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Is the Salut Programme an effective and cost-effective universal health promotion intervention for parents and their children? A register-based retrospective observational study

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Abstract

Objectives: This study aims to investigate the effectiveness and cost-effectiveness of the Salut Programme, a universal health promotion intervention, compared to care-as-usual, over the periods of pregnancy, delivery and the child's first two years of life.

Method: We adopted a register-based retrospective observational design using existing data sources with respect to both exposures and outcomes. Health outcomes and costs were compared between geographical areas that received care-as-usual (non-Salut area), and areas where the Programme was implemented (Salut area). We included mothers and their children from both the Salut area and non-Salut area if: i) the child was born 2002-2004 (premeasure period) or ii) the child was born 2006-2008 (postmeasure period). The effectiveness study adopted two strategies: i) a matched difference-in-difference analysis using data from all participants; and ii) a longitudinal analysis restricted to mothers who had given birth twice, i.e. both in the pre- and postmeasure periods. The economic evaluation was performed from a health care and a limited societal perspective. Outcomes were clustered during pregnancy, delivery and birth, and during the child's first two years.

Results: The difference-in-difference analyses did not result in any significant effect on the outcomes. The longitudinal analyses resulted in significant positive improvement in Apgar scores, reflecting the newborn's physical condition, with more children having a normal Apgar score (1 minute +3%, and 5 minutes +1%). The incremental cost of the Programme was INT$ 308 per child. From both a health care and a limited societal perspective, the Programme yielded higher effects and higher costs than care-as-usual, with ICERs of INT$ 2063 and INT$ 16 870, respectively, per prevented case (child with low 5 minute Apgar score).

Conclusions: The Salut Programme may be an effective universal intervention to improve maternal and child health, and is likely to represent good value for money.

Strengths and limitations of this study

- The Salut Programme may be an effective universal health promotion intervention to improve maternal and child health, and is likely to represent good value for money.
- Our study contributes to the limited evidence base regarding universal multi-sectorial health promotion approaches during pregnancy and early childhood.
- A major strength of this study is that the "state of the art" methods were used in the effectiveness analyses.
- Our analyses were limited to data available in registers. We lacked access to data on primary care and medication as well as on lifestyle and health-related quality of life.
- In the cost-effectiveness analyses, the limited societal perspective only included productivity losses due to mothers' inpatient and outpatient care, which might have contributed to the uncertainty in the results.

Background

Development during the prenatal period, infancy and childhood is known to influence lifelong health [1-4], and the link between early-life health and adult outcomes is strong and economically meaningful [5]. Promotion of optimal child development and wellbeing comprises early detection and treatment of whole families, and can potentially prevent the development of behavioural and emotional problems in children and adolescents [6].

Until now, the research community has failed to provide persuasive evidence about the effectiveness and cost-effectiveness of health promotion and preventive interventions. However, evaluation of intervention efforts is necessary for evidence-based decision-making [7 8]. Childhood obesity programmes have been suggested to be cost-effective [9], but other examples are rare. There are considerable methodological challenges when conducting such evaluations, and more thorough economic analyses of preventive programmes are encouraged. Economic evaluation is important for both those delivering and funding the interventions [10], and if demonstrated to be cost-effective, experiences and work modes can potentially be used in other settings.

The current project is nested within the Swedish Salut Child Health Intervention Programme, initiated in Västerbotten County in 2005 in addition to care-as-usual. The Programme is a multi-sectorial, family-centred approach to health promotion and prevention. One of the Programme aims is avoidance of maternal and foetal pregnancy complications related to maternal lifestyle. This study aimed to investigate the effectiveness and cost-effectiveness of the Salut Programme compared to care-as-usual, over the periods of pregnancy, delivery and the child's first two years of life. The study was guided by the following research questions:

1) Does the Salut Programme improve maternal and child health?
2) What are the resource implications of the Salut Programme in terms of intervention and societal costs?
3) Is the Salut Programme a cost-effective public health intervention?

Methods

Overall study design and participants

The current study adopted a register-based retrospective observational design using existing data sources with respect to both exposures and outcomes [11]. We simulated an experiment by taking

advantage of the stepwise implementation of the Programme and nationally available individual-level register data collected independently of our study [12].

Health outcomes and costs were compared between geographical areas that received care-as-usual (non-Salut area), and areas where the Programme was implemented from 2006 and onwards (Salut area). The mother's place of residence at the child's birth determined whether the child and mother were classified as belonging to the Salut area or the non-Salut area. Thus, an intention-to-treat approach was used [13]. We included mothers and their children from both the Salut area and non-Salut area if the child was born 2002-2004 (thus before the Salut Programme was implemented anywhere), defined as the premeasure period. Accordingly, we included mothers and their children if the child was born 2006-2008 (thus after the Salut Programme was implemented in some areas), defined as the postmeasure period. Henceforth, four study groups were formed: Salut pre, Salut post, non-Salut pre and non-Salut post.

We conducted an effectiveness study and an economic evaluation study. The effectiveness study adopted two complementary strategies: a matched difference-in-difference analysis using data from all participants, and a longitudinal analysis restricted to the subsample of mothers who had given birth twice during the study period, both in the pre- and postmeasure periods. The economic evaluation was conducted from both a healthcare and a limited societal perspective. In a recently published study protocol we have described the Salut Programme and our planned analysis strategies [14]. In the present study, this protocol has largely been followed. A few revisions have been made when necessary, and are described and motivated below.

Care-as-usual and the Salut Programme

Care-as-usual during pregnancy and childhood is free of charge and decentralised to locally-elected county councils with tax raising powers, which creates some variation across the country in delivery of services. Almost all parents attend antenatal care, and likewise almost all children attend child healthcare and dental care with an accompanying parent. Open pre-schools are free of charge, run by the municipality or churches, and attended on a drop-in basis by families.

The Salut Programme is integrated within care-as-usual, and comprises strengthening and restructuring of care-as-usual, and new specific interventions. Professionals in antenatal care, child healthcare, dental care and open pre-schools are invited to learning seminars and are encouraged to use manuals, specifically developed for the Salut Programme, to guide everyday practice. Following

countywide implementation, an evaluation showed significant improvements in professionals' health promotion practices and in collaboration across sectors [15]. The Programme is described in detail in appendix A and in previous publications [14 16-18].

Health outcomes

Health outcome measures were chosen to demonstrate the performance of the Salut Programme with respect to supporting normal pregnancy and birth, and in other ways contributing to the well-being of children and their mothers. Another prerequisite was that the measures were available through the Umeå SIMSAM Lab [12], compiled from national and local registers. Moreover, we were guided by a recent publication on frequently measured outcomes to assess maternity care performance [19]. A detailed description of the registers can be found elsewhere [14]. The following time periods and outcome measures were chosen:

1) **During pregnancy, delivery and at birth** – Mother's smoking status at first antenatal visit (yes/no); pregnancy length at delivery (≥37/<37 weeks); caesarean section (yes/no); birth weight (≥2500/<2500 g); birth length (cm); large for gestational age (LGA; ≥2 standard deviations above the reference population's mean weight); small for gestational age (SGA; ≤2 standard deviations below the reference population's mean weight); Apgar score 1, 5, and 10 minutes after delivery (≥7/<7 points); child diagnosed by paediatrician as healthy (yes/no); and duration of mother's inpatient care related to delivery (days).
2) **During the first two years after the child's birth** – Inpatient care not related to delivery within the two first months after child's birth (yes/no); cumulative duration of inpatient care (days); and cumulative number of outpatient visits, all for mother and child, respectively.

Effectiveness analyses

The samples are presented in figure 1. Assumptions and details regarding the analysis strategies are described elsewhere 14, and in appendix B. The matched difference-in-difference analyses utilized the total sample. For each child born in the Salut area at postmeasure, matching observations were found in each of the other three groups: Salut area pre, non-Salut area pre and non-Salut area post. For every outcome an observation was deemed a match if the mother, at the time of the child's birth, had the same level of education and similar age as the mother of a child born in the Salut area at postmeasure. The average difference over time in the Salut area was computed as the difference

between the mean outcome in the Salut area at postmeasure and the mean outcome of the matched observations from the Salut area at premeasure. Analogously, the average difference over time in the non-Salut area was computed as the difference between the mean outcome of the matched observations from the non-Salut area at postmeasure and the mean outcome of the matched observations from the non-Salut area at premeasure. The final difference-in-difference estimate of the average treatment effect on the treated was computed by subtracting the average difference over time in the non-Salut area from the average difference over time in the Salut area. Bootstrap standard errors were computed [20].

In the longitudinal analyses we utilized the subsample of mothers that gave birth to at least one child in each of the time periods, and living in the same geographical area over the whole time period (figure 1). For a given outcome of interest, focusing on this subsample allowed us to use the mother's premeasure outcome value as a covariate on which to match on, in addition to the matching variables used in the difference-in-difference analyses. The simple matching estimate of the average treatment effect on the treated was computed as the difference between the mean outcome in the Salut area at postmeasure, and the mean outcome of the matched observations from the non-Salut area at postmeasure. Abadie-Imbens standard errors were computed [21]. In all analyses, matching was performed separately for each outcome variable, namely the identity of the match was not fixed across analyses. Analyses were conducted in R 3.3.0 [22] using the Matching package [23] for matching and Abadie-Imbens standard errors.

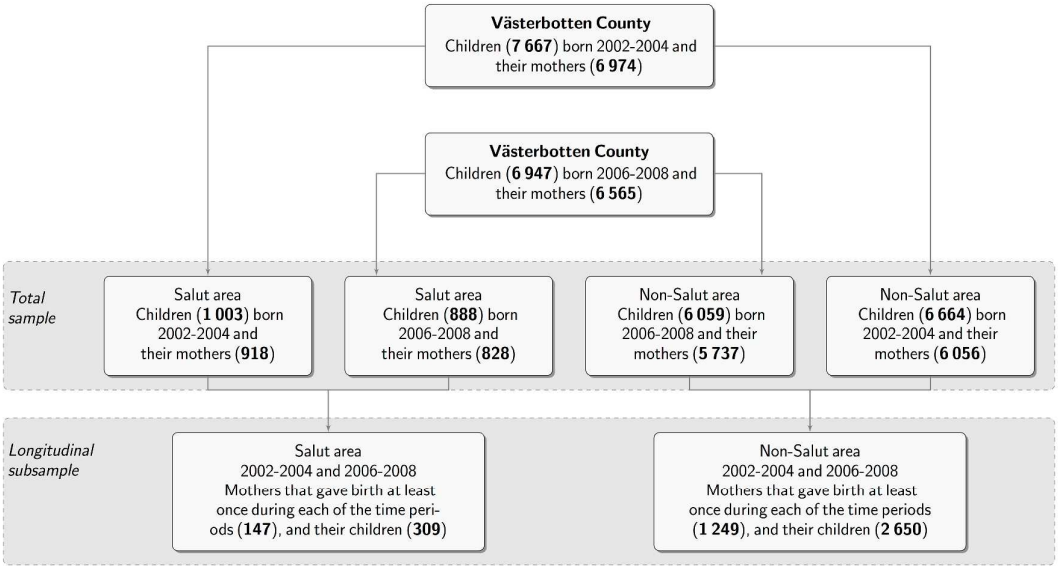

Figure 1 An overview of the study population and samples used in the analyses.

Economic evaluation

The economic analysis aimed to capture both the healthcare and the wider societal costs and benefits of the Salut Programme for the first two years of the children's lives, and their mothers. Two perspectives were adopted: a health care perspective, consisting of intervention costs and other healthcare resources used by children and mothers, and a limited societal perspective, additionally including productivity losses associated with mothers' illness [34]. Results are expressed in 2013 purchasing-power parity international dollars (8.71 SEK=INT$) after adjusting for inflation using the gross domestic product deflator [24].

Intervention cost

Programme costs were estimated between January 2005 and June 2010. We added the opportunity cost of professionals' time to attend learning seminars during 2005-2007 (appendix table D1). Calendar year-based allocation rules for joint costs and the division between start-up and implementation were decided upon retrospectively by the Salut Programme staff to capture the changing nature of activities over time (appendix table D2). Intervention costs were discounted at an annual rate of 3%.

Healthcare and other societal costs

Healthcare related costs were derived from information on the use of healthcare resources external to the Salut Programme, such as maternal inpatient care related to delivery and children's and mothers' inpatient and outpatient care due to illness. All healthcare related costs were calculated for the child's first two years. Productivity losses due to mothers' illness were included in the analysis conducted from a limited societal perspective. Productivity losses were calculated using the human capital approach, by multiplying time off work due to inpatient and outpatient care by the average gross salary (including social charges). The average number of parental benefit days during the first year is around 220 for women in Sweden [25]. Therefore, mothers were assumed to be on parental leave during the first year after childbirth, hence productivity losses were estimated for year two only. Contrary to the planned analyses in the study protocol [14], care of a sick child compensations were excluded from the analysis, as these were only linked to the parent and not to a particular child.

In addition, these costs can be considered transfer payments, thus including them would constitute double counting. Total costs were estimated by multiplying frequencies of resources by their respective unit cost. Costs incurred during year two were discounted at 3%. The difference in health care and other societal costs was compared between the Salut Programme and care-as-usual and between pre- and postmeasure using permutation tests. Unit costs used to value resource use are listed in appendix table E1.

Cost-effectiveness analysis

The economic framework of this study is a retrospective register-based cost-effectiveness analysis. We compared costs and outcomes of the Salut Programme to care-as-usual, from a healthcare and a limited societal perspective, and calculated incremental cost-effectiveness ratios (ICERs). For the probabilistic analysis, we used non-parametric bootstrapping with 1000 replications to obtain 95% confidence intervals around the ICER. The bootstrap results are presented on a cost-effectiveness plane. Bootstrapping was performed in Excel 2011.

Results

Characteristics of the study population

In the Salut area, 1003 and 888 children were born in the premeasure and postmeasure period, respectively (figure 1). In the non-Salut area, 6664 and 6059 children were born in the premeasure and postmeasure period, respectively. There were 147 mothers that gave birth at least once to 309 children in the Salut area and 1249 mothers that gave birth at least once to 2650 children in the non-Salut area. Characteristics of the total sample are given in table 1, and for the longitudinal subsample in appendix table C1. Mothers giving birth to children in the Salut area were on average younger and less educated compared to mothers in the non-Salut area. Missing values varied between measures (appendix tables C2-C3). Information on mother's education was missing for 2.1-2.4 % of the Salut area observations and 1.0-1.1% of the non-Salut area observations. All outcomes at birth exhibited some missingness, with the largest proportion for the smoking variable (10.4% in Salut-area pre). Outcomes during the first two years after birth were all fully observed.

Table 1 Characteristics of the participants in the total sample

	Salut area[a]		Non-Salut area[a]	
	pre[b]	post[b]	pre[b]	post[b]
Participants				
Mothers, n	918	828	6056	5737
Children, n	1003	888	6664	6059
Covariates				
Mother's age (years), M (SD)	29.7 (5.3)	29.7 (5.2)	30.3 (4.9)	30.3 (5.0)
Mother's education, %				
Compulsory school	11.0	11.3	7.5	7.5
Secondary school	51.2	48.1	44.5	36.8
Higher education	37.8	40.6	48.0	55.7
Health outcomes				
Pregnancy, delivery and around the child's birth				
Smoking[c] (yes), %	8.4	5.2	5.3	3.8
Pregnancy length (≥37 weeks), %	92.6	95.0	94.4	94.6
Caesarean section (yes), %	17.2	18.1	16.4	16.4
Birth weight (≥2 500 g), %	94.8	96.9	96.5	96.4
Birth length (cm), M (SD)	50.3 (2.8)	50.3 (2.9)	50.5 (2.5)	50.3 (2.5)
LGA[d] (yes), %	3.6	3.8	4.4	3.4
SGA[e] (yes), %	2.5	2.5	1.7	1.9
Apgar score[f] (≥7 points) at 1 minute, %	95.8	96.3	95.3	94.6
at 5 minutes, %	99.1	99.4	98.7	98.5
at 10 minutes, %	99.7	99.8	99.7	99.6
Healthy child[g] (yes), %	79.3	81.1	77.8	79.2
Mother's inpatient care[h] (days), M (SD)	3.7 (2.8)	3.1 (2.0)	3.6 (2.6)	2.9 (2.2)
During the first two years after the child's birth				
Mother with early inpatient care[i] (yes), %	1.1	2.4	1.8	1.3

Child with early inpatient care[i] (yes), %	6.9	4.2	6.9	4.3
Mother's inpatient care[j] (days), M (SD)	0.4 (2.1)	0.5 (3.2)	0.5 (5.3)	0.5 (4.5)
Child's inpatient care[j] (days), M (SD)	1.9 (12.8)	1.5 (8.2)	1.5 (8.1)	1.4 (9.6)
Mother's outpatient visits[k], M (SD)	0.0 (0.1)	0.0 (0.1)	0.0 (0.1)	0.0 (0.1)
Child's outpatient visits[k], M (SD)	0.0 (0.2)	0.1 (0.4)	0.0 (0.2)	0.1 (0.7)

M – mean; SD – Standard deviation.

[a] Difference-in-difference estimates of the average treatment effect on the treated (ATT) with 95% confidence intervals (CI). CIs and p-values were computed with the assumption that ATT was normally distributed and with a standard deviation equal to the bootstrap standard error.
[b] Simple matching estimates of the average treatment effect on the treated (ATT) with 95% confidence intervals (CI). CIs and p-values were computed with the assumption that ATT was normal distributed and with a standard deviation equal to the Abadie-Imbens standard error.
[c] Smoking status at first antenatal visit, around pregnancy week 12.
[d] Large for gestational age (LGA) – ≥2 SD above the reference population's mean weight.
[e] Small for gestational age (SGA) – ≤2 SD below the reference population's mean weight.
[f] A measure of the newborn's physical condition 1, 5 and 10 minutes after birth, range 0-10.
[g] A healthy child according to a paediatrician's examination.
[h] Mother's inpatient care related to delivery.
[i] Early inpatient care for mother and child, respectively, during the first two months after the child's birth but not related to the delivery.
[j] Cumulative duration of inpatient care for mother and child, respectively, over the child's first two years, excluding care due to delivery complications.
[k] Number of outpatient visits for mother and child, respectively, over the child's first two years, excluding care for the mother due to delivery complications.

Effectiveness analyses

Before conducting the difference-in-difference analyses, observations with missing values on outcome and/or matching variables were excluded. The analytical sample sizes differed between outcomes since exclusion of observations was done separately for each outcome (appendix tables C2-C3). The samples were well balanced before matching, but matching improved the covariate balance and resulted in standardized mean differences [26 27], close to zero for all covariates in all analyses. The difference-in-difference analyses did not result in any significant average treatment effect on the treated estimates. Hence, we conclude that for those individuals who were exposed to the Salut Programme, the Programme had on average no effect on the outcomes studied (table 2).

Before conducting the longitudinal analyses, the subsample of mothers giving birth at least once in each time period in the same area was further reduced in the following manner: for mothers who gave birth to more than one child in the same area at premeasure, observations from this period not

relating to the last birth in that area and period were excluded. Analogously, if there were multiple births in the same area at postmeasure, observations from this period not relating to the first birth in that area and period were excluded. These exclusions were performed so that the variables at premeasure could be used as baseline variables to match on. Due to multiple births in the same area and period, observations were excluded from Salut area post (6), Salut area pre (9), non-Salut area post (49), and non-Salut area pre (103). Finally, observations with missing values on outcome and/or covariates were excluded as in the difference-in-difference analyses (appendix tables C4-C5). Matching improved the covariate balance and resulted in standardized mean differences close to zero for all covariates. The longitudinal analyses resulted in significant positive average treatment effect on the treated estimates for the outcomes Apgar at 1 and 5 minutes (table 2).

We conclude that for those who were exposed to the Salut Programme, in the subpopulation of mothers giving birth at least twice, there were 3% (95% CI: 2-4%) more births with high Apgar at 1 minute compared to what would have been the case had they not been exposed to the Programme. Similarly, there were 1% (95% CI: 0.5-2%) more births with high Apgar at 5 minutes compared to what would have been the case had they not been exposed to the Salut Programme. For our sample, this translates to 3.6 and 1.2 additional children having high Apgar at 1 and 5 minutes, respectively. The results for the other outcomes showed no significant effects.

Table 2 Results of the effectiveness study, total sample and longitudinal subsample

Health outcomes	**Total sample**		**Longitudinal subsample**	
	ATT (95% CI)[a]	**p-value**	**ATT (95% CI)[b]**	**p-value**
Pregnancy, delivery and around the child's birth				
Smoking[c] (yes)	-0.02 (-0.05, 4e-03)	0.09	-0.02 (-0.06, 0.01)	0.11
Pregnancy length (≥37 weeks)	0.02 (3e-04, 0.04)	0.08	0.02 (0.02, 0.05)	0.34
Caesarean section (yes)	0.01 (-0.03, 0.05)	0.66	-4e-05 (-0.04, 0.04)	1.00
Birth weight (≥2500 g)	0.02 (-6e-04, 0.05)	0.06	0.01 (-8e-03, 0.03)	0.22
Birth length (cm)	0.11 (-0.19, 0.41)	0.47	0.10 (-0.31, 0.51)	0.63
LGA[d] (yes)	0.01 (-0.01, 0.03)	0.30	0.01 (-0.04, 0.05)	0.73
SGA[e] (yes)	-4e-03 (-0.02, 0.02)	0.72	-0.01 (-0.02, -4e-03)	0.01

Apgar score[f] (≥7 points) at 1 minute	0.02 (-2e-03, 0.04)	0.07	*0.03 (0.02, 0.04)*	*4e-12***
at 5 minutes	5e-03 (-0.01, 0.02)	0.34	*0.01 (5e-03, 0.02)*	*9e-05***
at 10 minutes	1e-03 (-4e-03, 7e-03)	0.61	2e-03 (-6e-04, 4e-03)	0.15
Healthy child[g] (yes)	0.01 (-0.04, 0.05)	0.81	0.01 (-0.06, 0.08)	0.73
Mother's inpatient care[h] (days)	-4e-03 (-0.26, 0.25)	0.98	-0.04 (-0.43, 0.34)	0.82
During the first two years after the child's birth				
Mother with early inpatient care[i] (yes)	0.02 (7e-03, 0.03)	3e-03	0.01 (-0.01, 0.04)	0.26
Child with early inpatient care[i] (yes)	0.01 (-0.01, 0.03)	0.44	-3e-04 (-0.03, 0.03)	0.98
Mother's inpatient care[j] (days)	0.08 (-0.25, 0.40)	0.64	-0.28 (-0.53, -0.04)	0.02
Child's inpatient care[j] (days)	-0.17 (-1.33, 0.99)	0.77	0.37 (-1.03, 1.77)	0.60
Mother's outpatient visits[k]	1e-03 (-0.01, 0.01)	0.86	-0.01 (-0.03, 0.01)	0.19
Child's outpatient visits[k]	0.02 (-0.02, 0.05)	0.40	-2e-03 (-0.04, 0.03)	0.92

[a] Difference-in-difference estimates of the average treatment effect on the treated (ATT) with 95% confidence intervals (CI). CIs and p-values were computed with the assumption that ATT was normally distributed and with a standard deviation equal to the bootstrap standard error.

[b] Simple matching estimates of the average treatment effect on the treated (ATT) with 95% confidence intervals (CI). CIs and p-values were computed with the assumption that ATT was normal distributed and with a standard deviation equal to the Abadie-Imbens standard error.

[c] Smoking status at first antenatal visit, around pregnancy week 12.

[d] Large for gestational age (LGA) – ≥2 SD above the reference population's mean weight.

[e] Small for gestational age (SGA) – ≤2 SD below the reference population's mean weight.

[f] A measure of the newborn's physical condition 1, 5 and 10 minutes after birth, range 0-10.

[g] A healthy child according to a paediatrician's examination.

[h] Mother's inpatient care related to delivery.

[i] Early inpatient care for mother and child, respectively, during the first two months after the child's birth but not related to the delivery.

[j] Cumulative duration of inpatient care for mother and child, respectively, over the child's first two years, excluding care due to delivery complications.

[k] Number of outpatient visits for mother and child, respectively, over the child's first two years, excluding care for the mother due to delivery complications.

*Statistically significant effect at the α=0.05 level after a Bonferroni correction for multiple comparisons, i.e. with the 38 outcome variables this implies a significance threshold of 0.05/38=0.001.

**Statistically significant effect at the α=0.01 level after a Bonferroni correction for multiple comparisons, i.e. with the 38 outcome variables this implies a significance threshold of 0.01/38=0.00026.

1

Intervention costs

The total cost of the Salut Programme was INT$ 273 063 (2 379 260 SEK). Averaged over the 888 children born in the Salut area at postmeasure gives a cost of INT$ 308 (2 679 SEK) per child. The largest cost components were staff (64%), and the opportunity cost of professionals' time to attend the learning seminars (16%) (appendix table D1). Of the total, 28% were start-up costs incurred during 2005-2007. The average annual implementation cost was INT$ 43 575 (379 677 SEK; averaged over 66 months).

Healthcare and other societal costs

The differences in mean healthcare costs and productivity losses between pre- and postmeasure for the Salut and the non-Salut area for the longitudinal subsample (n=1289) are shown in table 3. Healthcare costs were lower in the Salut area due to less inpatient care for both mothers and children. Healthcare costs were lower at postmeasure compared to premeasure in both areas, and although the decrease over time was slightly larger in the Salut area compared to the non-Salut area, the difference was not statistically significant.

Productivity losses increased in the non-Salut area from pre- to postmeasure (+INT$ 29; p=0.03), but remained unchanged in the Salut area, which explains the difference in productivity losses over time in the Salut area compared to the non-Salut area (-INT$ 31 per child; p= 0.38). Adding up healthcare costs and productivity losses, total costs (excluding intervention costs) were INT$ 1556 lower at postmeasure than at premeasure in the Salut area, and INT$ 1127 lower at postmeasure than at premeasure in the non-Salut area. Hence, total costs fell by INT$ 430 more per person in the Salut area compared to the non-Salut area (p=0.97). Analyses of healthcare costs and productivity losses for the total sample are found in the appendix table E2.

Table 3 Mean healthcare costs and productivity losses for the longitudinal sub-sample (2013 INT$)[a]

	Salut[b]		Difference Salut post-pre[d]		Non-Salut[b]		Difference Non-Salut post-pre[e]		Incremental costs Salut vs. Non-Salut[f]	
Costs	**pre[c]**	**post[c]**		**p-value***	**pre[c]**	**post[c]**		**p-value***		**p-value**
Intervention cost per child		308	308							
Children, n	121	121			1 168	1 168				
Healthcare costs, M (SD)										
Pregnancy, delivery and around the child's birth										
Delivery	5767 (979)	5842 (1063)	76 (131)	p=0.70	5855 (1072)	5894 (1110)	39 (45)	p=0.41	36 (147)	p=0.81
During the first two years after the child's birth										
Mother's inpatient care	604 (3089)	605 (2547)	1 (364)	p=1.00	1100 (8396)	1822 (15 637)	722 (519)	p=0.18	-721 (1618)	p=0.60
Child's inpatient care	10 773 (50 242)	9142 (43 492)	-1631 (6041)	p=0.82	15 245 (98 078)	13 331 (143 972)	-1914 (5097)	p=0.75	283 (15 960)	p=0.98
Mother's outpatient care	3 (28)	3 (28)	0 (4)	p=1.00	4 (36)	5 (40)	2 (2)	p=0.27	-2 (5)	p=0.75
Child's outpatient care	8 (49)	8 (50)	0 (6)	p=1.00	14 (97)	11 (64)	-4 (3)	p=0.28	4 (11)	p=0.68

Total healthcare costs	**17 154 (50 535)**	**15 599 (43 666)**	**-1555 (6072)**	**p=0.83**	**22 219 (98 650)**	**21 063 (144 736)**	**-1156 (5125)**	**p=0.86**	**-399 (16 048)**	**p=0.97**
Productivity losses, M (SD)										
During the second year after the child's birth										
Mother's outpatient care	2 (21)	2 (21)	0 (3)	p=1.00	2 (20)	2 (21)	0 (1)	p=1.00	0 (3)	p=0.94
Mother's inpatient care	17 (98)	15 (104)	-2 (13)	p=0.90	20 (170)	48 (440)	29 (14)	*p=0.03**	-31 (43)	p=0.38
Total productivity losses	**19 (99)**	**17 (106)**	**-2 (13)**	**p=1.00**	**21 (172)**	**50 (441)**	**29 (14)**	***p=0.02****	**-31 (43)**	**p=0.38**
Total healthcare costs + productivity losses	**17 173 (50 538)**	**15 616 (43 670)**	**-1556 (6072)**	**p=0.83**	**22 240 (98 660)**	**21 113 (144 768)**	**-1127 (5126)**	**p=0.85**	**-430 (16 051)**	**p=0.97**

*Statistical significance defined as p<0.05.

[a] Results expressed in 2013 purchasing-power parity adjusted international dollars (1 INT$=8.71 SEK).

[b] Salut area – Geographical area in Västerbotten county where the Salut Programme was implemented prior to 2009; Non-Salut area – remaining part of Västerbott county. Several of the health outcomes are further described in table 1.

[c] Premeasure period – 2002-2004; postmeasure period – 2006-2008.

[d] P-values are based on permutation tests of the difference in means between Salut post and Salut pre.

[e] P-values are based on permutation tests of the difference in means between Non-Salut post and N Salut pre.

[f] P-values are based on permutation tests of the difference in means between Salut and Non-Salut over time, i.e. the difference in means between Non-Salut post and Non-Salut pre subtracted from the difference in means between Salut post and Salut pre.

Cost-effectiveness analysis

Both Apgar at 1 and 5 minutes showed statistically significant differences between Salut and non-Salut areas in the longitudinal analysis. Previous studies suggest that a low Apgar score at 5 minutes correlates with neonatal mortality and confers an increased risk of neurologic disability and cognitive impairment [28-30]. In contrast, Apgar at 1 minute is not a good predictor of infant outcomes [31]. Hence, we considered Apgar at 5 minutes as the only relevant outcome in the cost-effectiveness analysis. Deterministic cost-effectiveness was expressed as the cost per low-Apgar case prevented. The cost-effectiveness results for both costing perspectives are given in table 4. From a healthcare perspective, the Salut Programme yielded higher effects and higher costs than care-as-usual (non-Salut), with an ICER of INT$ 2063 per low-Apgar case prevented, and a 47.4% probability of being cost-saving and entailing positive effects. From a limited societal perspective, the Salut Programme also yielded higher effects and higher costs than care-as-usual, with an ICER of INT$ 16 870 per low-Apgar case prevented, and a 44.7% probability of being cost-saving and entailing positive effects. We estimated the number needed to treat to prevent one case with low Apgar by dividing one by the absolute risk reduction between Salut and non-Salut (0.019); 52 mothers would need to be exposed to the Salut Programme to prevent one case of low Apgar.

Table 4 Results of the cost-effectiveness study, longitudinal sub-sample (costs in 2013 INT$)

	Salut area[a]				Non-Salut area[a]						
	Average cost post-pre[b, c] M (SD)		Average proportion of low Apgar[d] cases prevented post-pre M (SD)		Average cost post-pre M (SD)		Average proportion of low Apgar cases prevented post-pre M (SD)		Bootstrapped Incremental costs	Bootstrapped Incremental effects	ICER (95% CI)
	Base-case	Bootstrap	Base-case	Bootstrap	Base-case	Boot-strap	Base-case	Boot-strap			
Healthcare perspective	-1247 (66 657.78)	-1199.29 (5821.97)	0.016 (0.128)	0.016 (0.011)	-1155.75 (176 066.52)	-1240.12 (5243.67)	- 0.003 (0.149)	-0.003 (0.004)	41	0.020	2063 (dominant[e] - 312 910)
Limited societal perspective	-1248.87 (66 667.67)	-805.79 (5893.79)	0.016 (0.128)	0.015 (0.011)	-1126.69 (176 099.98)	-1126.36 (5142.54)	- 0.003 (0.149)	-0.003 (0.004)	321	0.019	16 870 (dominant[e,f] - 324 697)

ICER – Incremental cost-effectiveness ratio; CI – Confidence interval.

[a] Salut area – Geographical area in Västerbotten county where the Salut Programme was implemented from 2006 and onwards; non-Salut area – remaining part of Västerbotten county. Several of the health outcomes are further described in Table 1.

[b] Premeasure period – 2002-2004; postmeasure period – 2006-2008.

[c] The average cost per participant includes intervention costs and resource use costs

[d] Apgar at 5 minutes – a measure of the newborn's physical condition at 5 minutes after birth, range 0-10 points.

[e] The intervention is less costly and more effective than the comparator (dominant).

[f] 3% of the observations have negative effects and negative costs and fall on the south-west quadrant of the cost-effectiveness plane.

Figure E1 in the appendix presents the cost-effectiveness results on a cost-effectiveness plane for both costing perspectives. Most of the bootstrapped estimates of incremental costs and effects fall in the south-east and the north-east quadrants of the plane, with the Salut Programme having both a likelihood of being cost-saving (dominant, i.e. less costly and more effective than the comparator) and more costly and more effective than the comparator. This reflects the relatively large uncertainty around the cost and the cost-effectiveness estimates.

Discussion

Main study findings and comparison with other studies

Our results suggest that the Salut Programme may be an effective universal health promotion intervention to improve maternal and child health, and is likely to represent good value for money. The difference-in-difference analyses did not show significant improvements in health outcomes, but suggested changes in a positive direction. However, the longitudinal analyses resulted in a significant positive improvement in Apgar scores, reflecting the newborn's physical condition, with more children having a normal Apgar score (1 minute +3%, and 5 minutes +1%). The cost added by the Programme to care-as-usual was small, INT$ 308, representing only 4% of the average health care cost for the pregnancy, delivery and neonatal periods per woman/child, INT$ 7945 [32]. From both a healthcare and a limited societal perspective, the Programme yielded higher effects and higher costs than care-as-usual, with ICERs of INT$ 2063 and INT$ 16 870, respectively, per prevented case (child with low 5 minute Apgar score). The Programme has a 45% probability of being cost-saving and entailing positive effects.

Our study contributes to this limited evidence base regarding universal multi-sectorial health promotion approaches during pregnancy and early childhood. We are aware of only a few evaluations of the effectiveness and cost-effectiveness of such interventions. The universal parenting programme "All Children in Focus", offered to parents of children aged 3 and above, showed a positive effect on parental self-efficacy and child health [33]. However, the programme had a low probability of cost-effectiveness [34]. Another study of a nurse-led intensive home visiting programme for first-time teenage mothers found no short-term benefits concerning the selected primary outcomes [35].

Strengths and weaknesses of the study

We evaluated the Salut Programme as it was implemented in current practice, which increases the external validity and generalizability of the results. The use of existing register data, in which exposure

and outcomes have been routinely collected [12], reduces the amount of missing data. The "state of the art" methods used in the effectiveness analyses, which do not require strong assumptions regarding the data generating mechanisms, allowed us to identify the differential effect of the Programme on children and mothers born in Salut versus non-Salut areas in a natural experiment [36].

While intention-to-treat [13] was the only feasible approach, we may have underestimated the intervention effects. We controlled for mothers' age and education using matching as well as the premeasure value of the outcome in the longitudinal analyses. However, we are aware of the risk for residual confounding. In estimating intervention costs, opportunity costs of parents' or professionals' time were not considered, since professionals were expected to integrate the Programme interventions within care-as-usual. There might have been an initial learning period during when visits took longer than usual, and we may have underestimated the set-up costs due to limitations of the retrospective study design.

As the Programme is a universal health promotion intervention, medical outcome measures were not expected to show significant effects. However, our analyses were limited to data available in registers. In particular, we lacked access to data on primary care visits and medication as well as on lifestyle and health-related quality of life. In the cost-effectiveness analyses, the limited societal perspective only included productivity losses due to mothers' inpatient and outpatient care, which might have contributed to the uncertainty in the results. Furthermore, we could only use a clinical health outcome – the number of low-Apgar cases prevented. As there is no established willingness to pay for one prevented case of low-Apgar, it is difficult to estimate pragmatic value for money based on the cost-effectiveness results.

Implications for policy and clinical practice

The Apgar score is a well-established predictive index for neonatal morbidity and mortality in normal-birth weighted infants [37 38]. Low Apgar at 5 minutes is associated with an increased risk of neurological disabilities, such as cerebral palsy. As such, the estimated lifetime cost for a child with cerebral palsy is about INT$ 850 000 [39], which is almost 100 times higher than the cost to prevent one child with low Apgar at 5 minutes shown in our study (ICERs INT$ 2063 and INT$ 16 870). Although there is no study estimating willingness-to-pay for a low Apgar case prevented, the Salut Programme is likely to represent good value for money, given the potential societal cost-savings arising from preventing one case of low Apgar score.

Universal complex interventions implemented in real-life settings, such as the Salut Programme, are scarce and pose challenges with respect to implementation, dissemination and evaluation [40]. The reliability of our results depends on how the Salut Programme was implemented in current praxis. Interviews with professionals suggest that key issues for effective implementation are involvement of professionals in intervention development, regular meetings with professionals and process consultants, and the use of manuals [16]. On the other hand, more resources would likely have improved feasibility by providing professionals with more dedicated time to deliver the interventions. Continuous support from decision-makers is necessary [41] to sustain the effectiveness and cost-effectiveness of an evidence-based intervention, such as the Salut Programme, in the long-term.

Conclusions

Our study suggests that the Salut Programme may be an effective universal intervention to improve maternal and child health, and is likely to represent good value for money. The evaluation of public health interventions, including cost-effectiveness analyses, provides information that can guide decision-makers to allocate resources optimally.

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Contributors

The statistical analyses were carried out by JH, and the economic evaluation by FS, AMPB and IF. AI and IF conceived and designed the study. EE, ML and AI constitute the scientific steering group for the Salut Programme, and AI is principal investigator for the Umeå SIMSAM Lab, both prerequisites for the present study. All the authors (JH, FS, EE, AMPB, AI, ML and IF) contributed to the writing process and have approved the final manuscript.

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Competing interests

None declared.

Ethics approval

The Regional Ethical Review Board in Umeå gave clearance for the Salut Programme research (2010-63-31M) and for the Umeå SIMSAM Lab research (2010-157-31Ö).

Data sharing statement

No additional data are available.

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List of tables and figures

Appendix A The Swedish Salut child health intervention programme

Table A1 Västerbotten County Council's vision and the Salut Programme's aims and focus areas

Vision, aims, focus areas	Content
Vision	By 2020, the health and wellbeing of the population will be the best in the world.
Overall aim	Good health is achieved by salutogenic interventions in collaboration with societal actors and the family with the child's best in focus. Through systematic improvements, interventions are developed and implemented to promote satisfactory conditions during childhood, increased physical activity, and healthy eating habits.
Main focus areas	To promote healthy eating habits, physical activity and good psychosocial health, and to prevent obesity and caries.
Aims during pregnancy period	Avoidance of maternal and foetal pregnancy complications related to maternal lifestyle. Healthy maternal weight gain during pregnancy. A minimum of 30 minutes daily physical activity. Regular meals. Five fruits and vegetables a day. Tooth-brushing twice a day with fluoride toothpaste. Regular dental health care visits. Parents are feeling prepared for their parental roles. Pregnant women are living in relations free from intimate partner violence. Pregnant women refrain from tobacco, alcohol and drug use.
Aims for parents and children 0-18 months	Normal weight development for 18-month olds. Retain of pre-pregnancy weight. Sufficient sleep (parents and children). Environments free from tobacco and drug use, and alcohol use is limited. A minimum of one hour daily physical activity (play) for children. A minimum of 30 minutes daily physical activity for parents. Avoidance of TV-viewing and TV/computer games for children. Six months exclusive breastfeeding, and thereafter partly continued for 1 year or longer. Introduction of 5 fruits and vegetables a day for children. Five fruits and vegetables a day for parents. Regular meals for both parents and children. Avoidance of discretionary foods for children. Tooth-brushing twice a day with fluoride toothpaste (from the first tooth for the children). Regular dental health care visits. Parents feel confident in their parental roles. Satisfying parental-child attachment and interaction. Women/children live in an environment free from violence and violation.

Table A2 Care-as-usual and the Salut Programme's interventions targeting parents-to-be and their children during pregnancy and until the child is 18 months, and significant changes in professionals' practices post Salut implementation

Care-as-usual	**Arena**
Maternal and foetal surveillance (7-9 check-ups)	ANC
Psychosocial- and lifestyle counselling	ANC, CHC
Participation in parental support groups	ANC, CHC
Health and development check-ups, and immunizations (about 10 visits when the child is 0-18 months, and more often when needed)	CHC
Advice on teeth brushing twice a day	CHC, DHC
Oral health check-up and health promoting advice (child age 2-3 years)	DHC
Socialization at open preschools for children not yet enrolled in regular preschools and their parents	OPS
The Salut Programme	**Arena**
Strengthening or restructuring of 'care-as-usual'	
Motivational Interviewing (MI)	ANC, CHC*, DHC
Collaboration between any of involved sectors	ANC*, CHC*
Involvement in parental support groups	ANC, CHC
Lifestyle counselling	ANC, CHC*, DHC*
Edinburgh Postnatal Depression Scale (EPDS) at "mother's visit" (Child age 8 weeks)	ANC
Activities to enhance early parent-child attachment, parent relation-ships, children's physical activity and linguistic development	CHC, OPS
Activities to promote healthy snacks/food and drinks	OPS*
Activities to encourage physical activity	OPS
The Salut Programme specific interventions	
Questionnaires for health surveillance	ANC, CHC, DHC
Free dental health counselling for the parents-to-be	DHC
Collaboration between any of involved sectors	DHC*, OPS*
Contribution to parental support groups	DHC, OPS
Questions for domestic violence during pregnancy and at "mother's visit" (child age 8 weeks)	ANC*, CHC*
Focus on fathers' experiences of change in life situation at "father's visit" (child age 10 months)	CHC*
Oral health investigation (child age 12 months)	DHC

ANC- Antenatal Care; CHC- Child Health Care; DHC- Dental Health Care; OPS- Open Pre-Schools.
*Significant changes in professionals' practices pre- and 6 months' post-implementation ($p \leq 0.01$) according to.[1].

Appendix B Effectiveness analysis strategies

Matching strategy

In the difference-in-difference analyses exact matching was imposed on the categorical covariate (education) and caliper matching was used to find matches on age. A caliper of 0.6 was used which means that an observation is considered a match if it is equal to or within 0.6 sample standard deviations of the matching variable. For example, if the age sample standard deviation is 5 in the Salut area at postmeasure then a matching observation from one of the other three groups would have the same level of education and be within 3 years of the age of the considered observation in the Salut area at postmeasure. The reason for using caliper matching instead of exact matching is that it can be difficult to find exact matches on covariates that are not categorical. Using a caliper means that we avoid dropping observations due to no exact matches. In cases where there were tied matches, i.e., several observations matching the birth in Salut area at postmeasure, a weighted average of the outcomes from the tied observations was used. Matching was done "with replacement", i.e. the same observation could be used as a match for more than one observation in the Salut area at postmeasure. In the longitudinal subsample, for each birth in the Salut area at premeasure, a matching observation was found among the births in the non-Salut area at premeasure. An observation was considered a match if it, in the premeasure period, had similar values on the outcome variable as well as on mother's level of education and age. Matching was otherwise performed analogously to the difference-in-difference analysis.

Standard error computation

In the difference-in-difference analyses bootstrap estimates of the standard error was computed using ordinary non-parametric bootstrapping. Specifically, 1000 bootstrap samples were constructed by sampling with replacement from the original sample and, following the procedure described above, a difference-in-difference estimate was computed for each bootstrap sample. The estimated standard error was taken as the sample standard deviation of the 1000 bootstrap difference-in-difference estimates. Using the difference-in-difference estimate based on the original sample and the bootstrap estimated standard error, confidence intervals and p- values were computed under the assumption that the distribution of the difference-in-difference estimator could be approximated by a normal distribution. In the longitudinal analyses standard errors were computed according to Abadie and Imbens (2006). Using the simple matching estimate and the estimated Abadie-Imbens standard error, confidence intervals and p-values were computed under the assumption that the distribution of the simple matching estimator could be approximated by a normal distribution.

Appendix C Characteristics of the study population and analytical samples

Table C1 Characteristics of the participants in the longitudinal subsample

	Salut area[a]		Non-Salut area[a]	
	pre[b]	post[b]	pre[b]	post[b]
Participants				
Mothers, n	147	147	1249	1249
Children, n	156	153	1352	1298
Covariates				
Mother's age (years), M (SD)	27.6 (4.0)	31.8 (4.1)	28.3 (4.2)	32.1 (4.2)
Mother's education, %				
Compulsory school	9.3	9.9	7.4	6.3
Secondary school	53.3	51.3	43.5	41.4
Higher education	37.3	38.8	49.0	52.4
Health outcomes				
Pregnancy, delivery and around the child's birth				
Smoking[c] (yes), %	4.7	2.1	4.3	3.1
Pregnancy length (≥37 weeks), %	91.4	98.0	95.1	96.0
Caesarean section (yes), %	13.7	16.8	14.6	16.1
Birth weight (≥2 500 g), %	91.4	99.3	96.8	97.7
Birth length (cm), M (SD)	49.8 (3.4)	50.7 (2.1)	50.6 (2.5)	50.6 (2.3)
LGA[d] (yes), %	2.2	6.3	3.5	5.3
SGA[e] (yes), %	4.4	1.4	2.0	1.3
Apgar score[f] (≥7 points) at 1 minute, %	95.7	100.0	95.4	96.1
at 5 minutes, %	98.6	100.0	98.8	98.9
at 10 minutes, %	99.3	100.0	99.8	99.8
Healthy child[g] (yes), %	79.1	85.9	78.0	82.9
Mother's inpatient care[h] (days), M (SD)	4.1 (3.1)	2.7 (1.7)	3.7 (2.3)	2.5 (2.1)
During the first two years after the child's birth				
Mother with early inpatient care[i] (yes), %	0.0	2.6	2.1	1.0
Child with early inpatient care[i] (yes), %	5.8	3.3	6.4	3.9
Mother's inpatient care[j] (days), M (SD)	0.2 (0.8)	0.2 (0.6)	0.3 (2.5)	0.4 (3.7)
Child's inpatient care[j] (days), M (SD)	1.6 (5.8)	1.4 (6.9)	1.6 (8.8)	1.3 (12.0)
Mother's outpatient visits[k], M (SD)	0.0 (0.1)	0.0 (0.1)	0.0 (0.2)	0.0 (0.1)
Child's outpatient visits[k], M (SD)	0.0 (0.1)	0.0 (0.2)	0.0 (0.3)	0.0 (0.2)

M – mean; SD – Standard deviation.

[a] Salut area – Geographical area in Västerbotten county where the Salut Programme was implemented from 2006 and onwards; non-Salut area – remaining part of Västerbotten county.

[b] Premeasure period 2002-2004; postmeasure period 2006-2008.

[c] Smoking status at first antenatal visit, around pregnancy week 12.

[d] Large for gestational age (LGA) – ≥2 SD above the reference population's mean weight.

[e] Small for gestational age (SGA) – ≤2 SD below the reference population's mean weight.

[f] A measure of the newborn's physical condition 1, 5 and 10 minutes after birth, range 0-10 points.

[g] A healthy child according to a paediatrician's examination.
[h] Mother's inpatient care related to delivery.
[i] Early inpatient care for mother and child, respectively, during the first two months after the child's birth, but not related to the delivery.
[j] Cumulative duration of inpatient care for mother and child, respectively, over the child's first two years, excluding care due to delivery complications.
[k] Number of outpatient visits for mother and child, respectively, over the child's first two years, excluding care for the mother due to delivery complications.

Table C2 Number of observations with missing values in the total sample

	Salut area[a]		Non-Salut area[a]	
	pre[b]	post[b]	pre[b]	post[b]
Covariates				
Mother's age (years)	0	0	0	0
Mother's education (compulsory/secondary/higher)	24	19	67	67
Health outcomes				
Pregnancy, delivery and around the child's birth				
Smoking[c] (yes)	115	49	584	304
Pregnancy length (≥37 weeks)	63	20	257	137
Caesarean section (yes)	63	20	257	136
Birth weight (≥2 500 g)	63	21	262	139
Birth length (cm)	67	22	282	162
LGA[d] (yes)	91	41	440	273
SGA[e] (yes)	91	41	440	273
Apgar score[f] (≥7) at 1 minute	68	25	287	168
at 5 minutes	68	25	289	174
at 10 minutes	75	31	397	272
Healthy child[g] (yes)	63	20	257	136
Mother's inpatient care[h] (days)	0	0	0	0
During the first two years after the child's birth				
Mother with early inpatient care[i] (yes)	0	0	0	0
Child with early inpatient care[i] (yes)	0	0	0	0
Mother's inpatient care[j] (days)	0	0	0	0
Child's inpatient care[j] (days)	0	0	0	0
Mother's outpatient visits[k]	0	0	0	0
Child's outpatient visits[k]	0	0	0	0

[a] Salut area – Geographical area in Västerbotten county where the Salut Programme was implemented from 2006 and onwards; non-Salut area – remaining part of Västerbotten county.

[b] Premeasure period 2002-2004; postmeasure period 2006-2008.

[c] Smoking status at first antenatal visit, around pregnancy week 12.

[d] Large for gestational age (LGA) – ≥2 SD above the reference population's mean weight.

[e] Small for gestational age (SGA) – ≤2 SD below the reference population's mean weight.

[f] A measure of the newborn's physical condition 1, 5 and 10 minutes after birth, range 0-10 points.

[g] A healthy child according to a paediatrician's examination.

[h] Mother's inpatient care related to delivery.

[i] Early inpatient care for mother and child, respectively, during the first two months after the child's birth but not related to the delivery.

[j] Cumulative duration of inpatient care for mother and child, respectively, over the child's first two years, excluding care due to delivery complications.

[k] Number of outpatient visits for mother and child, respectively, over the child's first two years, excluding care for the mother due to delivery complications.

Table C3 Number of observations with missing values in the longitudinal subsample

	Salut[a] area		Non-Salut[a] area	
	pre[b]	post[b]	pre[b]	post[b]
Covariates				
Mother's age (years)	0	0	0	0
Mother's education (compulsory/secondary/higher)	6	1	8	3
Health outcomes				
Pregnancy, delivery and around the child's birth				
Smoking[c] (yes)	27	8	118	73
Pregnancy length (≥37 weeks)	17	4	57	21
Caesarean section (yes)	17	4	57	21
Birth weight (≥2 500 g)	17	5	58	21
Birth length (cm)	17	5	64	23
LGA[d] (yes)	21	9	71	49
SGA[e] (yes)	21	9	71	49
Apgar score[f] (≥7) at 1 minute	18	5	59	30
at 5 minutes	18	5	59	31
at 10 minutes	19	6	81	59
Healthy child[g] (yes)	17	4	57	21
Mother's inpatient care[h] (days)	0	0	0	0
During the first two years after the child's birth				
Mother with early inpatient care[i] (yes)	0	0	0	0
Child with early inpatient care[i] (yes)	0	0	0	0
Mother's inpatient care[j] (days)	0	0	0	0
Child's inpatient care[j] (days)	0	0	0	0
Mother's outpatient visits[k]	0	0	0	0
Child's outpatient visits[k]	0	0	0	0

[a] Salut area – Geographical area in Västerbotten county where the Salut Programme was implemented from 2006 and onwards; non-Salut area – remaining part of Västerbotten county.
[b] Premeasure period 2002-2004; postmeasure period 2006-2008.
[c] Smoking status at first antenatal visit, around pregnancy week 12.
[d] Large for gestational age (LGA) – ≥2 SD above the reference population's mean weight.
[e] Small for gestational age (SGA) – ≤2 SD below the reference population's mean weight.
[f] A measure of the newborn's physical condition 1, 5 and 10 minutes after birth, range 0-10 points.
[g] A healthy child according to a paediatrician's examination.
[h] Mother's inpatient care related to delivery.
[i] Early inpatient care for mother and child, respectively, during the first two months after the child's birth, but not related to the delivery.
[j] Cumulative duration of inpatient care for mother and child, respectively, over the child's first two years, excluding care due to delivery complications.
[k] Number of outpatient visits for mother and child, respectively, over the child's first two years, excluding care for the mother due to delivery complications.

Table C4 Exclusions and final analytical sample sizes in difference-in-difference analyses

		Exclusions due to missingness	Eligible for matching	Used for matching
Health outcomes				
Pregnancy, delivery and around the child's birth				
Smoking[c] (yes)	Salut[a] pre[b]	135	868	866
	Salut[a] post[b]	62	826	826
	Non-Salut[a] pre[b]	629	6 035	5 985
	Non-Salut[a] post[b]	354	5 705	5 653
Pregnancy length (≥37 weeks)	Salut pre	84	919	916
	Salut post	34	854	854
	Non-Salut pre	303	6 361	6 310
	Non-Salut post	189	5 870	5 820
Caesarean section (yes)	Salut pre	84	919	916
	Salut post	34	854	854
	Non-Salut pre	303	6 361	6 310
	Non-Salut post	188	5 871	5 821
Birth weight (≥2 500 g)	Salut pre	84	919	916
	Salut post	35	853	853
	Non-Salut pre	308	6 356	6 305
	Non-Salut post	191	5 868	5 818
Birth length (cm)	Salut pre	88	915	912
	Salut post	36	852	852
	Non-Salut pre	328	6 336	6 285
	Non-Salut post	214	5 845	5 795
LGA[d] (yes)	Salut pre	118	885	882
	Salut post	55	833	833
	Non-Salut pre	486	6 178	6 127
	Non-Salut post	325	5 734	5 688
SGA[e] (yes)	Salut pre	118	885	882
	Salut post	55	833	833
	Non-Salut pre	486	6 178	6 127
	Non-Salut post	325	5 734	5 688
Apgar score[f] (≥7) at 1 minute	Salut pre	89	914	911
	Salut post	39	849	849
	Non-Salut pre	333	6 331	6 280
	Non-Salut post	219	5 840	5 790
at 5 minutes	Salut pre	89	914	911
	Salut post	39	849	849
	Non-Salut pre	335	6 329	6 278
	Non-Salut post	225	5 834	5 784
at 10 minutes	Salut pre	96	907	904

	Salut post	45	843	843
	Non-Salut pre	442	6 222	6 174
	Non-Salut post	322	5 737	5 690
Healthy child[g] (yes)	Salut pre	84	919	912
	Salut post	34	854	854
	Non-Salut pre	303	6 361	6 310
	Non-Salut post	188	5 871	5 821
Mother's inpatient care[h] (yes)	Salut pre	24	979	976
	Salut post	19	869	869
	Non-Salut pre	67	6 597	6 545
	Non-Salut post	67	5 992	5 942
During the first two years after the child's birth				
Mother with early inpatient care[i] (yes)	Salut pre	24	979	976
	Salut post	19	869	869
	Non-Salut pre	67	6 597	6 545
	Non-Salut post	67	5 992	5 942
Child with early inpatient care[i] (yes)	Salut pre	24	979	976
	Salut post	19	869	869
	Non-Salut pre	67	6 597	6 545
	Non-Salut post	67	5 992	5 942
Mother's inpatient care[j] (days)	Salut pre	24	979	976
	Salut post	19	869	869
	Non-Salut pre	67	6 597	6 545
	Non-Salut post	67	5 992	5 942
Child's inpatient care[j] (days)	Salut pre	24	979	976
	Salut post	19	869	869
	Non-Salut pre	67	6 597	6 545
	Non-Salut post	67	5 992	5 942
Mother's outpatient visits[k]	Salut pre	24	979	976
	Salut post	19	869	869
	Non-Salut pre	67	6 597	6 545
	Non-Salut post	67	5 992	5 942
Child's outpatient visits[k]	Salut pre	24	979	976
	Salut post	19	869	869
	Non-Salut pre	67	6 597	6 545
	Non-Salut post	67	5 992	5 942

[a] Salut area – Geographical area in Västerbotten county where the Salut Programme was implemented from 2006 and onwards; non-Salut area – remaining part of Västerbotten county.
[b] Premeasure period 2002-2004; postmeasure period 2006-2008.
[c] Smoking status at first antenatal visit, around pregnancy week 12.
[d] Large for gestational age (LGA) – ≥2 SD above the reference population's mean weight.
[e] Small for gestational age (SGA) – ≤2 SD below the reference population's mean weight.
[f] A measure of the newborn's physical condition 1, 5 and 10 minutes after birth, range 0-10 points.
[g] A healthy child according to a paediatrician's examination.

[h] Mother's inpatient care related to delivery.
[i] Early inpatient care for mother and child, respectively, during the first two months after the child's birth, but not related to the delivery.
[j] Cumulative duration of inpatient care for mother and child, respectively, over the child's first two years, excluding care due to delivery complications.
[k] Number of outpatient visits for mother and child, respectively, over the child's first two years, excluding care for the mother due to delivery complications.

Table C5 Exclusions and final analytical sample sizes in the longitudinal subsample analyses

		Exclusions due to missingness	Eligible for matching	Used for matching	No matches found
Health outcomes					
Pregnancy, delivery and around the child's birth					
Smoking[c] (yes)	Salut[a]	36	111	111	0
	Non-Salut[a]	148	1 101	963	
Pregnancy length (≥37 weeks)	Salut	24	123	123	0
	Non-Salut	72	1 177	957	
Caesarean section (yes)	Salut	24	123	123	0
	Non-Salut	72	1 177	967	
Birth weight (≥2 500g)	Salut	25	122	121	1
	Non-Salut	72	1 177	984	
Birth length (cm)	Salut	25	122	121	1
	Non-Salut	79	1 170	439	
LGA[d] (yes)	Salut	28	119	119	0
	Non-Salut	91	1 158	965	
SGA[e] (yes)	Salut	28	119	117	2
	Non-Salut	91	1 158	971	
Apgar score[f] (≥7) at 1 minute	Salut	26	121	120	1
	Non-Salut	81	1 168	957	
at 5 minutes	Salut	26	121	120	1
	Non-Salut	82	1 167	1 048	
at 10 minutes	Salut	28	119	118	1
	Non-Salut	127	1 122	1 017	
Healthy child[g] (yes)	Salut	24	123	123	0
	Non-Salut	72	1 177	911	
Mother's inpatient care[h] (yes)	Salut	5	142	137	5
	Non-Salut	7	1 242	605	
During the first two years after the child's birth					
Mother with early inpatient care[i] (yes)	Salut	5	142	142	0
	Non-Salut	7	1 242	1 135	
Child with early inpatient care[i] (yes)	Salut	5	142	142	0
	Non-Salut	7	1 242	1 104	
Mother's inpatient care[j] (days)	Salut	5	142	141	1
	Non-Salut	7	1 242	1 081	
Child's inpatient care[j] (days)	Salut	5	142	141	1
	Non-Salut	7	1 242	972	
Mother's outpatient visits[k]	Salut	5	142	142	0
	Non-Salut	7	1 242	1 145	
Child's outpatient visits[k]	Salut	5	142	142	0
	Non-Salut	7	1 242	1 076	

[a] Salut area – Geographical area in Västerbotten county where the Salut Programme was implemented from 2006 and onwards; non-Salut area – remaining part of Västerbotten county.
[b] Premeasure period 2002-2004; postmeasure period 2006-2008.
[c] Smoking status at first antenatal visit, around pregnancy week 12.
[d] Large for gestational age (LGA) – ≥2 SD above the reference population's mean weight.
[e] Small for gestational age (SGA) – ≤2 SD below the reference population's mean weight.
[f] A measure of the new-borns physical condition 1, 5 and 10 minutes after birth, range 0-10 points.
[g] A healthy child according to a paediatrician's examination.
[h] Mother's inpatient care related to delivery.
[i] Early inpatient care for mother and child, respectively, during the first two months after the child's birth but not related to the delivery.
[j] Cumulative duration of inpatient care for mother and child, respectively, over the child's first two years, excluding care due to delivery complications.
[k] Number of outpatient visits for mother and child, respectively, over the child's first two years, excluding care for the mother due to delivery complications.

Appendix D Intervention costs

Costing methods

We estimated intervention costs as consisting of two main components: Salut Programme costs, and the opportunity cost of professionals to attend the learning seminars. Salut Programme staff consisted of healthcare developers (1-3 people), whose input amounted to 86 person-months, and seven other staff who contributed 10-20 person-months each (change process consultants, a paediatrician, researcher, midwife, dentist, and a statistician). Salut staff salaries and the costs of travel, materials (e.g. manuals, training materials, questionnaires and information leaflets), rent of venues and refreshments were extracted from the accounting system.

The opportunity cost associated with learning seminars was estimated by multiplying the number of attendees in each seminar by daily pay (assuming 8 hours per seminar). Table D1 describes the average hourly pay of professionals and total seminar attendance over 2005-2007. Speakers external to the Salut Programme staff who did not receive financial compensation for their efforts are also included here. Not all seminars were relevant for all professionals, e.g. midwives only attended seminars related to the unborn child. Where the number of attendees was missing, we used the median number of attendees per type of seminar and staff category. Average hourly pay was estimated for each staff category for the years 2005, 2006 and 2007 using average monthly pay for the sex and age group of the average participant from Statistics Sweden [32] to which social security contributions were added [33]. The total time contribution was estimated to equal 2464 hours or approximately 10 person-months.

Table D1 Professionals' seminar attendance and unit costs

Staff category	Hourly pay (INT$)	Total seminar attendance (hours)	Number of attendees (median, per seminar)
Midwife	22	312	4
Child health nurse	27	712	12
Dental hygienist / dental nurse	25	848	5.5
Pre-school teacher	44	200	3
Manager (child health care)	23	192	3
External speakers	29	200	1

Table D2 specifies the allocation rules applied to Salut Programme costs identified in the accounting data. Decision rules by calendar year was the most feasible way to separate between start-up up and intervention costs on the one hand, and between the Salut activities evaluated in this study and other activities on the other hand, because appropriate staff time use information was not available. Start-up costs were annualised over 10 years assuming straight-line depreciation. An equivalent of 4.5 years of annualised start-up costs were included in the total intervention cost, corresponding to the implementation period under study (January 2006-June 2010). In parallel to implementation of the Programme, interventions for older children were being developed. From 2008, Salut staff was preparing to scale up the intervention to the rest of the county.

Table D2 Joint cost allocation rules (%) and division of Salut Programme costs between start-up and implementation

Year	Salut Programme (%)	Interventions for older children (%)	Scale-up of the Salut Programme (%)
2005	100 (start-up)	0	0
2006	60 (of which 1/2 start-up, 1/2 implementation)	40	0
2007	50 (of which 1/3 start-up)	50	0
2008	30 (implementation)	30	40
2009	10 (implementation)	10	80
2010[a]	10 (implementation)	10	80

[a] First six months.

Appendix E Healthcare and other societal costs

Table E1 Unit costs used in costing analysis

Costs	Unit costs (2013 INT$)	Source
Healthcare costs		
Average cost of delivery[a]		Swedish Association of Local Authorities and Regions [2]
Vaginal delivery	5 414	
Caesarean section	8 460	
Average cost mother's inpatient care (per day)[b]	4 119	Swedish Association of Local Authorities and Regions [2]
Average cost child's inpatient care (per day)[c]		Swedish Association of Local Authorities and Regions [2]
<1 year olds	11 610	
1 year olds	5 208	
2 year olds	5 274	
Average cost mother's outpatient care (per visit)[b]	322	Swedish Association of Local Authorities and Regions [2]
Average cost child's outpatient care (per visit)[c]		Swedish Association of Local Authorities and Regions [2]
<1 year olds	312	
1 year olds	333	
2 year olds	335	
Productivity losses		
Mother's average salary (per day)[d]	233	Statistics Sweden [3]

[a] Average cost with and without complications. Each unit cost is weighted by the total number of vaginal deliveries and caesarean sections with or without complications registered in 2013.
[b] Average cost for mothers aged between 18-40 years.
[c] Average cost for males and females in each age group.
[d] Including social charges of 31.42%.

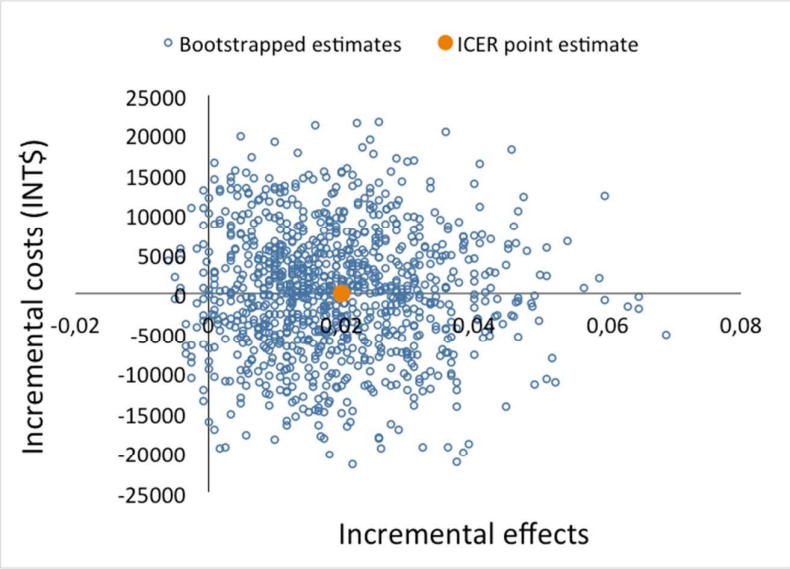
Table E2 Mean healthcare costs and productivity losses for the total sample (2013 INT$)

	Salut[a] pre[b]	Salut post[b]	Non-Salut[a] pre	Non-Salut post	Salut post vs. Salut pre[c]	Non-Salut post vs. Non-Salut pre[d]	Salut v Non-Sa over ti
Children, n	1 003	888	6 664	6 059			
Healthcare costs							
Pregnancy, delivery and around the child's birth							
Delivery[f]	51 443	51 849	51 342	51 414	406	72	
	(9 769)	(10 128)	(9 671)	(9 738)	(458)	(172)	(
					p=0.39	p=0.68	p=(
During the first two years after the child's birth							
Mother's inpatient care	13 581	16 381	179 178	15 925	2 800	-1 993	4
	(74 369)	(114 098)	(186 633)	(158 752)	(4 383)	(3 087)	8 8
					p=0.54	p=0.53	p=(
Child's inpatient care	178 499	131 243	137 163	120 308	-47 256	-16 855	30
	(1 250 316)	(714 282)	(777 528)	(904 385)	(47 636)	(14 917)	42 8
					p=0.36	p=0.26	p=(
Mother's outpatient visits	30	34	37	36	4	-1	
	(287)	(304)	(364)	(317)	(14)	(6)	
					p=0.80	p=0.81	p=(
Child's outpatient visits	85	160	100	139	74	38	
	(509)	(1 219)	(619)	(1 964)	(42)	(25)	
					p=0.05	p=0.08	p=(
Total healthcare costs	**243 639**	**199 667**	**206 561**	**187 822**	**-43 972**	**-18 739**	**25**
	(1 256 313)	**(725 027)**	**(817 517)**	**(919 472)**	**(47 975)**	**(15 400)**	**44 (**
					p=0.41	**p=0.23**	**p=(**
Productivity losses							
During the second year after the child's birth							
Mother's inpatient care	493	422	485	475	-72	-10	
	(3 513)	(4 054)	(6 818)	(6 197)	(174)	(116)	(
					p=0.69	p=0.93	p=(
Mother's outpatient visits	12	16	12	13	4	1	
	(152)	(174)	(158)	(160)	(8)	(3)	
					p=0.78	p=0.83	p=(
Total productivity losses	**505**	**437**	**497**	**488**	**-68**	**-9**	
	(3 538)	**(4 063)**	**(6 843)**	**(6 210)**	**(175)**	**(116)**	**(3**
					p=0.70	**p=0.94**	**p=(**
Total healthcare costs and productivity losses	**244 144**	**200 104**	**207 058**	**188 310**	**-44 040**	**-18 748**	**-25**
	(1 256 656)	**(725 624)**	**(819 261)**	**(920 400)**	**(47 994)**	**(15 424)**	**44 1**
					p=0.41	**p=0.22**	**p=(**

[a] Salut area – Geographical area in Västerbotten county where the Salut Programme was implemented from 2006 and onwards; non-Salut area – remaining part of Västerbotten county.
[b] Premeasure period – 2002-2004; postmeasure period – 2006-2008.
[c] P-values are based on permutation tests of the difference in means between Salut post and Salut pre.
[d] P-values are based on permutation tests of the difference in means between non-Salut post and non-Salut pre.
[e] P-values are based on permutation tests of the difference in means between Salut and non-Salut over time, i.e. the difference in means between non-Salut post and non-Salut pre subtracted from the difference in means between Salut post and Salut pre.

[f] For the 476 births with missing info on delivery type, the cost for Ceasarean section was imputed with probability 0.17 and with probability 0.83 the cost for vaginal delivery was imputed.

Healthcare perspective



Limited societal perspective

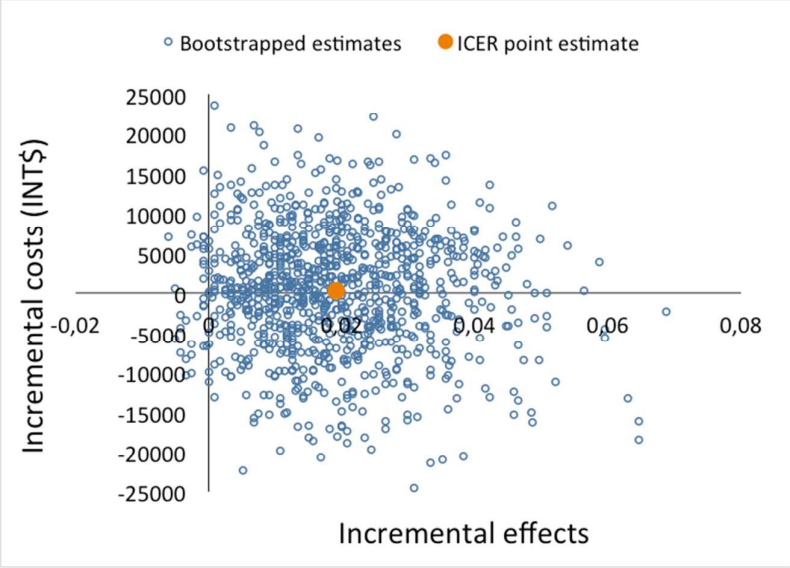


Figure E1. Cost-effectiveness planes for the healthcare and limited societal perspectives. The horizontal axis divides the plane according to incremental effect, and the vertical axis according to incremental cost, which divides the plane into four different quadrants. Each quadrant has a different implication for the cost-effectiveness decision. Iterations falling on the north-east quadrant are those where the intervention is more effective and more costly than the comparator; those on the south-east quadrant are more effective and less costly; those on the south-west quadrant are less effective and less costly; and those on the north-west quadrant are more costly and less effective.

References

1. Edvardsson K, Ivarsson A, Garvare R, Eurenius E, Lindkvist M, Mogren I, Small R, Nyström ME: **Improving child health promotion practices in multiple sectors - outcomes of the Swedish Salut Programme**. *BMC Public Health* 2012, **12**:920.
2. **Cost per Patient Database. Cost data 2013 per DRG.** [https://skl.se/ekonomijuridikstatistik/statistik/kostnadperpatientkpp/kppdatabas.1079.html]
3. **Statistical database.** [http://www.statistikdatabasen.scb.se]

Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement

Section/item	Item No	Recommendation	Reported on page No/ line No
Title and abstract			
Title	1	Identify the study as an economic evaluation or use more specific terms such as "cost-effectiveness analysis", and describe the interventions compared.	Title, page 1
Abstract	2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions.	Abstract, page 2
Introduction			
Background and objectives	3	Provide an explicit statement of the broader context for the study. Present the study question and its relevance for health policy or practice decisions	Page 4, lines 16-27
Methods			
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	Page 5, lines 1-15 Page 9, lines 29-31 Page 10, lines 1-10
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	Page 5, lines 16-23
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	Page 5, lines 20-21 Page 8, lines 5-10
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	Page 5, lines 26-32 Page 6, lines 1-8
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	Page 8, lines 5-7
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	Page 8, line 20 Page 9, lines 6-17
Choice of health outcomes	10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	Page 6, lines 10-29
Measurement of effectiveness	11a	*Single study-based estimates:* Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	Page 7, lines 1-29 Appendix B

Section/item	Item No	Recommendation	Reported on page No/ line No
	11b	*Synthesis-based estimates*: Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.	Not applicable
Measurement and valuation of preference based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	Not applicable
Estimating resources and costs	13a	*Single study-based economic evaluation:* Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	Page 8, lines 14-20 Page 9, lines 1-19
	13b	*Model-based economic evaluation:* Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	Not applicable
Currency, price date, and conversion	14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	Page 8, lines 4-20 Page 9, lines 1-19 Appendix D
Choice of model	15	Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended.	Not applicable
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytical model.	Not applicable
Analytical methods	17	Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	Page 7, lines 1-29 Page 11, lines 1-19 Page 12 lines 1-4 Appendix B
Results			

Section/item	Item No	Recommendation	Reported on page No/ line No
Study parameters	18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	Not applicable
Incremental costs and outcomes	19	For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.	Page 18, Table 4 in the main manuscript
Characterising uncertainty	20a	*Single study-based economic evaluation:* Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact of methodological assumptions (such as discount rate, study perspective).	Page 18, Table 4 in the main manuscript Appendix E, Figure E
	20b	*Model-based economic evaluation:* Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	Not applicable
Characterising heterogeneity	21	If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.	Not applicable
Discussion			
Study findings, limitations, generalisability, and current knowledge	22	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	Pages 19-21
Other			
Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	Page 22 “Funding”
Conflicts of interest	24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.	Page 22 “Competing interests”

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Is the Salut Programme an effective and cost-effective universal health promotion intervention for parents and their children? A register-based retrospective observational study.

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Is the Salut Programme an effective and cost-effective universal health promotion intervention for parents and their children? A register-based retrospective observational study

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Abstract

Objectives: This study investigates the effectiveness and cost-effectiveness of the Salut Programme, a universal health promotion intervention, compared to care-as-usual, over the periods of pregnancy, delivery and the child's first two years of life.

Method: We adopted a register-based retrospective observational design using existing data sources with respect to both exposures and outcomes. Health outcomes and costs were compared between geographical areas that received care-as-usual (non-Salut area), and areas where the Programme was implemented (Salut area). We included mothers and their children from both the Salut and non-Salut areas if: i) the child was born 2002-2004 (premeasure period) or ii) the child was born 2006-2008 (postmeasure period). The effectiveness study adopted two strategies: i) a matched difference-in-difference analysis using data from all participants; and ii) a longitudinal analysis restricted to mothers who had given birth twice, i.e. both in the pre- and postmeasure periods. The economic evaluation was performed from a health care and a limited societal perspective. Outcomes were clustered during pregnancy, delivery and birth, and the child's first two years.

Results: Difference-in-difference analyses did not yield any significant effect on the outcomes. Longitudinal analyses resulted in significant positive improvement in Apgar scores, reflecting the newborn's physical condition, with more children having a normal Apgar score (1 minute +3%, 5 minutes +1%). The cost of the Programme was INT$ 308/child. From both costing perspectives, the Programme yielded higher effects and lower costs than care-as-usual, being thus cost-saving (probability of around 50%).

Conclusions: Our findings suggest that the Salut Programme is an effective universal intervention to improve maternal and child health, and may be good value for money, however there is large uncertainty around the cost estimates.

Strengths and limitations of this study

- The findings suggest that the Salut Programme is an effective universal intervention to improve maternal and child health, and may be good value for money.
- Our study contributes to the limited evidence base regarding universal multi-sectorial health promotion approaches during pregnancy and early childhood.
- A major strength of this study is that the "state of the art" methods were used in the effectiveness analyses.
- Our analyses were limited to data available in registers. We lacked access to data on primary care and medication as well as on lifestyle and health-related quality of life.
- In the cost-effectiveness analyses, the limited societal perspective only included productivity losses due to mothers' inpatient and outpatient care, which might have contributed to the uncertainty in the results.

Background

Development during the prenatal period, infancy and childhood is known to influence lifelong health [1-4], and the link between early-life health and adult outcomes is strong and economically meaningful [5]. Promotion of optimal child development and wellbeing comprises early detection and treatment of whole families, and can potentially prevent the development of behavioural and emotional problems in children and adolescents [6].

Until now, the research community has failed to provide persuasive evidence about the effectiveness and cost-effectiveness of health promotion and preventive interventions. However, evaluation of intervention efforts is necessary for evidence-based decision-making [7 8]. Childhood obesity programmes have been suggested to be cost-effective [9], but other examples are rare. There are considerable methodological challenges when conducting such evaluations, and more thorough economic analyses of preventive programmes are encouraged. Economic evaluation is important for both those delivering and funding the interventions [10], and if demonstrated to be cost-effective, experiences and work modes can potentially be used in other settings.

The current project is nested within the Swedish Salut Child Health Intervention Programme, initiated in Västerbotten County in 2005 in addition to care-as-usual. The Programme is a multi-sectorial, family-centred approach to health promotion and prevention. One of the Programme aims is avoidance of maternal and foetal pregnancy complications related to maternal lifestyle. This study aimed to investigate the effectiveness and cost-effectiveness of the Salut Programme compared to care-as-usual, over the periods of pregnancy, delivery and the child's first two years of life. The study was guided by the following research questions:

1) Does the Salut Programme improve maternal and child health?
2) What are the resource implications of the Salut Programme in terms of intervention and societal costs?
3) Is the Salut Programme a cost-effective public health intervention?

Methods

Overall study design and participants

The current study adopted a register-based retrospective observational design using existing data sources with respect to both exposures and outcomes [11]. We simulated an experiment by taking

advantage of the stepwise implementation of the Programme and nationally available individual-level register data collected independently of our study [12].

Health outcomes and costs were compared between geographical areas that received care-as-usual (non-Salut area), and areas where the Programme was implemented from 2006 and onwards (Salut area). The mother's place of residence at the child's birth determined whether the child and mother were classified as belonging to the Salut area or the non-Salut area. Thus, an intention-to-treat approach was used [13]. We included mothers and their children from both the Salut area and non-Salut area if the child was born 2002-2004 (thus before the Salut Programme was implemented anywhere), defined as the premeasure period. Accordingly, we included mothers and their children if the child was born 2006-2008 (thus after the Salut Programme was implemented in some areas), defined as the postmeasure period. Henceforth, four study groups were formed: Salut pre, Salut post, non-Salut pre and non-Salut post.

We conducted an effectiveness study and an economic evaluation study. The effectiveness study adopted two complementary strategies: a matched difference-in-difference analysis using data from all participants, and a longitudinal analysis restricted to the subsample of mothers who had given birth twice during the study period, both in the pre- and postmeasure periods. The economic evaluation was conducted from both a healthcare and a limited societal perspective. In a recently published study protocol we have described the Salut Programme and our planned analysis strategies [14]. In the present study, this protocol has largely been followed. A few revisions have been made when necessary, and are described and motivated below.

Care-as-usual and the Salut Programme

Care-as-usual during pregnancy and childhood is free of charge and decentralised to locally-elected county councils with tax raising powers, which creates some variation across the country in delivery of services. Almost all parents attend antenatal care, and likewise almost all children attend child healthcare and dental care with an accompanying parent. Open pre-schools are free of charge, run by the municipality or churches, and attended on a drop-in basis by families.

The Salut Programme is integrated within care-as-usual, and comprises strengthening and restructuring of care-as-usual, and new specific interventions. Professionals in antenatal care, child healthcare, dental care and open pre-schools are invited to learning seminars and are encouraged to use manuals, specifically developed for the Salut Programme, to guide everyday practice. Following

countywide implementation, an evaluation showed significant improvements in professionals' health promotion practices and in collaboration across sectors [15]. The Programme is described in detail in appendix A and in previous publications [14 16-18].

Health outcomes

Health outcome measures were chosen to demonstrate the performance of the Salut Programme with respect to supporting normal pregnancy and birth, and in other ways contributing to the well-being of children and their mothers. Another prerequisite was that the measures were available through the Umeå SIMSAM Lab [12], compiled from national and local registers. Moreover, we were guided by a recent publication on frequently measured outcomes to assess maternity care performance [19]. A detailed description of the registers can be found elsewhere [14]. The following time periods and outcome measures were chosen:

1) During pregnancy, delivery and at birth – Mother's smoking status at first antenatal visit (yes/no); pregnancy length at delivery (≥37/<37 weeks); caesarean section (yes/no); birth weight (≥2500/<2500 g); birth length (cm); large for gestational age (LGA; ≥2 standard deviations above the reference population's mean weight); small for gestational age (SGA; ≤2 standard deviations below the reference population's mean weight); Apgar score 1, 5, and 10 minutes after delivery (≥7/<7 points); child diagnosed by paediatrician as healthy (yes/no); and duration of mother's inpatient care related to delivery (days).

2) During the first two years after the child's birth – Inpatient care not related to delivery within the two first months after child's birth (yes/no); cumulative duration of inpatient care (days); and cumulative number of outpatient visits, all for mother and child, respectively.

Effectiveness analyses

The samples are presented in figure 1. Assumptions and details regarding the analysis strategies are described elsewhere 14, and in appendix B. The matched difference-in-difference analyses utilized the total sample. For each child born in the Salut area at postmeasure, matching observations were found in each of the other three groups: Salut area pre, non-Salut area pre and non-Salut area post. For every outcome an observation was deemed a match if the mother, at the time of the child's birth, had the same level of education and similar age as the mother of a child born in the Salut area at postmeasure. The average difference over time in the Salut area was computed as the difference between the mean outcome in the Salut area at postmeasure and the mean outcome of the matched

observations from the Salut area at premeasure. Analogously, the average difference over time in the non-Salut area was computed as the difference between the mean outcome of the matched observations from the non-Salut area at postmeasure and the mean outcome of the matched observations from the non-Salut area at premeasure. The final difference-in-difference estimate of the average treatment effect on the treated was computed by subtracting the average difference over time in the non-Salut area from the average difference over time in the Salut area. To obtain confidence intervals reflecting the uncertainty around the average treatment effect on the treated (ATT) point estimates standard errors were computed using non-parametric bootstrapping with 1000 replications[20].

In the longitudinal analyses we utilized the subsample of mothers that gave birth to at least one child in each of the time periods, and living in the same geographical area over the whole time period (figure 1). For a given outcome of interest, focusing on this subsample allowed us to use the mother's premeasure outcome value as a covariate on which to match on, in addition to the matching variables used in the difference-in-difference analyses. The simple matching estimate of the average treatment effect on the treated was computed as the difference between the mean outcome in the Salut area at postmeasure, and the mean outcome of the matched observations from the non-Salut area at postmeasure. Abadie-Imbens standard errors[21] were computed to obtain confidence intervals reflecting the uncertainty around the ATT point estimates. The standard error computation is based on estimation of the asymptotic variance of the simple matching estimator and is preferable to bootstrapping in this case since the latter would lead to inconsistent standard error estimation[22].

In all analyses, matching was performed separately for each outcome variable, namely the identity of the match was not fixed across analyses. Analyses were conducted in R 3.3.0 [23] using the Matching package [24] for matching and Abadie-Imbens standard errors.

(figure 1 here)

Figure 1. An overview of the study population and samples used in the analyses.

Economic evaluation

The economic analysis aimed to capture both the healthcare and the wider societal costs and benefits of the Salut Programme for the first two years of the children's lives, and their mothers. Two perspectives were adopted: a health care perspective, consisting of intervention costs and other healthcare resources used by children and mothers, and a limited societal perspective, additionally including productivity losses associated with mothers' illness [34]. Results are expressed in 2013 purchasing-power parity international dollars (8.71 SEK=INT$) after adjusting for inflation using the gross domestic product deflator [25].

Intervention cost

Programme costs were estimated between January 2005 and June 2010. We added the opportunity cost of professionals' time to attend learning seminars during 2005-2007 (appendix table C1). Calendar year-based allocation rules for joint costs and the division between start-up and implementation were decided upon retrospectively by the Salut Programme staff to capture the changing nature of activities over time (appendix table C2). Intervention costs were discounted at an annual rate of 3%.

Healthcare and other societal costs

Healthcare related costs were derived from information on the use of healthcare resources external to the Salut Programme, such as maternal inpatient care related to delivery and children's and mothers' inpatient and outpatient care due to illness. All healthcare related costs were calculated for the child's first two years. Productivity losses due to mothers' illness were included in the analysis conducted from a limited societal perspective. Productivity losses were calculated using the human capital approach, by multiplying time off work due to inpatient and outpatient care by the average gross salary (including social charges). The average number of parental benefit days during the first year is around 220 for women in Sweden [26]. Therefore, mothers were assumed to be on parental leave during the first year after childbirth, hence productivity losses were estimated for year two only. Contrary to the planned analyses in the study protocol [14], care of a sick child compensations were excluded from the analysis, as these were only linked to the parent and not to a particular child. In addition, these costs can be considered transfer payments, thus including them would constitute double counting. Total costs were estimated by multiplying frequencies of resources by their

respective unit cost. Costs incurred during year two were discounted at 3%. The difference in health care and other societal costs was compared between the Salut Programme and care-as-usual and between pre- and postmeasure using permutation tests. Unit costs used to value resource use are listed in appendix table C3.

Cost-effectiveness analysis

The economic framework of this study is a retrospective register-based cost-effectiveness analysis. We compared costs and outcomes of the Salut Programme to care-as-usual, from a healthcare and a limited societal perspective, and calculated incremental cost-effectiveness ratios (ICERs). Deterministic cost-effectiveness was expressed as the cost per low-Apgar case prevented. For the probabilistic analysis, we used non-parametric bootstrapping with 1000 replications to obtain 95% confidence intervals around the ICER and investigate the uncertainty around the ICER estimates. The bootstrap results are presented on a cost-effectiveness plane. We explored the probability that Salut is cost-effective compared to care-as-usual, subject to a range of possible maximum values that a decision maker would be willing to pay for an additional low-Apgar case prevented. Cost-effectiveness acceptability curves (CEAC) for the healthcare and the limited societal perspectives were generated by plotting these probabilities for a range of willingness-to-pay values. CEACs are a recommended decision-making approach to dealing with uncertainty regarding the cost-effectiveness estimates and the maximum values decision makers would be willing to pay for these. A decision maker who knows their maximum willingness-to-pay for an additional unit of health gain can use the CEAC to determine the strength of the evidence on the cost-effectiveness of an intervention [27]. Bootstrapping and the CEACs were performed in Excel 2011.

Results

Characteristics of the study population

In the Salut area, 1003 and 888 children were born in the premeasure and postmeasure period, respectively (figure 1). In the non-Salut area, 6664 and 6059 children were born in the premeasure and postmeasure period, respectively. There were 147 mothers that gave birth at least once to 309 children in the Salut area and 1249 mothers that gave birth at least once to 2650 children in the non-Salut area. Characteristics of the total sample are given in table 1, and for the longitudinal subsample in appendix table D1. Mothers giving birth to children in the Salut area were on average younger and less educated compared to mothers in the non-Salut area. The differences in age and education

between Salut post and Non-Salut post on the one hand, and between Salut post and Non-Salut pre on the other hand, were all statistically significant with p-values below 0.001. Between Salut post and Salut pre there were no significant differences in age and education (p-values 0.78 and 0.30, respectively). Missing values varied between measures (appendix tables D2-D3). Information on mother's education was missing for 2.1-2.4% of the Salut area observations and 1.0-1.1% of the non-Salut area observations. All outcomes at birth exhibited some missingness, with the largest proportion for the smoking variable (10.4% in Salut-area pre). Outcomes during the first two years after birth were all fully observed.

Table 1 Characteristics of the participants in the total sample

	Salut area[a]		Non-Salut area[a]	
	pre[b]	post[b]	pre[b]	post[b]
Participants				
Mothers, n	918	828	6056	5737
Children, n	1003	888	6664	6059
Covariates				
Mother's age (years), M (SD)	29.7 (5.3)	29.7 (5.2)	30.3 (4.9)	30.3 (5.0)
Mother's education, %				
Compulsory school	11.0	11.3	7.5	7.5
Secondary school	51.2	48.1	44.5	36.8
Higher education	37.8	40.6	48.0	55.7
Health outcomes				
Pregnancy, delivery and around the child's birth				
Smoking[c] (yes), %	8.4	5.2	5.3	3.8
Pregnancy length (≥37 weeks), %	92.6	95.0	94.4	94.6
Caesarean section (yes), %	17.2	18.1	16.4	16.4
Birth weight (≥2 500 g), %	94.8	96.9	96.5	96.4

Birth length (cm), M (SD)	50.3 (2.8)	50.3 (2.9)	50.5 (2.5)	50.3 (2.5)
LGA[d] (yes), %	3.6	3.8	4.4	3.4
SGA[e] (yes), %	2.5	2.5	1.7	1.9
Apgar score[f] (≥7 points) at 1 minute, %	95.8	96.3	95.3	94.6
at 5 minutes, %	99.1	99.4	98.7	98.5
at 10 minutes, %	99.7	99.8	99.7	99.6
Healthy child[g] (yes), %	79.3	81.1	77.8	79.2
Mother's inpatient care[h] (days), M (SD)	3.7 (2.8)	3.1 (2.0)	3.6 (2.6)	2.9 (2.2)
During the first two years after the child's birth				
Mother with early inpatient care[i] (yes), %	1.1	2.4	1.8	1.3
Child with early inpatient care[i] (yes), %	6.9	4.2	6.9	4.3
Mother's inpatient care[j] (days), M (SD)	0.4 (2.1)	0.5 (3.2)	0.5 (5.3)	0.5 (4.5)
Child's inpatient care[j] (days), M (SD)	1.9 (12.8)	1.5 (8.2)	1.5 (8.1)	1.4 (9.6)
Mother's outpatient visits[k], M (SD)	0.0 (0.1)	0.0 (0.1)	0.0 (0.1)	0.0 (0.1)
Child's outpatient visits[k], M (SD)	0.0 (0.2)	0.1 (0.4)	0.0 (0.2)	0.1 (0.7)

M – mean; SD – Standard deviation.

[a] Difference-in-difference estimates of the average treatment effect on the treated (ATT) with 95% confidence intervals (CI). CIs and p-values were computed with the assumption that ATT was normally distributed and with a standard deviation equal to the bootstrap standard error.

[b] Simple matching estimates of the average treatment effect on the treated (ATT) with 95% confidence intervals (CI).
CIs and p-values were computed with the assumption that ATT was normal distributed and with a standard deviation equal to the Abadie-Imbens standard error.

[c] Smoking status at first antenatal visit, around pregnancy week 12.

[d] Large for gestational age (LGA) – ≥2 SD above the reference population's mean weight.

[e] Small for gestational age (SGA) – ≤2 SD below the reference population's mean weight.

[f] A measure of the newborn's physical condition 1, 5 and 10 minutes after birth, range 0-10.

[g] A healthy child according to a paediatrician's examination.

[h] Mother's inpatient care related to delivery.

[i] Early inpatient care for mother and child, respectively, during the first two months after the child's birth but not related to the delivery.

[j] Cumulative duration of inpatient care for mother and child, respectively, over the child's first two years, excluding care due to delivery complications.

[k] Number of outpatient visits for mother and child, respectively, over the child's first two years, excluding care

for the mother due to delivery complications.

Effectiveness analyses

Before conducting the difference-in-difference analyses, observations with missing values on outcome and/or matching variables were excluded. The analytical sample sizes differed between outcomes since exclusion of observations was done separately for each outcome (appendix tables D2-D3). The samples were well balanced before matching, but matching improved the covariate balance and resulted in standardized mean differences [28 29], close to zero for all covariates in all analyses. The difference-in-difference analyses did not result in any significant average treatment effect on the treated estimates. Hence, we conclude that for those individuals who were exposed to the Salut Programme, the Programme had on average no effect on the outcomes studied (table 2).

Before conducting the longitudinal analyses, the subsample of mothers giving birth at least once in each time period in the same area was further reduced in the following manner: for mothers who gave birth to more than one child in the same area at premeasure, observations from this period not relating to the last birth in that area and period were excluded. Analogously, if there were multiple births in the same area at postmeasure, observations from this period not relating to the first birth in that area and period were excluded. These exclusions were performed so that the variables at premeasure could be used as baseline variables to match on. Due to multiple births in the same area and period, observations were excluded from Salut area post (6), Salut area pre (9), non-Salut area post (49), and non-Salut area pre (103). Finally, observations with missing values on outcome and/or covariates were excluded as in the difference-in-difference analyses (appendix tables D4-D5). Matching improved the covariate balance and resulted in standardized mean differences close to zero for all covariates. The longitudinal analyses resulted in significant positive average treatment effect on the treated estimates for the outcomes Apgar at 1 and 5 minutes (table 2).

We conclude that for those who were exposed to the Salut Programme, in the subpopulation of mothers giving birth at least twice, there were 3% (95% CI: 2-4%) more births with high Apgar at 1 minute compared to what would have been the case had they not been exposed to the Programme. Similarly, there were 1% (95% CI: 0.5-2%) more births with high Apgar at 5 minutes compared to what would have been the case had they not been exposed to the Salut Programme. For our sample, this translates to 3.6 and 1.2 additional children having high Apgar at 1 and 5 minutes, respectively. We estimated the number needed to treat to prevent one case with low Apgar at 5 minutes by dividing one by the absolute risk reduction between Salut and non-Salut (0.02); 50 mothers would need to be

exposed to the Salut Programme to prevent one case of low Apgar. The results for the other outcomes showed no significant effects.

To assess how sensitive the results are to the exclusion of observations with missing values, analogous analyses where performed on samples where missing values had been imputed using multivariate imputations by chained equations with predictive mean matching[30]. The results from analyses based on the samples with imputed values do not differ substantially from the results presented in table 2 and the conclusions that can be drawn are the same (appendix table D6).

Table 2 Results of the effectiveness study, total sample and longitudinal subsample

Health outcomes	Total sample		Longitudinal subsample	
	ATT (95% CI)[a]	p-value	ATT (95% CI)[b]	p-value
Pregnancy, delivery and around the child's birth				
Smoking[c] (yes)	-0.02 (-0.05, 4e-03)	0.09	-0.02 (-0.06, 0.01)	0.11
Pregnancy length (≥37 weeks)	0.02 (3e-04, 0.04)	0.08	0.02 (-0.02, 0.05)	0.34
Caesarean section (yes)	0.01 (-0.03, 0.05)	0.66	-4e-05 (-0.04, 0.04)	1.00
Birth weight (≥2500 g)	0.02 (-6e-04, 0.05)	0.06	0.01 (-8e-03, 0.03)	0.22
Birth length (cm)	0.11 (-0.19, 0.41)	0.47	0.10 (-0.31, 0.51)	0.63
LGA[d] (yes)	0.01 (-0.01, 0.03)	0.30	0.01 (-0.04, 0.05)	0.73
SGA[e] (yes)	-4e-03 (-0.02, 0.02)	0.72	-0.01 (-0.02, -4e-03)	0.01
Apgar score[f] (≥7 points) at 1 minute	0.02 (-2e-03, 0.04)	0.07	*0.03 (0.02, 0.04)*	*4e-12***
at 5 minutes	5e-03 (-0.01, 0.02)	0.34	*0.01 (5e-03, 0.02)*	*9e-05***
at 10 minutes	1e-03 (-4e-03, 7e-03)	0.61	2e-03 (-6e-04, 4e-03)	0.15
Healthy child[g] (yes)	0.01 (-0.04, 0.05)	0.81	0.01 (-0.06, 0.08)	0.73

Mother's inpatient care[h] (days)	-4e-03 (-0.26, 0.25)	0.98	-0.04 (-0.43, 0.34)	0.82
During the first two years after the child's birth				
Mother with early inpatient care[i] (yes)	0.02 (7e-03, 0.03)	3e-03	0.01 (-0.01, 0.04)	0.26
Child with early inpatient care[i] (yes)	0.01 (-0.01, 0.03)	0.44	-3e-04 (-0.03, 0.03)	0.98
Mother's inpatient care[j] (days)	0.08 (-0.25, 0.40)	0.64	-0.28 (-0.53, -0.04)	0.02
Child's inpatient care[j] (days)	-0.17 (-1.33, 0.99)	0.77	0.37 (-1.03, 1.77)	0.60
Mother's outpatient visits[k]	1e-03 (-0.01, 0.01)	0.86	-0.01 (-0.03, 0.01)	0.19
Child's outpatient visits[k]	0.02 (-0.02, 0.05)	0.40	-2e-03 (-0.04, 0.03)	0.92

[a] Difference-in-difference estimates of the average treatment effect on the treated (ATT) with 95% confidence intervals (CI). CIs and p-values were computed with the assumption that ATT was normally distributed and with a standard deviation equal to the bootstrap standard error.

[b] Simple matching estimates of the average treatment effect on the treated (ATT) with 95% confidence intervals (CI). CIs and p-values were computed with the assumption that ATT was normal distributed and with a standard deviation equal to the Abadie-Imbens standard error.

[c] Smoking status at first antenatal visit, around pregnancy week 12.

[d] Large for gestational age (LGA) – ≥2 SD above the reference population's mean weight.

[e] Small for gestational age (SGA) – ≤2 SD below the reference population's mean weight.

[f] A measure of the newborn's physical condition 1, 5 and 10 minutes after birth, range 0-10.

[g] A healthy child according to a paediatrician's examination.

[h] Mother's inpatient care related to delivery.

[i] Early inpatient care for mother and child, respectively, during the first two months after the child's birth but not related to the delivery.

[j] Cumulative duration of inpatient care for mother and child, respectively, over the child's first two years, excluding care due to delivery complications.

[k] Number of outpatient visits for mother and child, respectively, over the child's first two years, excluding care for the mother due to delivery complications.

*Statistically significant effect at the α=0.05 level after a Bonferroni correction for multiple comparisons, i.e. with the 38 outcome variables this implies a significance threshold of 0.05/38=0.001.

**Statistically significant effect at the α=0.01 level after a Bonferroni correction for multiple comparisons, i.e. with the 38 outcome variables this implies a significance threshold of 0.01/38=0.00026.

Intervention costs

The total cost of the Salut Programme was INT$ 273 063 (2 379 260 SEK). Averaged over the 888 children born in the Salut area at postmeasure gives a cost of INT$ 308 (2 679 SEK) per child. The largest cost components were staff (64%), and the opportunity cost of professionals' time to attend

the learning seminars (16%). Of the total, 28% were start-up costs incurred during 2005-2007. The average annual implementation cost was INT$ 43 575 (379 677 SEK; averaged over 66 months).

Healthcare and other societal costs

Mean healthcare costs and productivity losses at pre- and postmeasure for the Salut and the non-Salut areas for the longitudinal subsample (n=1289) are shown in table 3. Healthcare costs were lower in the Salut area due to less inpatient care for both mothers and children. Healthcare costs tended to be lower at postmeasure compared to premeasure in both areas, but the differences were not statistically significant. The standard deviation around the mean healthcare cost estimates was large mostly because of large variation in inpatient care costs.

Productivity losses increased in the non-Salut area from pre- to postmeasure (+INT$ 29; p=0.03), but remained unchanged in the Salut area, which explains the difference in productivity losses over time in the Salut area compared to the non-Salut area (-INT$ 31 per child; p= 0.38). Adding up healthcare costs and productivity losses, total costs (excluding intervention costs) were INT$ 1556 lower at postmeasure than at premeasure in the Salut area, and INT$ 1127 lower at postmeasure than at premeasure in the non-Salut area. Hence, total costs fell by INT$ 430 more per person in the Salut area compared to the non-Salut area (p=0.97). Analyses of healthcare costs and productivity losses for the total sample are found in the appendix table E1.

Table 3 Mean healthcare costs and productivity losses for the longitudinal sub-sample (2013 INT$)[a]

	Salut[b]		Difference Salut post-pre[d]		Non-Salut[b]		Difference Non-Salut post-pre[e]		Incremental costs Salut vs. Non-Salut[f]	
Costs	pre[c]	post[c]		p-value*	pre[c]	post[c]		p-value*		p-value
Intervention cost per child		308	308						308	
Children, n	121	121			1 168	1 168				
Healthcare costs, M (SD)										
Pregnancy, delivery and around the child's birth										
Delivery	5767 (979)	5842 (1063)	76 (131)	p=0.70	5855 (1072)	5894 (1110)	39 (45)	p=0.41	36 (147)	p=0.81
During the first two years after the child's birth										
Mother's inpatient care	604 (3089)	605 (2547)	1 (364)	p=1.00	1100 (8396)	1822 (15 637)	722 (519)	p=0.18	-721 (1618)	p=0.60
Child's inpatient care	10 773 (50 242)	9142 (43 492)	-1631 (6041)	p=0.82	15 245 (98 078)	13 331 (143 972)	-1914 (5097)	p=0.75	283 (15 960)	p=0.98
Mother's outpatient care	3 (28)	3 (28)	0 (4)	p=1.00	4 (36)	5 (40)	2 (2)	p=0.27	-2 (5)	p=0.75

Child's outpatient care	8 (49)	8 (50)	0 (6)	p=1.00	14 (97)	11 (64)	-4 (3)	p=0.28	4 (11)	p=0.68
Total healthcare costs	17 154 (50 535)	15 599 (43 666)	-1555 (6072)	p=0.83	22 219 (98 650)	21 063 (144 736)	-1156 (5125)	p=0.86	-399 (16 048)	p=0.97
Productivity losses, M (SD)										
During the second year after the child's birth										
Mother's outpatient care	2 (21)	2 (21)	0 (3)	p=1.00	2 (20)	2 (21)	0 (1)	p=1.00	0 (3)	p=0.94
Mother's inpatient care	17 (98)	15 (104)	-2 (13)	p=0.90	20 (170)	48 (440)	29 (14)	*p=0.03**	-31 (43)	p=0.38
Total productivity losses	19 (99)	17 (106)	-2 (13)	p=1.00	21 (172)	50 (441)	29 (14)	*p=0.02**	-31 (43)	p=0.38
Total healthcare costs + productivity losses	17 173 (50 538)	15 616 (43 670)	-1556 (6072)	p=0.83	22 240 (98 660)	21 113 (144 768)	-1127 (5126)	p=0.85	-430 (16 051)	p=0.97

*Statistical significance defined as p<0.05.

[a] Results expressed in 2013 purchasing-power parity adjusted international dollars (1 INT$=8.71 SEK).

[b] Salut area – Geographical area in Västerbotten county where the Salut Programme was implemented prior to 2009; Non-Salut area – remaining pai
Västerbotten county. Several of the health outcomes are further described in table 1.

[c] Premeasure period – 2002-2004; postmeasure period – 2006-2008.

[d] P-values are based on permutation tests of the difference in means between Salut post and Salut pre.

[e] P-values are based on permutation tests of the difference in means between Non-Salut pc
and Non-Salut pre.

[f] P-values are based on permutation tests of the difference in means between Salut and Non-Salut over time, i.e. the difference in means between Non-Salut post and Non-Salut pre subtracted from the difference in means between Salut post and Salut pre.

Cost-effectiveness analysis

Both Apgar at 1 and 5 minutes showed statistically significant differences between Salut and non-Salut areas in the longitudinal analysis. Previous studies suggest that a low Apgar score at 5 minutes correlates with neonatal mortality and confers an increased risk of neurologic disability and cognitive impairment [31-33]. In contrast, Apgar at 1 minute is not a good predictor of infant outcomes [34]. Hence, we considered Apgar at 5 minutes as the only relevant outcome in the cost-effectiveness analysis. The cost-effectiveness results for both costing perspectives are given in table 4. From both a healthcare and a limited societal perspective, the Salut Programme yields higher effects and lower costs (i.e. "dominant) than care-as-usual (non-Salut). The probability that the Salut Programme is cost-saving and entails positive effects compared to care-as-usual is approximately 50% (48.3% for the healthcare perspective and 49.7% for the limited societal perspective).

Figure E1 in the appendix presents the cost-effectiveness results on a cost-effectiveness plane for both costing perspectives. The bootstrapped estimates of incremental costs and effects fall approximately equally in the south-east and north-east quadrants of the plane. This is consistent with the Salut Programme having positive effects and a approximately 50% probability of being cost-saving compared to care-as-usual. The cost effectiveness plane demonstrates that the uncertainty around the cost estimates is indeed very large. This is further evidenced when plotting the cost effectiveness acceptability curve (CEAC, Figure E2 in the appendix) for different willingness-to-pay (WTP) values. With a zero WTP for preventing a case of low-Apgar, the probability that the Salut Programme is cost-effective is approximately 50%. This probability hardly increases with WTP until very high ceiling values of 100.000 INT$ and above.

Table 4 Results of the cost-effectiveness study, longitudinal sub-sample (costs in 2013 INT$)

	Salut area[a]				Non-Salut area[a]						
	Average cost post-pre[b, c] M (SD)		Average proportion of low Apgar[d] cases prevented post-pre M (SD)		Average cost post-pre M (SD)		Average proportion of low Apgar cases prevented post-pre M (SD)		Bootstrapped Incremental costs	Bootstrapped Incremental effects	ICER
	Base-case	Bootstrap	Base-case	Bootstrap	Base-case	Boot-strap	Base-case	Boot-strap			
Healthcare perspective	-1247 (66 658)	-1207 (5892)	0.016 (0.128)	0.016 (0.011)	-1156 (176 067)	-1131 (5294)	- 0.003 (0.149)	-0.003 (0.004)	-76	0.02	dominant[ef]
Limited societal perspective	-1249 (66 668)	-1398 (5941)	0.016 (0.128)	0.016 (0.011)	-1127 (176 099.98)	-922 (5284)	- 0.003 (0.149)	-0.003 (0.004)	-476	0.02	dominant[ef]

ICER – Incremental cost-effectiveness ratio; CI – Confidence interval.

[a] Salut area – Geographical area in Västerbotten county where the Salut Programme was implemented from 2006 and onwards; non-Salut area – remaining part of Västerbotten county. Several of the health outcomes are further described in Table 1.

[b] Premeasure period – 2002-2004; postmeasure period – 2006-2008.

[c] The average cost per participant includes intervention costs and resource use costs

[d] Apgar at 5 minutes – a measure of the newborn's physical condition at 5 minutes after birth, range 0-10 points.

[e] The intervention is less costly and more effective than the comparator (dominant).

[f] Approximately 3% of the observations have negative effects.

Discussion

Main study findings and comparison with other studies

Our results suggest that the Salut Programme is an effective universal child health promotion intervention, and is likely to represent good value for money. The difference-in-difference analyses did not show significant improvements in maternal and child health outcomes, but suggested changes in a positive direction. However, the longitudinal analyses resulted in a significant positive improvement in Apgar scores, reflecting the newborn's physical condition, with more children having a normal Apgar score (1 minute +3%, and 5 minutes +1%). The cost added by the Programme to care-as-usual was small, INT$ 308, representing only 4% of the average health care cost for the pregnancy, delivery and neonatal periods per woman/child, INT$ 7945 [35]. From both a healthcare and a limited societal perspective, the Programme yielded higher effects and lower costs than care-as-usual, with approximately 50% probability of being cost-saving and entailing positive effects. Exploration of the uncertainty around the cost-effectiveness data showed that there was relatively large uncertainty around the cost estimates. In our view the most likely explanation is that the noted differences in costs may not have been directly impacted by the intervention. Importantly, the Salut Programme would only have a higher probability of cost-effectiveness compared to care-as-usual if decision makers would be willing to pay much more (what seem unreasonably high financial figures) for an additional low-Apgar case prevented. Thus, our findings show that Salut can be good value for money. However, more evidence is needed about costs, in particular how Salut may impact on healthcare costs in the long-term.

Our study contributes to the limited evidence base regarding universal multi-sectorial health promotion interventions during pregnancy and early childhood. We are aware of only a few evaluations of the effectiveness and cost-effectiveness of such interventions. The universal parenting programme "All Children in Focus", offered to parents of children aged 3 and above, showed a positive effect on parental self-efficacy and child health [36]. However, the programme had a low probability of cost-effectiveness [37]. Another study of a nurse-led intensive home visiting programme for first-time teenage mothers found no short-term benefits concerning the selected primary outcomes [38].

Strengths and weaknesses of the study

We evaluated the Salut Programme as it was implemented in current practice, which increases the external validity and generalisability of the results. The use of existing register data, in which exposure

and outcomes have been routinely collected [12], reduces the amount of missing data. The "state of the art" methods used in the effectiveness analyses, which do not require strong assumptions regarding the data generating mechanisms, allowed us to identify the differential effect of the Programme on children and mothers born in Salut versus non-Salut areas in a natural experiment [39].

While intention-to-treat [13] was the only feasible approach, we may have underestimated the intervention effects. We controlled for mothers' age and education using matching as well as the premeasure value of the outcome in the longitudinal analyses. However, we are aware of the risk for residual confounding. Another possible source of underestimation of effects is that the intervention development period (2005-2007) in part overlaps with the postmeasure period (children born 2006-2008). The retrospective study design limited us in terms of evaluating whether there was an initial learning period, during which effectiveness of the Programme was lower. If such a learning period indeed existed, we may also have underestimated the opportunity cost of the Programme, because we assumed that (as stipulated by the Programme), professionals integrated the Programme interventions within care-as-usual. In the case visits took more time than usual early on during implementation, a full societal perspective should also consider the incremental opportunity cost of parents' time. Due to the limitations of the retrospective design we were not able to evaluate whether such a learning period existed.

As the Programme is a universal health promotion intervention, medical outcome measures were not expected to show significant effects. However, our analyses were limited to data available in registers. In particular, we lacked access to data on primary care visits and medication as well as on lifestyle and health-related quality of life. In the cost-effectiveness analyses, the limited societal perspective only included productivity losses due to mothers' inpatient and outpatient care, which might have contributed to the uncertainty in the results.

Implications for policy and clinical practice

The Apgar score is a well-established predictive index for neonatal morbidity and mortality in normal-birth weighted infants [40-42]. Low Apgar at 5 minutes is associated with an increased risk of neurological disabilities[32 43]. For example, 1.7 % of newborns with low Apgar are diagnosed with cerebral palsy, compared with 0.05 % of newborns with normal Apgar at 5 minutes[44]. Hence, to prevent one case of cerebral palsy, one would have to prevent 55 cases of low Apgar at 5 minutes. As such, the estimated lifetime cost for a child with cerebral palsy is about INT$ 850 000 [45], while the broad implementation of

the Salut programme would result in additional health benefits (cases of normal Apgar score) at no additional costs. Although there is no study estimating the willingness-to-pay for a low-Apgar case prevented, this comparison might serve as a reference frame.

Universal complex interventions implemented in real-life settings, such as the Salut Programme, are scarce and pose challenges with respect to implementation, dissemination and evaluation [46]. The reliability of our results depends on how the Salut Programme was implemented in current praxis. Interviews with professionals suggest that key issues for effective implementation are involvement of professionals in intervention development, regular meetings with professionals and process consultants, and the use of manuals [16]. On the other hand, more resources would likely have improved feasibility by providing professionals with more dedicated time to deliver the interventions. Continuous support from decision-makers is necessary [47] to sustain the effectiveness and cost-effectiveness of an evidence-based intervention, such as the Salut Programme, in the long-term.

Conclusions

Our study suggests that the Salut Programme is an effective universal intervention to improve maternal and child health, and may be good value for money. The probability that the Salut Programme is cost-saving and entails positive effects is around 50% over a wide range of willingness to pay ceiling values, although with a large uncertainty around the cost estimates

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Contributors

The statistical analyses were carried out by JH, and the economic evaluation by FS, AMPB and IF. AI and IF conceived and designed the study. EE, ML and AI constitute the scientific steering group for the Salut Programme, and AI is principal investigator for the Umeå SIMSAM Lab, both prerequisites for the

present study. All the authors (JH, FS, EE, AMPB, AI, ML and IF) contributed to the writing process and have approved the final manuscript.

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Competing interests

None declared.

Ethics approval

The Regional Ethical Review Board in Umeå gave clearance for the Salut Programme research (2010-63-31M) and for the Umeå SIMSAM Lab research (2010-157-31Ö).

Data sharing statement

No additional data are available.

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List of tables and figures

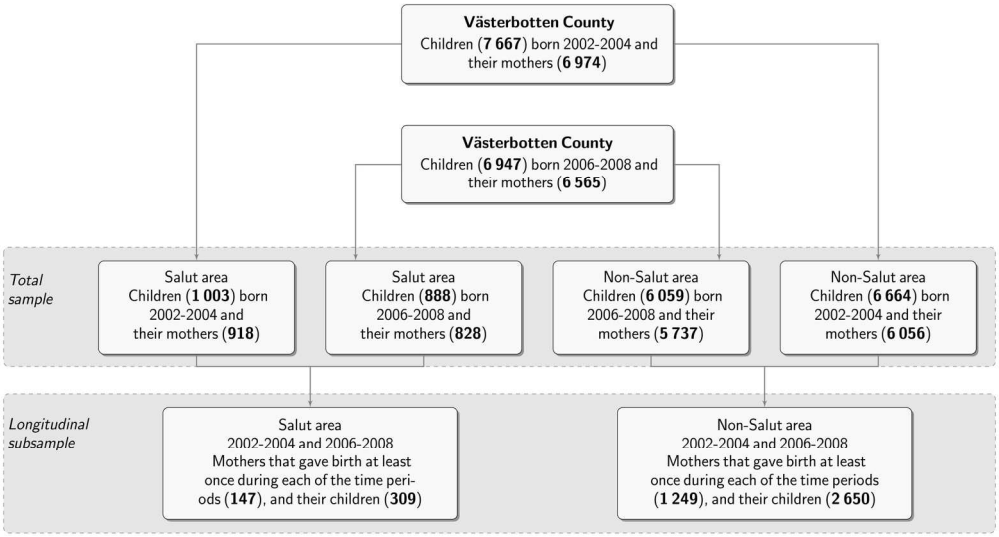


Figure 1. An overview of the study population and samples used in the analyses

84x45mm (600 x 600 DPI)

Appendix A The Swedish Salut child health intervention programme

Table A1 Västerbotten County Council's vision and the Salut Programme's aims and focus areas

Vision, aims, focus areas	Content
Vision	By 2020, the health and wellbeing of the population will be the best in the world.
Overall aim	Good health is achieved by salutogenic interventions in collaboration with societal actors and the family with the child's best in focus. Through systematic improvements, interventions are developed and implemented to promote satisfactory conditions during childhood, increased physical activity, and healthy eating habits.
Main focus areas	To promote healthy eating habits, physical activity and good psychosocial health, and to prevent obesity and caries.
Aims during pregnancy period	Avoidance of maternal and foetal pregnancy complications related to maternal lifestyle. Healthy maternal weight gain during pregnancy. A minimum of 30 minutes daily physical activity. Regular meals. Five fruits and vegetables a day. Tooth-brushing twice a day with fluoride toothpaste. Regular dental health care visits. Parents are feeling prepared for their parental roles. Pregnant women are living in relations free from intimate partner violence. Pregnant women refrain from tobacco, alcohol and drug use.
Aims for parents and children 0-18 months	Normal weight development for 18-month olds. Retain of pre-pregnancy weight. Sufficient sleep (parents and children). Environments free from tobacco and drug use, and alcohol use is limited. A minimum of one hour daily physical activity (play) for children. A minimum of 30 minutes daily physical activity for parents. Avoidance of TV-viewing and TV/computer games for children. Six months exclusive breastfeeding, and thereafter partly continued for 1 year or longer. Introduction of 5 fruits and vegetables a day for children. Five fruits and vegetables a day for parents. Regular meals for both parents and children. Avoidance of discretionary foods for children. Tooth-brushing twice a day with fluoride toothpaste (from the first tooth for the children). Regular dental health care visits. Parents feel confident in their parental roles. Satisfying parental-child attachment and interaction. Women/children live in an environment free from violence and violation.

Table A2 Care-as-usual and the Salut Programme's interventions targeting parents-to-be and their children during pregnancy and until the child is 18 months, and significant changes in professionals' practices post Salut implementation

Care-as-usual	**Arena**
Maternal and foetal surveillance (7-9 check-ups)	ANC
Psychosocial- and lifestyle counselling	ANC, CHC
Participation in parental support groups	ANC, CHC
Health and development check-ups, and immunizations (about 10 visits when the child is 0-18 months, and more often when needed)	CHC
Advice on teeth brushing twice a day	CHC, DHC
Oral health check-up and health promoting advice (child age 2-3 years)	DHC
Socialization at open preschools for children not yet enrolled in regular preschools and their parents	OPS
The Salut Programme	**Arena**
Strengthening or restructuring of 'care-as-usual'	
Motivational Interviewing (MI)	ANC, CHC*, DHC
Collaboration between any of involved sectors	ANC*, CHC*
Involvement in parental support groups	ANC, CHC
Lifestyle counselling	ANC, CHC*, DHC*
Edinburgh Postnatal Depression Scale (EPDS) at "mother's visit" (Child age 8 weeks)	ANC
Activities to enhance early parent-child attachment, parent relation-ships, children's physical activity and linguistic development	CHC, OPS
Activities to promote healthy snacks/food and drinks	OPS*
Activities to encourage physical activity	OPS
The Salut Programme specific interventions	
Questionnaires for health surveillance	ANC, CHC, DHC
Free dental health counselling for the parents-to-be	DHC
Collaboration between any of involved sectors	DHC*, OPS*
Contribution to parental support groups	DHC, OPS
Questions for domestic violence during pregnancy and at "mother's visit" (child age 8 weeks)	ANC*, CHC*
Focus on fathers' experiences of change in life situation at "father's visit" (child age 10 months)	CHC*
Oral health investigation (child age 12 months)	DHC

ANC- Antenatal Care; CHC- Child Health Care; DHC- Dental Health Care; OPS- Open Pre-Schools.
*Significant changes in professionals' practices pre- and 6 months' post-implementation ($p \leq 0.01$) according to.[1].

Appendix B Effectiveness analysis strategies

Matching strategy

In the difference-in-difference analyses exact matching was imposed on the categorical covariate (education) and caliper matching was used to find matches on age. A caliper of 0.6 was used which means that an observation is considered a match if it is equal to or within 0.6 sample standard deviations of the matching variable. For example, if the age sample standard deviation is 5 in the Salut area at postmeasure then a matching observation from one of the other three groups would have the same level of education and be within 3 years of the age of the considered observation in the Salut area at postmeasure. The reason for using caliper matching instead of exact matching is that it can be difficult to find exact matches on covariates that are not categorical. Using a caliper means that we avoid dropping observations due to no exact matches. In cases where there were tied matches, i.e., several observations matching the birth in Salut area at postmeasure, a weighted average of the outcomes from the tied observations was used. Matching was done "with replacement", i.e. the same observation could be used as a match for more than one observation in the Salut area at postmeasure. In the longitudinal subsample, for each birth in the Salut area at premeasure, a matching observation was found among the births in the non-Salut area at premeasure. An observation was considered a match if it, in the premeasure period, had similar values on the outcome variable as well as on mother's level of education and age. Matching was otherwise performed analogously to the difference-in-difference analysis.

Standard error computation

In the difference-in-difference analyses bootstrap estimates of the standard error was computed using ordinary non-parametric bootstrapping. Specifically, 1000 bootstrap samples were constructed by sampling with replacement from the original sample and, following the procedure described above, a difference-in-difference estimate was computed for each bootstrap sample. The estimated standard error was taken as the sample standard deviation of the 1000 bootstrap difference-in-difference estimates. Using the difference-in-difference estimate based on the original sample and the bootstrap estimated standard error, confidence intervals and p- values were computed under the assumption that the distribution of the difference-in-difference estimator could be approximated by a normal distribution. In the longitudinal analyses standard errors were computed according to Abadie and Imbens (2006). Using the simple matching estimate and the estimated Abadie-Imbens standard error, confidence intervals and p-values were computed under the assumption that the distribution of the simple matching estimator could be approximated by a normal distribution.

Appendix C Costing analysis

Costing methods

We estimated intervention costs as consisting of two main components: Salut Programme costs, and the opportunity cost of professionals to attend the learning seminars. Salut Programme staff consisted of healthcare developers (1-3 people), whose input amounted to 86 person-months, and seven other staff who contributed 10-20 person-months each (change process consultants, a paediatrician, researcher, midwife, dentist, and a statistician). Salut staff salaries and the costs of travel, materials (e.g. manuals, training materials, questionnaires and information leaflets), rent of venues and refreshments were extracted from the accounting system.

The opportunity cost associated with learning seminars was estimated by multiplying the number of attendees in each seminar by daily pay (assuming 8 hours per seminar). Table D1 describes the average hourly pay of professionals and total seminar attendance over 2005-2007. Speakers external to the Salut Programme staff who did not receive financial compensation for their efforts are also included here. Not all seminars were relevant for all professionals, e.g. midwives only attended seminars related to the unborn child. Where the number of attendees was missing, we used the median number of attendees per type of seminar and staff category. Average hourly pay was estimated for each staff category for the years 2005, 2006 and 2007 using average monthly pay for the sex and age group of the average participant from Statistics Sweden [32] to which social security contributions were added [33]. The total time contribution was estimated to equal 2464 hours or approximately 10 person-months.

Table C1 Professionals' seminar attendance and unit costs

Staff category	Hourly pay (INT$)	Total seminar attendance (hours)	Number of attendees (median, per seminar)
Midwife	22	312	4
Child health nurse	27	712	12
Dental hygienist / dental nurse	25	848	5.5
Pre-school teacher	44	200	3
Manager (child health care)	23	192	3
External speakers	29	200	1

Table C2 specifies the allocation rules applied to Salut Programme costs identified in the accounting data. Decision rules by calendar year was the most feasible way to separate between start-up up and intervention costs on the one hand, and between the Salut activities evaluated in this study and other activities on the other hand, because appropriate staff time use information was not available. Start-up costs were annualised over 10 years assuming straight-line depreciation. An equivalent of 4.5 years of annualised start-up costs were included in the total intervention cost, corresponding to the implementation period under study (January 2006-June 2010). In parallel to implementation of the Programme, interventions for older children were being developed. From 2008, Salut staff was preparing to scale up the intervention to the rest of the county.

Table C2 Joint cost allocation rules (%) and division of Salut Programme costs between start-up and implementation

Year	Salut Programme (%)	Interventions for older children (%)	Scale-up of the Salut Programme (%)
2005	100 (start-up)	0	0
2006	60 (of which 1/2 start-up, 1/2 implementation)	40	0
2007	50 (of which 1/3 start-up)	50	0
2008	30 (implementation)	30	40
2009	10 (implementation)	10	80
2010[a]	10 (implementation)	10	80

[a] First six months.

Table C3 Unit costs used in costing analysis, healthcare and other societal costs

Costs	Unit costs (2013 INT$)	Source
Healthcare costs		
Average cost of delivery[a]		Swedish Association of Local Authorities and Regions [2]
Vaginal delivery	5 414	
Caesarean section	8 460	
Average cost mother's inpatient care (per day)[b]	4 119	Swedish Association of Local Authorities and Regions [2]
Average cost child's inpatient care (per day)[c]		Swedish Association of Local Authorities and Regions [2]
<1 year olds	11 610	
1 year olds	5 208	
2 year olds	5 274	
Average cost mother's outpatient care (per visit)[b]	322	Swedish Association of Local Authorities and Regions [2]
Average cost child's outpatient care (per visit)[c]		Swedish Association of Local Authorities and Regions [2]
<1 year olds	312	
1 year olds	333	
2 year olds	335	
Productivity losses		
Mother's average salary (per day)[d]	233	Statistics Sweden [3]

[a] Average cost with and without complications. Each unit cost is weighted by the total number of vaginal deliveries and caesarean sections with or without complications registered in 2013.
[b] Average cost for mothers aged between 18-40 years.

[c] Average cost for males and females in each age group.
[d] Including social charges of 31.42%.

Appendix D Characteristics of the study population and analytical samples

Table D1 Characteristics of the participants in the longitudinal subsample

	Salut area[a]		Non-Salut area[a]	
	pre[b]	**post[b]**	**pre[b]**	**post[b]**
Participants				
Mothers, n	147	147	1249	1249
Children, n	156	153	1352	1298
Covariates				
Mother's age (years), M (SD)	27.6 (4.0)	31.8 (4.1)	28.3 (4.2)	32.1 (4.2)
Mother's education, %				
Compulsory school	9.3	9.9	7.4	6.3
Secondary school	53.3	51.3	43.5	41.4
Higher education	37.3	38.8	49.0	52.4
Health outcomes				
Pregnancy, delivery and around the child's birth				
Smoking[c] (yes), %	4.7	2.1	4.3	3.1
Pregnancy length (≥37 weeks), %	91.4	98.0	95.1	96.0
Caesarean section (yes), %	13.7	16.8	14.6	16.1
Birth weight (≥2 500 g), %	91.4	99.3	96.8	97.7
Birth length (cm), M (SD)	49.8 (3.4)	50.7 (2.1)	50.6 (2.5)	50.6 (2.3)
LGA[d] (yes), %	2.2	6.3	3.5	5.3
SGA[e] (yes), %	4.4	1.4	2.0	1.3
Apgar score[f] (≥7 points) at 1 minute, %	95.7	100.0	95.4	96.1
at 5 minutes, %	98.6	100.0	98.8	98.9
at 10 minutes, %	99.3	100.0	99.8	99.8
Healthy child[g] (yes), %	79.1	85.9	78.0	82.9
Mother's inpatient care[h] (days), M (SD)	4.1 (3.1)	2.7 (1.7)	3.7 (2.3)	2.5 (2.1)
During the first two years after the child's birth				
Mother with early inpatient care[i] (yes), %	0.0	2.6	2.1	1.0
Child with early inpatient care[i] (yes), %	5.8	3.3	6.4	3.9
Mother's inpatient care[j] (days), M (SD)	0.2 (0.8)	0.2 (0.6)	0.3 (2.5)	0.4 (3.7)
Child's inpatient care[j] (days), M (SD)	1.6 (5.8)	1.4 (6.9)	1.6 (8.8)	1.3 (12.0)
Mother's outpatient visits[k], M (SD)	0.0 (0.1)	0.0 (0.1)	0.0 (0.2)	0.0 (0.1)
Child's outpatient visits[k], M (SD)	0.0 (0.1)	0.0 (0.2)	0.0 (0.3)	0.0 (0.2)

M – mean; SD – Standard deviation.

[a] Salut area – Geographical area in Västerbotten county where the Salut Programme was implemented from 2006 and onwards; non-Salut area – remaining part of Västerbotten county.

[b] Premeasure period 2002-2004; postmeasure period 2006-2008.

[c] Smoking status at first antenatal visit, around pregnancy week 12.

[d] Large for gestational age (LGA) – ≥2 SD above the reference population's mean weight.

[e] Small for gestational age (SGA) – ≤2 SD below the reference population's mean weight.

[f] A measure of the newborn's physical condition 1, 5 and 10 minutes after birth, range 0-10 points.

[g] A healthy child according to a paediatrician's examination.
[h] Mother's inpatient care related to delivery.
[i] Early inpatient care for mother and child, respectively, during the first two months after the child's birth, but not related to the delivery.
[j] Cumulative duration of inpatient care for mother and child, respectively, over the child's first two years, excluding care due to delivery complications.
[k] Number of outpatient visits for mother and child, respectively, over the child's first two years, excluding care for the mother due to delivery complications.

Table D2 Number of observations with missing values in the total sample

	Salut area[a]		Non-Salut area[a]	
	pre[b]	post[b]	pre[b]	post[b]
Covariates				
Mother's age (years)	0	0	0	0
Mother's education (compulsory/secondary/higher)	24	19	67	67
Health outcomes				
Pregnancy, delivery and around the child's birth				
Smoking[c] (yes)	115	49	584	304
Pregnancy length (≥37 weeks)	63	20	257	137
Caesarean section (yes)	63	20	257	136
Birth weight (≥2 500 g)	63	21	262	139
Birth length (cm)	67	22	282	162
LGA[d] (yes)	91	41	440	273
SGA[e] (yes)	91	41	440	273
Apgar score[f] (≥7) at 1 minute	68	25	287	168
at 5 minutes	68	25	289	174
at 10 minutes	75	31	397	272
Healthy child[g] (yes)	63	20	257	136
Mother's inpatient care[h] (days)	0	0	0	0
During the first two years after the child's birth				
Mother with early inpatient care[i] (yes)	0	0	0	0
Child with early inpatient care[i] (yes)	0	0	0	0
Mother's inpatient care[j] (days)	0	0	0	0
Child's inpatient care[j] (days)	0	0	0	0
Mother's outpatient visits[k]	0	0	0	0
Child's outpatient visits[k]	0	0	0	0

[a] Salut area – Geographical area in Västerbotten county where the Salut Programme was implemented from 2006 and onwards; non-Salut area – remaining part of Västerbotten county.
[b] Premeasure period 2002-2004; postmeasure period 2006-2008.
[c] Smoking status at first antenatal visit, around pregnancy week 12.
[d] Large for gestational age (LGA) – ≥2 SD above the reference population's mean weight.
[e] Small for gestational age (SGA) – ≤2 SD below the reference population's mean weight.
[f] A measure of the newborn's physical condition 1, 5 and 10 minutes after birth, range 0-10 points.
[g] A healthy child according to a paediatrician's examination.
[h] Mother's inpatient care related to delivery.
[i] Early inpatient care for mother and child, respectively, during the first two months after the child's birth but not related to the delivery.
[j] Cumulative duration of inpatient care for mother and child, respectively, over the child's first two years, excluding care due to delivery complications.
[k] Number of outpatient visits for mother and child, respectively, over the child's first two years, excluding care for the mother due to delivery complications.

Table D3 Number of observations with missing values in the longitudinal subsample

	Salut[a] area		Non-Salut[a] area	
	pre[b]	post[b]	pre[b]	post[b]
Covariates				
Mother's age (years)	0	0	0	0
Mother's education (compulsory/secondary/higher)	6	1	8	3
Health outcomes				
Pregnancy, delivery and around the child's birth				
Smoking[c] (yes)	27	8	118	73
Pregnancy length (≥37 weeks)	17	4	57	21
Caesarean section (yes)	17	4	57	21
Birth weight (≥2 500 g)	17	5	58	21
Birth length (cm)	17	5	64	23
LGA[d] (yes)	21	9	71	49
SGA[e] (yes)	21	9	71	49
Apgar score[f] (≥7) at 1 minute	18	5	59	30
at 5 minutes	18	5	59	31
at 10 minutes	19	6	81	59
Healthy child[g] (yes)	17	4	57	21
Mother's inpatient care[h] (days)	0	0	0	0
During the first two years after the child's birth				
Mother with early inpatient care[i] (yes)	0	0	0	0
Child with early inpatient care[i] (yes)	0	0	0	0
Mother's inpatient care[j] (days)	0	0	0	0
Child's inpatient care[j] (days)	0	0	0	0
Mother's outpatient visits[k]	0	0	0	0
Child's outpatient visits[k]	0	0	0	0

[a] Salut area – Geographical area in Västerbotten county where the Salut Programme was implemented from 2006 and onwards; non-Salut area – remaining part of Västerbotten county.
[b] Premeasure period 2002-2004; postmeasure period 2006-2008.
[c] Smoking status at first antenatal visit, around pregnancy week 12.
[d] Large for gestational age (LGA) – ≥2 SD above the reference population's mean weight.
[e] Small for gestational age (SGA) – ≤2 SD below the reference population's mean weight.
[f] A measure of the newborn's physical condition 1, 5 and 10 minutes after birth, range 0-10 points.
[g] A healthy child according to a paediatrician's examination.
[h] Mother's inpatient care related to delivery.
[i] Early inpatient care for mother and child, respectively, during the first two months after the child's birth, but not related to the delivery.
[j] Cumulative duration of inpatient care for mother and child, respectively, over the child's first two years, excluding care due to delivery complications.
[k] Number of outpatient visits for mother and child, respectively, over the child's first two years, excluding care for the mother due to delivery complications.

Table D4 Exclusions and final analytical sample sizes in difference-in-difference analyses

		Exclusions due to missingness	Eligible for matching	Used for matching
Health outcomes				
Pregnancy, delivery and around the child's birth				
Smoking[c] (yes)	Salut[a] pre[b]	135	868	866
	Salut[a] post[b]	62	826	826
	Non-Salut[a] pre[b]	629	6 035	5 985
	Non-Salut[a] post[b]	354	5 705	5 653
Pregnancy length (≥37 weeks)	Salut pre	84	919	916
	Salut post	34	854	854
	Non-Salut pre	303	6 361	6 310
	Non-Salut post	189	5 870	5 820
Caesarean section (yes)	Salut pre	84	919	916
	Salut post	34	854	854
	Non-Salut pre	303	6 361	6 310
	Non-Salut post	188	5 871	5 821
Birth weight (≥2 500 g)	Salut pre	84	919	916
	Salut post	35	853	853
	Non-Salut pre	308	6 356	6 305
	Non-Salut post	191	5 868	5 818
Birth length (cm)	Salut pre	88	915	912
	Salut post	36	852	852
	Non-Salut pre	328	6 336	6 285
	Non-Salut post	214	5 845	5 795
LGA[d] (yes)	Salut pre	118	885	882
	Salut post	55	833	833
	Non-Salut pre	486	6 178	6 127
	Non-Salut post	325	5 734	5 688
SGA[e] (yes)	Salut pre	118	885	882
	Salut post	55	833	833
	Non-Salut pre	486	6 178	6 127
	Non-Salut post	325	5 734	5 688
Apgar score[f] (≥7) at 1 minute	Salut pre	89	914	911
	Salut post	39	849	849
	Non-Salut pre	333	6 331	6 280
	Non-Salut post	219	5 840	5 790
at 5 minutes	Salut pre	89	914	911
	Salut post	39	849	849
	Non-Salut pre	335	6 329	6 278
	Non-Salut post	225	5 834	5 784

at 10 minutes	Salut pre	96	907	904
	Salut post	45	843	843
	Non-Salut pre	442	6 222	6 174
	Non-Salut post	322	5 737	5 690
Healthy child[g] (yes)	Salut pre	84	919	912
	Salut post	34	854	854
	Non-Salut pre	303	6 361	6 310
	Non-Salut post	188	5 871	5 821
Mother's inpatient care[h] (yes)	Salut pre	24	979	976
	Salut post	19	869	869
	Non-Salut pre	67	6 597	6 545
	Non-Salut post	67	5 992	5 942
During the first two years after the child's birth				
Mother with early inpatient care[i] (yes)	Salut pre	24	979	976
	Salut post	19	869	869
	Non-Salut pre	67	6 597	6 545
	Non-Salut post	67	5 992	5 942
Child with early inpatient care[i] (yes)	Salut pre	24	979	976
	Salut post	19	869	869
	Non-Salut pre	67	6 597	6 545
	Non-Salut post	67	5 992	5 942
Mother's inpatient care[j] (days)	Salut pre	24	979	976
	Salut post	19	869	869
	Non-Salut pre	67	6 597	6 545
	Non-Salut post	67	5 992	5 942
Child's inpatient care[j] (days)	Salut pre	24	979	976
	Salut post	19	869	869
	Non-Salut pre	67	6 597	6 545
	Non-Salut post	67	5 992	5 942
Mother's outpatient visits[k]	Salut pre	24	979	976
	Salut post	19	869	869
	Non-Salut pre	67	6 597	6 545
	Non-Salut post	67	5 992	5 942
Child's outpatient visits[k]	Salut pre	24	979	976
	Salut post	19	869	869
	Non-Salut pre	67	6 597	6 545
	Non-Salut post	67	5 992	5 942

[a] Salut area – Geographical area in Västerbotten county where the Salut Programme was implemented from 2006 and onwards; non-Salut area – remaining part of Västerbotten county.
[b] Premeasure period 2002-2004; postmeasure period 2006-2008.
[c] Smoking status at first antenatal visit, around pregnancy week 12.
[d] Large for gestational age (LGA) – ≥2 SD above the reference population's mean weight.
[e] Small for gestational age (SGA) – ≤2 SD below the reference population's mean weight.
[f] A measure of the newborn's physical condition 1, 5 and 10 minutes after birth, range 0-10 points.

[g] A healthy child according to a paediatrician's examination.
[h] Mother's inpatient care related to delivery.
[i] Early inpatient care for mother and child, respectively, during the first two months after the child's birth, but not related to the delivery.
[j] Cumulative duration of inpatient care for mother and child, respectively, over the child's first two years, excluding care due to delivery complications.
[k] Number of outpatient visits for mother and child, respectively, over the child's first two years, excluding care for the mother due to delivery complications.

Table D5 Results of the effectiveness study when missing values have been imputed, total sample and longitudinal subsample

Health outcomes	Total sample		Longitudinal subsample	
	ATT (95% CI)[a]	p-value	ATT (95% CI)[b]	p-value
Pregnancy, delivery and around the child's birth				
Smoking[c] (yes)	-0.02 (-0.04, 0.01)	0.21	-0.02 (-0.05, 0.01)	0.24
Pregnancy length (≥37 weeks)	0.02 (5e-03, 0.04)	0.12	0.01 (-0.02, 0.04)	0.43
Caesarean section (yes)	0.01 (-0.03, 0.05)	0.66	0.02 (-0.04, 0.07)	0.53
Birth weight (≥2500 g)	0.02 (7e-04, 0.04)	0.04	0.01 (-0.02, 0.03)	0.59
Birth length (cm)	0.13 (-0.10, 0.38)	0.27	0.07 (-0.35, 0.49)	0.74
LGA[d] (yes)	0.01 (-0.01, 0.03)	0.26	0.02 (-0.03, 0.07)	0.47
SGA[e] (yes)	-0.01 (-0.02, 0.01)	0.47	-1e-03 (-0.03, 0.02)	0.93
Apgar score[f] (≥7 points) at 1 minute	0.02 (-3e-03, 0.04)	0.10	*0.03 (0.02, 0.04)*	*4e-12***
at 5 minutes	3e-03 (-0.01, 0.01)	0.57	*0.01 (5e-03, 0.01)*	*2e-04***
at 10 minutes	1e-03 (-5e-03, 7e-03)	0.65	2e-03 (-4e-04, 4e-03)	0.11
Healthy child[g] (yes)	-1e-04 (-0.04, 0.04)	1.00	0.01 (-0.06,0.08)	0.73
Mother's inpatient care[h] (days)	0.02 (-0.22, 0.25)	0.95	0.08 (-0.30, 0.46)	0.67
During the first two years after the child's birth				
Mother with early inpatient care[i] (yes)	0.02 (6e-03, 0.03)	3e-03	0.02 (-0.01, 0.05)	0.15
Child with early inpatient care[i] (yes)	3e-03 (-0.02, 0.02)	0.95	-0.01 (-0.05, 0.03)	0.60
Mother's inpatient care[j] (days)	0.14 (-0.31, 0.60)	0.57	-0.30 (-0.57, -0.03)	0.03
Child's inpatient care[j] (days)	-0.32 (-1.21, 0.56)	0.55	0.44 (-0.88, 1.77)	0.51
Mother's outpatient visits[k]	1e-03 (-0.01, 0.01)	0.75	-0.01 (-0.02, 0.01)	0.20
Child's outpatient visits[k]	0.01 (-0.04, 0.06)	0.60	-0.01 (-0.04, 0.03)	0.65

[a] Difference-in-difference estimates of the average treatment effect on the treated (ATT) with 95% confidence intervals (CI). CIs and p-values were computed with the assumption that ATT was normally distributed and with a standard deviation equal to the bootstrap standard error.

[b] Simple matching estimates of the average treatment effect on the treated (ATT) with 95% confidence intervals (CI). CIs and p-values were computed with the assumption that ATT was normal distributed and with a standard deviation equal to the Abadie-Imbens standard error.

[c] Smoking status at first antenatal visit, around pregnancy week 12.

[d] Large for gestational age (LGA) – ≥2 SD above the reference population's mean weight.

[e] Small for gestational age (SGA) – ≤2 SD below the reference population's mean weight.

[f] A measure of the newborn's physical condition 1, 5 and 10 minutes after birth, range 0-10.

[g] A healthy child according to a paediatrician's examination.

[h] Mother's inpatient care related to delivery.

[i] Early inpatient care for mother and child, respectively, during the first two months after the child's birth but not related to the delivery.
[j] Cumulative duration of inpatient care for mother and child, respectively, over the child's first two years, excluding care due to deliver complications.
[k] Number of outpatient visits for mother and child, respectively, over the child's first two years, excluding care for the mother due to delivery complications.
*Statistically significant effect at the α=0.05 level after a Bonferroni correction for multiple comparisons, i.e. with the 38 outcome variables this implies a significance threshold of 0.05/38=0.001.
**Statistically significant effect at the α=0.01 level after a Bonferroni correction for multiple comparisons, i.e. with the 38 outcome variables this implies a significance threshold of 0.01/38=0.00026.

Table D6 Exclusions and final analytical sample sizes in the longitudinal subsample analyses

		Exclusions due to missingness	Eligible for matching	Used for matching	No matches found
Health outcomes					
Pregnancy, delivery and around the child's birth					
Smoking[c] (yes)	Salut[a]	36	111	111	0
	Non-Salut[a]	148	1 101	963	
Pregnancy length (≥37 weeks)	Salut	24	123	123	0
	Non-Salut	72	1 177	957	
Caesarean section (yes)	Salut	24	123	123	0
	Non-Salut	72	1 177	967	
Birth weight (≥2 500g)	Salut	25	122	121	1
	Non-Salut	72	1 177	984	
Birth length (cm)	Salut	25	122	121	1
	Non-Salut	79	1 170	439	
LGA[d] (yes)	Salut	28	119	119	0
	Non-Salut	91	1 158	965	
SGA[e] (yes)	Salut	28	119	117	2
	Non-Salut	91	1 158	971	
Apgar score[f] (≥7) at 1 minute	Salut	26	121	120	1
	Non-Salut	81	1 168	957	
at 5 minutes	Salut	26	121	120	1
	Non-Salut	82	1 167	1 048	
at 10 minutes	Salut	28	119	118	1
	Non-Salut	127	1 122	1 017	
Healthy child[g] (yes)	Salut	24	123	123	0
	Non-Salut	72	1 177	911	
Mother's inpatient care[h] (yes)	Salut	5	142	137	5
	Non-Salut	7	1 242	605	
During the first two years after the child's birth					
Mother with early inpatient care[i] (yes)	Salut	5	142	142	0
	Non-Salut	7	1 242	1 135	
Child with early inpatient care[i] (yes)	Salut	5	142	142	0
	Non-Salut	7	1 242	1 104	
Mother's inpatient care[j] (days)	Salut	5	142	141	1
	Non-Salut	7	1 242	1 081	
Child's inpatient care[j] (days)	Salut	5	142	141	1
	Non-Salut	7	1 242	972	
Mother's outpatient visits[k]	Salut	5	142	142	0
	Non-Salut	7	1 242	1 145	
Child's outpatient visits[k]	Salut	5	142	142	0
	Non-Salut	7	1 242	1 076	

[a] Salut area – Geographical area in Västerbotten county where the Salut Programme was implemented from 2006 and onwards; non-Salut area – remaining part of Västerbotten county.
[b] Premeasure period 2002-2004; postmeasure period 2006-2008.
[c] Smoking status at first antenatal visit, around pregnancy week 12.
[d] Large for gestational age (LGA) – ≥2 SD above the reference population's mean weight.
[e] Small for gestational age (SGA) – ≤2 SD below the reference population's mean weight.
[f] A measure of the new-borns physical condition 1, 5 and 10 minutes after birth, range 0-10 points.
[g] A healthy child according to a paediatrician's examination.
[h] Mother's inpatient care related to delivery.
[i] Early inpatient care for mother and child, respectively, during the first two months after the child's birth but not related to the delivery.
[j] Cumulative duration of inpatient care for mother and child, respectively, over the child's first two years, excluding care due to delivery complications.
[k] Number of outpatient visits for mother and child, respectively, over the child's first two years, excluding care for the mother due to delivery complications.

Appendix E Healthcare and other societal costs

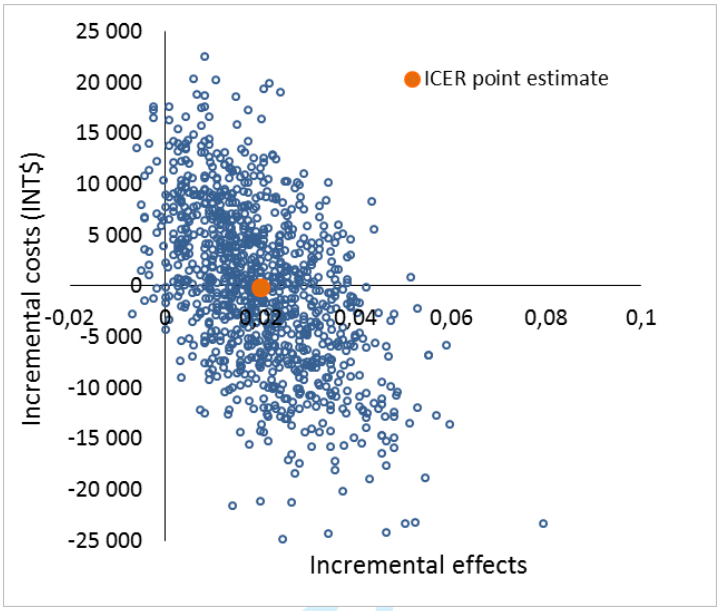
Table E1 Mean healthcare costs and productivity losses for the total sample (2013 INT$)

	Salut[a]	Salut	Non-Salut[a]	Non-Salut	Salut post vs. Salut pre[c]	Non-Salut post vs. Non-Salut pre[d]
	pre[b]	post[b]	pre	post		
Children, n	1 003	888	6 664	6 059		
Healthcare costs						
Pregnancy, delivery and around the child's birth						
Delivery[f]	51 443	51 849	51 342	51 414	406	72
	(9 769)	(10 128)	(9 671)	(9 738)	(458)	(172)
					p=0.39	p=0.68
During the first two years after the child's birth						
Mother's inpatient care	13 581	16 381	179 178	15 925	2 800	-1 993
	(74 369)	(114 098)	(186 633)	(158 752)	(4 383)	(3 087)
					p=0.54	p=0.53
Child's inpatient care	178 499	131 243	137 163	120 308	-47 256	-16 855
	(1 250 316)	(714 282)	(777 528)	(904 385)	(47 636)	(14 917)
					p=0.36	p=0.26
Mother's outpatient visits	30	34	37	36	4	-1
	(287)	(304)	(364)	(317)	(14)	(6)
					p=0.80	p=0.81
Child's outpatient visits	85	160	100	139	74	38
	(509)	(1 219)	(619)	(1 964)	(42)	(25)
					p=0.05	p=0.08
Total healthcare costs	**243 639**	**199 667**	**206 561**	**187 822**	**-43 972**	**-18 739**
	(1 256 313)	**(725 027)**	**(817 517)**	**(919 472)**	**(47 975)**	**(15 400)**
					p=0.41	**p=0.23**
Productivity losses						
During the second year after the child's birth						
Mother's inpatient care	493	422	485	475	-72	-10
	(3 513)	(4 054)	(6 818)	(6 197)	(174)	(116)
					p=0.69	p=0.93
Mother's outpatient visits	12	16	12	13	4	1
	(152)	(174)	(158)	(160)	(8)	(3)
					p=0.78	p=0.83
Total productivity losses	**505**	**437**	**497**	**488**	**-68**	**-9**
	(3 538)	**(4 063)**	**(6 843)**	**(6 210)**	**(175)**	**(116)**
					p=0.70	**p=0.94**
Total healthcare costs and productivity losses	**244 144**	**200 104**	**207 058**	**188 310**	**-44 040**	**-18 748**
	(1 256 656)	**(725 624)**	**(819 261)**	**(920 400)**	**(47 994)**	**(15 424)**
					p=0.41	**p=0.22**

[a] Salut area – Geographical area in Västerbotten county where the Salut Programme was implemented from 2006 and onwards; non-Salut area – remaining part of Västerbotten county.
[b] Premeasure period – 2002-2004; postmeasure period – 2006-2008.
[c] P-values are based on permutation tests of the difference in means between Salut post and Salut pre.
[d] P-values are based on permutation tests of the difference in means between non-Salut post and non-Salut pre.

[e] P-values are based on permutation tests of the difference in means between Salut and non-Salut over time, i.e. the difference in means between non-Salut post and non-Salut pre subtracted from the difference in means between Salut post and Salut pre.
[f] For the 476 births with missing info on delivery type, the cost for Ceasarean section was imputed with probability 0.17 and with probability 0.83 the cost for vaginal delivery was imputed.

Healthcare perspective



Limited societal perspective

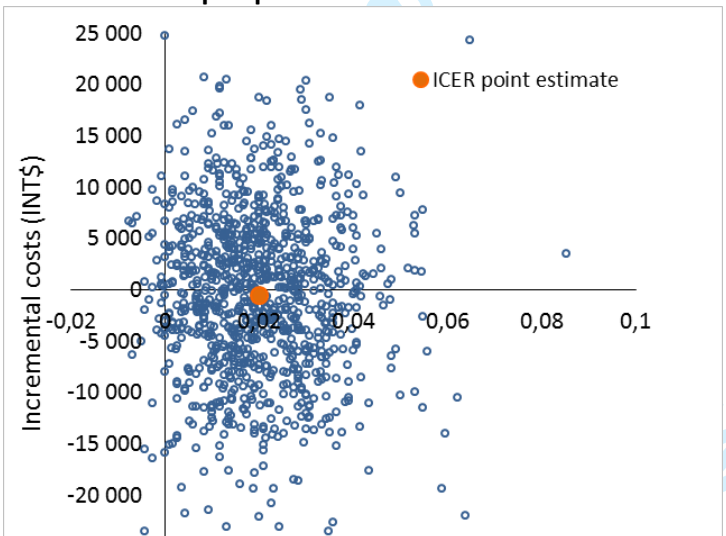
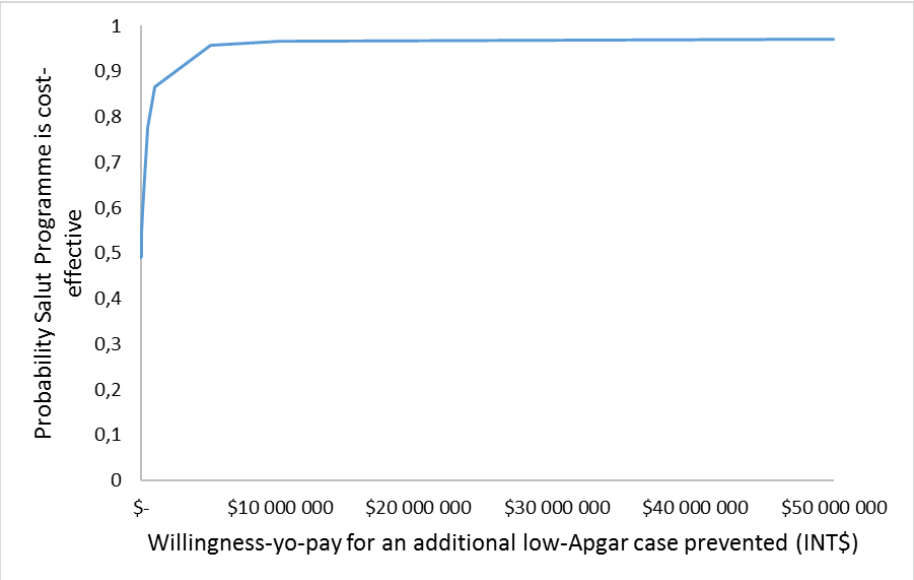


Figure E1. Cost-effectiveness planes for the healthcare and limited societal perspectives. The horizontal axis divides the plane according to incremental effect, and the vertical axis according to incremental cost, which divides the plane into four different quadrants. Each quadrant has a different implication for the cost-effectiveness decision. Iterations falling on the north-east quadrant are those where the intervention is more effective and more costly than the comparator; those on the south-east quadrant are more effective and less costly; those on the south-west quadrant are less effective and less costly; and those on the north-west quadrant are more costly and less effective.

Healthcare perspective



Limited societal perspective

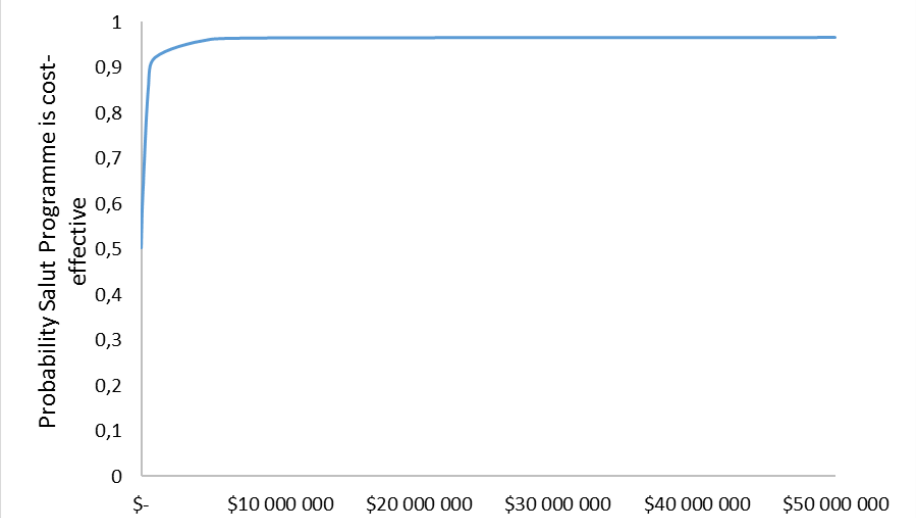


Figure E2. Cost-effectiveness acceptability curve (CEAC) for the healthcare and limited societal perspectives. The CEAC shows the probability that the Salut Programme is cost-effective compared to care-as-usual, subject to a range of possible maximum values that a decision-maker would be willing to pay for an additional low-Apgar case prevented.

References

1. Edvardsson K, Ivarsson A, Garvare R, Eurenius E, Lindkvist M, Mogren I, Small R, Nyström ME: **Improving child health promotion practices in multiple sectors - outcomes of the Swedish Salut Programme**. *BMC Public Health* 2012, **12**:920.
2. **Cost per Patient Database. Cost data 2013 per DRG.** [https://skl.se/ekonomijuridikstatistik/statistik/kostnadperpatientkpp/kppdatabas.1079.html]
3. **Statistical database.** [http://www.statistikdatabasen.scb.se]

Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement

Section/item	Item No	Recommendation	Reported on page No/ line No
Title and abstract			
Title	1	Identify the study as an economic evaluation or use more specific terms such as "cost-effectiveness analysis", and describe the interventions compared.	Title, page 1
Abstract	2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions.	Abstract, page 2
Introduction			
Background and objectives	3	Provide an explicit statement of the broader context for the study. Present the study question and its relevance for health policy or practice decisions	Page 4, lines 15-25
Methods			
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	Page 4, lines 28-31 Page 5, lines 1-10 Page 9, lines 20-32 Page 10, lines 1-2
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	Page 5, lines 5-17
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	Page 5, lines 8-17 Page 8, lines 5-10
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	Page 5, lines 26-32 Page 6, lines 1-8
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	Page 8, lines 5-7
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	Page 8, line 26 Page 9, lines 6-17
Choice of health outcomes	10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	Page 6, lines 9-19
Measurement of effectiveness	11a	*Single study-based estimates:* Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	Page 6, lines 21-32 Page 7, lines 1-20 Appendix B

Section/item	Item No	Recommendation	Reported on page No/ line No
	11b	*Synthesis-based estimates*: Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.	Not applicable
Measurement and valuation of preference based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	Not applicable
Estimating resources and costs	13a	*Single study-based economic evaluation:* Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	Page 8, lines 4-29
	13b	*Model-based economic evaluation:* Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	Not applicable
Currency, price date, and conversion	14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	Page 7, lines 30-32 Page 8, lines 1-10 Appendix C
Choice of model	15	Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended.	Not applicable
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytical model.	Not applicable
Analytical methods	17	Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	Page 7, lines 3-29 Page 11, lines 2-19 Page 12 lines 1-4 Appendix B
Results			

Section/item	Item No	Recommendation	Reported on page No/ line No
Study parameters	18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	Not applicable
Incremental costs and outcomes	19	For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.	Page 19, Table 4 in the main manuscript
Characterising uncertainty	20a	*Single study-based economic evaluation:* Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact of methodological assumptions (such as discount rate, study perspective).	Page 19, Table 4 in the main manuscript Appendix E, Figure E1 and E2
	20b	*Model-based economic evaluation:* Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	Not applicable
Characterising heterogeneity	21	If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.	Not applicable
Discussion			
Study findings, limitations, generalisability, and current knowledge	22	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	Pages 21-23
Other			
Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	Page 24 “Funding”
Conflicts of interest	24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.	Page 24 “Competing interests”

The CHEERS statement checklist format is based on the format of the CONSORT statement checklist

BMJ Open

Is the Salut Programme an effective and cost-effective universal health promotion intervention for parents and their children? A register-based retrospective observational study.

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Is the Salut Programme an effective and cost-effective universal health promotion intervention for parents and their children? A register-based retrospective observational study

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Abstract

Objectives: This study investigates the effectiveness and cost-effectiveness of the Salut Programme, a universal health promotion intervention, compared to care-as-usual, over the periods of pregnancy, delivery and the child's first two years of life.

Method: We adopted a register-based retrospective observational design using existing data sources with respect to both exposures and outcomes. Health outcomes and costs were compared between geographical areas that received care-as-usual (non-Salut area), and areas where the Programme was implemented (Salut area). We included mothers and their children from both the Salut and non-Salut areas if: i) the child was born 2002-2004 (premeasure period) or ii) the child was born 2006-2008 (postmeasure period). The effectiveness study adopted two strategies: i) a matched difference-in-difference analysis using data from all participants; and ii) a longitudinal analysis restricted to mothers who had given birth twice, i.e. both in the pre- and postmeasure periods. The economic evaluation was performed from a health care and a limited societal perspective. Outcomes were clustered during pregnancy, delivery and birth, and the child's first two years.

Results: Difference-in-difference analyses did not yield any significant effect on the outcomes. Longitudinal analyses resulted in significant positive improvement in Apgar scores, reflecting the newborn's physical condition, with more children having a normal Apgar score (1 minute +3%, 5 minutes +1%). The cost of the Programme was INT$ 308/child. From both costing perspectives, the Programme yielded higher effects and lower costs than care-as-usual, being thus cost-saving (probability of around 50%).

Conclusions: Our findings suggest that the Salut Programme is an effective universal intervention to improve maternal and child health, and may be good value for money, however there is large uncertainty around the cost estimates.

Strengths and limitations of this study

- The findings suggest that the Salut Programme is an effective universal intervention to improve maternal and child health, and may be good value for money.
- Our study contributes to the limited evidence base regarding universal multi-sectorial health promotion approaches during pregnancy and early childhood.
- A major strength of this study is that the "state of the art" methods were used in the effectiveness analyses.
- Our analyses were limited to data available in registers. We lacked access to data on primary care and medication as well as on lifestyle and health-related quality of life.
- In the cost-effectiveness analyses, the limited societal perspective only included productivity losses due to mothers' inpatient and outpatient care, which might have contributed to the uncertainty in the results.

Background

Development during the prenatal period, infancy and childhood is known to influence lifelong health [1-4], and the link between early-life health and adult outcomes is strong and economically meaningful [5]. Promotion of optimal child development and wellbeing comprises early detection and treatment of whole families, and can potentially prevent the development of behavioural and emotional problems in children and adolescents [6].

Until now, the research community has failed to provide persuasive evidence about the effectiveness and cost-effectiveness of health promotion and preventive interventions. However, evaluation of intervention efforts is necessary for evidence-based decision-making [7 8]. Childhood obesity programmes have been suggested to be cost-effective [9], but other examples are rare. There are considerable methodological challenges when conducting such evaluations, and more thorough economic analyses of preventive programmes are encouraged. Economic evaluation is important for both those delivering and funding the interventions [10], and if demonstrated to be cost-effective, experiences and work modes can potentially be used in other settings.

The current project is nested within the Swedish Salut Child Health Intervention Programme, initiated in Västerbotten County in 2005 in addition to care-as-usual. The Programme is a multi-sectorial, family-centred approach to health promotion and prevention. One of the Programme aims is avoidance of maternal and foetal pregnancy complications related to maternal lifestyle. This study aimed to investigate the effectiveness and cost-effectiveness of the Salut Programme compared to care-as-usual, over the periods of pregnancy, delivery and the child's first two years of life. The study was guided by the following research questions:

1) Does the Salut Programme improve maternal and child health?
2) What are the resource implications of the Salut Programme in terms of intervention and societal costs?
3) Is the Salut Programme a cost-effective public health intervention?

Methods

Overall study design and participants

The current study adopted a register-based retrospective observational design using existing data sources with respect to both exposures and outcomes [11]. We simulated an experiment by taking

advantage of the stepwise implementation of the Programme and nationally available individual-level register data collected independently of our study [12].

Health outcomes and costs were compared between geographical areas that received care-as-usual (non-Salut area), and areas where the Programme was implemented from 2006 and onwards (Salut area). The mother's place of residence at the child's birth determined whether the child and mother were classified as belonging to the Salut area or the non-Salut area. Thus, an intention-to-treat approach was used [13]. We included mothers and their children from both the Salut area and non-Salut area if the child was born 2002-2004 (thus before the Salut Programme was implemented anywhere), defined as the premeasure period. Accordingly, we included mothers and their children if the child was born 2006-2008 (thus after the Salut Programme was implemented in some areas), defined as the postmeasure period. Henceforth, four study groups were formed: Salut pre, Salut post, non-Salut pre and non-Salut post.

We conducted an effectiveness study and an economic evaluation study. The effectiveness study adopted two complementary strategies: a matched difference-in-difference analysis using data from all participants, and a longitudinal analysis restricted to the subsample of mothers who had given birth twice during the study period, both in the pre- and postmeasure periods. The economic evaluation was conducted from both a healthcare and a limited societal perspective. In a recently published study protocol we have described the Salut Programme and our planned analysis strategies [14]. In the present study, this protocol has largely been followed. A few revisions have been made when necessary, and are described and motivated below.

Care-as-usual and the Salut Programme

Care-as-usual during pregnancy and childhood is free of charge and decentralised to locally-elected county councils with tax raising powers, which creates some variation across the country in delivery of services. Almost all parents attend antenatal care, and likewise almost all children attend child healthcare and dental care with an accompanying parent. Open pre-schools are free of charge, run by the municipality or churches, and attended on a drop-in basis by families.

The Salut Programme is integrated within care-as-usual, and comprises strengthening and restructuring of care-as-usual, and new specific interventions. Professionals in antenatal care, child healthcare, dental care and open pre-schools are invited to learning seminars and are encouraged to use manuals, specifically developed for the Salut Programme, to guide everyday practice. Following

countywide implementation, an evaluation showed significant improvements in professionals' health promotion practices and in collaboration across sectors [15]. The Programme is described in detail in appendix A, table A1 -A2 and in previous publications [14 16-18].

Health outcomes

Health outcome measures were chosen to demonstrate the performance of the Salut Programme with respect to supporting normal pregnancy and birth, and in other ways contributing to the well-being of children and their mothers. Another prerequisite was that the measures were available through the Umeå SIMSAM Lab [12], compiled from national and local registers. Moreover, we were guided by a recent publication on frequently measured outcomes to assess maternity care performance [19]. A detailed description of the registers can be found elsewhere [14]. The following time periods and outcome measures were chosen:

1) During pregnancy, delivery and at birth – Mother's smoking status at first antenatal visit (yes/no); pregnancy length at delivery (≥37/<37 weeks); caesarean section (yes/no); birth weight (≥2500/<2500 g); birth length (cm); large for gestational age (LGA; ≥2 standard deviations above the reference population's mean weight); small for gestational age (SGA; ≤2 standard deviations below the reference population's mean weight); Apgar score 1, 5, and 10 minutes after delivery (≥7/<7 points); child diagnosed by paediatrician as healthy (yes/no); and duration of mother's inpatient care related to delivery (days).

2) During the first two years after the child's birth – Inpatient care not related to delivery within the two first months after child's birth (yes/no); cumulative duration of inpatient care (days); and cumulative number of outpatient visits, all for mother and child, respectively.

Effectiveness analyses

The samples are presented in figure 1. Assumptions and details regarding the analysis strategies are described elsewhere 14, and in appendix B. The matched difference-in-difference analyses utilized the total sample. For each child born in the Salut area at postmeasure, matching observations were found in each of the other three groups: Salut area pre, non-Salut area pre and non-Salut area post. For every outcome an observation was deemed a match if the mother, at the time of the child's birth, had the same level of education and similar age as the mother of a child born in the Salut area at postmeasure. The average difference over time in the Salut area was computed as the difference between the mean outcome in the Salut area at postmeasure and the mean outcome of the matched

observations from the Salut area at premeasure. Analogously, the average difference over time in the non-Salut area was computed as the difference between the mean outcome of the matched observations from the non-Salut area at postmeasure and the mean outcome of the matched observations from the non-Salut area at premeasure. The final difference-in-difference estimate of the average treatment effect on the treated was computed by subtracting the average difference over time in the non-Salut area from the average difference over time in the Salut area. To obtain confidence intervals reflecting the uncertainty around the average treatment effect on the treated (ATT) point estimates standard errors were computed using non-parametric bootstrapping with 1000 replications[20].

In the longitudinal analyses we utilized the subsample of mothers that gave birth to at least one child in each of the time periods, and living in the same geographical area over the whole time period (figure 1). For a given outcome of interest, focusing on this subsample allowed us to use the mother's premeasure outcome value as a covariate on which to match on, in addition to the matching variables used in the difference-in-difference analyses. The simple matching estimate of the average treatment effect on the treated was computed as the difference between the mean outcome in the Salut area at postmeasure, and the mean outcome of the matched observations from the non-Salut area at postmeasure. Abadie-Imbens standard errors[21] were computed to obtain confidence intervals reflecting the uncertainty around the ATT point estimates. The standard error computation is based on estimation of the asymptotic variance of the simple matching estimator and is preferable to bootstrapping in this case since the latter would lead to inconsistent standard error estimation[22].

In all analyses, matching was performed separately for each outcome variable, namely the identity of the match was not fixed across analyses. Analyses were conducted in R 3.3.0 [23] using the Matching package [24] for matching and Abadie-Imbens standard errors.

(figure 1 here)

Figure 1. An overview of the study population and samples used in the analyses.

Economic evaluation

The economic analysis aimed to capture both the healthcare and the wider societal costs and benefits of the Salut Programme for the first two years of the children's lives, and their mothers. Two perspectives were adopted: a health care perspective, consisting of intervention costs and other healthcare resources used by children and mothers, and a limited societal perspective, additionally including productivity losses associated with mothers' illness [34]. Results are expressed in 2013 purchasing-power parity international dollars (8.71 SEK=INT$) after adjusting for inflation using the gross domestic product deflator [25].

Intervention cost

Programme costs were estimated between January 2005 and June 2010. We added the opportunity cost of professionals' time to attend learning seminars during 2005-2007 (appendix C, table C1). Calendar year-based allocation rules for joint costs and the division between start-up and implementation were decided upon retrospectively by the Salut Programme staff to capture the changing nature of activities over time (appendix C, table C2). Intervention costs were discounted at an annual rate of 3%.

Healthcare and other societal costs

Healthcare related costs were derived from information on the use of healthcare resources external to the Salut Programme, such as maternal inpatient care related to delivery and children's and mothers' inpatient and outpatient care due to illness. All healthcare related costs were calculated for the child's first two years. Productivity losses due to mothers' illness were included in the analysis conducted from a limited societal perspective. Productivity losses were calculated using the human capital approach, by multiplying time off work due to inpatient and outpatient care by the average gross salary (including social charges). The average number of parental benefit days during the first year is around 220 for women in Sweden [26]. Therefore, mothers were assumed to be on parental leave during the first year after childbirth, hence productivity losses were estimated for year two only. Contrary to the planned analyses in the study protocol [14], care of a sick child compensations were excluded from the analysis, as these were only linked to the parent and not to a particular child. In addition, these costs can be considered transfer payments, thus including them would constitute double counting. Total costs were estimated by multiplying frequencies of resources by their

respective unit cost. Costs incurred during year two were discounted at 3%. The difference in health care and other societal costs was compared between the Salut Programme and care-as-usual and between pre- and postmeasure using permutation tests. Unit costs used to value resource use are listed in appendix C, table C3.

Cost-effectiveness analysis

The economic framework of this study is a retrospective register-based cost-effectiveness analysis. We compared costs and outcomes of the Salut Programme to care-as-usual, from a healthcare and a limited societal perspective, and calculated incremental cost-effectiveness ratios (ICERs). Deterministic cost-effectiveness was expressed as the cost per low-Apgar case prevented. For the probabilistic analysis, we used non-parametric bootstrapping with 1000 replications to obtain 95% confidence intervals around the ICER and investigate the uncertainty around the ICER estimates. The bootstrap results are presented on a cost-effectiveness plane. We explored the probability that Salut is cost-effective compared to care-as-usual, subject to a range of possible maximum values that a decision maker would be willing to pay for an additional low-Apgar case prevented. Cost-effectiveness acceptability curves (CEAC) for the healthcare and the limited societal perspectives were generated by plotting these probabilities for a range of willingness-to-pay values. CEACs are a recommended decision-making approach to dealing with uncertainty regarding the cost-effectiveness estimates and the maximum values decision makers would be willing to pay for these. A decision maker who knows their maximum willingness-to-pay for an additional unit of health gain can use the CEAC to determine the strength of the evidence on the cost-effectiveness of an intervention [27]. Bootstrapping and the CEACs were performed in Excel 2011.

Results

Characteristics of the study population

In the Salut area, 1003 and 888 children were born in the premeasure and postmeasure period, respectively (figure 1). In the non-Salut area, 6664 and 6059 children were born in the premeasure and postmeasure period, respectively. There were 147 mothers that gave birth at least once to 309 children in the Salut area and 1249 mothers that gave birth at least once to 2650 children in the non-Salut area. Characteristics of the total sample are given in table 1, and for the longitudinal subsample in appendix D, table D1. Mothers giving birth to children in the Salut area were on average younger and less educated compared to mothers in the non-Salut area. The differences in age and education

between Salut post and Non-Salut post on the one hand, and between Salut post and Non-Salut pre on the other hand, were all statistically significant with p-values below 0.001. Between Salut post and Salut pre there were no significant differences in age and education (p-values 0.78 and 0.30, respectively). Missing values varied between measures (appendix D, tables D2-D3). Information on mother's education was missing for 2.1-2.4% of the Salut area observations and 1.0-1.1% of the non-Salut area observations. All outcomes at birth exhibited some missingness, with the largest proportion for the smoking variable (10.4% in Salut-area pre). Outcomes during the first two years after birth were all fully observed.

Table 1 Characteristics of the participants in the total sample

	Salut area[a]		Non-Salut area[a]	
	pre[b]	post[b]	pre[b]	post[b]
Participants				
Mothers, n	918	828	6056	5737
Children, n	1003	888	6664	6059
Covariates				
Mother's age (years), M (SD)	29.7 (5.3)	29.7 (5.2)	30.3 (4.9)	30.3 (5.0)
Mother's education, %				
Compulsory school	11.0	11.3	7.5	7.5
Secondary school	51.2	48.1	44.5	36.8
Higher education	37.8	40.6	48.0	55.7
Health outcomes				
Pregnancy, delivery and around the child's birth				
Smoking[+c] (yes), %	8.4	5.2	5.3	3.8
Pregnancy length[+] (≥37 weeks), %	92.6	95.0	94.4	94.6
Caesarean section[+] (yes), %	17.2	18.1	16.4	16.4
Birth weight[++] (≥2 500 g), %	94.8	96.9	96.5	96.4

Birth length[++] (cm), M (SD)	50.3 (2.8)	50.3 (2.9)	50.5 (2.5)	50.3 (2.5)
LGA[++d] (yes), %	3.6	3.8	4.4	3.4
SGA[++e] (yes), %	2.5	2.5	1.7	1.9
Apgar score[++f] (≥7 points) at 1 minute, %	95.8	96.3	95.3	94.6
at 5 minutes, %	99.1	99.4	98.7	98.5
at 10 minutes, %	99.7	99.8	99.7	99.6
Healthy child[++g] (yes), %	79.3	81.1	77.8	79.2
Mother's inpatient care[+h] (days), M (SD)	3.7 (2.8)	3.1 (2.0)	3.6 (2.6)	2.9 (2.2)
During the first two years after the child's birth				
Mother with early inpatient care[+i] (yes), %	1.1	2.4	1.8	1.3
Child with early inpatient care[++i] (yes), %	6.9	4.2	6.9	4.3
Mother's inpatient care[+j] (days), M (SD)	0.4 (2.1)	0.5 (3.2)	0.5 (5.3)	0.5 (4.5)
Child's inpatient care[++j] (days), M (SD)	1.9 (12.8)	1.5 (8.2)	1.5 (8.1)	1.4 (9.6)
Mother's outpatient visits[+k], M (SD)	0.0 (0.1)	0.0 (0.1)	0.0 (0.1)	0.0 (0.1)
Child's outpatient visits[++k], M (SD)	0.0 (0.2)	0.1 (0.4)	0.0 (0.2)	0.1 (0.7)

M – mean; SD – Standard deviation.

[+] Outcome maternal health

[++] Outcome child health

[a] Salut area – Geographical area in Västerbotten county where the Salut Programme was implemented prior to 2009; Non-Salut area – remaining part of Västerbotten county.

[b] Premeasure period – 2002-2004; postmeasure period – 2006-2008.

[c] Smoking status at first antenatal visit, around pregnancy week 12.

[d] Large for gestational age (LGA) – ≥2 SD above the reference population's mean weight.

[e] Small for gestational age (SGA) – ≤2 SD below the reference population's mean weight.

[f] A measure of the newborn's physical condition 1, 5 and 10 minutes after birth, range 0-10.

[g] A healthy child according to a paediatrician's examination.

[h] Mother's inpatient care related to delivery.

[i] Early inpatient care for mother and child, respectively, during the first two months after the child's birth but not related to the delivery.

[j] Cumulative duration of inpatient care for mother and child, respectively, over the child's first two years, excluding care due to delivery complications.

[k] Number of outpatient visits for mother and child, respectively, over the child's first two years, excluding care for the mother due to delivery complications.

Effectiveness analyses

Before conducting the difference-in-difference analyses, observations with missing values on outcome and/or matching variables were excluded. The analytical sample sizes differed between outcomes since exclusion of observations was done separately for each outcome (appendix D, tables D2-D3). The samples were well balanced before matching, but matching improved the covariate balance and resulted in standardized mean differences [28 29], close to zero for all covariates in all analyses. The difference-in-difference analyses did not result in any significant average treatment effect on the treated estimates. Hence, we conclude that for those individuals who were exposed to the Salut Programme, the Programme had on average no significant effect on the outcomes studied (table 2), but the data suggest changes in a positive direction for the majority of health outcomes.

Before conducting the longitudinal analyses, the subsample of mothers giving birth at least once in each time period in the same area was further reduced in the following manner: for mothers who gave birth to more than one child in the same area at premeasure, observations from this period not relating to the last birth in that area and period were excluded. Analogously, if there were multiple births in the same area at postmeasure, observations from this period not relating to the first birth in that area and period were excluded. These exclusions were performed so that the variables at premeasure could be used as baseline variables to match on. Due to multiple births in the same area and period, observations were excluded from Salut area post (6), Salut area pre (9), non-Salut area post (49), and non-Salut area pre (103). Finally, observations with missing values on outcome and/or covariates were excluded as in the difference-in-difference analyses (appendix D, tables D4-D5). Matching improved the covariate balance and resulted in standardized mean differences close to zero for all covariates. The longitudinal analyses resulted in significant positive average treatment effect on the treated estimates for the outcomes Apgar at 1 and 5 minutes (table 2).

We conclude that for those who were exposed to the Salut Programme, in the subpopulation of mothers giving birth at least twice, there were 3% (95% CI: 2-4%) more births with high Apgar at 1 minute compared to what would have been the case had they not been exposed to the Programme. Similarly, there were 1% (95% CI: 0.5-2%) more births with high Apgar at 5 minutes compared to what would have been the case had they not been exposed to the Salut Programme. For our sample, this translates to 3.6 and 1.2 additional children having high Apgar at 1 and 5 minutes, respectively. We estimated the number needed to treat to prevent one case with low Apgar at 5 minutes by dividing one by the absolute risk reduction between Salut and non-Salut (0.02); 50 mothers would need to be exposed to the Salut Programme to prevent one case of low Apgar. The results for the other outcomes

showed no significant effects; however, even for this population we can see changes in a positive direction.

To assess how sensitive the results are to the exclusion of observations with missing values, analogous analyses where performed on samples where missing values had been imputed using multivariate imputations by chained equations with predictive mean matching[30]. The results from analyses based on the samples with imputed values do not differ substantially from the results presented in table 2 and the conclusions that can be drawn are the same (appendix D, table D6).

Table 2 Results of the effectiveness study, total sample and longitudinal subsample

Health outcomes	Total sample		Longitudinal subsample	
	ATT (95% CI)[a]	p-value	ATT (95% CI)[b]	p-value
Pregnancy, delivery and around the child's birth				
Smoking[+c] (yes), %	-0.02 (-0.05, 4e-03)	0.09	-0.02 (-0.06, 0.01)	0.11
Pregnancy length[+] (≥37 weeks), %	0.02 (3e-04, 0.04)	0.08	0.02 (-0.02, 0.05)	0.34
Caesarean section[+] (yes), %	0.01 (-0.03, 0.05)	0.66	-4e-05 (-0.04, 0.04)	1.00
Birth weight[++] (≥2 500 g), %	0.02 (-6e-04, 0.05)	0.06	0.01 (-8e-03, 0.03)	0.22
Birth length[++] (cm), M (SD)	0.11 (-0.19, 0.41)	0.47	0.10 (-0.31, 0.51)	0.63
LGA[++d] (yes), %	0.01 (-0.01, 0.03)	0.30	0.01 (-0.04, 0.05)	0.73
SGA[++e] (yes), %	-4e-03 (-0.02, 0.02)	0.72	-0.01 (-0.02, -4e-03)	0.01
Apgar score[++f] (≥7 points) at 1 minute, %	0.02 (-2e-03, 0.04)	0.07	*0.03 (0.02, 0.04)*	*4e-12***
at 5 minutes, %	5e-03 (-0.01, 0.02)	0.34	*0.01 (5e-03, 0.02)*	*9e-05***
at 10 minutes, %	1e-03 (-4e-03, 7e-03)	0.61	2e-03 (-6e-04, 4e-03)	0.15
Healthy child[++g] (yes), %	0.01 (-0.04, 0.05)	0.81	0.01 (-0.06, 0.08)	0.73

Mother's inpatient care[+h] (days), M (SD)	-4e-03 (-0.26, 0.25)	0.98	-0.04 (-0.43, 0.34)	0.82
During the first two years after the child's birth				
Mother with early inpatient care[+i] (yes), %	0.02 (7e-03, 0.03)	3e-03	0.01 (-0.01, 0.04)	0.26
Child with early inpatient care[++i] (yes), %	0.01 (-0.01, 0.03)	0.44	-3e-04 (-0.03, 0.03)	0.98
Mother's inpatient care[+j] (days), M (SD)	0.08 (-0.25, 0.40)	0.64	-0.28 (-0.53, -0.04)	0.02
Child's inpatient care[++j] (days), M (SD)	-0.17 (-1.33, 0.99)	0.77	0.37 (-1.03, 1.77)	0.60
Mother's outpatient visits[+k], M (SD)	1e-03 (-0.01, 0.01)	0.86	-0.01 (-0.03, 0.01)	0.19
Child's outpatient visits[++k], M (SD)	0.02 (-0.02, 0.05)	0.40	-2e-03 (-0.04, 0.03)	0.92

[+] Outcome maternal health
[++] Outcome child health
[a] Difference-in-difference estimates of the average treatment effect on the treated (ATT) with 95% confidence intervals (CI). CIs and p-values were computed with the assumption that ATT was normally distributed and with a standard deviation equal to the bootstrap standard error.
[b] Simple matching estimates of the average treatment effect on the treated (ATT) with 95% confidence intervals (CI). CIs and p-values were computed with the assumption that ATT was normal distributed and with a standard deviation equal to the Abadie-Imbens standard error.
[c] Smoking status at first antenatal visit, around pregnancy week 12.
[d] Large for gestational age (LGA) – ≥2 SD above the reference population's mean weight.
[e] Small for gestational age (SGA) – ≤2 SD below the reference population's mean weight.
[f] A measure of the newborn's physical condition 1, 5 and 10 minutes after birth, range 0-10.
[g] A healthy child according to a paediatrician's examination.
[h] Mother's inpatient care related to delivery.
[i] Early inpatient care for mother and child, respectively, during the first two months after the child's birth but not related to the delivery.
[j] Cumulative duration of inpatient care for mother and child, respectively, over the child's first two years, excluding care due to delivery complications.
[k] Number of outpatient visits for mother and child, respectively, over the child's first two years, excluding care for the mother due to delivery complications.
*Statistically significant effect at the α=0.05 level after a Bonferroni correction for multiple comparisons, i.e. with the 38 outcome variables this implies a significance threshold of 0.05/38=0.001.
**Statistically significant effect at the α=0.01 level after a Bonferroni correction for multiple comparisons, i.e. with the 38 outcome variables this implies a significance threshold of 0.01/38=0.00026.

1

2 ## Intervention costs

3 The total cost of the Salut Programme was INT$ 273 063 (2 379 260 SEK). Averaged over the 888
4 children born in the Salut area at postmeasure gives a cost of INT$ 308 (2 679 SEK) per child. The
5 largest cost components were staff (64%), and the opportunity cost of professionals' time to attend

the learning seminars (16%). Of the total, 28% were start-up costs incurred during 2005-2007. The average annual implementation cost was INT$ 43 575 (379 677 SEK; averaged over 66 months).

Healthcare and other societal costs

Mean healthcare costs and productivity losses at pre- and postmeasure for the Salut and the non-Salut areas for the longitudinal subsample (n=1289) are shown in table 3. Healthcare costs were lower in the Salut area due to less inpatient care for both mothers and children. Healthcare costs tended to be lower at postmeasure compared to premeasure in both areas, but the differences were not statistically significant. The standard deviation around the mean healthcare cost estimates was large mostly because of large variation in inpatient care costs.

Productivity losses increased in the non-Salut area from pre- to postmeasure (+INT$ 29; p=0.03), but remained unchanged in the Salut area, which explains the difference in productivity losses over time in the Salut area compared to the non-Salut area (-INT$ 31 per child; p= 0.38). Adding up healthcare costs and productivity losses, total costs (excluding intervention costs) were INT$ 1556 lower at postmeasure than at premeasure in the Salut area, and INT$ 1127 lower at postmeasure than at premeasure in the non-Salut area. Hence, total costs fell by INT$ 430 more per person in the Salut area compared to the non-Salut area (p=0.97). Analyses of healthcare costs and productivity losses for the total sample are found in the appendix E, table E1.

Table 3 Mean healthcare costs and productivity losses for the longitudinal sub-sample (2013 INT$)[a]

	Salut[b]		Difference Salut post-pre[d]		Non-Salut[b]		Difference Non-Salut post-pre[e]		Incremental costs Salut vs. Non-Salut[f]	
Costs	pre[c]	post[c]		p-value*	pre[c]	post[c]		p-value*		p-value
Intervention cost per child		308	308						308	
Children, n	121	121			1 168	1 168				
Healthcare costs, M (SD)										
Pregnancy, delivery and around the child's birth										
Delivery	5767 (979)	5842 (1063)	76 (131)	p=0.70	5855 (1072)	5894 (1110)	39 (45)	p=0.41	36 (147)	p=0.81
During the first two years after the child's birth										
Mother's inpatient care	604 (3089)	605 (2547)	1 (364)	p=1.00	1100 (8396)	1822 (15 637)	722 (519)	p=0.18	-721 (1618)	p=0.60
Child's inpatient care	10 773 (50 242)	9142 (43 492)	-1631 (6041)	p=0.82	15 245 (98 078)	13 331 (143 972)	-1914 (5097)	p=0.75	283 (15 960)	p=0.98
Mother's outpatient care	3 (28)	3 (28)	0 (4)	p=1.00	4 (36)	5 (40)	2 (2)	p=0.27	-2 (5)	p=0.75

Child's outpatient care	8 (49)	8 (50)	0 (6)	p=1.00	14 (97)	11 (64)	-4 (3)	p=0.28	4 (11)	p=0.68
Total healthcare costs	17 154 (50 535)	15 599 (43 666)	-1555 (6072)	p=0.83	22 219 (98 650)	21 063 (144 736)	-1156 (5125)	p=0.86	-399 (16 048)	p=0.97
Productivity losses, M (SD)										
During the second year after the child's birth										
Mother's outpatient care	2 (21)	2 (21)	0 (3)	p=1.00	2 (20)	2 (21)	0 (1)	p=1.00	0 (3)	p=0.94
Mother's inpatient care	17 (98)	15 (104)	-2 (13)	p=0.90	20 (170)	48 (440)	29 (14)	*p=0.03**	-31 (43)	p=0.38
Total productivity losses	19 (99)	17 (106)	-2 (13)	p=1.00	21 (172)	50 (441)	29 (14)	*p=0.02**	-31 (43)	p=0.38
Total healthcare costs + productivity losses	17 173 (50 538)	15 616 (43 670)	-1556 (6072)	p=0.83	22 240 (98 660)	21 113 (144 768)	-1127 (5126)	p=0.85	-430 (16 051)	p=0.97

*Statistical significance defined as p<0.05.

[a] Results expressed in 2013 purchasing-power parity adjusted international dollars (1 INT$=8.71 SEK).

[b] Salut area – Geographical area in Västerbotten county where the Salut Programme was implemented prior to 2009; Non-Salut area – remaining pai
Västerbotten county. Several of the health outcomes are further described in table 1.

[c] Premeasure period – 2002-2004; postmeasure period – 2006-2008.

[d] P-values are based on permutation tests of the difference in means between Salut post and Salut pre.

[e] P-values are based on permutation tests of the difference in means between Non-Salut pc
and Non-Salut pre.

[f] P-values are based on permutation tests of the difference in means between Salut and Non-Salut over time, i.e. the difference in means between Non-Salut post and Non-Salut pre subtracted from the difference in means between Salut post and Salut pre.

Cost-effectiveness analysis

Both Apgar at 1 and 5 minutes showed statistically significant differences between Salut and non-Salut areas in the longitudinal analysis. Previous studies suggest that a low Apgar score at 5 minutes correlates with neonatal mortality and confers an increased risk of neurologic disability and cognitive impairment [31-33]. In contrast, Apgar at 1 minute is not a good predictor of infant outcomes [34]. Hence, we considered Apgar at 5 minutes as the only relevant outcome in the cost-effectiveness analysis. The cost-effectiveness results for both costing perspectives are given in table 4. From both a healthcare and a limited societal perspective, the Salut Programme yields higher effects and lower costs (i.e. "dominant) than care-as-usual (non-Salut). The probability that the Salut Programme is cost-saving and entails positive effects compared to care-as-usual is approximately 50% (48.3% for the healthcare perspective and 49.7% for the limited societal perspective).

Figure E1 in the appendix E presents the cost-effectiveness results on a cost-effectiveness plane for both costing perspectives. The bootstrapped estimates of incremental costs and effects fall approximately equally in the south-east and north-east quadrants of the plane. This is consistent with the Salut Programme having positive effects and a approximately 50% probability of being cost-saving compared to care-as-usual. The cost effectiveness plane demonstrates that the uncertainty around the cost estimates is indeed very large. This is further evidenced when plotting the cost effectiveness acceptability curve (CEAC, Figure E2 in the appendix E) for different willingness-to-pay (WTP) values. With a zero WTP for preventing a case of low-Apgar, the probability that the Salut Programme is cost-effective is approximately 50%. This probability hardly increases with WTP until very high ceiling values of 100.000 INT$ and above.

Table 4 Results of the cost-effectiveness study, longitudinal sub-sample (costs in 2013 INT$)

	Salut area[a]				Non-Salut area[a]						
	Average cost post-pre[b, c] M (SD)		Average proportion of low Apgar[d] cases prevented post-pre M (SD)		Average cost post-pre M (SD)		Average proportion of low Apgar cases prevented post-pre M (SD)		Bootstrapped Incremental costs	Bootstrapped Incremental effects	ICER
	Base-case	Bootstrap	Base-case	Bootstrap	Base-case	Boot-strap	Base-case	Boot-strap			
Healthcare perspective	-1247 (66 658)	-1207 (5892)	0.016 (0.128)	0.016 (0.011)	-1156 (176 067)	-1131 (5294)	- 0.003 (0.149)	-0.003 (0.004)	-76	0.02	dominant[ef]
Limited societal perspective	-1249 (66 668)	-1398 (5941)	0.016 (0.128)	0.016 (0.011)	-1127 (176 099.98)	-922 (5284)	- 0.003 (0.149)	-0.003 (0.004)	-476	0.02	dominant[ef]

ICER – Incremental cost-effectiveness ratio; CI – Confidence interval.

[a] Salut area – Geographical area in Västerbotten county where the Salut Programme was implemented from 2006 and onwards; non-Salut area – remaining part of Västerbotten county. Several of the health outcomes are further described in Table 1.

[b] Premeasure period – 2002-2004; postmeasure period – 2006-2008.

[c] The average cost per participant includes intervention costs and resource use costs

[d] Apgar at 5 minutes – a measure of the newborn's physical condition at 5 minutes after birth, range 0-10 points.

[e] The intervention is less costly and more effective than the comparator (dominant).

[f] Approximately 3% of the observations have negative effects.

Discussion

Main study findings and comparison with other studies

Our results suggest that the Salut Programme is an effective universal child health promotion intervention, and is likely to represent good value for money. The difference-in-difference analyses did not show significant improvements in maternal and child health outcomes, but suggested changes in a positive direction. However, the longitudinal analyses resulted in a significant positive improvement in Apgar scores, reflecting the newborn's physical condition, with more children having a normal Apgar score (1 minute +3%, and 5 minutes +1%). Notably, a recent publication suggests that a low Apgar score at 5 minutes may also serve as an indicator of poor maternal health [35]. This recent published six-year study of over 600,000 newborns has extended the application of Apgar and identified a link between the newborn's Apgar score and the mother's need for intensive care.

The cost added by the Programme to care-as-usual was small, INT$ 308, representing only 4% of the average health care cost for the pregnancy, delivery and neonatal periods per woman/child, INT$ 7945 [36]. From both a healthcare and a limited societal perspective, the Programme yielded higher effects and lower costs than care-as-usual, with approximately 50% probability of being cost-saving and entailing positive effects. Exploration of the uncertainty around the cost-effectiveness data showed that there was relatively large uncertainty around the cost estimates. In our view the most likely explanation is that the noted differences in costs may not have been directly impacted by the intervention. Importantly, the Salut Programme would only have a higher probability of cost-effectiveness compared to care-as-usual if decision makers would be willing to pay much more (what seem unreasonably high financial figures) for an additional low-Apgar case prevented. Thus, our findings show that Salut can be good value for money. However, more evidence is needed about costs, in particular how Salut may impact on healthcare costs in the long-term.

Our study contributes to the limited evidence base regarding universal multi-sectorial health promotion interventions during pregnancy and early childhood. We are aware of only a few evaluations of the effectiveness and cost-effectiveness of such interventions. The universal parenting programme "All Children in Focus", offered to parents of children aged 3 and above, showed a positive effect on parental self-efficacy and child health [37]. However, the programme had a low probability of cost-effectiveness [38]. Another study of a nurse-led intensive home visiting programme for first-time teenage mothers found no short-term benefits concerning the selected primary outcomes [39].

Strengths and weaknesses of the study

We evaluated the Salut Programme as it was implemented in current practice, which increases the external validity and generalisability of the results. The use of existing register data, in which exposure and outcomes have been routinely collected [12], reduces the amount of missing data. The "state of the art" methods used in the effectiveness analyses, which do not require strong assumptions regarding the data generating mechanisms, allowed us to identify the differential effect of the Programme on children and mothers born in Salut versus non-Salut areas in a natural experiment [40].

While intention-to-treat [13] was the only feasible approach, we may have underestimated the intervention effects. We controlled for mothers' age and education using matching as well as the premeasure value of the outcome in the longitudinal analyses. However, we are aware of the risk for residual confounding. Another possible source of underestimation of effects is that the intervention development period (2005-2007) in part overlaps with the postmeasure period (children born 2006-2008). The retrospective study design limited us in terms of evaluating whether there was an initial learning period, during which effectiveness of the Programme was lower. If such a learning period indeed existed, we may also have underestimated the opportunity cost of the Programme, because we assumed that (as stipulated by the Programme), professionals integrated the Programme interventions within care-as-usual. In the case visits took more time than usual early on during implementation, a full societal perspective should also consider the incremental opportunity cost of parents' time. Due to the limitations of the retrospective design we were not able to evaluate whether such a learning period existed.

As the Programme is a universal health promotion intervention, medical outcome measures were not expected to show significant effects. However, our analyses were limited to data available in registers. In particular, we lacked access to data on primary care visits and medication as well as on lifestyle and health-related quality of life. In the cost-effectiveness analyses, the limited societal perspective only included productivity losses due to mothers' inpatient and outpatient care, which might have contributed to the uncertainty in the results.

Implications for policy and clinical practice

Apgar scores have long been used as a measure for assessing infant wellbeing at birth, but 5-minute Apgar scores in particular have also become a well-established predictive index for long-term outcomes such as neonatal morbidity and mortality in normal-birth weighted infants [41-43]. Low Apgar score at 5 minutes is associated with an increased risk of neurological disabilities[32 44]. For example, 1.7 % of newborns with low Apgar scores are diagnosed with cerebral palsy, compared with 0.05 % of

newborns with normal Apgar score at 5 minutes[45]. Hence, to prevent one case of cerebral palsy, one would have to prevent 55 cases of low Apgar at 5 minutes. As such, the estimated lifetime cost for a child with cerebral palsy is about INT$ 850 000 [46], while the broad implementation of the Salut programme would result in additional health benefits (cases of normal Apgar score) at no additional costs. Although there is no study estimating the willingness-to-pay for a low-Apgar case prevented, this comparison might serve as a reference frame.

Universal complex interventions implemented in real-life settings, such as the Salut Programme, are scarce and pose challenges with respect to implementation, dissemination and evaluation [47]. The reliability of our results depends on how the Salut Programme was implemented in current praxis. Interviews with professionals suggest that key issues for effective implementation are involvement of professionals in intervention development, regular meetings with professionals and process consultants, and the use of manuals [16]. On the other hand, more resources would likely have improved feasibility by providing professionals with more dedicated time to deliver the interventions. Continuous support from decision-makers is necessary [48] to sustain the effectiveness and cost-effectiveness of an evidence-based intervention, such as the Salut Programme, in the long-term.

Conclusions

Our study suggests that the Salut Programme is an effective universal intervention to improve maternal and child health, and may be good value for money. The probability that the Salut Programme is cost-saving and entails positive effects is around 50% over a wide range of willingness to pay ceiling values, although with a large uncertainty around the cost estimates.

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Contributors

The statistical analyses were carried out by JH, and the economic evaluation by FS, AMPB and IF. AI and IF conceived and designed the study. EE, ML and AI constitute the scientific steering group for the Salut Programme, and AI is principal investigator for the Umeå SIMSAM Lab, both prerequisites for the present study. All the authors (JH, FS, EE, AMPB, AI, ML and IF) contributed to the writing process and have approved the final manuscript.

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Competing interests

None declared.

Ethics approval

The Regional Ethical Review Board in Umeå gave clearance for the Salut Programme research (2010-63-31M) and for the Umeå SIMSAM Lab research (2010-157-31Ö).

Data sharing statement

No additional data are available.

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List of tables and figures

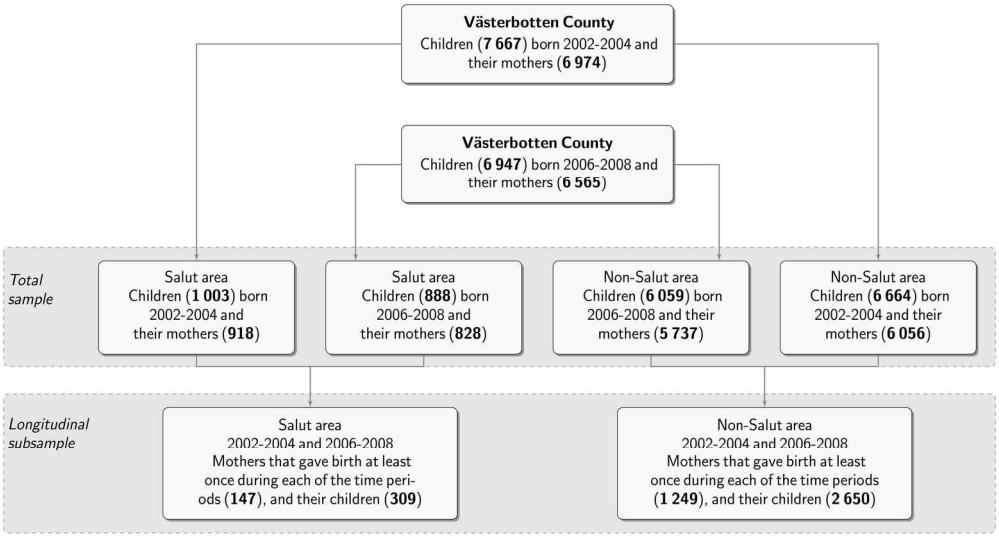


Figure 1. An overview of the study population and samples used in the analyses

84x45mm (600 x 600 DPI)

Appendix A The Swedish Salut child health intervention programme

Table A1 Västerbotten County Council's vision and the Salut Programme's aims and focus areas

Vision, aims, focus areas	Content
Vision	By 2020, the health and wellbeing of the population will be the best in the world.
Overall aim	Good health is achieved by salutogenic interventions in collaboration with societal actors and the family with the child's best in focus. Through systematic improvements, interventions are developed and implemented to promote satisfactory conditions during childhood, increased physical activity, and healthy eating habits.
Main focus areas	To promote healthy eating habits, physical activity and good psychosocial health, and to prevent obesity and caries.
Aims during pregnancy period	Avoidance of maternal and foetal pregnancy complications related to maternal lifestyle. Healthy maternal weight gain during pregnancy. A minimum of 30 minutes daily physical activity. Regular meals. Five fruits and vegetables a day. Tooth-brushing twice a day with fluoride toothpaste. Regular dental health care visits. Parents are feeling prepared for their parental roles. Pregnant women are living in relations free from intimate partner violence. Pregnant women refrain from tobacco, alcohol and drug use.
Aims for parents and children 0-18 months	Normal weight development for 18-month olds. Retain of pre-pregnancy weight. Sufficient sleep (parents and children). Environments free from tobacco and drug use, and alcohol use is limited. A minimum of one hour daily physical activity (play) for children. A minimum of 30 minutes daily physical activity for parents. Avoidance of TV-viewing and TV/computer games for children. Six months exclusive breastfeeding, and thereafter partly continued for 1 year or longer. Introduction of 5 fruits and vegetables a day for children. Five fruits and vegetables a day for parents. Regular meals for both parents and children. Avoidance of discretionary foods for children. Tooth-brushing twice a day with fluoride toothpaste (from the first tooth for the children). Regular dental health care visits. Parents feel confident in their parental roles. Satisfying parental-child attachment and interaction. Women/children live in an environment free from violence and violation.

Table A2 Care-as-usual and the Salut Programme's interventions targeting parents-to-be and their children during pregnancy and until the child is 18 months, and significant changes in professionals' practices post Salut implementation

Care-as-usual	**Arena**
Maternal and foetal surveillance (7-9 check-ups)	ANC
Psychosocial- and lifestyle counselling	ANC, CHC
Participation in parental support groups	ANC, CHC
Health and development check-ups, and immunizations (about 10 visits when the child is 0-18 months, and more often when needed)	CHC
Advice on teeth brushing twice a day	CHC, DHC
Oral health check-up and health promoting advice (child age 2-3 years)	DHC
Socialization at open preschools for children not yet enrolled in regular preschools and their parents	OPS
The Salut Programme	**Arena**
Strengthening or restructuring of 'care-as-usual'	
Motivational Interviewing (MI)	ANC, CHC*, DHC
Collaboration between any of involved sectors	ANC*, CHC*
Involvement in parental support groups	ANC, CHC
Lifestyle counselling	ANC, CHC*, DHC*
Edinburgh Postnatal Depression Scale (EPDS) at "mother's visit" (Child age 8 weeks)	ANC
Activities to enhance early parent-child attachment, parent relation-ships, children's physical activity and linguistic development	CHC, OPS
Activities to promote healthy snacks/food and drinks	OPS*
Activities to encourage physical activity	OPS
The Salut Programme specific interventions	
Questionnaires for health surveillance	ANC, CHC, DHC
Free dental health counselling for the parents-to-be	DHC
Collaboration between any of involved sectors	DHC*, OPS*
Contribution to parental support groups	DHC, OPS
Questions for domestic violence during pregnancy and at "mother's visit" (child age 8 weeks)	ANC*, CHC*
Focus on fathers' experiences of change in life situation at "father's visit" (child age 10 months)	CHC*
Oral health investigation (child age 12 months)	DHC

ANC- Antenatal Care; CHC- Child Health Care; DHC- Dental Health Care; OPS- Open Pre-Schools.
*Significant changes in professionals' practices pre- and 6 months' post-implementation ($p \leq 0.01$) according to.[1].

Appendix B Effectiveness analysis strategies

Matching strategy

In the difference-in-difference analyses exact matching was imposed on the categorical covariate (education) and caliper matching was used to find matches on age. A caliper of 0.6 was used which means that an observation is considered a match if it is equal to or within 0.6 sample standard deviations of the matching variable. For example, if the age sample standard deviation is 5 in the Salut area at postmeasure then a matching observation from one of the other three groups would have the same level of education and be within 3 years of the age of the considered observation in the Salut area at postmeasure. The reason for using caliper matching instead of exact matching is that it can be difficult to find exact matches on covariates that are not categorical. Using a caliper means that we avoid dropping observations due to no exact matches. In cases where there were tied matches, i.e., several observations matching the birth in Salut area at postmeasure, a weighted average of the outcomes from the tied observations was used. Matching was done "with replacement", i.e. the same observation could be used as a match for more than one observation in the Salut area at postmeasure. In the longitudinal subsample, for each birth in the Salut area at premeasure, a matching observation was found among the births in the non-Salut area at premeasure. An observation was considered a match if it, in the premeasure period, had similar values on the outcome variable as well as on mother's level of education and age. Matching was otherwise performed analogously to the difference-in-difference analysis.

Standard error computation

In the difference-in-difference analyses bootstrap estimates of the standard error was computed using ordinary non-parametric bootstrapping. Specifically, 1000 bootstrap samples were constructed by sampling with replacement from the original sample and, following the procedure described above, a difference-in-difference estimate was computed for each bootstrap sample. The estimated standard error was taken as the sample standard deviation of the 1000 bootstrap difference-in-difference estimates. Using the difference-in-difference estimate based on the original sample and the bootstrap estimated standard error, confidence intervals and p- values were computed under the assumption that the distribution of the difference-in-difference estimator could be approximated by a normal distribution. In the longitudinal analyses standard errors were computed according to Abadie and Imbens (2006). Using the simple matching estimate and the estimated Abadie-Imbens standard error, confidence intervals and p-values were computed under the assumption that the distribution of the simple matching estimator could be approximated by a normal distribution.

Appendix C Costing analysis

Costing methods

We estimated intervention costs as consisting of two main components: Salut Programme costs, and the opportunity cost of professionals to attend the learning seminars. Salut Programme staff consisted of healthcare developers (1-3 people), whose input amounted to 86 person-months, and seven other staff who contributed 10-20 person-months each (change process consultants, a paediatrician, researcher, midwife, dentist, and a statistician). Salut staff salaries and the costs of travel, materials (e.g. manuals, training materials, questionnaires and information leaflets), rent of venues and refreshments were extracted from the accounting system.

The opportunity cost associated with learning seminars was estimated by multiplying the number of attendees in each seminar by daily pay (assuming 8 hours per seminar). Table D1 describes the average hourly pay of professionals and total seminar attendance over 2005-2007. Speakers external to the Salut Programme staff who did not receive financial compensation for their efforts are also included here. Not all seminars were relevant for all professionals, e.g. midwives only attended seminars related to the unborn child. Where the number of attendees was missing, we used the median number of attendees per type of seminar and staff category. Average hourly pay was estimated for each staff category for the years 2005, 2006 and 2007 using average monthly pay for the sex and age group of the average participant from Statistics Sweden [32] to which social security contributions were added [33]. The total time contribution was estimated to equal 2464 hours or approximately 10 person-months.

Table C1 Professionals' seminar attendance and unit costs

Staff category	Hourly pay (INT$)	Total seminar attendance (hours)	Number of attendees (median, per seminar)
Midwife	22	312	4
Child health nurse	27	712	12
Dental hygienist / dental nurse	25	848	5.5
Pre-school teacher	44	200	3
Manager (child health care)	23	192	3
External speakers	29	200	1

Table C2 specifies the allocation rules applied to Salut Programme costs identified in the accounting data. Decision rules by calendar year was the most feasible way to separate between start-up up and intervention costs on the one hand, and between the Salut activities evaluated in this study and other activities on the other hand, because appropriate staff time use information was not available. Start-up costs were annualised over 10 years assuming straight-line depreciation. An equivalent of 4.5 years of annualised start-up costs were included in the total intervention cost, corresponding to the implementation period under study (January 2006-June 2010). In parallel to implementation of the Programme, interventions for older children were being developed. From 2008, Salut staff was preparing to scale up the intervention to the rest of the county.

Table C2 Joint cost allocation rules (%) and division of Salut Programme costs between start-up and implementation

Year	Salut Programme (%)	Interventions for older children (%)	Scale-up of the Salut Programme (%)
2005	100 (start-up)	0	0
2006	60 (of which 1/2 start-up, 1/2 implementation)	40	0
2007	50 (of which 1/3 start-up)	50	0
2008	30 (implementation)	30	40
2009	10 (implementation)	10	80
2010[a]	10 (implementation)	10	80

[a] First six months.

Table C3 Unit costs used in costing analysis, healthcare and other societal costs

Costs	Unit costs (2013 INT$)	Source
Healthcare costs		
Average cost of delivery[a]		Swedish Association of Local Authorities and Regions [2]
Vaginal delivery	5 414	
Caesarean section	8 460	
Average cost mother's inpatient care (per day)[b]	4 119	Swedish Association of Local Authorities and Regions [2]
Average cost child's inpatient care (per day)[c]		Swedish Association of Local Authorities and Regions [2]
<1 year olds	11 610	
1 year olds	5 208	
2 year olds	5 274	
Average cost mother's outpatient care (per visit)[b]	322	Swedish Association of Local Authorities and Regions [2]
Average cost child's outpatient care (per visit)[c]		Swedish Association of Local Authorities and Regions [2]
<1 year olds	312	
1 year olds	333	
2 year olds	335	
Productivity losses		
Mother's average salary (per day)[d]	233	Statistics Sweden [3]

[a] Average cost with and without complications. Each unit cost is weighted by the total number of vaginal deliveries and caesarean sections with or without complications registered in 2013.
[b] Average cost for mothers aged between 18-40 years.

[c] Average cost for males and females in each age group.
[d] Including social charges of 31.42%.

Appendix D Characteristics of the study population and analytical samples

Table D1 Characteristics of the participants in the longitudinal subsample

	Salut area[a]		Non-Salut area[a]	
	pre[b]	**post[b]**	**pre[b]**	**post[b]**
Participants				
Mothers, n	147	147	1249	1249
Children, n	156	153	1352	1298
Covariates				
Mother's age (years), M (SD)	27.6 (4.0)	31.8 (4.1)	28.3 (4.2)	32.1 (4.2)
Mother's education, %				
Compulsory school	9.3	9.9	7.4	6.3
Secondary school	53.3	51.3	43.5	41.4
Higher education	37.3	38.8	49.0	52.4
Health outcomes				
Pregnancy, delivery and around the child's birth				
Smoking[c] (yes), %	4.7	2.1	4.3	3.1
Pregnancy length (≥37 weeks), %	91.4	98.0	95.1	96.0
Caesarean section (yes), %	13.7	16.8	14.6	16.1
Birth weight (≥2 500 g), %	91.4	99.3	96.8	97.7
Birth length (cm), M (SD)	49.8 (3.4)	50.7 (2.1)	50.6 (2.5)	50.6 (2.3)
LGA[d] (yes), %	2.2	6.3	3.5	5.3
SGA[e] (yes), %	4.4	1.4	2.0	1.3
Apgar score[f] (≥7 points) at 1 minute, %	95.7	100.0	95.4	96.1
at 5 minutes, %	98.6	100.0	98.8	98.9
at 10 minutes, %	99.3	100.0	99.8	99.8
Healthy child[g] (yes), %	79.1	85.9	78.0	82.9
Mother's inpatient care[h] (days), M (SD)	4.1 (3.1)	2.7 (1.7)	3.7 (2.3)	2.5 (2.1)
During the first two years after the child's birth				
Mother with early inpatient care[i] (yes), %	0.0	2.6	2.1	1.0
Child with early inpatient care[i] (yes), %	5.8	3.3	6.4	3.9
Mother's inpatient care[j] (days), M (SD)	0.2 (0.8)	0.2 (0.6)	0.3 (2.5)	0.4 (3.7)
Child's inpatient care[j] (days), M (SD)	1.6 (5.8)	1.4 (6.9)	1.6 (8.8)	1.3 (12.0)
Mother's outpatient visits[k], M (SD)	0.0 (0.1)	0.0 (0.1)	0.0 (0.2)	0.0 (0.1)
Child's outpatient visits[k], M (SD)	0.0 (0.1)	0.0 (0.2)	0.0 (0.3)	0.0 (0.2)

M – mean; SD – Standard deviation.

[a] Salut area – Geographical area in Västerbotten county where the Salut Programme was implemented from 2006 and onwards; non-Salut area – remaining part of Västerbotten county.

[b] Premeasure period 2002-2004; postmeasure period 2006-2008.

[c] Smoking status at first antenatal visit, around pregnancy week 12.

[d] Large for gestational age (LGA) – ≥2 SD above the reference population's mean weight.

[e] Small for gestational age (SGA) – ≤2 SD below the reference population's mean weight.

[f] A measure of the newborn's physical condition 1, 5 and 10 minutes after birth, range 0-10 points.

[g] A healthy child according to a paediatrician's examination.
[h] Mother's inpatient care related to delivery.
[i] Early inpatient care for mother and child, respectively, during the first two months after the child's birth, but not related to the delivery.
[j] Cumulative duration of inpatient care for mother and child, respectively, over the child's first two years, excluding care due to delivery complications.
[k] Number of outpatient visits for mother and child, respectively, over the child's first two years, excluding care for the mother due to delivery complications.

Table D2 Number of observations with missing values in the total sample

	Salut area[a]		Non-Salut area[a]	
	pre[b]	post[b]	pre[b]	post[b]
Covariates				
Mother's age (years)	0	0	0	0
Mother's education (compulsory/secondary/higher)	24	19	67	67
Health outcomes				
Pregnancy, delivery and around the child's birth				
Smoking[c] (yes)	115	49	584	304
Pregnancy length (≥37 weeks)	63	20	257	137
Caesarean section (yes)	63	20	257	136
Birth weight (≥2 500 g)	63	21	262	139
Birth length (cm)	67	22	282	162
LGA[d] (yes)	91	41	440	273
SGA[e] (yes)	91	41	440	273
Apgar score[f] (≥7) at 1 minute	68	25	287	168
at 5 minutes	68	25	289	174
at 10 minutes	75	31	397	272
Healthy child[g] (yes)	63	20	257	136
Mother's inpatient care[h] (days)	0	0	0	0
During the first two years after the child's birth				
Mother with early inpatient care[i] (yes)	0	0	0	0
Child with early inpatient care[i] (yes)	0	0	0	0
Mother's inpatient care[j] (days)	0	0	0	0
Child's inpatient care[j] (days)	0	0	0	0
Mother's outpatient visits[k]	0	0	0	0
Child's outpatient visits[k]	0	0	0	0

[a] Salut area – Geographical area in Västerbotten county where the Salut Programme was implemented from 2006 and onwards; non-Salut area – remaining part of Västerbotten county.
[b] Premeasure period 2002-2004; postmeasure period 2006-2008.
[c] Smoking status at first antenatal visit, around pregnancy week 12.
[d] Large for gestational age (LGA) – ≥2 SD above the reference population's mean weight.
[e] Small for gestational age (SGA) – ≤2 SD below the reference population's mean weight.
[f] A measure of the newborn's physical condition 1, 5 and 10 minutes after birth, range 0-10 points.
[g] A healthy child according to a paediatrician's examination.
[h] Mother's inpatient care related to delivery.
[i] Early inpatient care for mother and child, respectively, during the first two months after the child's birth but not related to the delivery.
[j] Cumulative duration of inpatient care for mother and child, respectively, over the child's first two years, excluding care due to delivery complications.
[k] Number of outpatient visits for mother and child, respectively, over the child's first two years, excluding care for the mother due to delivery complications.

Table D3 Number of observations with missing values in the longitudinal subsample

	Salut[a] area		Non-Salut[a] area	
	pre[b]	post[b]	pre[b]	post[b]
Covariates				
Mother's age (years)	0	0	0	0
Mother's education (compulsory/secondary/higher)	6	1	8	3
Health outcomes				
Pregnancy, delivery and around the child's birth				
Smoking[c] (yes)	27	8	118	73
Pregnancy length (≥37 weeks)	17	4	57	21
Caesarean section (yes)	17	4	57	21
Birth weight (≥2 500 g)	17	5	58	21
Birth length (cm)	17	5	64	23
LGA[d] (yes)	21	9	71	49
SGA[e] (yes)	21	9	71	49
Apgar score[f] (≥7) at 1 minute	18	5	59	30
at 5 minutes	18	5	59	31
at 10 minutes	19	6	81	59
Healthy child[g] (yes)	17	4	57	21
Mother's inpatient care[h] (days)	0	0	0	0
During the first two years after the child's birth				
Mother with early inpatient care[i] (yes)	0	0	0	0
Child with early inpatient care[i] (yes)	0	0	0	0
Mother's inpatient care[j] (days)	0	0	0	0
Child's inpatient care[j] (days)	0	0	0	0
Mother's outpatient visits[k]	0	0	0	0
Child's outpatient visits[k]	0	0	0	0

[a] Salut area – Geographical area in Västerbotten county where the Salut Programme was implemented from 2006 and onwards; non-Salut area – remaining part of Västerbotten county.
[b] Premeasure period 2002-2004; postmeasure period 2006-2008.
[c] Smoking status at first antenatal visit, around pregnancy week 12.
[d] Large for gestational age (LGA) – ≥2 SD above the reference population's mean weight.
[e] Small for gestational age (SGA) – ≤2 SD below the reference population's mean weight.
[f] A measure of the newborn's physical condition 1, 5 and 10 minutes after birth, range 0-10 points.
[g] A healthy child according to a paediatrician's examination.
[h] Mother's inpatient care related to delivery.
[i] Early inpatient care for mother and child, respectively, during the first two months after the child's birth, but not related to the delivery.
[j] Cumulative duration of inpatient care for mother and child, respectively, over the child's first two years, excluding care due to delivery complications.
[k] Number of outpatient visits for mother and child, respectively, over the child's first two years, excluding care for the mother due to delivery complications.

Table D4 Exclusions and final analytical sample sizes in difference-in-difference analyses

		Exclusions due to missingness	Eligible for matching	Used for matching
Health outcomes				
Pregnancy, delivery and around the child's birth				
Smoking[c] (yes)	Salut[a] pre[b]	135	868	866
	Salut[a] post[b]	62	826	826
	Non-Salut[a] pre[b]	629	6 035	5 985
	Non-Salut[a] post[b]	354	5 705	5 653
Pregnancy length (≥37 weeks)	Salut pre	84	919	916
	Salut post	34	854	854
	Non-Salut pre	303	6 361	6 310
	Non-Salut post	189	5 870	5 820
Caesarean section (yes)	Salut pre	84	919	916
	Salut post	34	854	854
	Non-Salut pre	303	6 361	6 310
	Non-Salut post	188	5 871	5 821
Birth weight (≥2 500 g)	Salut pre	84	919	916
	Salut post	35	853	853
	Non-Salut pre	308	6 356	6 305
	Non-Salut post	191	5 868	5 818
Birth length (cm)	Salut pre	88	915	912
	Salut post	36	852	852
	Non-Salut pre	328	6 336	6 285
	Non-Salut post	214	5 845	5 795
LGA[d] (yes)	Salut pre	118	885	882
	Salut post	55	833	833
	Non-Salut pre	486	6 178	6 127
	Non-Salut post	325	5 734	5 688
SGA[e] (yes)	Salut pre	118	885	882
	Salut post	55	833	833
	Non-Salut pre	486	6 178	6 127
	Non-Salut post	325	5 734	5 688
Apgar score[f] (≥7) at 1 minute	Salut pre	89	914	911
	Salut post	39	849	849
	Non-Salut pre	333	6 331	6 280
	Non-Salut post	219	5 840	5 790
at 5 minutes	Salut pre	89	914	911
	Salut post	39	849	849
	Non-Salut pre	335	6 329	6 278
	Non-Salut post	225	5 834	5 784

at 10 minutes	Salut pre	96	907	904
	Salut post	45	843	843
	Non-Salut pre	442	6 222	6 174
	Non-Salut post	322	5 737	5 690
Healthy child[g] (yes)	Salut pre	84	919	912
	Salut post	34	854	854
	Non-Salut pre	303	6 361	6 310
	Non-Salut post	188	5 871	5 821
Mother's inpatient care[h] (yes)	Salut pre	24	979	976
	Salut post	19	869	869
	Non-Salut pre	67	6 597	6 545
	Non-Salut post	67	5 992	5 942
During the first two years after the child's birth				
Mother with early inpatient care[i] (yes)	Salut pre	24	979	976
	Salut post	19	869	869
	Non-Salut pre	67	6 597	6 545
	Non-Salut post	67	5 992	5 942
Child with early inpatient care[i] (yes)	Salut pre	24	979	976
	Salut post	19	869	869
	Non-Salut pre	67	6 597	6 545
	Non-Salut post	67	5 992	5 942
Mother's inpatient care[j] (days)	Salut pre	24	979	976
	Salut post	19	869	869
	Non-Salut pre	67	6 597	6 545
	Non-Salut post	67	5 992	5 942
Child's inpatient care[j] (days)	Salut pre	24	979	976
	Salut post	19	869	869
	Non-Salut pre	67	6 597	6 545
	Non-Salut post	67	5 992	5 942
Mother's outpatient visits[k]	Salut pre	24	979	976
	Salut post	19	869	869
	Non-Salut pre	67	6 597	6 545
	Non-Salut post	67	5 992	5 942
Child's outpatient visits[k]	Salut pre	24	979	976
	Salut post	19	869	869
	Non-Salut pre	67	6 597	6 545
	Non-Salut post	67	5 992	5 942

[a] Salut area – Geographical area in Västerbotten county where the Salut Programme was implemented from 2006 and onwards; non-Salut area – remaining part of Västerbotten county.
[b] Premeasure period 2002-2004; postmeasure period 2006-2008.
[c] Smoking status at first antenatal visit, around pregnancy week 12.
[d] Large for gestational age (LGA) – ≥2 SD above the reference population's mean weight.
[e] Small for gestational age (SGA) – ≤2 SD below the reference population's mean weight.
[f] A measure of the newborn's physical condition 1, 5 and 10 minutes after birth, range 0-10 points.

[g] A healthy child according to a paediatrician's examination.
[h] Mother's inpatient care related to delivery.
[i] Early inpatient care for mother and child, respectively, during the first two months after the child's birth, but not related to the delivery.
[j] Cumulative duration of inpatient care for mother and child, respectively, over the child's first two years, excluding care due to delivery complications.
[k] Number of outpatient visits for mother and child, respectively, over the child's first two years, excluding care for the mother due to delivery complications.

Table D5 Results of the effectiveness study when missing values have been imputed, total sample and longitudinal subsample

Health outcomes	Total sample		Longitudinal subsample	
	ATT (95% CI)[a]	p-value	ATT (95% CI)[b]	p-value
Pregnancy, delivery and around the child's birth				
Smoking[c] (yes)	-0.02 (-0.04, 0.01)	0.21	-0.02 (-0.05, 0.01)	0.24
Pregnancy length (≥37 weeks)	0.02 (5e-03, 0.04)	0.12	0.01 (-0.02, 0.04)	0.43
Caesarean section (yes)	0.01 (-0.03, 0.05)	0.66	0.02 (-0.04, 0.07)	0.53
Birth weight (≥2500 g)	0.02 (7e-04, 0.04)	0.04	0.01 (-0.02, 0.03)	0.59
Birth length (cm)	0.13 (-0.10, 0.38)	0.27	0.07 (-0.35, 0.49)	0.74
LGA[d] (yes)	0.01 (-0.01, 0.03)	0.26	0.02 (-0.03, 0.07)	0.47
SGA[e] (yes)	-0.01 (-0.02, 0.01)	0.47	-1e-03 (-0.03, 0.02)	0.93
Apgar score[f] (≥7 points) at 1 minute	0.02 (-3e-03, 0.04)	0.10	*0.03 (0.02, 0.04)*	*4e-12***
at 5 minutes	3e-03 (-0.01, 0.01)	0.57	*0.01 (5e-03, 0.01)*	*2e-04***
at 10 minutes	1e-03 (-5e-03, 7e-03)	0.65	2e-03 (-4e-04, 4e-03)	0.11
Healthy child[g] (yes)	-1e-04 (-0.04, 0.04)	1.00	0.01 (-0.06,0.08)	0.73
Mother's inpatient care[h] (days)	0.02 (-0.22, 0.25)	0.95	0.08 (-0.30, 0.46)	0.67
During the first two years after the child's birth				
Mother with early inpatient care[i] (yes)	0.02 (6e-03, 0.03)	3e-03	0.02 (-0.01, 0.05)	0.15
Child with early inpatient care[i] (yes)	3e-03 (-0.02, 0.02)	0.95	-0.01 (-0.05, 0.03)	0.60
Mother's inpatient care[j] (days)	0.14 (-0.31, 0.60)	0.57	-0.30 (-0.57, -0.03)	0.03
Child's inpatient care[j] (days)	-0.32 (-1.21, 0.56)	0.55	0.44 (-0.88, 1.77)	0.51
Mother's outpatient visits[k]	1e-03 (-0.01, 0.01)	0.75	-0.01 (-0.02, 0.01)	0.20
Child's outpatient visits[k]	0.01 (-0.04, 0.06)	0.60	-0.01 (-0.04, 0.03)	0.65

[a] Difference-in-difference estimates of the average treatment effect on the treated (ATT) with 95% confidence intervals (CI). CIs and p-values were computed with the assumption that ATT was normally distributed and with a standard deviation equal to the bootstrap standard error.

[b] Simple matching estimates of the average treatment effect on the treated (ATT) with 95% confidence intervals (CI). CIs and p-values were computed with the assumption that ATT was normal distributed and with a standard deviation equal to the Abadie-Imbens standard error.

[c] Smoking status at first antenatal visit, around pregnancy week 12.

[d] Large for gestational age (LGA) – ≥2 SD above the reference population's mean weight.

[e] Small for gestational age (SGA) – ≤2 SD below the reference population's mean weight.

[f] A measure of the newborn's physical condition 1, 5 and 10 minutes after birth, range 0-10.

[g] A healthy child according to a paediatrician's examination.

[h] Mother's inpatient care related to delivery.

[i] Early inpatient care for mother and child, respectively, during the first two months after the child's birth but not related to the delivery.
[j] Cumulative duration of inpatient care for mother and child, respectively, over the child's first two years, excluding care due to deliver complications.
[k] Number of outpatient visits for mother and child, respectively, over the child's first two years, excluding care for the mother due to delivery complications.
*Statistically significant effect at the α=0.05 level after a Bonferroni correction for multiple comparisons, i.e. with the 38 outcome variables this implies a significance threshold of 0.05/38=0.001.
**Statistically significant effect at the α=0.01 level after a Bonferroni correction for multiple comparisons, i.e. with the 38 outcome variables this implies a significance threshold of 0.01/38=0.00026.

Table D6 Exclusions and final analytical sample sizes in the longitudinal subsample analyses

		Exclusions due to missingness	Eligible for matching	Used for matching	No matches found
Health outcomes					
Pregnancy, delivery and around the child's birth					
Smoking[c] (yes)	Salut[a]	36	111	111	0
	Non-Salut[a]	148	1 101	963	
Pregnancy length (≥37 weeks)	Salut	24	123	123	0
	Non-Salut	72	1 177	957	
Caesarean section (yes)	Salut	24	123	123	0
	Non-Salut	72	1 177	967	
Birth weight (≥2 500g)	Salut	25	122	121	1
	Non-Salut	72	1 177	984	
Birth length (cm)	Salut	25	122	121	1
	Non-Salut	79	1 170	439	
LGA[d] (yes)	Salut	28	119	119	0
	Non-Salut	91	1 158	965	
SGA[e] (yes)	Salut	28	119	117	2
	Non-Salut	91	1 158	971	
Apgar score[f] (≥7) at 1 minute	Salut	26	121	120	1
	Non-Salut	81	1 168	957	
at 5 minutes	Salut	26	121	120	1
	Non-Salut	82	1 167	1 048	
at 10 minutes	Salut	28	119	118	1
	Non-Salut	127	1 122	1 017	
Healthy child[g] (yes)	Salut	24	123	123	0
	Non-Salut	72	1 177	911	
Mother's inpatient care[h] (yes)	Salut	5	142	137	5
	Non-Salut	7	1 242	605	
During the first two years after the child's birth					
Mother with early inpatient care[i] (yes)	Salut	5	142	142	0
	Non-Salut	7	1 242	1 135	
Child with early inpatient care[i] (yes)	Salut	5	142	142	0
	Non-Salut	7	1 242	1 104	
Mother's inpatient care[j] (days)	Salut	5	142	141	1
	Non-Salut	7	1 242	1 081	
Child's inpatient care[j] (days)	Salut	5	142	141	1
	Non-Salut	7	1 242	972	
Mother's outpatient visits[k]	Salut	5	142	142	0
	Non-Salut	7	1 242	1 145	
Child's outpatient visits[k]	Salut	5	142	142	0
	Non-Salut	7	1 242	1 076	

[a] Salut area – Geographical area in Västerbotten county where the Salut Programme was implemented from 2006 and onwards; non-Salut area – remaining part of Västerbotten county.
[b] Premeasure period 2002-2004; postmeasure period 2006-2008.
[c] Smoking status at first antenatal visit, around pregnancy week 12.
[d] Large for gestational age (LGA) – ≥2 SD above the reference population's mean weight.
[e] Small for gestational age (SGA) – ≤2 SD below the reference population's mean weight.
[f] A measure of the new-borns physical condition 1, 5 and 10 minutes after birth, range 0-10 points.
[g] A healthy child according to a paediatrician's examination.
[h] Mother's inpatient care related to delivery.
[i] Early inpatient care for mother and child, respectively, during the first two months after the child's birth but not related to the delivery.
[j] Cumulative duration of inpatient care for mother and child, respectively, over the child's first two years, excluding care due to delivery complications.
[k] Number of outpatient visits for mother and child, respectively, over the child's first two years, excluding care for the mother due to delivery complications.

Appendix E Healthcare and other societal costs

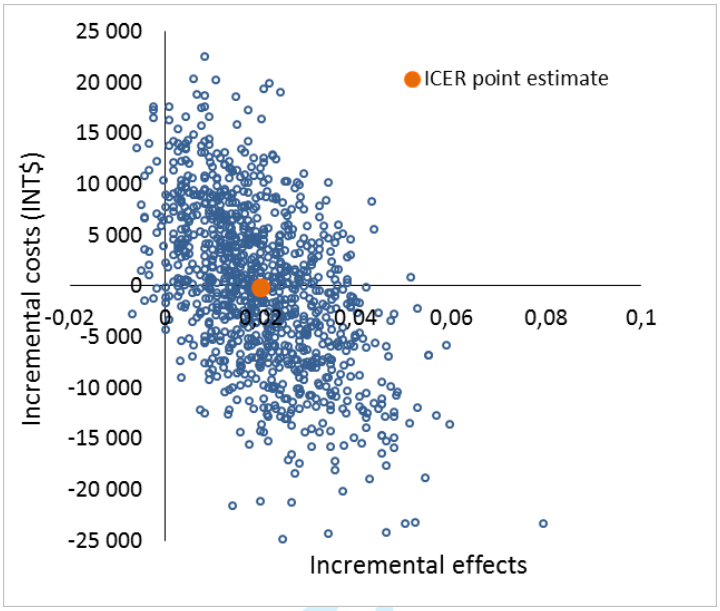
Table E1 Mean healthcare costs and productivity losses for the total sample (2013 INT$)

	Salut[a]	Salut	Non-Salut[a]	Non-Salut	Salut post vs. Salut pre[c]	Non-Salut post vs. Non-Salut pre[d]
	pre[b]	post[b]	pre	post		
Children, n	1 003	888	6 664	6 059		
Healthcare costs						
Pregnancy, delivery and around the child's birth						
Delivery[f]	51 443	51 849	51 342	51 414	406	72
	(9 769)	(10 128)	(9 671)	(9 738)	(458)	(172)
					p=0.39	p=0.68
During the first two years after the child's birth						
Mother's inpatient care	13 581	16 381	179 178	15 925	2 800	-1 993
	(74 369)	(114 098)	(186 633)	(158 752)	(4 383)	(3 087)
					p=0.54	p=0.53
Child's inpatient care	178 499	131 243	137 163	120 308	-47 256	-16 855
	(1 250 316)	(714 282)	(777 528)	(904 385)	(47 636)	(14 917)
					p=0.36	p=0.26
Mother's outpatient visits	30	34	37	36	4	-1
	(287)	(304)	(364)	(317)	(14)	(6)
					p=0.80	p=0.81
Child's outpatient visits	85	160	100	139	74	38
	(509)	(1 219)	(619)	(1 964)	(42)	(25)
					p=0.05	p=0.08
Total healthcare costs	**243 639**	**199 667**	**206 561**	**187 822**	**-43 972**	**-18 739**
	(1 256 313)	**(725 027)**	**(817 517)**	**(919 472)**	**(47 975)**	**(15 400)**
					p=0.41	**p=0.23**
Productivity losses						
During the second year after the child's birth						
Mother's inpatient care	493	422	485	475	-72	-10
	(3 513)	(4 054)	(6 818)	(6 197)	(174)	(116)
					p=0.69	p=0.93
Mother's outpatient visits	12	16	12	13	4	1
	(152)	(174)	(158)	(160)	(8)	(3)
					p=0.78	p=0.83
Total productivity losses	**505**	**437**	**497**	**488**	**-68**	**-9**
	(3 538)	**(4 063)**	**(6 843)**	**(6 210)**	**(175)**	**(116)**
					p=0.70	**p=0.94**
Total healthcare costs and productivity losses	**244 144**	**200 104**	**207 058**	**188 310**	**-44 040**	**-18 748**
	(1 256 656)	**(725 624)**	**(819 261)**	**(920 400)**	**(47 994)**	**(15 424)**
					p=0.41	**p=0.22**

[a] Salut area – Geographical area in Västerbotten county where the Salut Programme was implemented from 2006 and onwards; non-Salut area – remaining part of Västerbotten county.
[b] Premeasure period – 2002-2004; postmeasure period – 2006-2008.
[c] P-values are based on permutation tests of the difference in means between Salut post and Salut pre.
[d] P-values are based on permutation tests of the difference in means between non-Salut post and non-Salut pre.

[e] P-values are based on permutation tests of the difference in means between Salut and non-Salut over time, i.e. the difference in means between non-Salut post and non-Salut pre subtracted from the difference in means between Salut post and Salut pre.
[f] For the 476 births with missing info on delivery type, the cost for Ceasarean section was imputed with probability 0.17 and with probability 0.83 the cost for vaginal delivery was imputed.

Healthcare perspective



Limited societal perspective

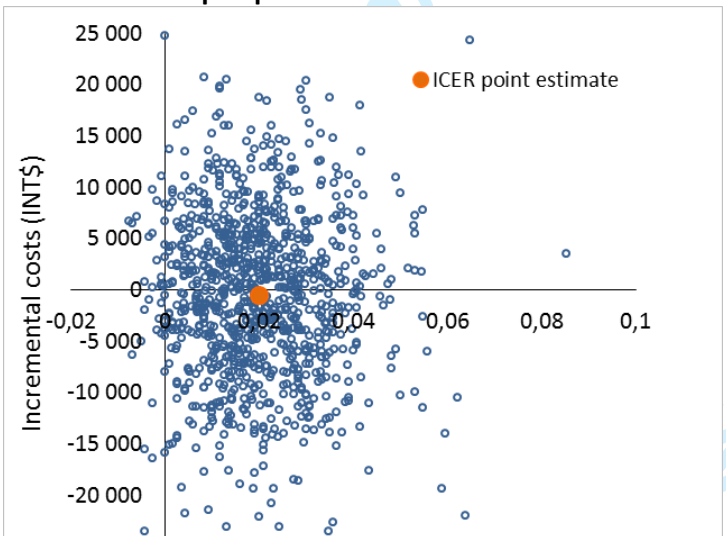
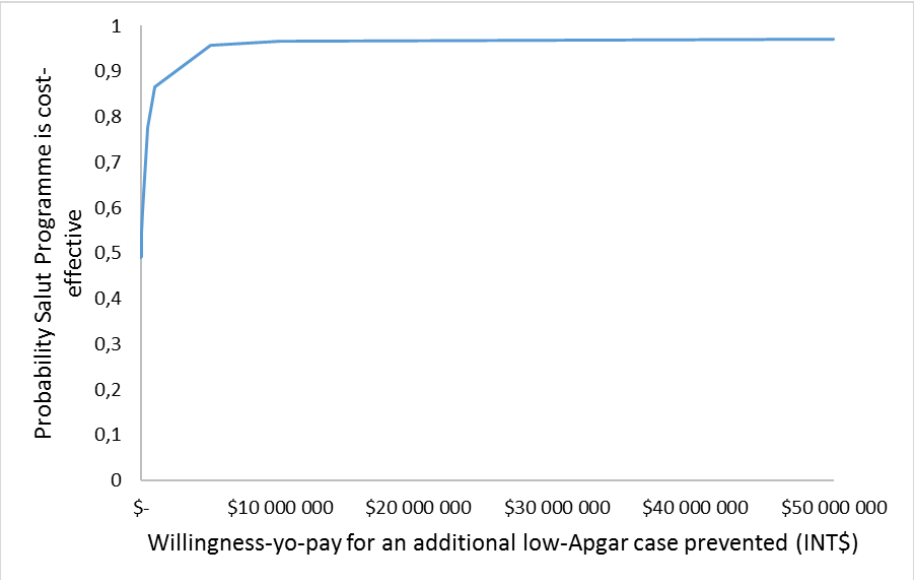


Figure E1. Cost-effectiveness planes for the healthcare and limited societal perspectives. The horizontal axis divides the plane according to incremental effect, and the vertical axis according to incremental cost, which divides the plane into four different quadrants. Each quadrant has a different implication for the cost-effectiveness decision. Iterations falling on the north-east quadrant are those where the intervention is more effective and more costly than the comparator; those on the south-east quadrant are more effective and less costly; those on the south-west quadrant are less effective and less costly; and those on the north-west quadrant are more costly and less effective.

Healthcare perspective



Limited societal perspective

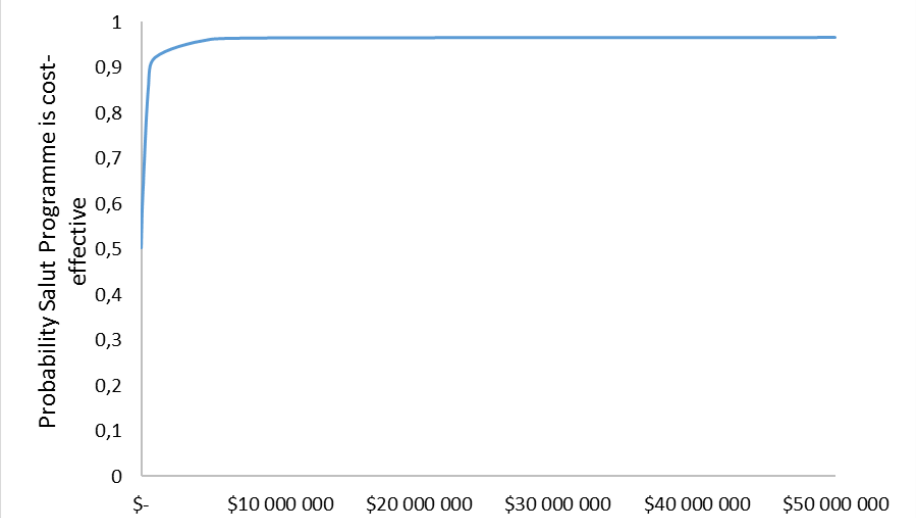


Figure E2. Cost-effectiveness acceptability curve (CEAC) for the healthcare and limited societal perspectives. The CEAC shows the probability that the Salut Programme is cost-effective compared to care-as-usual, subject to a range of possible maximum values that a decision-maker would be willing to pay for an additional low-Apgar case prevented.

References

1. Edvardsson K, Ivarsson A, Garvare R, Eurenius E, Lindkvist M, Mogren I, Small R, Nyström ME: **Improving child health promotion practices in multiple sectors - outcomes of the Swedish Salut Programme**. *BMC Public Health* 2012, **12**:920.
2. **Cost per Patient Database. Cost data 2013 per DRG.** [https://skl.se/ekonomijuridikstatistik/statistik/kostnadperpatientkpp/kppdatabas.1079.html]
3. **Statistical database.** [http://www.statistikdatabasen.scb.se]

Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement

Section/item	Item No	Recommendation	Reported on page No/ line No
Title and abstract			
Title	1	Identify the study as an economic evaluation or use more specific terms such as "cost-effectiveness analysis", and describe the interventions compared.	Title, page 1
Abstract	2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions.	Abstract, page 2
Introduction			
Background and objectives	3	Provide an explicit statement of the broader context for the study. Present the study question and its relevance for health policy or practice decisions	Page 4, lines 15-25
Methods			
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	Page 4, lines 28-31 Page 5, lines 1-10 Page 9, lines 20-32 Page 10, lines 1-2
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	Page 5, lines 5-17
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	Page 5, lines 8-17 Page 8, lines 5-10
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	Page 5, lines 26-32 Page 6, lines 1-8
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	Page 8, lines 5-7
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	Page 8, line 26 Page 9, lines 6-17
Choice of health outcomes	10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	Page 6, lines 9-19
Measurement of effectiveness	11a	*Single study-based estimates:* Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	Page 6, lines 21-32 Page 7, lines 1-20 Appendix B

Section/item	Item No	Recommendation	Reported on page No/ line No
	11b	*Synthesis-based estimates*: Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.	Not applicable
Measurement and valuation of preference based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	Not applicable
Estimating resources and costs	13a	*Single study-based economic evaluation:* Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	Page 8, lines 4-29
	13b	*Model-based economic evaluation:* Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	Not applicable
Currency, price date, and conversion	14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	Page 7, lines 30-32 Page 8, lines 1-10 Appendix C
Choice of model	15	Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended.	Not applicable
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytical model.	Not applicable
Analytical methods	17	Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	Page 7, lines 3-29 Page 11, lines 2-19 Page 12 lines 1-4 Appendix B
Results			

Section/item	Item No	Recommendation	Reported on page No/ line No
Study parameters	18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	Not applicable
Incremental costs and outcomes	19	For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.	Page 19, Table 4 in the main manuscript
Characterising uncertainty	20a	*Single study-based economic evaluation:* Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact of methodological assumptions (such as discount rate, study perspective).	Page 19, Table 4 in the main manuscript Appendix E, Figure E1 and E2
	20b	*Model-based economic evaluation:* Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	Not applicable
Characterising heterogeneity	21	If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.	Not applicable
Discussion			
Study findings, limitations, generalisability, and current knowledge	22	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	Pages 21-23
Other			
Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	Page 24 “Funding”
Conflicts of interest	24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.	Page 24 “Competing interests”

The CHEERS statement checklist format is based on the format of the CONSORT statement checklist