was made that these were all twin births making a total of 21,978 twin births.

Birth

The relative frequency of different modes of birth differs systematically between singleton and twin pregnancies with a higher caesarean section rate for multiple pregnancies (CG132). Therefore, the cost analysis incorporated the costs associated with the mode of birth. We were unable to find data sources that would allow mode of birth by both multiplicity and gestational age to be taken into account and therefore the analysis assumes that the mode of birth is unaffected by gestational age.

Table 13 reports the unit costs used in the cost analysis by mode of birth, derived from NHS Reference Costs 2015/16.

Table 13: Cost of delivery

Mode of delivery		Total elective long-stay including excess bed days	Non-elective long-stay including excess bed days	Non-elective short stay	Weighted average cost
Normal	FCEs	1,401	153,795	223,283	£2,117
	Cost	£2,367	£3,070	£1,459	
Assisted	FCEs	316	60,400	23,161	£3,191
	Cost	£3,751	£3,699	£1,860	
Planned CS	FCEs	3,081	47,597	20,927	£3,440
	Cost	£3,375	£3,905	£2,393	
Emergency CS	FCEs	542	89,476	9,027	£4,563
	Cost	£4,404	£4,728	£2,938	

FCEs – Finished Consultant Episodes

The number of FCEs for each type of birth (normal birth, assisted birth, planned caesarean section and emergency caesarean section) along with the type of in-patient stay was used to calculate a weighted average cost for each mode of birth. The number and cost of excess bed days, all reported in the NHS Reference Costs 2015-16, was also included in the weighted cost of each birth. These costs were further weighted to reflect the relative frequency of alternative modes of birth in multiple and singleton pregnancies.

The proportion of singletons and twins delivered by each method was taken from The National Sentinel CS Audit Report 2001 (Table 14). Furthermore, in the base case analysis we adopted the approach of a previously published study[2] by applying a multiplier of 1.34 to twin births to reflect that a twin birth would incur more health care resource use (e.g. time, staffing) than a singleton birth.

Table 14: Mode of delivery used to inform the model taken from The National Sentinel CS audit Report 2001

Mode of delivery	Single	Twin
Normal delivery	67.0%	36.3%
Assisted delivery	11.7%	4.7%
Planned CS	7.9%	22%
Emergency CS	13.4%	37%

Neonatal care

It is reported that 11.5% of babies admitted to Neonatal Intensive Care Units (NICU) are from multiple pregnancies (Neonatal Data Analysis Unit 2014 Report) but multiple pregnancies account for only 1.6% of live births. However, in order to estimate the risk of a conception ultimately leading to a neonatal care admission, it is necessary to take into account the proportion of births that will be stillbirth (see Figure 3). The proportion of stillbirths by gestational age was taken from UK data (ONS, 2015) and is reported in Table 15. A small number of births occurring below 24 weeks were excluded because no stillbirths are given for this data.

The model uses the same stillbirth rate at a given gestational age for both singleton and twin pregnancies, but as the distribution of twin births by gestational age differs from that of singletons, the stillbirth rate for twin births will differ from that of singletons overall.

Table 15: Stillbirth rate by gestational age (ONS, 2014 – England & Wales)

Gestational age	Stillbirths	All births	Stillbirth rate
24 weeks	236	650	0.3631
25 weeks	255	730	0.3493
26 weeks	195	817	0.2387
27 weeks	168	872	0.1927
28 weeks	149	1,106	0.1347
29 weeks	131	1,218	0.1076
30 weeks	124	1,592	0.0779
31 weeks	132	2,095	0.0630
32 weeks	140	2,850	0.0491
33 weeks	134	3,947	0.0339
34 weeks	150	6,963	0.0215
35 weeks	145	10,159	0.0143
36 weeks	202	20,699	0.0098
37 weeks	211	46,701	0.0045
38 weeks	221	93,000	0.0024
39 weeks	201	167,487	0.0012
40 weeks	215	184,930	0.0012
41 weeks	175	127,334	0.0014
42 weeks	29	20,729	0.0014

The per diem unit costs of neonatal care were taken from critical care are available from NHS Reference costs 2015-16. These costs are shown in Table 16

Table 16: Cost of neonatal care

Neonatal care	Cost/ day	Source
NICU level 1	£437	NHSRC 2015/16, critical care, Neonatal Critical Care, Normal Care, XA05Z
NICU level 2	£1,218	NHSRC 2015/16, critical care, Neonatal Critical Care, Intensive Care, XA01Z
HDU	£872	NHSRC 2015/16, critical care, Neonatal Critical Care, High dependency, XA02Z
SCBU	£520*	NHSRC 2015/16, critical care, Neonatal Critical Care. Weighted average of: Special Care without External Carer, XA03Z £560 & Special Care with External Carer, XA04Z £384

The total cost of a neonatal care admission is determined by the daily cost and length of hospital stay. Following the approach of most of this costing report we assumed that gestational age rather than multiplicity per se was the key determinant of the length of stay. Data from the Neonatal Data Analysis Unit (NDAU 2012 Service Provision v1.0;https://www1.imperial.ac.uk/resources/195C8F2D-0CBD-4B80-8C7A-C957242DF614/ndau2012serviceprovisionreportv1.pdf) was used to estimate the length of stay in neonatal care by gestational age, see Table 17.

Table 17: Length of stay and postmenstrual age at discharge by gestational age, infants discharged to home or foster care in 2012

Gestational age at birth	Median length of stay in days (IQR)
≤ 27 weeks	92 (76-112)
28-31 weeks	44 (34-57)
32-36 weeks	13 (8-19)
≥ 37 weeks	4 (3-7)

Reproduced with kindly permission of the Neonatal Data Analysis Unit
IQR – Inter Quartile Range

It was assumed that the median length of stay was equivalent to the mean length of stay, which may underestimate the mean if length of stay is right skewed, as it generally is expected to be[6]. In order to get a break down by each week of gestational age a curve was fitted to the four data points shown in Table 17 and an estimated length of stay by week of gestational age was estimated from the fitted equation, see Figure 10 and Table 18. It was assumed that the mean length of stay did not increase below a gestational age of 27 weeks and did not decrease above 37 weeks.

Figure 10: Observed length of stay by gestational age and fitted curve

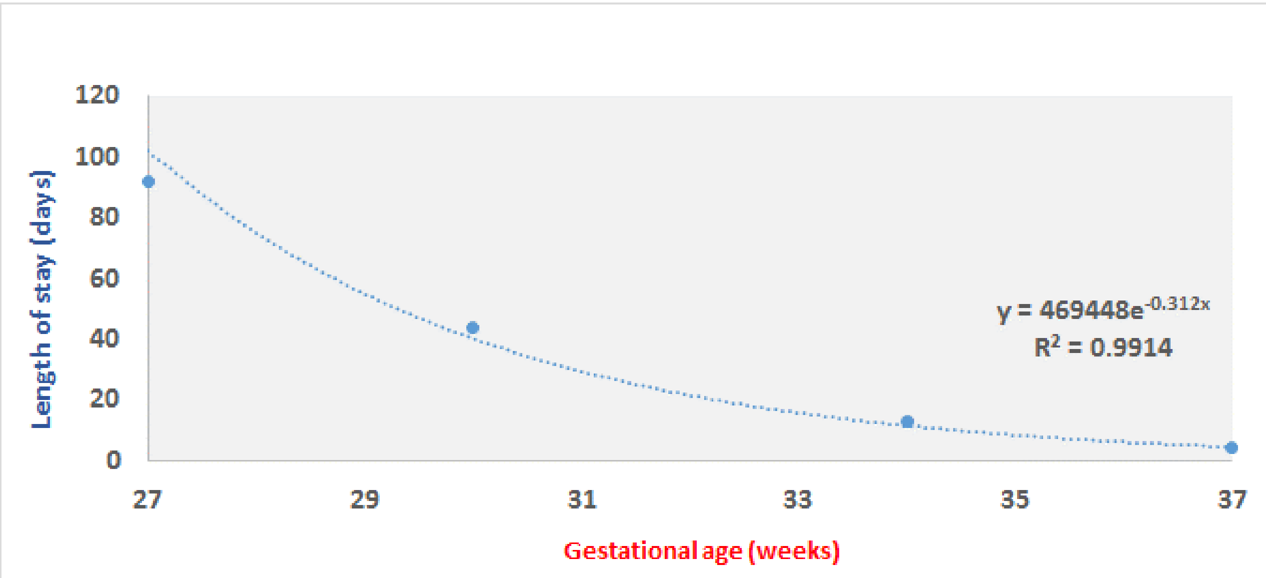


Table 18: Observed and fitted mean length of stay in neonatal care

Gestational age	Observed LOS	Fitted LOS
24 weeks	-	103
25 weeks	-	103
26 weeks	-	103
27 weeks	92	103
28 weeks	-	75
29 weeks	-	55
30 weeks	44	40
31 weeks	-	29
32 weeks	-	21
33 weeks	-	15
34 weeks	13	11
35 weeks	-	8
36 weeks	-	6
37 weeks	4	4
38 weeks	-	4
39 weeks	-	4
40 weeks	-	4
41 weeks	-	4
42 weeks	-	4

Table 16 shows the per diem unit cost for different levels of neonatal care. To calculate the weighted cost of a NICU admission, the estimated proportion of length of stay spent in each level of care was estimated using assumptions made in a costing of neonatal costs in the NICE guideline on multiple pregnancy (CG129).

Table 19: Length of stay by gestational age at birth (CG129)

Gestational age at birth	Length of stay (weeks)			
	SCBU (%)	NICU level 1 (%)	NICU level 2 (%)	HDU (%)
30 weeks	5 (56%)	2 (22%)	0	2 (22%)
32 weeks	4 (67%)	0	2 (33%)	0
36 weeks	1 (100%)	0	0	0

NICU, neonatal intensive care unit; SCBU, special care baby unit; HDU, high dependency care unit

It was assumed that neonatal admissions from babies born between 24-31 weeks would be allocated to the different levels of neonatal care as per babies born at a gestational age of 30 weeks (see Table 19). For babies born at gestational ages of 32-35 weeks the length of neonatal stay by level of care would be as for the proportions for babies born at a gestational age of 32 weeks. Finally, all babies born at 36 weeks gestational age and older are assumed to receive all their neonatal care in a special care baby unit. The model does not take into account any potential independent effect of multiplicity and mode of birth on either the length or type of hospital stay.

The final component of costing neonatal care involved estimating the proportion of babies who would be admitted to neonatal care by gestational age. Data from the Neonatal Data Analysis Unit (https://www1.imperial.ac.uk/resources/98E6A2BD-03B3-4D5D-89B8-A7DEC031537D/ndau2014reportv1.2.pdf) provided a breakdown of the number of infants discharged from neonatal care for 182 neonatal units in England, Scotland and Wales in 2014 by gestational age. These data are reproduced in Table 20. Other birth statistics used in the costing report have largely used data based on England and Wales only and therefore a multiplier was applied to estimate the equivalent numbers for England and Wales. The total number of birth in England and Wales in 2014 was 694,610 whereas in Scotland the total was 55,098 and therefore a multiplier of 0.93 was used to estimate the number of infants discharged from neonatal care by gestational age in England and Wales[e].

Table 20: Number of babies admitted to Neonatal Care by gestational age at birth

Gestational age at birth	Numbers of babies admitted England, Wales & Scotland	Estimated babies admitted England & Wales	Cumulative frequency (%)
≤ 25 weeks	1,144	1,060	1.27%
26-32 weeks	9,637	8,929	11.95%
33-36 weeks	24,470	22,950	39.40%
≥ 37 weeks	54,674	50,656	100%

To obtain an estimate of cumulative frequency by week of gestational age the observed data depicted in Table 20 was plotted on a graph using Microsoft Excel® and a curve fitted as shown in Figure 11:. The equation of the fitted curve was used to estimate the cumulative frequency of neonatal care admissions by gestational age, see Table 21.

For all babies born at term (≥ 37 weeks) it was assumed that the proportion of births admitted to neonatal care was constant irrespective of gestational age. From Table 21 it can be seen that it is estimated that 39.6% of neonatal care admission occur in babies born at a gestational age of 36 weeks and under, implying that 60.4% of neonatal care admissions are to babies born at term. Of the 639,129 term births (see Table 12), the proportion occurring at gestational ages of 37, 38, 39, 40, 41 and 42 weeks was calculated. This 'weight' was then used to estimate the proportion of the remaining neonatal care admissions that would occur at each of those gestational ages[f].

---

[e] Total Birth in England, Wales and Scotland: 694,610 + 55,098 = 749,708
Multiplier: 694,610 ÷ 749,708 = 0.93

[f] Births at a gestational age of 37 weeks = 46,490
Proportion of term babies born at 37 weeks = 0.073
Proportion of neonatal care admissions from babies born at 37 weeks: 0.604 x 0.0703 = 0.042

Figure 11: Cumulative frequency of neonatal care admission by gestational age

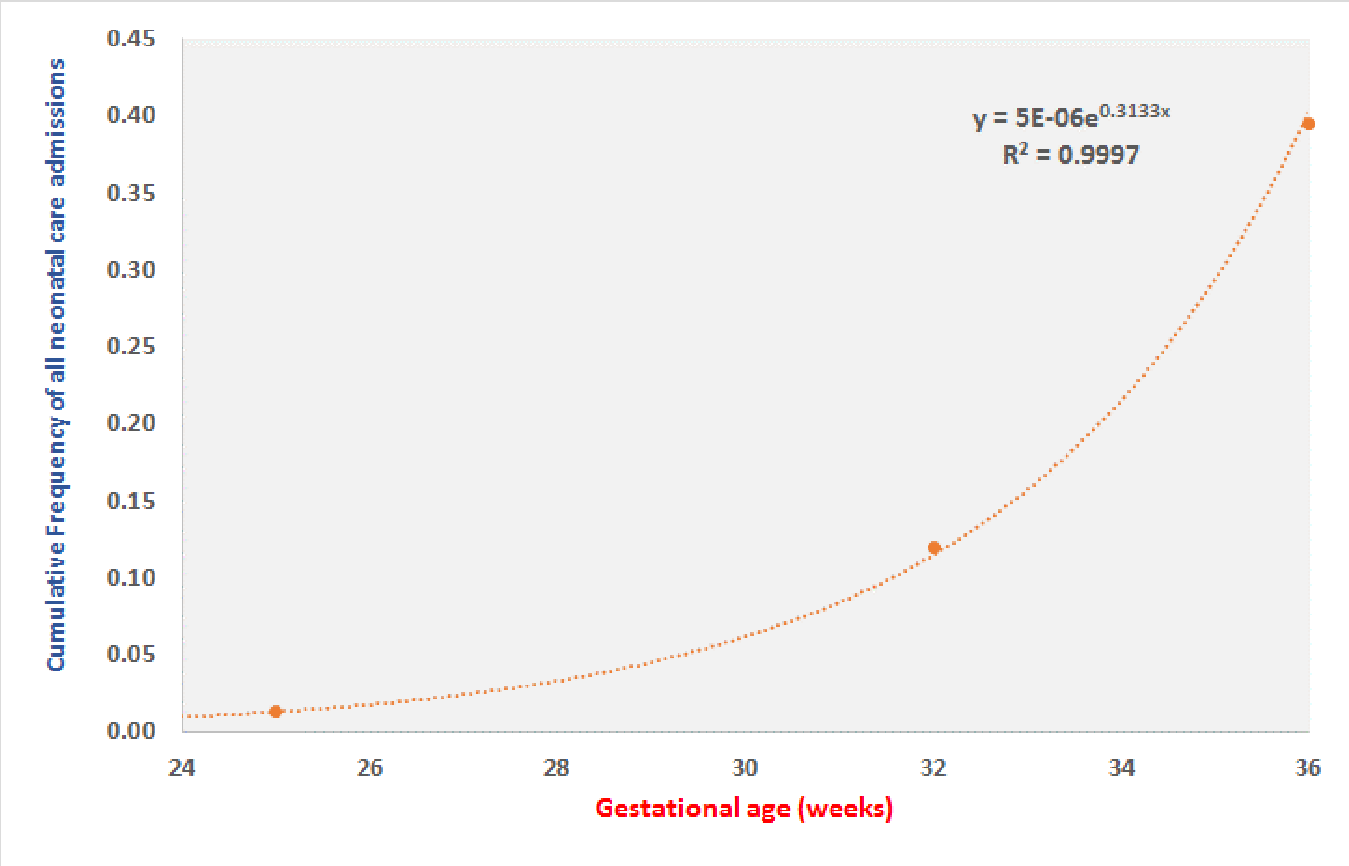


Table 21: Observed and fitted cumulative frequency of neonatal care admission by gestational age

Gestational age	Observed cumulative frequency	Fitted cumulative frequency
24 weeks	-	0.009
25 weeks	0.0127	0.013
26 weeks	-	0.017
27 weeks	-	0.024
28 weeks	-	0.032
29 weeks	-	0.044
30 weeks	-	0.060
31 weeks	-	0.083
32 weeks	0.1195	0.113
33 weeks	-	0.155
34 weeks	13	0.211
35 weeks	-	0.289
36 weeks	0.3940	0.396
37 weeks	-	0.440
38 weeks	-	0.527
39 weeks	-	0.686
40 weeks	-	0.860
41 weeks	-	0.980
42 weeks	-	1.000

The fitted cumulative frequency rates listed in Table 21 was used in conjunction with data on livebirths by gestational age to derive a neonatal care admission rate by gestational age. However, it was assumed that all live births of 25 weeks or under would be admitted to neonatal care. The neonatal care admission rates derived for use in the model are given in Table 22.

Table 22: Neonatal care admission rates

Gestational age	Live births (ONS, 2015)	Fitted cumulative frequency	Estimated births admitted to neonatal care	Neonatal care admission rate
24 weeks	414	0.009	414	1.0000
25 weeks	475	0.013	475	1.0000
26 weeks	622	0.017	553	0.8883
27 weeks	704	0.024	530	0.7534
28 weeks	957	0.032	726	0.7581
29 weeks	1,087	0.044	992	0.9130
30 weeks	1,468	0.060	1,358	0.9248
31 weeks	1,963	0.083	1,857	0.9461
32 weeks	2,710	0.113	2,540	0.9374
33 weeks	3,813	0.155	3,475	0.9114
34 weeks	6,813	0.211	4,754	0.6978
35 weeks	10,014	0.289	6,503	0.6494
36 weeks	20,497	0.396	8,895	0.4340
37 weeks	46,490	0.440	3,675	0.0790
38 weeks	92,779	0.527	7,334	0.0790
39 weeks	167,286	0.686	13,224	0.0790
40 weeks	184,715	0.860	14,601	0.0790
41 weeks	127,159	0.980	10,052	0.0790
42 weeks	20,700	1.000	1,636	0.0790

Long terms costs (associated with prematurity)

NHS costs in the first 2-years of life post initial hospital discharge

A recently published UK study reported on a population study to compare the economic costs associated with moderate and late preterm birth.[7] Table 23 shows the costs reported in that study for post-discharge NHS costs in moderate preterm, late preterm and term babies.

Table 23: Cost of NHS post-discharge costs in the first 2 years of life (2010-11 prices)

Gestational age	0-6 months	6-12 months	12-24 months
32-33 weeks (moderate preterm)	£1,351	£809	£424
34-36 weeks (late preterm)	£1,073	£796	£886
≥37 weeks (term)	£773	£682	£289

For the purposes of the model discharge costs were estimated for preterm (<37 weeks gestational age) and term babies. Preterm costs were calculated as a weighted average of the costs reported in Table 23 for moderate and late preterm births. The weights were based on the number of surviving babies from each category of prematurity (moderate and late). For 0-12 months this was based on the births surviving the neonatal period and for 12-24 months it was based on the births surviving the first 12 months. These proportions are derived from the model inputs for neonatal and post neonatal mortality. Table 24 shows the neonatal and post neonatal mortality by gestational age (Pregnancy and ethnic factors influencing births and infant mortality: England and Wales (ONS, 2015)) and Table 25 shows the weights for estimating the discharge costs associated with prematurity.

Table 24: Neonatal and post neonatal mortality (ONS, 2015)

Gestational age	Births	Neonatal deaths	Postnatal deaths	NND rate	PND rate
24 weeks	690	158	28	0.2290	0.0406
25 weeks	693	86	25	0.1241	0.0361
26 weeks	779	77	25	0.0988	0.0321
27 weeks	851	54	23	0.0635	0.0270
28 weeks	1,081	60	22	0.0555	0.0204
29 weeks	1,227	41	10	0.0334	0.0081
30 weeks	1,449	32	14	0.0213	0.0093
31 weeks	1,922	39	9	0.0203	0.0047
32 weeks	2,740	23	15	0.0084	0.0055
33 weeks	3,864	30	21	0.0078	0.0054
34 weeks	6,470	37	22	0.0057	0.0034
35 weeks	9,597	45	35	0.0047	0.0036
36 weeks	19,209	48	36	0.0025	0.0019
37 weeks	42,445	82	58	0.0019	0.0014
38 weeks	87,793	94	107	0.0011	0.0012
39 weeks	157,793	91	93	0.0006	0.0006
40 weeks	178,577	111	91	0.0005	0.0005
41 weeks	125,612	69	42	0.0005	0.0003
42 weeks	21,784	16	11	0.0006	0.0005

NND – Neonatal death; PND Post neonatal death

Table 25: Weights for moderate and late preterm discharge costs

Gestational age	0-12 months	12-24 months
32-33 weeks (moderate preterm)	0.1491	0.1487
34-36 weeks (late preterm)	0.8509	0.8513

As the costs reported in Table 23 were for a price year of 2010-2011 these were updated for inflation using the Hospital and Community Health Services (HCHS) index (www.info.doh.gov.uk/doh/finman.../2015.16%20Pay%20&%20Price%20series.xlsx), that gives a multiplier of 1.07 to convert those values into 2015-2016 prices.

Table 26 gives the NHS costs in the first 2 years after initial discharge by gestational age.

Table 26: NHS Costs in the first 2 years after initial discharge

Gestational age	0-6 months	6-12 months	12-24 months
24 weeks	£1,196	£856	£877
25 weeks	£1,196	£856	£877
26 weeks	£1,196	£856	£877
27 weeks	£1,196	£856	£877
28 weeks	£1,196	£856	£877
29 weeks	£1,196	£856	£877
30 weeks	£1,196	£856	£877
31 weeks	£1,196	£856	£877
32 weeks	£1,196	£856	£877
33 weeks	£1,196	£856	£877
34 weeks	£1,196	£856	£877
35 weeks	£1,196	£856	£877
36 weeks	£1,196	£856	£877
37 weeks	£830	£732	£310
38 weeks	£830	£732	£310
39 weeks	£830	£732	£310
40 weeks	£830	£732	£310
41 weeks	£830	£732	£310
42 weeks	£830	£732	£310

The model assumes that all babies who survive the neonatal period incur the 0-6 months post discharge NHS costs, but only infants who survive to one year incur the 6-12 months and 12-24 months discharge costs. This is tantamount to assuming that all post neonatal death occur at six months.

Neonatal morbidity and long term disability

A twin pregnancy has a greater risk of preterm birth which in turn is associated with increased neonatal morbidity (including respiratory distress syndrome and intra-ventricular haemorrhage). Long term disability arises as a result of the effects on the neurological system (leading to an increased risk of cerebral palsy and lower educational attainment, for example) and respiratory system. The more premature the birth the greater the risk of adverse outcomes, which means that babies born extremely preterm (before 28 weeks) have significantly worse outcomes than those born moderately preterm.

It is extremely difficult to capture the complex relationships between prematurity and adverse neonatal and long term outcomes and thus this part of the analysis relies on a number of simplifying assumptions. Based on economic modelling undertaken for the NICE guideline on preterm labour and birth (NG25) this cost analysis included neonatal morbidity resulting from respiratory distress syndrome (RDS) and intra-ventricular haemorrhage (IVH). In addition cerebral palsy was included as an outcome as approximately 40-50% of cerebral palsy occurs in those born prematurely.[8]

A published meta-analysis estimated the prevalence of cerebral age according to gestational age at birth.[9] A curve was fitted to the observed data using Microsoft Excel®, see Figure 12. The equation for that curve was used to estimate the risk of cerebral palsy for each week of gestational age, see Table 27.

Figure 12: Risk of cerebral palsy by gestational age

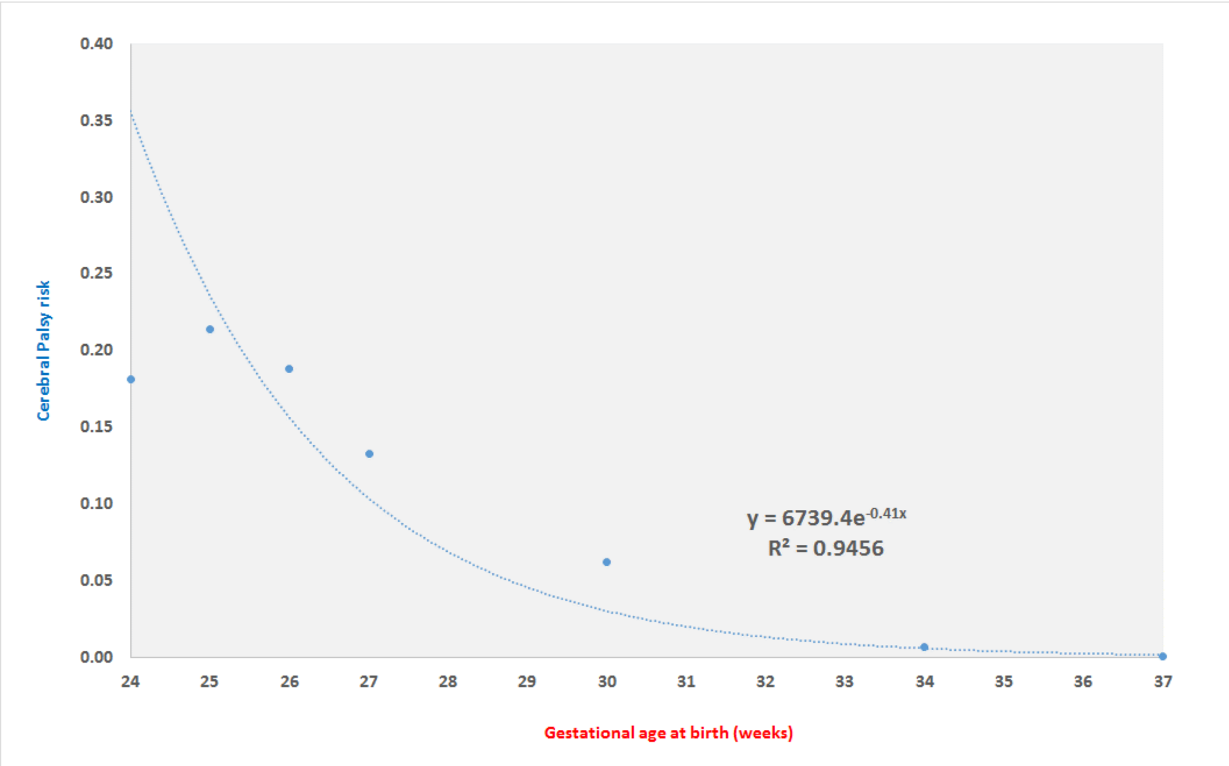


Table 27: Risk of cerebral palsy by gestational age

Gestational age	Observed cerebral palsy prevalence	Fitted cerebral palsy risk
24 weeks	0.181	0.3591
25 weeks	0.214	0.2383
26 weeks	0.188	0.1581
27 weeks	0.133	0.1050
28 weeks	-	0.0697
29 weeks	-	0.0462
30 weeks	0.062	0.0307
31 weeks	-	0.0204
32 weeks	-	0.0135
33 weeks	-	0.0090
34 weeks	0.007	0.0060
35 weeks	-	0.0039
36 weeks	-	0.0026
37 weeks	0.001	0.0017
38 weeks	-	0.0012
39 weeks	-	0.0008
40 weeks	-	0.0005
41 weeks	-	0.0003
42 weeks	-	0.0002

In terms of the model pathway, the risk of cerebral palsy is applied to babies surviving the neonatal period.

As with the NICE guideline on preterm birth (NG25) the risk of RDS and IVH by gestational age at birth was mostly estimated using a Medscape article on preterm labour (Ross, 2017). The risks of RDS for babies born after 34 weeks were based on the values reported in the NICE guideline on preterm birth (NG25).

As there is a mortality risk associated with RDS and IVH not all cases will incur long-term consequences. The model factored in that a proportion of neonatal death would be due to RDS and IVH and costs were only ascribed to RDS/IVH babies who did not die from the condition. It was assumed that mortality risk due to RDS and IVH did not vary by gestational age. RDS mortality was estimated using published US data (American Lung Association Lung Disease Data 2008). The mortality risk from IVH is taken from the NICE guideline on preterm birth (NG25).

RDS and IVH related risks used in the costing model are shown in Table 28.

Table 28: Risk of RDS, IVH and associated mortality

Gestational age	RDS rate	IVH rate	RDS mortality rate	IVH mortality rate
24 weeks	0.700	0.249	0.054	0.300
25 weeks	0.899	0.300	0.054	0.300
26 weeks	0.929	0.300	0.054	0.300
27 weeks	0.839	0.160	0.054	0.300
28 weeks	0.649	0.040	0.054	0.300
29 weeks	0.622	0.035	0.054	0.300
30 weeks	0.550	0.020	0.054	0.300
31 weeks	0.370	0.010	0.054	0.300
32 weeks	0.280	0.000	0.054	0.300
33 weeks	0.340	0.000	0.054	0.300
34 weeks	0.140	0.000	0.054	0.300
35 weeks	0.120	0.000	0.054	0.300
36 weeks	0.007	0.000	0.054	0.300
37 weeks	0.035	0.000	0.054	0.300
38 weeks	0.035	0.000	0.054	0.300
39 weeks	0.035	0.000	0.054	0.300
40 weeks	0.035	0.000	0.054	0.300
41 weeks	0.035	0.000	0.054	0.300
42 weeks	0.035	0.000	0.054	0.300

Due to the complexity of such an approach and a likely dearth of data, the model does not consider the relative severity of these outcomes by gestational age, but that should be recognised as a simplifying assumption as the economic consequences of cerebral palsy, for example, vary hugely with severity.

A Danish study[10] was used to estimate the average cost of cerebral palsy per individual in a lifetime utilising the data on 2,367 individuals in the Danish Cerebral Palsy Register. Using those registers they assessed the costs to the health and social care sectors, as well as the costs to society constituted by lost productivity. However, for the perspective of this analysis, only hospital costs alone are included in the results but social care costs are additionally reported to illustrate the broader societal perspective. The lifetime costs (discounted at a rate of 5% per year) reported in this study are provided in

Table 29 alongside sterling costs inflated to a 2015/16 cost year. The discount rate used in this study greater than the 3.5% discount rate recommended in the NICE Reference Case and therefore the values will be underestimated compared to NICE methods.

Table 29: Estimate of lifetime cost of cerebral palsy

Cost	€ cost year 2000			£ cost year 2000	£ cost year 2015/16
	Men	Women	Mean		
Hospital costs	51,968	49,921	50,945	£41,284	£65,014
Primary health care costs	7,182	8,269	7,726	£6,261	£9,859
Pharmaceutical costs	7,005	7,068	7,037	£5,702	£8,980
Total health care costs	66,155	65,258	65,707	£53,247	**£83,853**
Total social costs	462,578	470,386	466,482	£378,024	£595,312

Social costs include: child care, education, housing, day activities, other
HCHS (2000) to) (2015/16) = 1.57 inflation multiplier
HM Revenue and Customs monthly exchange rate (February 2017) £1.00/€1.234 = £0.810/€1

The costs of RDS were taken from a published UK study[11] and we used the reported mean one-year post-hospital costs to the NHS in one-year survivors. As per the NICE guideline on preterm labour and birth (NG25) it was assumed that IVH would have the same cost as intracranial haemorrhage (ICH) and that Grade III and Grade IV ICH would be similar in cost to cerebral palsy. As it was estimated that 30% of ICH is of severity Grade III and Grade IV, the cost of IVH was assumed to be 30% of the cost of cerebral palsy. The model costs attached to RDS and IVH are given in Table 30.

Table 30: Costs of respiratory distress syndrome and intraventricular haemorrhage

Outcome	Cost
Respiratory distress syndrome	£3,935
Intraventricular haemorrhage	£25,156

Results

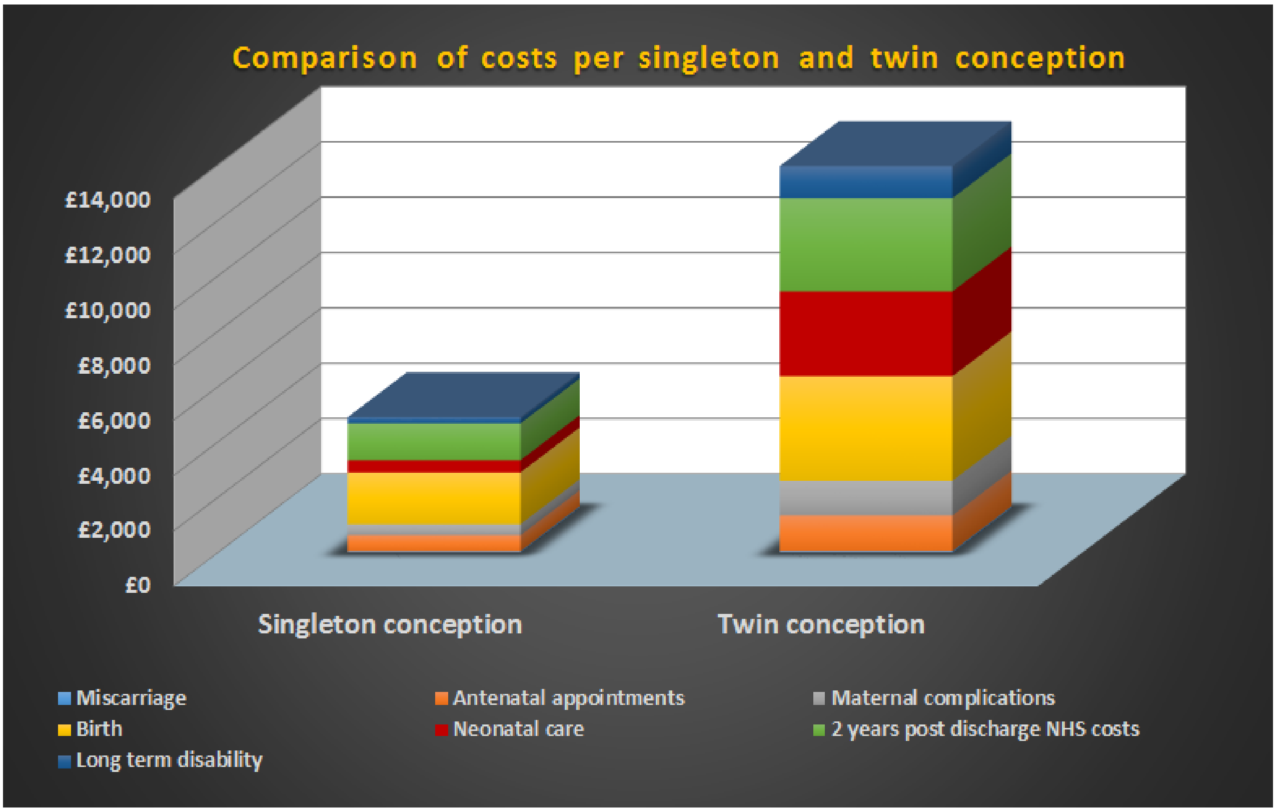
The model's results are presented first as the mean cost per conception. It should be remembered that a significant number of conceptions will result in an early pregnancy loss and that some pregnancies that commence with two fetal sacs will nevertheless result in a singleton birth.

The base case results, using the models default values are shown in Table 31 and Figure 13.

Table 31: Summary of cost differences for a singleton versus a twin conception

Category	Singleton conception	Twin conception
Miscarriage	£47	£54
Antenatal appointments	£577	£1,284
Maternal complications	£937	£1,257
Birth	£1,870	£3,777
Neonatal care	£442	£3,062
2-year post discharge NHS costs	£1,328	£3,369
Long term disability	£229	£1,156
Total	**£4,892**	**£13,959**

Figure 13: Chart showing a comparison of the costs of a singleton and twin conception

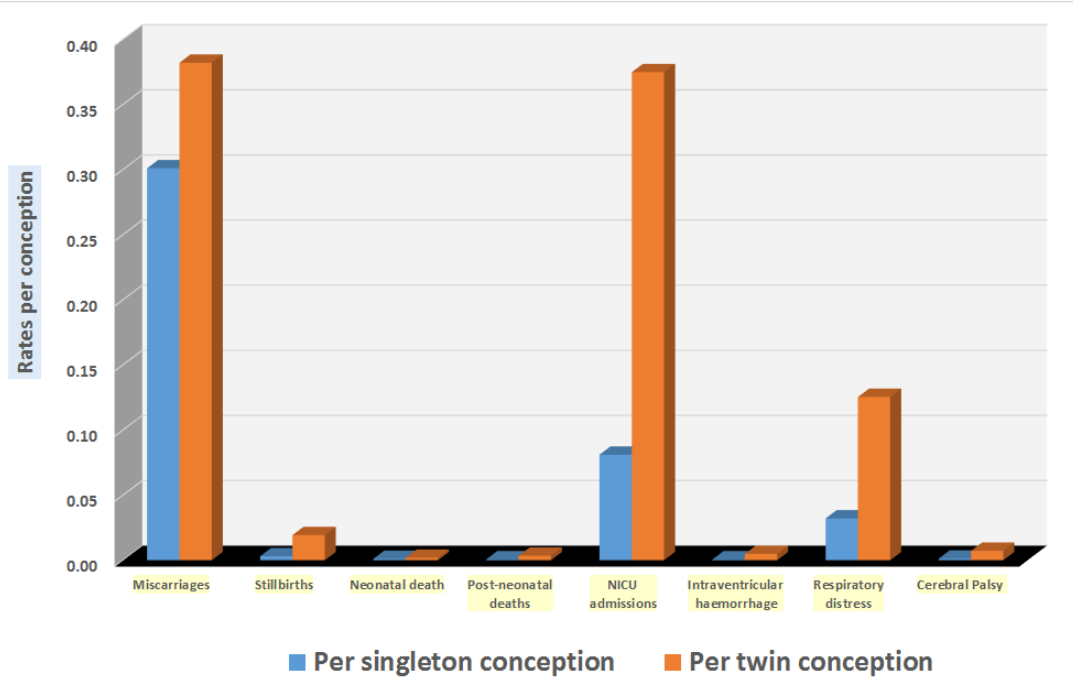


Driving much of these differences in cost are the differences in baby outcomes from a singleton and twin conception. Table 32 and Figure 14 summarise the differences in the rates of the various clinical outcomes used in this costing report. Figure 15 is a chart which depicts the increased relative risk of these clinical outcomes for a twin conception versus a singleton conception.[g]

Table 32: A comparison of the rates of adverse baby outcomes per singleton conception and per twin conception

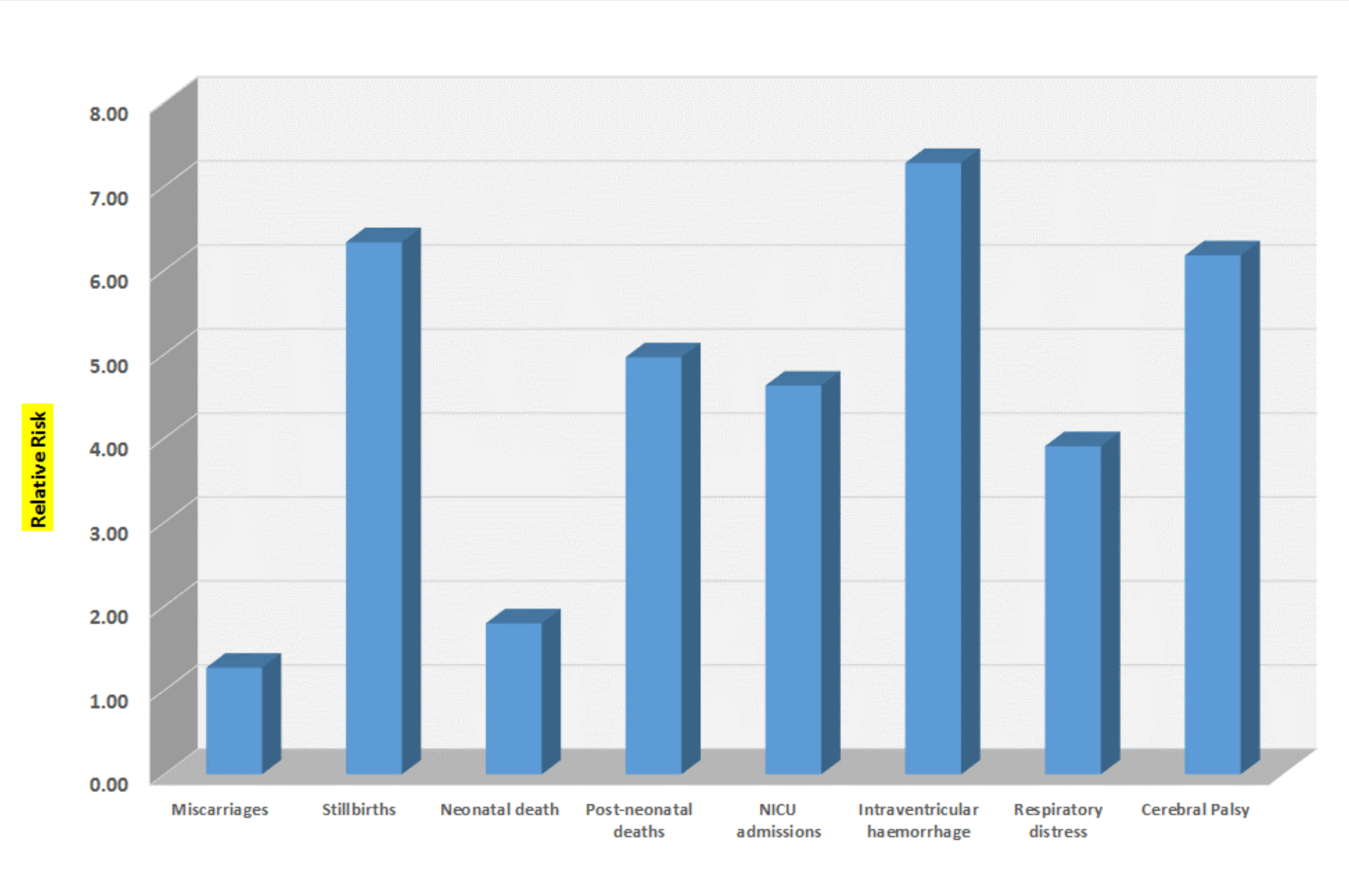
Outcome	Singleton conception	Twin conception	Relative risk[h]
Miscarriage	0.3010	0.3820	1.27
Stillbirths	0.0030	0.0193	6.34
Neonatal death	0.0010	0.0019	1.8
Post neonatal death	0.0007	0.0034	4.96
Neonatal care admissions	0.0810	0.3748	4.63
Intraventricular haemorrhage	0.0007	0.0048	7.28
Respiratory distress syndrome	0.0321	0.1254	3.91
Cerebral palsy	0.0012	0.0072	6.18

Figure 14: A comparison of the risks of adverse outcomes of birth for singleton and twin conceptions



[g] Note these relative risks are per conception and not per birth
[h] The increased risk for a twin conception relative to a singleton conception

Figure 15: Relative risks of a twin conception when compared to a singleton conception



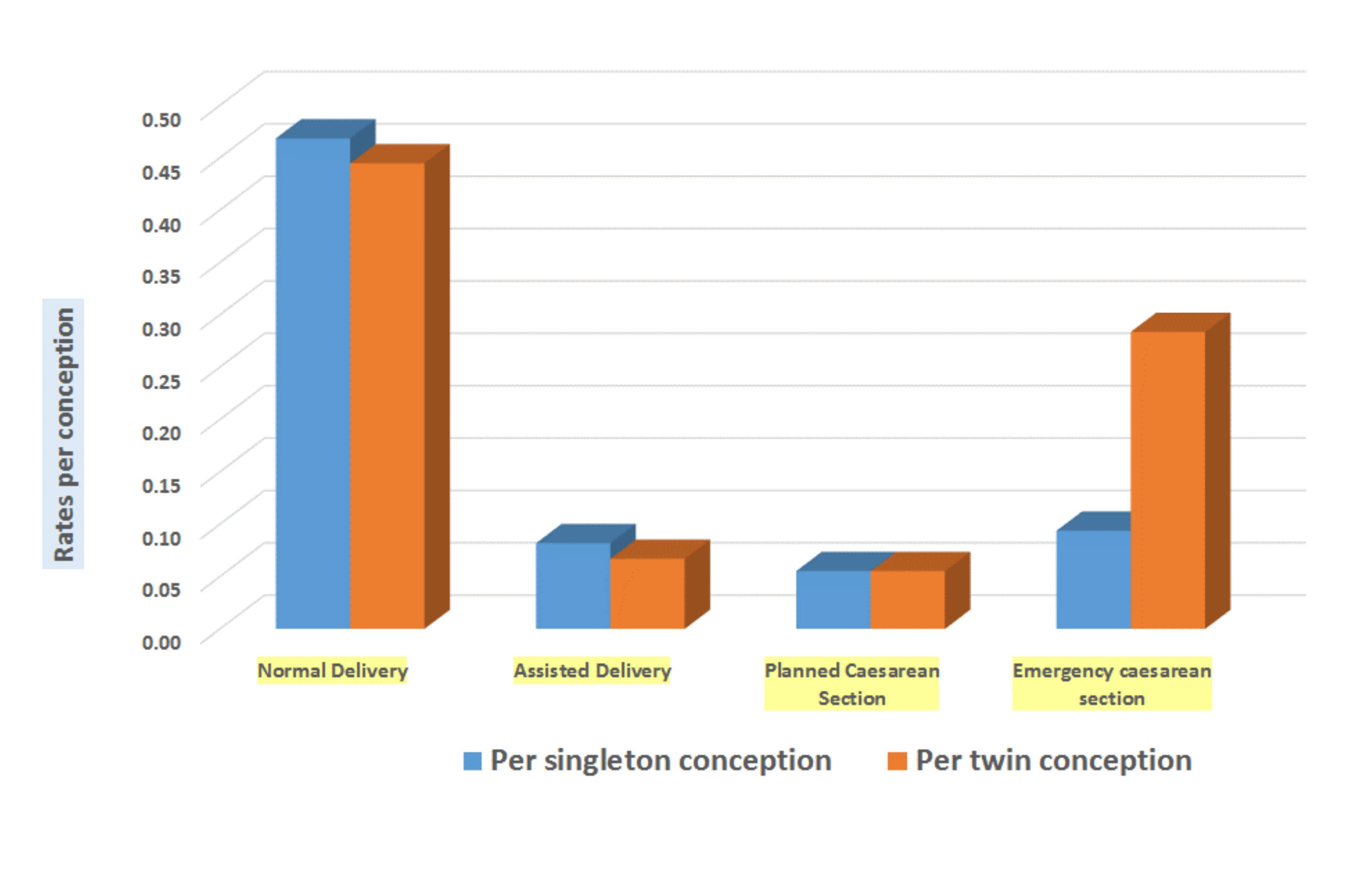
Another factor leading to increased costs of a twin conception is the reduced chance of a normal vaginal birth, with the impact of this illustrated in Table 33 and Figure 16.

Table 33: A comparison of the mode of birth per singleton and twin conception

Mode of birth	Per singleton conception	Per twin conception	Relative risk[i]
Normal delivery	0.468	0.445	0.95
Assisted delivery	0.082	0.067	0.82
Planned caesarean section	0.055	0.055	1.00
Emergency caesarean section	0.094	0.284	3.03

[i] The increased risk for a twin conception relative to a singleton conception

Figure 16: Rates of different modes of birth by twin and singleton conception



The One at a time campaign [https://www.hfea.gov.uk/about-us/our-campaign-to-reduce-multiple-births/] raised awareness amongst patients and professionals about the risks associated with multiple births to ensure that as many women as possible have a healthy baby. As part of this campaign in 2009 the Human Fertilisation and Embryology Authority (HFEA) started setting multiple pregnancy targets for fertility clinics in an attempt to reduce the multiple pregnancy rate. When the campaign started, one in four births from IVF were multiple births – 20 times higher than natural conception. The aim is to get to one in 10. The most recent national data shows that around 11% of IVF births are multiple births, showing that the sector has almost met that target, by transferring fewer embryos. However, the overall birth rate has slightly increased, suggesting that elective single embryo transfer policies have not led to a discernible reduction in the chance of having a baby.

The costing tool which was produced to accompany this report allows the user to stipulate a percentage reduction in twin conceptions and, under the assumption that a twin conception will be replaced by a singleton, calculates the saving to the NHS from such a reduction. The model uses UK data on pregnancy outcomes to estimate the current number of singleton and twin conceptions.

Singleton birth = 671,901
Twin births = 21,978
Singleton births from twin conception = 5,189
Singleton births from singleton conceptions = 666,712

Twin conception multiplier = 1.52
Singleton conception multiplier = 1.43
Twin conceptions = 16,790
Singleton conceptions = 953,808

The conception multipliers are estimated from the outcomes of the Markov modelling pathway, which indicates the proportion of pregnancies that are on-going and lead to birth. Table 34 below shows the impact of a 10% reduction in the twin conception rate from its current estimated level.

Table 34: Costs to the NHS before and after a 10% reduction in the rate of twin conceptions

Category	Before reduction	After reduction	Saving
Miscarriage	£46,113,204	£46,101,424	£11,780
Antenatal appointments	£571,674,964	£570,487,929	£1,187,035
Maternal complications	£399,618,227	£398,175,516	£1,442,711
Birth	£1,844,951,252	£1,841,749,851	£3,201,401
Neonatal care	£473,025,101	£468,626,248	£4,398,853
2-year post discharge NHS costs	£1,322,158,195	£1,318,732,149	£3,426,046
Long term disability	£237,594,075	£236,037,314	£1,556,761
Total	**£4,895,135,019**	**£4,879,910,431**	**£15,224,588**

Discussion

We believe this report to be a valued addition to other studies previously published in this area. First, it uses recent costs and in that sense updates the work of previous studies. However, we also think this study has some originality in its approach by its greater focus on linking outcomes directly to prematurity rather than multiplicity. It is widely accepted that most of the adverse outcomes of multiple pregnancy arise from the increased risk these pregnancies have of prematurity. The costing model generally did not include any independent risk of twin pregnancy over and above the effects mediated through prematurity, although some may exist.

In the context of all NHS spending on pregnancy, birth and the complications arising from it, any potential savings from reducing the twin or multiple conception rate are relatively small. So the £15 million saving estimated from reducing the twin conception rate by 10% from its current level only represented only 0.3% of the total NHS spend listed in the categories in Table 34. This is because twin births only account for approximately 1.6% of all births and whilst the relative risk of adverse outcomes is much higher for a singleton birth, the absolute risk remains relatively small. As Table 12 suggests, approximately two-thirds of twin births occur by 37 weeks. Nevertheless a saving of £15 million would be considerably in excess of what NICE would regard as a significant resource impact when considering the impact of their recommendations on the NHS.

Whilst this was a comprehensive analysis it was by necessity a huge simplification of the complex reality and the assumptions made in undertaking this evaluation reflected that. Not all the complications of prematurity have been taken into account in the analysis and to really accurately model the lifelong costs of cerebral palsy, for example, it would be necessary to have good knowledge of the whole disease pathway over a very long time frame, with data on complications and the use of interventions. Furthermore, this would have to reflect different disease severity and its link to the degree of prematurity. The uncertainty around our cost estimates is almost certainly greatest with respect to the lifelong consequences of adverse neonatal outcomes and long term morbidity. There is also likely to be a degree of double counting between costs estimated for the first two years post the initial hospital discharge and the lifelong costs associated with outcomes such as cerebral palsy.

Nevertheless, the cost analysis does utilise real UK data on birth and neonatal outcomes in conjunction with well-established links between prematurity and adverse outcomes. We therefore think the estimates are plausible and not inconsistent with other published work.[2]

This was not a formal economic evaluation as it did not explicitly compare two competing alternatives, as it would if it contrasted single embryo transfer versus double embryo transfer for example. Furthermore, it only considers the cost side of the equation and not any benefits arising from the expenditure, which is often likely to represent a cost-effective use of NHS resources at least in terms of the context of when the resource allocation decision is made. Nor does this analysis explicitly address any of the ethical issues or economic trade-offs that might follow from a reduction in twin conceptions.

Reducing twin conceptions would reduce morbidity, but it could also reduce the number of healthy births as the majority of multiple births result in that outcome. However, in this context it is worth noting that two singleton conceptions cost the NHS less than a single twin conception and therefore if the twin conception rate were reduced, the possibility would exist for “replacement” children from singleton conception with this option resulting in lower morbidity and at reduced cost.

Finally, this analysis focused on twin conception rather than multiple conception more generally. This is reasonable as twin births represent by far the biggest proportion of all multiple births, as indicated in Table 35. However, there is some suggestion that the costs rise exponentially with higher order multiples[2] and therefore the cost saving from reducing the number of such conceptions would be much greater per conception, even though the impact would be smaller in absolute terms.

Table 35: All maternities: age of mother, multiplicity and type of outcome in England and Wales (ONS, 2014)

Mode of birth	Number (%)
All maternities	687,346
Singleton maternities	676,357 (98.4%)
Twins	10,839 (1.6%)
Triplets	148 (0.02%)
Quads and above	2 (0.00%)

Conclusion

This cost analysis suggests that the cost of a twin conception is approximately three times greater than the cost of a singleton conception and that therefore there are savings to be made from reducing the twin conception rate. Whilst, these savings are not that large in the context of overall NHS expenditure, they are likely to reach a level that would be considered a "significant resource impact" by bodies such as NICE. Furthermore, this analysis has focused only on NHS costs and, especially in the context of neurodevelopmental problems arising from prematurity, the wider costs to society will be far in excess of those just experienced by the NHS. It is also important to remember that most of the savings from reducing twin conceptions are a result of reduced morbidity and not from increased antenatal monitoring or differences in the mode of birth.

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