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REVIEW

Rural healthcare delivery and maternal and infant outcomes for diabetes in pregnancy: A systematic review

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Abstract

Aim: The aim of this systematic review was to examine the literature regarding rural healthcare delivery for women with any type of diabetes in pregnancy, and subsequent maternal and infant outcomes.

Methods: Eight databases were searched in September 2020, including Medline, EMCare, CINAHL, EMBASE, Maternity and Infant Care, Cochrane, Rural and Remote Health and Aboriginal and Torres Strait Islander Health bibliography. Studies from high-income countries in rural, regional or remote areas with interventions conducted during the antenatal period were included. Intervention details were reported using the template for intervention description and replication template. Two reviewers independently assessed for risk of bias using the RoB2 and ROBINS I tools.

Results: Three articles met the inclusion criteria: two conducted in Australia and one in the United States. A multidisciplinary approach was reported in two of the included studies, which were modified specifically for their respective rural settings. All three studies reported rates of caesarean section, birthweight (grams) and gestational age at birth as maternal and infant outcomes. One study was considered at moderate risk of bias, and two studies were at serious risk of bias.

Conclusion: There is a significant gap in research relating to healthcare delivery for women with diabetes in pregnancy in rural areas. This lack of research is concerning given that 19% of individuals in high-income countries reside rurally. Further research is required to understand the implications of healthcare delivery models for diabetes in pregnancy in rural areas.

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diabetes in pregnancy, gestational diabetes, healthcare delivery, models of care, rural health

1 | INTRODUCTION

Diabetes in pregnancy (DIP) is one of the most common conditions experienced in pregnancy.[1] It refers to pregnant women with a diagnosis of either type 1, type 2 or gestational diabetes mellitus (GDM). Globally, in 2019, an estimated 20.4 million or approximately 16% of births were adversely affected by DIP.[2] Of these, 84.6% were classified as GDM, 7.9% were from diabetes detected before pregnancy including type 1 or type 2 diabetes mellitus and the remaining 8.5% were diabetes types apart from GDM (including type 1 and type 2 diabetes) that were first detected in pregnancy.[2] GDM is the most rapidly rising diabetes category in Australia, with rates of diagnosis tripling over the last decade from 5% in 2008–2009 to 16% in 2017–2018.[3,4] In 2015, type 1 and 2 diabetes mellitus in pregnancy accounted for approximately 1% of all cases of DIP.[5]

Suboptimal glycaemic control in pregnancy is associated with an increased risk of a range of adverse maternal[5] and infant outcomes.[5–7] This disease burden extends past the perinatal period, with women who experienced GDM having a seven-fold increased risk of developing type 2 diabetes mellitus, typically within 5–10 years of their diagnosis.[8,9] The risk of both short- and long-term adverse outcomes can be minimised through the comprehensive management of DIP.[10–14] A reduction in adverse outcomes has been achieved in intervention studies with a focus on optimising glycaemic control through dietary advice, self-monitoring of blood glucose levels and pharmacotherapy as required.[12,13] A randomised controlled trial of usual care ($n = 473$) and specialised treatment ($n = 485$) for mild GDM showed significant reductions in birthweight, rates of shoulder dystocia, and caesarean delivery in the treatment group compared to the control.[13]

Internationally, management guidelines for DIP focus on the goal of strict glycaemic control with some variation in recommendations according to diabetes type and by country.[14–18] However, there are similarities in the recommendations in developed countries.[14–18] The first is the recommendation of close monitoring and regular contact with a specialist multidisciplinary team of allied health and medical professionals before delivery.[14,15,17,19,20] Second, women should be referred to a dietitian for individualised and culturally appropriate dietary advice,[14,15,17] and for those with GDM, this should occur within 1 week of diagnosis.[16,18] Self-monitoring of blood glucose levels is recommended for women with all diabetes types throughout pregnancy.[14,17,18] Lastly, medication initiation is to occur in women with GDM where blood glucose targets are not met with lifestyle change alone,[14,16,17] and insulin therapy is likely required in women with pre-existing DIP.[15–17]

It has been well established that access to health services is limited for people living in rural and remote areas compared to those in metropolitan areas.[3,21] There were only 11 doctors per 10 000 people in non-metropolitan America in 2018, compared to 31 per 10 000 in metropolitan areas.[22] In 2017–2018, the number of full-time equivalent clinical specialists was 143 per 100 000 population in major cities in Australia, compared to 22 per 100 000 in very remote areas.[21] This deficit extends to maternal health services globally.[23,24] The lack of specialised healthcare in rural areas contributes to the increased risk of adverse maternal and perinatal outcomes.[24–27] This risk increases further for women with DIP in rural areas, with 37.6% of babies born pre-term to mothers living in remote or very remote areas in Australia with DIP, compared to 17.8% of babies in major cities.[5]

The limited number of health professionals in rural areas relative to metropolitan areas means that metropolitan-based models of care may not be feasible in rural areas. However, there is a lack of research investigating the healthcare accessible to women with DIP in rural areas.[28] The disparity may be magnified when high-income countries, such as Australia and the United States, are compared to low- to middle-income countries, where lack of clinician expertise and resources result in further deficiencies in the diagnosis and management of DIP.[29–31] Previous studies investigating models of care have used cross-sectional methods such as surveys, with a lack of reporting on detailed model of care processes and subsequent health outcomes.[32–34] To date, there has been one review with a target population of women with pre-pregnancy diabetes mellitus.[7] This review addressed exposures and subsequent outcomes and focused on Australian studies only.[7] There are no known systematic reviews investigating healthcare delivery for women with DIP in rural areas. Therefore, the aim of this systematic review was to identify and describe the current characteristics of healthcare delivery models of care internationally for women with DIP in rural areas, and describe the relationship with maternal and infant health outcomes.

2 | METHODS

The protocol for this review was registered with PROSPERO International prospective register of systematic reviews [CRD42020209956]. A search strategy was developed in consultation with a research librarian. Key search terms relating to diabetes and pregnancy and rural, regional or remoteness were used. Limits included the English language and papers published from 1990 onwards. This year was chosen as a cut off so that interventions reflect recent management recommendations in line with DIP research and technology developments, such as self-monitoring of blood glucose levels.[35,36] An initial systematic search of eight databases was conducted in September 2020. Databases searched included Medline (Ovid), EMCare (Ovid), CINAHL (EBSCOhost), EMBASE (Ovid), Maternity and Infant Care (Ovid), the Cochrane Library, Rural and Remote Health (Informit) and Aboriginal and Torres Strait Islander Health bibliography (Informit). The reference lists of included articles were hand searched to identify any additional studies that met the selection criteria. The full Medline search strategy is available as Appendix I (online supplementary material).

Studies were considered for inclusion if the target population was women with type 1 or type 2 diabetes mellitus in pregnancy or GDM. Any intervention conducted or observed in a regional, rural, remote or otherwise defined non-metropolitan setting by the study's authors and in a high-income country as defined by the World Bank (2019) was included.[37] The search was limited to high-income countries so that healthcare resourcing was comparable, as healthcare challenges and priorities for rural populations in low-income countries can vary greatly compared to high-income countries.[29,31] Studies were included if both metropolitan and non-metropolitan populations were represented, but the outcomes for the non-metropolitan group were reported separately. Interventions conducted or observed in the antenatal period were considered eligible. Studies with any comparator, such as an intervention or control group or pre/post study design were included. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were used to report results based on these criteria.[38]

Primary outcomes were defined as any maternal or infant physical or biochemical outcome related to glycaemic control, due to the broad range of outcomes associated with poor glycaemic control during pregnancy.[39] Physical outcomes included those such as caesarean section, preeclampsia, APGAR score and birthweight. Biochemical outcomes included blood glucose levels, neonatal hypoglycaemia and diabetic ketoacidosis. Secondary outcomes were also reported, and included nutrition, medication, behavioural, exercise, mental health related and healthcare delivery outcomes.

The title and abstract of identified studies were screened for eligibility independently by two reviewers. Full texts were then screened independently against the inclusion and exclusion criteria. If two reviewers disagreed at either the title and abstract or full-text stage, a third reviewer resolved this conflict. A data extraction template was developed and standardised, to ensure all relevant information was recorded. Data extracted included study design, participant characteristics, setting, rural description, maternal and infant outcomes, study results and conclusions. The template for intervention description and replication (TIDieR) template was used to extract specific intervention details and replication data.[40] The first reviewer extracted the relevant information, and this was checked by a second reviewer. A quality assessment was conducted independently by two reviewers on studies that met the inclusion criteria using either the Cochrane RoB2 or ROBINS-I tools,[41,42] depending on study design.

3 | RESULTS

The results of the search strategy are detailed in Appendix II (online supplementary material) using the PRISMA flow diagram.[38] Database searches returned 3177 articles, with a total of 1827 articles after duplicates were removed. Following title and abstract screening, 272 articles were considered for full-text inclusion. Three articles were identified as eligible and were included in the review.

Study and participant characteristics are outlined in Table 1. Two studies were conducted in Australia,[43,44] and one in the United States,[45] with sample sizes ranging from 87 to 303. One study was a pre-post design,[44] another was a retrospective cohort study with a control group, and the other was a non-randomised controlled trial.[45] All studies included women with GDM and type 2 diabetes mellitus in pregnancy. The two Australian studies also included women with type 1 diabetes mellitus in pregnancy.[43,45] Two studies described their location as a rural area,[44,45] and one as a regional hospital.[43] None of the studies included a specific rural, regional or remote definition.

Details of the interventions provided in each paper are shown using the TIDieR template in Table 2. The overall goals of each study varied substantially. One study involved referral to a lactation consultant to encourage antenatal expression and storage of colostrum.[43] The goal of this intervention was to compare rates of neonatal hypoglycaemia in women with any type of DIP who expressed antenatal colostrum to those who did not. Murfet et al.[44] investigated the effect of a nurse practitioner-led model of care on maternal and infant outcomes. The final article described a modified version of the "Sweet Success" program where rural antenatal

TABLE 1 Location, study design, sample size, demographics and rural descriptors for observational and intervention studies for women with diabetes in pregnancy in rural areas

Authors, year	Country; locality	Study design	Sample size	Demographics (age, ethnicity, SES)	Diabetes type/s	Rural/regional/remote description
Murfet et al. (2014)[44]	Australia; North West Tasmania	Pre-post	261	Mean age 31 years Caucasian 84% Aboriginal and/or Torres Strait Islander 7% Index of Relative Socioeconomic Advantage and Disadvantage deciles 1–4 99%	Pre GDM 57.1% T1DM 13.4% T2DM 4.5% Unknown (suspected GDM) 25.0% Post GDM 87.9% T1DM 7.4% T2DM 4.0% Unknown (suspected GDM) 3.4%	Describes study location as a "rural locality"
Casey et al. (2019)[43]	Australia; North Queensland	Retrospective cohort study with control group	303	Intervention Mean age 30 years Caucasian 88% Aboriginal and/or Torres Strait Islander 3.8% Filipino 2.5% Control Mean age 29 Caucasian 73% Aboriginal and/or Torres Strait Islander 7.2% Filipino 8.1% SES not reported	GDM 96% T1DM and T2DM % not individually specified	Regional public hospital
Weiderman and Marcuz (1996)[45]	United States; far North California	Non-randomised controlled trial Control group: usual care at a multidisciplinary "Sweet Success" program site[48]	87	Intervention Women <20 y 5% Women 20–29 y 46% Women 30–39 y 49% Caucasian 79% African American 0% Native American 3% Asian 5% Other 13% Control Women <20 y 6% Women 20–29 y 43% Women 30–39 y 45% Women >40 y 6% Caucasian 82% African American 4% Native American 8% Asian 4% Other 2% SES not reported	Intervention GDM 100% Control GDM 96% T2DM 4%	Rural geographic area of 5000 square miles

Abbreviations: DIP, diabetes in pregnancy; GDM, gestational diabetes mellitus; SES, socioeconomic status; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus.

TABLE 2 Description of interventions provided to women with diabetes in pregnancy in rural areas using the template for intervention description and replication—checklist[42]

Author, year	Why? Rationale/theory/goal	What? Materials and procedures	Who provided? How and where?	When and how much?	Tailoring and modifications
Murfet et al. (2014)[44]	Investigate maternal and infant outcomes following the implementation of a nurse practitioner-led model of care	Management protocol for insulin initiation in GDM and referral to physician Insulin initiated by obstetrician/credentialed diabetes educator for women with GDM Same day dispensing of insulin from hospital pharmacy Women with type 1 or type 2 diabetes mellitus were referred to diabetes physician at initial consult Use of continuous glucose monitoring and after-hours diabetes nurse educator contact	Coordinated by diabetes nurse practitioner Multidisciplinary clinic with: - Credentialed diabetes educator - Dietitian - Antenatal nurse - Obstetrician Face-to-face at one private and two local public hospitals	Initial 30 min credentialed diabetes educator—individual Initial 30 min dietitian—individual Joint credentialed diabetes educator/dietitian 20 min individual reviews—fortnightly until 36 weeks gestation then weekly Midwifery and obstetrics reviews as required	Individualised for low resource region Patients with type 1 and type 2 diabetes mellitus frequency of visits tailored to glycaemic control, use of insulin and obstetric reasons Modifications not reported
Casey et al. (2019)[43]	To compare rates of hypoglycaemia in babies born to mothers who express antenatal colostrum and mothers who do not, to inform local protocols	All women with diabetes in pregnancy were referred to a lactation consultant Women were educated on how to express and store colostrum daily between 34–36 weeks until birth Women were given syringes and labels to collect and store colostrum	Lactation consultant (referred to following an education session by the diabetes educator midwife) Face-to-face at a hospital site	Not reported	Not reported
Weiderman and Marcuz (1996)[45]	Establish GDM care plan for rural primary perinatal providers including a triage system for surveillance, diagnosis and management	Provider training materials and education packets, blood glucose meters and associated supplies were provided to each project site Following GDM diagnosis, patients were triaged into varying levels of care by the pilot guidelines and protocols	Obstetrician, diabetes educator, dietitian, mental health counsellor team streamlined "Sweet Success" program guidelines for each site + triage protocols developed Travelling multidisciplinary team, including the diabetes educator, dietitian and counsellor, provided	Followed up on a weekly or biweekly basis	Guidelines from the "Sweet Success" program were modified by specialist clinicians for each rural project site Focus on individualised patient care within pilot guidelines and protocols Modifications not reported

TABLE 2 (Continued)

Author, year	Why? Rationale/theory/goal	What? Materials and procedures	Who provided? How and where?	When and how much?	Tailoring and modifications
		Patients recorded blood glucose levels 3–4 times daily using blood glucose meters and kept daily dietary and fasting urine ketone levels	on-site training for project site staff Staff that were trained at clinic sites were either nurse midwives, certified nurse practitioners or registered nurses Face-to-face in a rural clinic setting		

Abbreviations: DIP, diabetes in pregnancy; GDM, gestational diabetes mellitus.

care providers including nurse practitioners, nurse midwives and registered nurses were upskilled in the diagnosis and management of GDM.[45]

Two studies described multidisciplinary care approaches, tailored for use in low resource rural settings.[44,45] Murfet et al.[44] included a multidisciplinary team coordinated by a nurse practitioner and included a dietitian, diabetes educator, obstetrician and antenatal nurse.[44] At the initial clinic visit, women were seen by each of these professionals. Follow up visits were scheduled fortnightly as joint consults with the dietitian and diabetes educator, with review by the antenatal nurse and obstetrician as necessary. Weiderman and Marcuz[45] described a visiting team consisting of a dietitian, diabetes educator and mental health counsellor. These health professionals, based at a non-rural site, upskilled existing staff in their respective rural locations to manage women with DIP.[45] All interventions were delivered face-to-face in a clinic or hospital setting.

Two studies reported some form of tailoring in their interventions.[44,45] One did not specify how this occurred, only that the intervention was developed for a low resource setting.[44] Weiderman and Marcuz (1996) described the modification of the "Sweet Success" program,[45] by clinicians specifically for rural sites.[45] Intervention modifications, planned and actual fidelity were not reported by any of the included articles.

Maternal and infant outcomes reported are outlined in Table 3. All studies reported rates of caesarean section, birthweight in grams and gestational age at birth.[43–45] Pre-eclampsia, polyhydramnios, emergency caesarean section, neonatal hypoglycaemia and APGAR score were included as maternal and infant outcomes in two articles.[43,44] Murfet et al.[44] analysed their primary outcomes using adjusted relative risk as pooled adverse maternal outcomes and pooled adverse neonatal outcomes, respectively.

The primary outcomes, results and conclusions are reported in Appendix III (online supplementary material). Secondary outcomes are listed in Appendix IV. The article evaluating a nurse practitioner-led rural model of care concluded that neonatal outcomes improved, without increasing specialist referral load.[44] This was reported as a reduction in the adjusted relative risk of pooled neonatal adverse outcomes, which was 0.76 (95% confidence interval [CI] 0.61–0.94) for all diabetes types and 0.60 for GDM (95% CI 0.48–0.76).[44] Weiderman and Marcuz[45] reported that their smaller-than-expected sample size limited the ability to draw conclusions. However, trends suggested that adequately upskilled rural clinicians were able to provide comprehensive care with no difference in maternal or infant outcomes when compared to the multidisciplinary team model.[45] The article examining antenatal colostrum expression reported no difference in neonatal hypoglycaemia between women who expressed

TABLE 3 Maternal and infant outcomes for women with diabetes in pregnancy in rural areas

		Author, year		
		Murfet et al. (2014)[44]	Casey et al. (2019)[43]	Weiderman and Marcuz (1996)[45]
Maternal outcomes	Maternal hypoglycaemia	✓		
	Loss of consciousness	✓		
	Diabetic ketoacidosis	✓		
	Maternal metabolic complications	✓		
	Threatened abortion requiring sutures	✓		
	Preeclampsia	✓	✓	
	Oligohydramnios/polyhydramnios	✓	✓	
	Premature labour/placenta previa	✓		
	2nd–4th degree tear	✓		
	Emergency caesarean		✓	
	Failure to progress/emergency caesarean	✓	✓	✓
	Postpartum haemorrhage	✓		
	Instrumental delivery		✓	
Infant outcomes	Gestational age at birth	✓	✓	✓
	Preterm delivery	✓		
	Birthweight	✓	✓	✓
	Neonatal hypoglycaemia	✓	✓	
	Neonatal respiratory distress syndrome	✓		
	Neonatal macrosomia	✓		
	Birth injuries	✓		
	Neural tube defect	✓		
	Neonatal congenital abnormality	✓		
	Stillbirth or neonatal death	✓		
	Apgar score		✓	✓
	Other neonatal complications	✓	✓	

and stored colostrum antenatally, with the intention of feeding their infant this after birth, and those who did not (p value 0.89).[43]

Two studies were considered as at serious risk of bias,[44,45] and one was considered at moderate risk[43] using the ROBINS-I tool (Appendix V, online supplementary material).[41]

4 | DISCUSSION

This review highlights a major gap in published research regarding antenatal interventions for women with DIP in rural areas, globally. There were only three studies identified that observed or conducted an antenatal intervention in a rural area for women with DIP and reported maternal and infant outcomes. Two studies were interventions,[44,45] one a pre-post design,[44] and the second a non-randomised controlled trial.[45] The third study was a retrospective cohort study.[43] No randomised controlled trials were identified despite a broad search strategy.

There was variation in maternal and infant outcomes reporting between articles, which were highly dependent on the primary aim of the study. Two of the included studies reported tailoring their interventions to a rural setting.[44,45] Due to the heterogenous nature of these three studies and the variation in reporting, it is difficult to draw any practice-based conclusions regarding delivery of healthcare for women with DIP in rural settings, but it flags that this issue has been neglected to date.

Guidelines issued by national bodies such as the American Diabetes Association and the Australasian Diabetes in Pregnancy Society vary between diabetes types.[14–18] Current GDM management guidelines recommend referral to the diabetes educator and dietitian for education

regarding lifestyle management and blood glucose self-monitoring as the first line of treatment, with medication initiated if glycaemic control remains sub-optimal.[14,16,18] Commencement of pharmacotherapy should be individualised, using metformin or insulin as both are considered safe and effective for use during pregnancy.[14,16,17] Pre-existing DIP requires ongoing lifestyle management from conception, with insulin therapy essential for women with type 1 diabetes and likely required for women with type 2 diabetes.[14,15,17,18] Multidisciplinary team management is recommended, which typically includes a credentialled diabetes educator, dietitian, obstetrician, endocrinologist and midwife or antenatal nurse, and may also include an Aboriginal health worker, lactation consultant and exercise physiologist.[14,16,17,18] The extent to which these guidelines are met in practice is unknown, as demonstrated by the lack of reporting on models of care found by this systematic review.

Current guidelines recommend women with GDM see a dietitian for a minimum of three appointments.[16] The feasibility of translating guidelines such as these to rural areas, where there are fewer allied health and specialists available,[21] is unknown. To plan and implement best practice models of care, details of current practices need to be described and evaluated.[46,47] This should include reporting of specific adaptions for the rural context such as tertiary clinic support, availability of specialist clinical staff and utilisation of telehealth in models. Context-specific solutions can then be implemented to address key issues within rural models of care.

This article is the first, to the best of the authors' knowledge, to report the published interventions on rural healthcare delivery for women with DIP. Although systematic reviews have been conducted previously which centred on outcomes for women with GDM, none have had a rural focus.[48,49] One review article investigated pregnancy outcomes of women and infants in metropolitan and rural areas; however, the type of review was not specified and was limited to pre-pregnancy diabetes in the Australian context.[7] A lack of large Australian studies in rural areas limited the ability of the review to draw conclusions when comparing rural and metropolitan outcomes.[7] A systematic review explored the prevalence of DIP for Aboriginal and Indigenous women globally; however, minimal focus was placed on the level of remoteness of studies.[50] Neither of these reviews reported on the models of care resulting in the specified outcomes.[7,50]

The lack of research targeting rural women with DIP, especially when considering healthcare delivery, reflects the wider gaps in research. There is a well-established gap in healthcare access and health outcomes for rural residents compared to those in metropolitan areas.[21,51] Additionally, it is known that healthcare delivery models must be modified to fit with the challenges of rural settings.[52] The services offered in rural areas are typically at facilities with less infrastructure, and are required to provide a broader range of services to a geographically dispersed population due to reduced access to specialist services.[52] The lack of studies meeting the criteria for this review demonstrates the limited research being undertaken into how models of care can be modified and evaluated in a rural context.

One of the challenges in conducting this review was the lack of international consensus on the definition of *rural*. Similar terms used by various organisations include remote, regional and non-metropolitan.[53] Definitions of rurality has evolved greatly over time to fit with changes in population density and increasing consideration of rural based policy and resource allocation.[53,54] As an example the Modified Monash Model, which is the current Australian measure, is predominantly focussed around the relationship between population size, geographical location and healthcare service access.[55]

Research on GDM management has been conducted in Australia.[56] A model of care based on the Queensland GDM management guidelines was adapted from metropolitan sites and implemented in two regional areas.[56,57] This research focused on the dietetic component of the model of care, aiming to increase adherence to Queensland Health clinical guidelines.[16] These guidelines recommended that women were seen by a dietitian within 1 week of a GDM diagnosis, and had a minimum of three appointments with a dietitian throughout their pregnancy.[16,56] Although this did not meet the inclusion criteria here due to a lack of maternal and infant outcome reporting, it highlighted the disparity between evidence-based practice and the current GDM model of care.[57]

Strengths of the current review include that a comprehensive search strategy across several databases was conducted to reduce the likelihood of missing eligible articles. Also, both intervention and observational studies were included, providing a thorough review of the available evidence. A limitation of this review is that some older studies may have been missed given that only published articles from 1990 onwards were considered. Additionally, the small number and heterogeneity of included articles limited the ability to draw practice-based conclusions on DIP care in rural areas.

Considering nearly one fifth of individuals in high-income countries reside in rural areas,[51] and the established worse health outcomes for rural mothers with DIP and their babies,[24,26] there is a significant lack of research to reflect this population.[28,58] A structured treatment approach has shown to improve outcomes in women with GDM.[12,13,19] However, it is unknown if

these approaches can be translated to a rural setting. More research is required to investigate and evaluate the current models of care in rural areas and their impact on maternal and infant outcomes.

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CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

AUTHOR CONTRIBUTIONS

Conceptualisation: EP, MR, LB, CC, KW, TS; methodology: EP, MR, TS; data curation: EP, GP; investigation: EP, GP, KR, SH; data analysis: EP; validation: EP, TS; writing: EP, MR, LB, TS; editing: EP, GP, MR, LB, KR, SH, CC, KW, TS; supervision: MR, LB, CC, TS; visualisation: MR, LB, TS; project administration: TS. All authors approved the final version of the manuscript for publication.

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