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National PReCePT Programme: a before-and-after evaluation of the implementation of a national quality improvement programme to increase the uptake of magnesium sulfate in preterm deliveries

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► Additional supplemental material is published online only. To view, please visit the journal online (<http://dx.doi.org/10.1136/archdischild-2022-324579>).

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Received 5 July 2022

Accepted 26 November 2022



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To cite: Edwards HB, Redaniel MT, Sillero-Rejon C, et al. *Arch Dis Child Fetal Neonatal Ed* Epub ahead of print: [please include Day Month Year]. doi:10.1136/archdischild-2022-324579

ABSTRACT

Objective To evaluate the effectiveness and cost-effectiveness of the National PReCePT Programme (NPP) in increasing use of magnesium sulfate ($MgSO_4$) in preterm births.

Design Before-and-after study.

Setting Maternity units (N=137) within NHS England and the Academic Health Science Network (AHSN) in 2018.

Participants Babies born ≤ 30 weeks' gestation admitted to neonatal units in England.

Interventions The NPP was a quality improvement (QI) intervention including the PReCePT (Preventing Cerebral Palsy in Pre Term labour) QI toolkit and materials (preterm labour proforma, staff training presentations, parent leaflet, posters for the unit and learning log), regional AHSN-level support, and up to 90 hours funded backfill for a midwife 'champion' to lead implementation.

Main outcome measures $MgSO_4$ uptake post implementation was compared with pre-NPP implementation uptake. Implementation and lifetime costs were estimated.

Results Compared with pre-implementation estimates, the average $MgSO_4$ uptake for babies born ≤ 30 weeks' gestation, in 137 maternity units in England, increased by 6.3 percentage points (95% CI 2.6 to 10.0 percentage points) to 83.1% post implementation, accounting for unit size, maternal, baby and maternity unit factors, time trends, and AHSN. Further adjustment for early/late initiation of NPP activities increased the estimate to 9.5 percentage points (95% CI 4.3 to 14.7 percentage points). From a societal and lifetime perspective, the health gains and cost savings associated with the NPP effectiveness generated a net monetary benefit of £866 per preterm baby and the probability of the NPP being cost-effective was greater than 95%.

Conclusion This national QI programme was effective and cost-effective. National programmes delivered via coordinated regional clinical networks can accelerate uptake of evidence-based therapies in perinatal care.

INTRODUCTION

Since 2015, the UK National Institute for Health and Care Excellence (NICE) has recommended administration of magnesium sulfate ($MgSO_4$) to

WHAT IS ALREADY KNOWN ON THIS TOPIC

- ⇒ Since 2015, the UK National Institute for Health and Care Excellence (NICE) has recommended administration of magnesium sulfate ($MgSO_4$) for fetal neuroprotection in very preterm deliveries (24–30 weeks' gestation).
- ⇒ By 2017, only two-thirds of eligible women in England were given $MgSO_4$, with wide regional variations.
- ⇒ The PReCePT (Preventing Cerebral Palsy in Pre Term labour) pilot study increased uptake from 21% to 88% (2015).
- ⇒ The National PReCePT Programme (NPP) aimed to increase $MgSO_4$ uptake to 85% by 2020.

WHAT THIS STUDY ADDS

- ⇒ The NPP, providing a quality improvement (QI) toolkit, regional Academic Health Science Network support and clinical backfill funding, was effective in increasing $MgSO_4$ uptake in preterm deliveries.
- ⇒ The NPP was highly cost-effective, generating a net monetary benefit of £866 per preterm baby and ~£3 million over the 12 months following implementation.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

- ⇒ Research evidence can take decades to become embedded in perinatal clinical practice, as was the case for antenatal steroids.
- ⇒ This study shows that national, network-supported QI programmes can accelerate uptake of evidence-based therapies and promote improvements in perinatal care.
- ⇒ The PReCePT model may serve as a blueprint for future interventions to improve perinatal care.

women at risk of preterm birth as a core part of maternity care.¹ $MgSO_4$ is a neuroprotective treatment that reduces the risk of cerebral palsy (CP) in preterm babies,² and is a highly cost-effective

intervention at approximately £1 per dose and an estimated £1 million of lifetime societal savings per case of CP avoided.^{3 4} However, by 2017, only 64% of eligible women received it.⁵ High regional variations in uptake (range 49%–78%) also indicated inequalities in perinatal care.⁵

The PRaCePT (Preventing Cerebral Palsy in Pre Term labour) quality improvement (QI) toolkit was developed to improve maternity staff awareness and increase the use of MgSO₄ in mothers at risk of giving birth ≤30 weeks' gestation. The pilot study (five maternity units) found an increase in uptake from 21% to 88% associated with the PRaCePT approach.⁶ In 2018, NHS England funded the National PRaCePT Programme (NPP), which scaled up this QI intervention for national roll-out. Maternity units received regional implementation support through the 15 Academic Health Science Networks (AHSNs), with the aim of increasing MgSO₄ use to 85% by 2020. The NPP provided the PRaCePT QI toolkit (preterm labour proforma, staff training presentations, parent information leaflet, posters for the unit and a learning log)⁷ to each unit ('National PRaCePT Programme Provisions' in online supplemental file 1). Each unit had a lead 'PRaCePT champion' midwife with 90 hours funded backfill. AHSN-level coaching and support from a regional clinical lead (obstetrician and/or neonatologist) and NPP manager were available to each unit. The NPP was launched in two tranches (May and September 2018). A nested cluster randomised trial to determine the effectiveness of standard versus enhanced support was conducted alongside the NPP.⁸

This study was an effectiveness and cost-effectiveness evaluation of the NPP QI intervention in increasing MgSO₄ uptake in mothers at risk of giving birth ≤30 weeks' gestational age. We hypothesised that it would help increase MgSO₄ uptake beyond the expected increase due to the underlying trend rate.

METHODS

The intervention evaluated was a QI programme as described in the previous section. The method used to evaluate the intervention followed a quasi-experimental before-and-after design, comparing absolute difference in mean MgSO₄ uptake between 12 months pre-implementation and 12 months post implementation, adjusted for possible confounders. A quasi-experimental approach was appropriate as the PRaCePT intervention had been widely implemented in maternity units in England, making a standard randomised controlled trial (RCT) infeasible.^{9–11} Additionally, as there was already indication that the intervention was effective from the pilot study, sufficient clinical equipoise for an RCT with a no-intervention control group was arguably not present.

Data

Pseudonymised patient-level data from the UK National Neonatal Research Database (NNRD) were used. This collates information from neonatal units and includes clinical data and mother and baby sociodemographic characteristics. All NNRD data undergo multiple quality assurance procedures and are considered to have high accuracy and completeness.^{12 13}

Estimated NPP adoption dates for each unit, demarcating the two periods, were provided by the AHSNs. Adoption date was defined as the month when the unit had initiated an implementation plan. The total period pre-implementation and post implementation across all units covered the months between October 2017 and June 2020. The month of initiation of the NPP in the maternity unit was excluded from the analysis.

Outcome

For consistency with nationally reported audit data, MgSO₄ uptake was defined as the number of mothers receiving MgSO₄ divided by the total number of eligible mothers, excluding missing values from the denominator. This was expressed as a percentage and computed per month per unit. For the cost-effectiveness analysis only, missing MgSO₄ uptake was considered as 'not given' and included in the denominator.

The analysis included data on babies born ≤30 weeks' gestational age. Singletons and one baby (the first born) from each multiple birth were included, for consistency with nationally reported figures. All multiples were included in the description of baby-level demographics. In cases where only one baby had a record for MgSO₄, we recoded the missing MgSO₄ status of the other multiples to match that for their twin/triplet who did have a record. For multiples with conflicting records (eg, Baby 1=given, Baby 2=not given), we recorded MgSO₄ as given.

The secondary outcomes were trends in MgSO₄ uptake, missing MgSO₄ data, reasons MgSO₄ was not given, cost of the NPP per preterm baby and the incremental net monetary benefit of the NPP per preterm baby from a lifetime societal perspective.

Possible confounders and other model terms

Possible confounding factors adjusted for included baby birth weight (grams) adjusted for gestational age (weeks) and sex expressed as a z-score, whether the baby was part of a multiple birth, maternal age, ethnicity, level of deprivation (Index of Multiple Deprivation decile), hypertension during pregnancy, type of unit (high dependency unit or special care unit (HDU/SCU) vs neonatal intensive care unit (NICU)), time and clustering by AHSN. The cost-effectiveness analysis also adjusted for type of birth (imminent or threatened).

Mother and baby characteristics were aggregated to the maternity unit level (using non-missing information) per study month, for example, mean maternal age and proportion with pregnancy hypertension. Missing information was minimal, except for mother's ethnicity (online supplemental table S1). The cost-effectiveness analysis used baby-level data, and missing data on possible confounders were imputed through chained equations.¹⁴

Statistical analyses

Effectiveness analysis

To compare the difference in mean monthly MgSO₄ uptake pre-implementation and post implementation, we conducted a multilevel mixed-effects linear regression using the maternity unit as the primary level of analysis. The model was weighted on unit size (number of eligible mothers at each unit) and adjusted for clustering by AHSN and potential confounders as listed in the previous section.

To account for early and late start of NPP activities in many units (as reported by AHSNs), we excluded records within three months either side of the NPP adoption month as a sensitivity analysis.

As additional sensitivity analyses, we evaluated the effect of (1) including the 13 maternity units receiving enhanced support in the PRaCePT trial intervention arm and (2) excluding units in one AHSN that started adoption significantly later than other AHSNs.

Cost-effectiveness analysis

The mean implementation cost per maternity unit was estimated from data supplied by the national programme team. This

included NPP management, AHSN support, and clinical backfill for midwives and clinical leads. The mean implementation cost per baby was calculated as the cost per unit divided by the total number of eligible babies per unit delivered during the follow-up period.

A decision tree analysis estimated the net monetary benefit of the NPP using a lifetime horizon and societal perspective.¹⁵ Model parameters were based on NNRD data for MgSO₄ uptake, and reported estimates for lifetime gains in quality-adjusted life-years (QALYs) and societal cost savings relating to healthcare, education, housing and work productivity from preventing CP via MgSO₄ treatment.⁴ Cost estimates were converted to pounds sterling and inflated to 2019 prices (online supplemental table S2). Babies delivered by caesarean section were defined as ‘imminent’ births (certain to occur within 24 hours) and all others as ‘threatened’. Deterministic analysis used a willingness-to-pay threshold of £20 000 per QALY gained, in line with the NICE guidance.¹⁶

The difference in uptake between the baseline and follow-up periods was estimated using a multilevel mixed-effects linear logistic regression at the baby level, adjusted for clustering by AHSN and unit, listed confounders, and interaction between type of birth and time period.

Probabilistic analysis to characterise parameter uncertainty and to estimate cost-effectiveness used Monte Carlo simulation with 10 000 samples drawn from the parameter distributions.¹⁵ For lifetime costs and health utilities estimates, we used the incremental differences. Point estimates, distribution assumptions and parameter source estimates are reported in online supplemental table S3. Incremental costs and effects were plotted on the cost-effectiveness plane and a cost-effectiveness acceptability curve plotted for willingness-to-pay thresholds from 0 to £100 000 per QALY gained. Subgroup analysis explored differences in cost-effectiveness between types of maternity unit (SCU/HDU or NICU).

RESULTS

Of the 155 maternity units in England, 150 participated in the NPP (the five units not participating were study pilot sites).⁶ The 13 units comprising the nested cluster RCT intervention group were also excluded, leaving 137 maternity units for evaluation.

The NPP adoption dates of the participating units ranged from October 2018 to October 2020, with almost all starting by April 2019. On average, there were 2.9 preterm births per unit per month. Maternal and baby characteristics were similar pre-implementation and post implementation (table 1). The average MgSO₄ uptake across all units in the 12 months pre-implementation was 70.9%, increasing to 83.1% across the 12 months post implementation (table 2). The average amount of missing MgSO₄ data reduced from 2.9% to 1.4%.

Imminent delivery was the most common reason why MgSO₄ was not given. Pre-implementation, MgSO₄ was ‘not offered’ in 16.1% of cases, and post implementation this reduced to 11.4% (table 2).

Overall, the trend in MgSO₄ uptake increased steadily (figure 1, online supplemental figures S1–S3). The average uptake varied by AHSN, and within each AHSN there was high monthly variation (online supplemental figure S3). The lowest average uptake was around 65% at the end of 2017 and the highest was around 94% around May 2020.

The unadjusted average increase in uptake from pre-implementation to post implementation was 12.2 percentage points. After adjusting for confounding factors, this reduced to

Table 1 Sociodemographic and clinical characteristics of mothers and babies born at ≤30 weeks’ gestation in NPP maternity units in England, October 2017–June 2020

Variable	Pre-implementation*	Post implementation*
Sociodemographic characteristics of babies†		
Babies (n)	3630	3441
Gestational age (weeks), median (IQR)	27.9 (25.9–29.0)	27.9 (26.0–29.1)
Birth weight (g), median (IQR)	982 (770–1210)	980 (769–1205)
Birth weight adjusted for gestational age (z-score), median (IQR)	0.1 (–0.6 to 0.7)	0.1 (–0.6 to 0.7)
Male sex, n (%)	1960 (54.0)	1851 (53.8)
Multiple births, n (%)	871 (24.0)	817 (23.7)
Sociodemographic and clinical characteristics of mothers		
Mothers (n)	3189	3016
Maternal age (years), mean (SD)	31 (6)	31 (6)
White ethnicity, n (%)	1711 (60.2)	1610 (61.2)
Level of deprivation (IMD quintile), n (%)		
1 (most deprived)	1108 (31.0)	1112 (32.9)
2	912 (25.6)	773 (22.9)
3	643 (18.0)	621 (18.4)
4	485 (14.0)	454 (13.4)
5 (least deprived)	422 (11.82)	418 (12.4)
Hypertension in pregnancy, n (%)	128 (3.5)	157 (4.6)
Antenatal steroids given, n (%)	3340 (92.1)	3220 (93.9)
Maternity unit characteristics		
Special care unit/high dependency unit, n (%)	1336 (36)	1226 (35.6)
Neonatal intensive care unit, n (%)	2294 (63.2)	2215 (64.4)
Average number of eligible births per hospital per month, mean (SD)	2.9 (2.1)	2.9 (2.1)
*Figures cover the 12 months prior to, and 12 months following the recorded NPP adoption date at each unit, excluding the month of adoption itself.		
†All babies in the dataset including multiples		
IMD, Index of Multiple Deprivation; NPP, National PreCePT Programme; PreCePT, Preventing Cerebral Palsy in Pre Term labour.		

6.3 percentage points (95% CI 2.6 to 10.0 percentage points, $p < 0.001$). Sensitivity analysis excluding data three months either side of the adoption month changed the estimate to 9.5% (95% CI 4.3 to 14.7, $p < 0.001$) (table 3). Neither including the nested RCT intervention units nor excluding units from one late-starting AHSN had any substantial effect on the estimate.

The proportion of missing MgSO₄ data fluctuated between 0% and 7%, but overall decreased over time (online supplemental figures S4 and S5). Around April 2020, the time of the first COVID-19 lockdown in England, missing MgSO₄ data appeared to increase and uptake decrease.

Costs and cost-effectiveness analyses

The mean implementation cost of the NPP was £6044 per unit: £738 for NPP management, £2764 for AHSN funding and £2500 for clinical backfill funding. The mean implementation cost per eligible preterm baby (≤30 weeks’ gestation) was £267.

The NPP was associated with a mean increase of 0.01 QALYs per preterm baby and £649 total incremental savings over a baby’s lifetime (table 4). This equates to a net monetary benefit of £886 per eligible preterm baby at a willingness-to-pay threshold of £20 000 per QALY gained (table 4). Applying this finding across all the preterm babies delivered during the year

Table 2 MgSO₄ uptake in babies born at ≤30 weeks' gestation in NPP maternity units in England, October 2017–June 2020*

Variable	Pre-implementation†	Post implementation†
Total number of eligible births	3172	3014
Total number of mothers given MgSO ₄ , n (%)	2279 (71.9)	2527 (83.8)
Total number of mothers not given MgSO ₄ , n (%)	803 (25.3)	447 (14.8)
Total number with MgSO ₄ data missing, n (%)	90 (2.8)	40 (1.3)
Mean MgSO ₄ uptake across all units, % (SD)	70.9 (3.6)	83.1 (3.5)
Mean MgSO ₄ missing data across all units, % (SD) (% range)	2.9 (1.3) (1.1–5.6)	1.4 (1.0) (0–3.1)
Reason MgSO ₄ not given, n (%)		
Contraindicated	9 (1.2)	6 (1.3)
Declined	7 (0.7)	3 (0.7)
Delivery imminent	499 (62.1)	337 (75.4)
Not appropriate	69 (8.6)	24 (5.4)
Not offered	129 (16.1)	51 (11.4)
Data missing	90 (11.2)	26 (5.8)

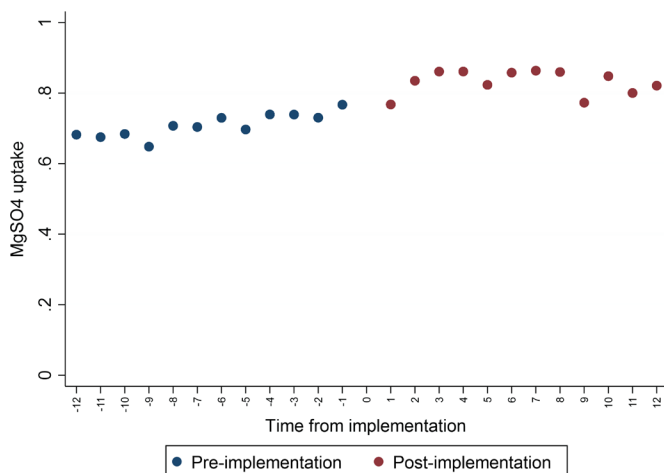
*MgSO₄ data from records on singleton births and the first born of multiples with records in the data set.
†Figures cover the 12 months prior to, and 12 months following the recorded NPP adoption date at each unit, excluding the month of adoption itself.
MgSO₄, magnesium sulfate; NPP, National PReCePT Programme; PReCePT, Preventing Cerebral Palsy in Pre Term labour.

post implementation, the NPP was associated with savings to the society accruing over their lifetime totalling £3 million (£886 multiplied by 3441). The probability of the NPP being cost-effective was greater than 95% (table 4, online supplemental figures S6–S8).

Although the cost per baby was higher in smaller (SCU/HDU) units than in NICUs (table 4), the probability of cost-effectiveness in small units was still high at about 85% (online supplemental figures S6–S8).

DISCUSSION

This is the first evaluation of a UK universally implemented national perinatal QI programme to increase administration of

**Figure 1** Magnesium sulfate (MgSO₄) uptake pre-implementation and post implementation.**Table 3** Difference in MgSO₄ uptake in babies born at ≤30 weeks' gestation after implementation of the NPP in maternity units in England††

Models	Difference in MgSO ₄ uptake (percentage points)*	95% CI (percentage points)	P value
1 Unadjusted†	12.2	9.5 to 15.0	<0.001
2 Adjusted for unit size‡	11.0	8.9 to 13.1	<0.001
3 Adjusted for unit size and clustering by AHSN§	11.0	8.4 to 13.5	<0.001
4 Adjusted for unit size, clustering by AHSN and NPP month¶	6.7	2.8 to 10.5	0.001
5 Fully adjusted**	6.3	2.6 to 10.0	0.001
6 Fully adjusted model** and excluding records within 3 months either side of the start month	9.5	4.3 to 14.7	<0.001
Additional analyses			
7 Model 6 and including the 13 PReCePT trial intervention units	9.6	4.4 to 14.8	<0.001
8 Model 6 and excluding units in one AHSN where implementation was delayed	10.0	3.9 to 16.0	0.001

*Percentage point changes, post implementation minus pre-implementation.
†Crude regression of uptake post implementation compared with pre-implementation.
‡As per model 1, plus additionally weighted on the number of eligible records per unit, with robust SEs.
§As per model 2, plus additionally accounting for clustering by AHSN, with robust SEs.
¶As per model 3, plus additionally adjusted for recorded start month.
**As per model 4, plus additionally adjusted for birth weight adjusted for gestational age and sex, maternal age, IMD, ethnicity, multiple birth, maternal hypertension (all unit-level aggregates), level of unit and study month.
††MgSO₄ data from records on singleton births and the first born of multiples with records in the data set.
AHSN, Academic Health Science Network; IMD, Index of Multiple Deprivation; MgSO₄, magnesium sulfate; NPP, National PReCePT Programme; PReCePT, Preventing Cerebral Palsy in Pre Term labour.

an evidence-based drug. We found that the NPP increased the uptake of MgSO₄ in babies born at ≤30 weeks' gestation and was cost-effective. It generated an estimated net monetary benefit to the society of £3 million over the lifetime of the preterm babies delivered during the 12 months following implementation. The reduction in the amount of missing MgSO₄ data indicates an improvement in record-keeping and is likely an indirect beneficial effect of the NPP.

MgSO₄ uptake varies across countries, with estimates of 0%–12.3% in Europe (2011–2015)¹⁷ and 43.0% in Canada (2011–2015).¹⁸ We found one similar QI strategy (MAG-CP (MAGNESIUM sulphate for fetal neuroprotection to prevent Cerebral Palsy) in Canada) which included educational rounds, focus groups and surveys of barriers/facilitators, and online training in addition to national guidelines.¹⁸ This was associated with an absolute increase in uptake of 44.3%, from 2.0% pre-implementation (2005–2010) to 46.3% post implementation (2011–2015).¹⁸ For context, UK uptake was 38% in 2014.¹⁹

Strengths

Routinely collected maternal, neonatal and cost data from the NNRD and the NPP provided robust, high-quality data for evaluation. Almost all maternity units in England were included, making the results generalisable. Mixed-effects models

Table 4 Probabilistic analysis results of the NPP cost-effectiveness

NPP	Combined			SCU/HDU			NICU		
	Point estimate	Lower 95% limit	Upper 95% limit	Point estimate	Lower 95% limit	Upper 95% limit	Point estimate	Lower 95% limit	Upper 95% limit
Incremental implementation costs, £	294	32	808	553	134	1277	98	57	149
Incremental lifetime costs, £	-943	-1486	-469	-909	-1514	-362	-867	-1443	-357
Incremental total costs, £	-649	-1284	35	-356	-1131	539	-769	-1344	258
Incremental QALYs	0.01	0.01	0.02	0.01	0.01	0.02	0.01	0.01	0.02
Net monetary benefit*, £	886	130	1621	586	-372	1475	987	355	1675

*We used a willingness-to-pay threshold of £20 000 per QALY gained.

HDU, high dependency unit; NICU, neonatal intensive care unit; NPP, National PRCePT Programme; PRCePT, Preventing Cerebral Palsy in Pre Term labour; QALYs, quality-adjusted life-years; SCU, special care unit.

enabled the effect estimates to be adjusted for known potential confounders and clustering by AHSN. As NPP implementation was directed by AHSNs, unmeasured similarities and differences between units within AHSNs need to be taken into account as we have done here.

The National Neonatal Audit Programme report on 2020 data concurred with our conclusions.²⁰ They found uptake in Scotland and Wales was comparable with the national average pre-NPP, but below afterwards. This is suggestive that English units' exposure to the NPP was associated with their higher average uptake. Their data on improvements in other audit measures are also illuminating. Their audit shows the increase in uptake of antenatal steroids from 75.6% to 85.8% took 5–6 years, where the comparable increase in the uptake of MgSO₄ from 72% to 85.7% took place over just 2 years. A key difference in the journey of these treatments was the dedicated national QI programme for MgSO₄. Again this is suggestive of the NPP's role in the relatively rapid improvement in uptake of MgSO₄.

Limitations

In a pragmatic before-and-after observational evaluation of this kind, it is impossible to conclusively attribute the observed increase in uptake to the NPP alone. For example, some of the observed improvements in uptake could be explained by improvements in record-keeping. However, the reduction in missing data was much smaller than the observed improvement in uptake, so it is unlikely to be a significant explanatory factor. Historically, uptake has been increasing since 2014 (online supplemental figure S2). This historical trend has been accounted for in the analysis. The estimate is the increased slope (increased improvement in uptake) over and above the pre-implementation slope. The statistical methods used minimised the impact of known biases and confounders, giving reason to believe that the NPP did have a positive impact on uptake. Analyses were limited to the available data (to June 2020), but it is expected that NPP benefits will persist. Sustainability needs to be addressed in future studies. Adoption dates used to demarcate the exposure periods were not firmly defined, and NPP activities were reported to have started before or after the stated start dates in some units, possibly diluting the observable effects of the NPP on uptake. Despite this, the various sensitivity analyses did not alter the main findings.

The adjusted effect estimate was smaller than expected from previous audit figures.²¹ This suggests that other factors (eg, organisational context²²) could have also contributed to the observed increase in uptake. From our 4-year experience post implementation in the five pilot sites, the improved uptake is likely to be sustained, meaning that longer-term analyses may

show the NPP to be even more cost-effective than estimated here as implementation costs are non-recurring.

The observed decrease in uptake and increase in missing MgSO₄ data around April 2020 may be a random fluctuation, but is consistent with a possible impact of the first wave of COVID-19 in England. Staffing pressures of a pandemic are likely to affect the quality of care. Also, women may have presented to hospital later during this time due to caution about contact, meaning missed opportunities to give MgSO₄ due to imminent delivery. Further analysis of future data would be valuable to identify clearer trends in uptake or missing data associated with the course of the pandemic.

Implications for clinical practice

Uptake of new evidence or guidelines is often slow due to practical barriers, lack of knowledge, and need for behaviour change, as illustrated by the case of antenatal steroids which took decades to become embedded in routine practice. This comes at a high clinical and economic cost. The NPP demonstrates that active implementation of national initiatives using QI toolkits, clinical leadership and regional QI support can have a substantial effect on accelerating uptake of evidence-based therapies.

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Acknowledgements We would like to thank all the participants who contributed to this evaluation. We also acknowledge the support of many staff in the AHSN Network and Brent Opmeer for their support and guidance.

Contributors KL, JD, NS and EW conceptualised the evaluation. KL and JM are the chief investigators. TJP, KT and MTR are the quantitative evaluation leads. SR is the process evaluation lead. WH and HM are the health economic evaluation leads. PC and EH are the study managers. EW is the NPP manager. ET, EW, NS and GAF advised on the study methodology, implementation and analysis. HBE, MTR, RM, CS-R, EW and PC acquired NNRD, NPP and cost data. HBE, MTR and RM conducted the effectiveness analysis. CS-R, HM and WH conducted the cost-effectiveness analysis. HBE, MTR and CS-R wrote the original manuscript. All authors reviewed and edited the manuscript for content and approved the submission. The corresponding author attests that all listed authors meet the authorship criteria and that no others meeting the criteria have been omitted. KL is the guarantor.

Funding This work was jointly funded by the National Institute for Health and Care Research Applied Research Collaboration West (NIHR ARC West; core NIHR

infrastructure-funded: NIHR200181) and the AHSN Network funded by NHS England. The Health Foundation funded the health economics evaluation (funder's reference: 557668). The views expressed are those of the authors and not necessarily those of the Health Foundation, NHS England, NHS Improvement, the NIHR or the Department of Health and Social Care.

Competing interests GAF received grant funding from the NIHR and the British Heart Foundation and is a party to partnership agreements with industry partners as CEO of the Oxford Academic Health Science Network. He is chair of the Buckinghamshire, Oxfordshire and West Berkshire Integrated Stroke Delivery Network, the Academic Health Science Network, the European Stroke Organisation Council of Fellows and the Academy of Medical Sciences Fellowship Sectional Committee 7. He is Director of the Cogentis and Accelerate companies and Non-Executive Director of the National Institute for Health and Care Excellence, and serves on the Board of Trustees of the Picker Institute and Health Services Research UK, and the governing body of Green Templeton College, Oxford University. He is data monitoring committee member for the PREVENT-SVD study, trial steering group member for OPTIMAS, R4VaD, ATTEST-2 and SENIOR-RITA trials, grants review panel member for Pfizer/Bristol Myers Squibb, and round table member for the Bristol Myers Squibb/Price Waterhouse Cooper Life Sciences 2030 Cancer Moonshot and Astellas Company Conference. KT acted as expert witness to the High Court in England, called by the UK MHRA, defendant in a case on hormonal pregnancy tests and congenital anomalies in 2021/2022. All other authors in this manuscript have no conflict of interest to declare aside from funding from NIHR ARC West, AHSN, NHS England and Health Foundation. The authors declare that the study management group has no competing financial, professional or personal interests that might have influenced the study design or conduct.

Patient and public involvement statement Public and patient involvement for this study was built on the involvement work in the PreCePT pilot study. This used a codesign and coproduction approach, including a partnership with BLISS, a support organisation for mothers experiencing preterm births, and two mothers who had experienced preterm births. These mothers were involved in study design.

Patient consent for publication Not required.

Ethics approval The UK National Health Service Health Research Authority (HRA project ID: 260504) and the University of Bristol Faculty of Health Sciences Research Ethics Committee (FREC Ref: 84582) approved the conduct of the study.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Anonymised individual-level data for this study are from the NNRD. Our data sharing agreement with the NNRD prohibits sharing data extracts outside of the University of Bristol research team. The NNRD data dictionary is available online and copies of the Statistical analysis plan are available at the University of Bristol's institutional repository (<https://research-information.bris.ac.uk/en/projects/national-precept-prevention-of-cerebral-palsy-in-pre-term-labour->).

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REFERENCES

- National Institute for Health and Care Excellence (NICE) guideline NG25. Preterm labour and birth NG25. UK NICE; 2015.
- Doyle LW, Crowther CA, Middleton P, *et al*. Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus. *Cochrane Database Syst Rev* 2009;1:CD004661.
- Shih ST, Tonmukayakul U, Imms C, *et al*. Economic evaluation and cost of interventions for cerebral palsy: a systematic review. *Dev Med Child Neurol* 2018;60:543–58.
- Bickford CD, Magee LA, Mitton C, *et al*. Magnesium sulphate for fetal neuroprotection: a cost-effectiveness analysis. *BMC Health Serv Res* 2013;13:527.
- NNAP. National neonatal audit programme (NNAP) annual report 2017. UK RCPCH; 2018.
- Burhouse A, Lea C, Ray S, *et al*. Preventing cerebral palsy in preterm labour: a multiorganisational quality improvement approach to the adoption and spread of magnesium sulphate for neuroprotection. *BMJ Open Qual* 2017;6:e000189.
- AHSN. Precept national programme resources. Available: <http://www.ahsnnetwork.com/about-academic-health-science-networks/national-programmes-priorities/precept/precept-resources>
- Edwards HB, Redaniel MT, Sillero-Rejon C, *et al*. Evaluation of standard and enhanced quality improvement methods to increase the uptake of magnesium sulphate in pre-term deliveries for the prevention of Neurodisability (PRECEPT study): a cluster randomized controlled trial. *medRxiv* 2022.
- Bernal JL, Cummins S, Gasparrini A. Interrupted time series regression for the evaluation of public health interventions: a tutorial. *International Journal of Epidemiology* 2016;46:348–55.
- Craig P, Katikireddi SV, Leyland A, *et al*. Natural experiments: an overview of methods, approaches, and contributions to public health intervention research. *Annu Rev Public Health* 2017;38:39–56.
- de Vocht F, Katikireddi SV, McQuire C, *et al*. Conceptualising natural and quasi experiments in public health. *BMC Med Res Methodol* 2021;21:32.
- Battersby C, Statnikov Y, Santhakumaran S, *et al*. The United Kingdom national neonatal research database: a validation study. *PLoS One* 2018;13:e0201815.
- Gale C, Morris I. The UK national neonatal research database: using neonatal data for research, quality improvement and more. *Archives of disease in childhood - Education & practice edition* 2016;101:216–8.
- Lee KJ, Tilling KM, Cornish RP, *et al*. Framework for the treatment and reporting of missing data in observational studies: the treatment and reporting of missing data in observational studies framework. *J Clin Epidemiol* 2021;134:79–88.
- Drummond MSM, Claxton K, Stoddart G. *Methods for the economic evaluation of health care programmes*. 4th ed. Oxford: Oxford University Press, 2015.
- NICE. *Developing NICE guidelines: the manual*. London: NICE, 2014.
- Wolf HT, Huusom L, Weber T, *et al*. Use of magnesium sulfate before 32 weeks of gestation: a European population-based cohort study. *BMJ Open* 2017;7:e013952.
- De Silva DA, Synnes AR, von Dadelszen P, *et al*. MAGnesium sulphate for fetal neuroprotection to prevent Cerebral Palsy (MAG-CP)-implementation of a national guideline in Canada. *Implement Sci* 2018;13:8.
- Lea CL, Smith-Collins A, Luyt K. Protecting the premature brain: current evidence-based strategies for minimising perinatal brain injury in preterm infants. *Arch Dis Child Fetal Neonatal Ed* 2017;102:F176–82.
- NNAP. National neonatal audit programme (NNAP) annual report 2020. UK RCPCH; 2021.
- NNAP. National neonatal audit programme (NNAP) annual report 2018. UK RCPCH; 2019.
- Bain E, Bubner T, Ashwood P, *et al*. Barriers and enablers to implementing antenatal magnesium sulphate for fetal neuroprotection guidelines: a study using the theoretical domains framework. *BMC Pregnancy Childbirth* 2015;15:176.