

Statistical Analysis Plan (SAP)

Economic evaluation of specialised antenatal care: Tommy's National Rainbow Clinic model

Protocol / project	Economic evaluation of Tommy's National Rainbow Clinic model compared to standard antenatal care
SAP version	Version 1.0
Date	24 February 2026
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Sponsor / setting	University of Manchester; Rainbow Clinic sites and NHS England routine datasets (MSDS/HES)/REVAL-Rose-NET

1. Background and rationale

Rainbow Clinics provide specialist antenatal care for pregnant women following a previous stillbirth, second trimester pregnancy loss, neonatal death, or termination of pregnancy for medical reasons (TFMR). The model (established in Manchester in 2013) combines consultant-led multidisciplinary care, enhanced fetal surveillance (additional ultrasound scanning), continuity, and tailored psychological support (Alex Heazell 2020, Bailey, Blocksidge et al. 2025, Barron, Tomlinson et al. 2025). Early evaluations suggest improved maternal and fetal outcomes, including reductions in preterm birth and low birthweight alongside positive patient experiences citing better communication and continuity of care (Abiola, Warrander et al. 2016, Le Vance, Plant et al. 2025). Tommy's National Rainbow Clinic Study collected standardized clinical, utilization and experience data across multiple UK sites.

Evidence on clinical and experiential benefits is emerging, but robust evidence on NHS costs and value for money is limited. This project therefore evaluates incremental healthcare utilisation and costs, alongside key maternal and neonatal outcomes.

2. Objectives

- To evaluate whether there are measurable differences in maternal and neonatal outcomes between women with a history of perinatal death or previous high-risk pregnancy who attend Rainbow Clinics and comparable women who meet eligibility criteria but receive standard antenatal care.
- To assess whether healthcare service utilization differs between women attending Rainbow Clinics and comparable women who meet eligibility criteria but receiving standard antenatal care.
- To estimate and compare the NHS resource costs associated with the Rainbow Clinic model and standard care, and to evaluate its overall economic value in relation to clinical outcomes using a cost-consequence framework.

- To examine variation in outcomes and healthcare service utilization across NHS sites with and without Rainbow Clinics, and to determine whether differences exist across key demographic and clinical subgroups.

3. Study design and data sources

Observational comparative evaluation combining: (i) Rainbow Clinic intervention cohort from REDCap case report forms and (ii) a matched/weighted comparator cohort from NHS England MSDS linked to HES (APC and OP). Comparator data will be restricted to women meeting Rainbow Clinic eligibility criteria at Trusts without Rainbow Clinics (years requested: 2021/22-2023/24). Within NHS England datasets, MSDS-HES linkage will use the common de-identified person-level identifier. The Rainbow Clinic cohort will not be individually linked to MSDS/HES; instead, variables and definitions will be harmonised across sources.

4. Study population.

Intervention cohort

The intervention group comprises women who received care through Rainbow Clinics during a pregnancy following a prior perinatal loss (stillbirth, neonatal death or TFMR). Data is collected from 21 NHS Trusts across England and Wales where the Rainbow Clinic model has been implemented. These include Manchester (Oxford Road Campus and South), Hampshire, Kettering, Leicester, Mid Yorkshire, Newcastle, Norfolk and Norwich, North Durham, Oldham, Ipswich, Portsmouth, Preston, Wigan, Leeds, East Lancashire, Bolton, Cambridge, Cardiff, Darlington Memorial, and Berkshire. Data is collected using the REDCap online database. The current dataset includes approximately 1,700 pregnancies for analysis across all sites.

Comparator cohort

Women with a pregnancy episode recorded in the MSDS/HES within the study period (most recent three full years), at participating NHS trusts (sites without Rainbow Clinics), who meet Rainbow Clinic eligibility criteria, as operationalized using routinely collected data

Exclusion criteria

- Age under 16 years.
- Insufficient maternity activity during the study period (no evidence of booking/contact and no birth outcome record).
- Rainbow Clinic attendance/referral in comparator data (where identifiable).

5. Outcomes

Economic outcomes

- Number of antenatal contacts (midwife/doctor/other), ultrasound scans, antenatal inpatient admissions/bed-days, and neonatal unit admission/length of stay (where available).
- Total NHS cost per pregnancy (aggregation of costed resource items; plus relevant hospital activity in HES where included).

Clinical outcomes

- Stillbirth in the subsequent pregnancy (primary clinical outcome).
- Gestational age at delivery, mode of delivery, onset of labour, birthweight and Apgar score at 5 minutes.
- Neonatal death before discharge; neonatal diagnoses (HIE, respiratory distress requiring ventilation, intracranial haemorrhage).
- Neonatal unit admission

6. Baseline covariates/risk factors

Risk factors have been selected as *a priori* based on published population-based registry evidence on pregnancy outcomes following prior loss (Al Khalaf, Kublickiene et al. 2024), which consistently adjusts for maternal age, BMI, smoking during pregnancy, diabetes and hypertension. These factors are routinely captured within MSDS and HES and enable appropriate control for confounding in non-randomized analyses. Core adjustment variables also include ethnicity, deprivation (IMD in comparator data), gravidity/parity, prior obstetric history (stillbirth/neonatal death/TFMR/miscarriage 16-23 weeks) and site/time indicators.

7. Data preparation and quality assurance

- REDCap repeating instruments: economic evaluation will use the case report form records; where multiple records exist, select the most complete post-birth form using a pre-specified completeness rule.
- Range and plausibility checks (age, BMI inputs, gestation, birthweight), and internal consistency checks (outcome fields vs neonatal admission).
- Harmonise definitions across REDCap and MSDS/HES with a documented mapping (e.g., ethnicity groupings; inpatient admission definitions).

8. Statistical methods

All analyses will compare women attending Rainbow Clinics with eligible women receiving standard antenatal care. Given the non-randomized implementation of the Rainbow Clinic model, causal effects will be estimated using a combination of regression adjustment and a staggered Difference-in-Differences (DiD) framework. Propensity score methods will be used to improve baseline comparability. Effect estimates will be reported with 95% confidence intervals. Standard errors will be clustered at NHS Trust level.

Control of Confounding and Group Comparability

Given the non-randomized nature of the study, propensity score methods will be used to improve comparability between groups. Propensity scores representing the probability of Rainbow Clinic exposure conditional on baseline covariates will be estimated using logistic regression. The primary approach will use inverse probability of treatment weighting (IPTW). Covariate balance will be assessed using standardized mean differences. All outcome models will additionally include multivariable regression adjustment for baseline covariates to reduce residual confounding. These include maternal age, body mass index, smoking, diabetes, hypertension, ethnicity, area-level deprivation, parity, and prior obstetric history.

Primary Causal Estimation Strategy

To account for staggered implementation across NHS sites, DiD framework will be used. Models will include Site fixed effects; Calendar time fixed effects; An interaction between intervention exposure and post-implementation period. The coefficient on this interaction term will represent the estimated causal effect of the Rainbow Clinic model. The parallel trends assumption will be assessed using pre-implementation trend analysis.

Analysis of Clinical Outcomes

Binary outcomes will be analyzed using logistic regression. Continuous outcomes will be analyzed using linear regression. Models will incorporate: Propensity score weighting, DiD specification, Baseline covariate adjustment. Results will be presented as adjusted odds ratios or mean differences with 95% confidence intervals. Absolute differences will be reported where appropriate.

Analysis of Healthcare Utilization

Count outcomes will be analyzed using Poisson regression, with negative binomial models used if over-dispersion is present. Models will follow the same weighted DiD specification described above. Adjusted incidence rate ratios and absolute differences will be reported.

Missing Data

The extent and patterns of missing data will be described. Missing covariate data will be handled using multiple imputations by chained equations under a Missing at Random assumption. The imputation model will include exposure, outcomes, and all covariates used in the analytical models. Estimates will be combined using Rubin's rules (White, Royston et al. 2011, Faria, Gomes et al. 2014). Complete case analyses will be conducted as sensitivity analyses.

9. Economic Methods

An economic evaluation will be conducted alongside the effectiveness analysis to assess the economic impact of the Rainbow Clinic model compared with standard antenatal care. The evaluation will adopt a cost-consequence framework, presenting incremental costs alongside incremental clinical and health services utilization outcomes. All economic analyses will be conducted at an individual level using linked routine healthcare data (National Institute for Health and Care Excellence 2025).

Perspective and Time Horizon

The economic evaluation will be undertaken from the perspective of the NHS. Only direct healthcare costs will be included. These will comprise antenatal care contacts, diagnostic investigations, emergency attendances, inpatient admissions, delivery-related care, and neonatal care. Indirect costs and wider societal costs will not be included.

The time horizon will extend from booking appointment through delivery and the immediate neonatal period, consistent with the available MSDS and HES data. Discounting will not be applied due to the short time horizon.

Measurement of Resource Use & Costing

Healthcare resource utilization will be measured at the individual level using linked MSDS and HES datasets. Resource categories will include antenatal visits, ultrasound scans, emergency department attendances, inpatient admissions, length of stay, delivery mode, and neonatal care utilization. Resource use will be aggregated per pregnancy episode. Unit costs will be obtained from nationally published NHS reference costs (England 2022). Total cost per pregnancy will be calculated by multiplying resource quantities by corresponding unit costs and summing across categories. All costs will be expressed in pounds sterling for the most recent available financial year. Where necessary, earlier costs will be inflated using appropriate NHS inflation indices.

Given the expected right-skewed distribution of cost data, generalized linear models (GLM) will be used to estimate adjusted mean costs. The appropriate distributional family (e.g., gamma with log link) will be selected based on diagnostic testing with robustness checks (e.g., two-part models). The primary cost analysis will apply the same propensity weighted staggered DiD framework used in the clinical analyses. Site and time fixed effects will be included. The adjusted incremental cost associated with Rainbow Clinic implementation will be reported with 95% confidence intervals.

Cost-Consequence Analysis

A cost-consequence analysis (CCA) will be conducted to present incremental costs and incremental clinical outcomes in a disaggregated format. Adjusted DiD estimates will be used to calculate summary measures, including:

- Incremental cost per stillbirth avoided
- Incremental cost per NICU admission prevented

These ratios will be calculated by dividing the adjusted incremental cost difference by the adjusted difference in outcome rates. Results will be presented transparently without aggregation into a single cost-effectiveness ratio.

Uncertainty and Sensitivity Analyses

Uncertainty around cost estimates and cost-consequence ratios will be assessed using non-parametric bootstrapping (Drummond, Sculpher et al. 2015). Sensitivity analyses will examine the robustness of results to:

- Alternative unit cost sources
- Alternative model specifications for cost data
- Complete case versus imputed datasets
- Alternative propensity score specifications

Subgroup economic analyses will be conducted to explore heterogeneity in cost impacts across key demographic and clinical groups.

10. Reporting, governance and amendments

Reporting will follow STROBE (observational comparisons) and CHEERS principles (economic evaluation). Any deviations from this SAP will be documented in an amendment log and reported in study outputs.

References

Abiola, J., et al. (2016). "The Manchester rainbow clinic, a dedicated clinical service for parents who have experienced a previous stillbirth improves outcomes in subsequent pregnancies." *BJOG* **123**(Suppl 1): 46.

Al Khalaf, S., et al. (2024). "Risk of stillbirth and adverse pregnancy outcomes in a third pregnancy when an earlier pregnancy has ended in stillbirth." *Acta Obstetrica et Gynecologica Scandinavica* **103**(1): 111-120.

Alex Heazell (2020). "The Tommy's National Rainbow Clinic Study." <https://www.tommys.org/our-research/our-research-projects/stillbirth-research/rainbow-clinic-improving-maternity-care>.

Bailey, E., et al. (2025). "Management of Pregnancy after Loss." *Clinics in Perinatology*.

Barron, R. L., et al. (2025). "Tommy's National Rainbow Clinic Study: a protocol for a multi-site cohort study to evaluate a specialist antenatal service for women and families following a stillbirth or neonatal death." *BMJ open* **15**(8): e103294.

Drummond, M. F., et al. (2015). *Methods for the economic evaluation of health care programmes*, Oxford university press.

England, N. (2022). "National cost collection for the NHS <https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection>." Accessed 1st Sep.

Faria, R., et al. (2014). "A guide to handling missing data in cost-effectiveness analysis conducted within randomised controlled trials." *Pharmacoeconomics* **32**(12): 1157-1170.

Le Vance, J., et al. (2025). "Impact of a dedicated antenatal specialist service for women with a history of stillbirth: the rainbow clinic." *BMC Pregnancy and Childbirth* **25**(1): 317.

National Institute for Health and Care Excellence (2025). "NICE health technology evaluations: the manual, <https://www.nice.org.uk/process/pmg36/chapter/economic-evaluation-2#evidence-on-resource-use-and-costs> (accessed on Feb, 2026).".

White, I. R., et al. (2011). "Multiple imputation using chained equations: issues and guidance for practice." *Statistics in medicine* **30**(4): 377-399.

