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TEDI-Prem: a multisite randomised controlled trial protocol assessing the effect of a telehealth early intervention program on neurodevelopmental outcomes of infants born very preterm and their parent's well-being

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Abbreviations:
VPT: Very Preterm
TEDI-Prem: Telehealth for Early Developmental Intervention in babies born very preterm
CA: Corrected Age
NICU: Neonatal Intensive Care Unit
SCN: Special Care Nursery

Bayley-4: Bayley Scales of Infant and Toddler Development- 4th edition
KPSE: Karitane Parenting Confidence Scale
DASS-21: Depression Anxiety and Stress Scale 21
SF-6D: Short-Form Six-Dimension Quality of Life
EQ-TIPS: EuroQol Toddler and Infant Populations measure
ITSEA: Infant Toddler Social Emotional Assessment
EAS: Emotional Availability Scale
SMD: Standardised Mean Difference
CI: Confidence Interval
SPEEDI: Supporting Play Exploration and Early Development Intervention
RCT: Randomised Controlled Trial
SPIRIT: Standard Protocol Items: Recommendations for Interventional Trials
REDCap: Research Electronic Data Capture

Author's contributions
Stacey C Dusing, Peter J Anderson, Kim Dalziel, Anne E Holland, Rod W Hunt, Katherine J Lee, Angela Morgan, and Karli Treyvaud were involved in conception and design of the study. Abbey L Eeles and Alicia J Spittle were involved in the conception and design of the study, and initial manuscript preparation. All authors provided critical review of the protocol, approved the final version as submitted, and agree to be accountable for all aspects of the work.

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ABSTRACT

Introduction
Infants born very preterm (VPT, <32 weeks' gestation) are at increased risk for neurodevelopmental impairments including motor, cognitive and behavioural delay. Parents of infants born VPT also have poorer mental health outcomes compared with parents of infants born at term.

We have developed an intervention program called TEDI-Prem (Telehealth for Early Developmental Intervention in babies born very preterm) based on previous research. TEDI-

Prem aims to improve neurodevelopmental outcomes and parental well-being in children born VPT. Here we present the protocol outlining a multicentre, pragmatic, parallel group, randomised controlled trial (RCT) to determine the efficacy of TEDI-Prem plus usual care, compared with usual care alone.

Methods and analysis
We will recruit 466 VPT infants from the neonatal units of five hospitals in Victoria, Australia. Participants will be randomised, stratified by site of recruitment and multiple birth, to TEDI-Prem plus usual care or usual care alone. The TEDI-Prem intervention program involves 13 sessions across three phases. Phase one commences in the neonatal unit with four face to face sessions with parent/s and a physiotherapist/occupational therapist. Once discharged, sessions across phase two and three (six and three sessions, respectively) continue until infants are 12 months' corrected age (CA) via telehealth.

The primary outcome is the Bayley Scales of Infant and Toddler Development- 4th edition (Bayley-4) motor composite score at 12 months' CA. Secondary outcomes address other neurodevelopmental domains (Bayley-4 cognitive and language composite score; Infant Toddler Social Emotional Assessment), parental mental health (Depression Anxiety and Stress Scale 21), parent-child interaction (Emotional Availability Scale), parent quality of life (Short-Form Six-Dimension Quality of Life), child quality of life (Toddler and Infant Questionnaire), service delivery (Measures of Processes of Care), and program cost-effectiveness at 12 and 24 months' CA.

Ethics and dissemination
This trial has Royal Children's Hospital Human Research and Ethics committee approval (HREC/67604/RCHM-2020) with specific site approval for all participating sites. Findings will be disseminated through peer-reviewed publications, conference presentations, digital and print media and to participants.

Registration details
This trial is registered with the Australian New Zealand Clinical Trials Registry (ACTRN12621000364875).

Strengths and limitations of this study

- We have adapted and combined two pilot-tested intervention programs targeted at very preterm infants and their families.
- The intervention was adapted in partnership with consumers.
- The intervention sessions are delivered in hospital and post-discharge with face to face and telehealth modes utilised. This increases access to intervention for families, including those who face barriers to service use such as living in regional or rural communities.
- This study will recruit a large sample size from 5 out of 6 Victorian neonatal intensive care units.

INTRODUCTION

Worldwide, over 2.5 million babies are born very preterm (VPT, <32 weeks' gestation) each year.[1] In Australia alone, there are approximately 5000 VPT births each year, and whilst most of these infants survive,[2] over 50% of VPT infants will have a neurodevelopmental impairment.[3, 4] The neurodevelopmental deficits resulting from early birth may compromise physical function, academic achievement and quality of life.[5-7] While survival rates are improving in children born VPT, the rates of neurodevelopmental impairments are not improving over time[8] and are associated with substantial economic costs.[9] Further, following the VPT birth parents have higher rates of mental health problems than their peers with term-born infants, which is itself associated with poorer child outcomes.[10, 11]

Very preterm birth occurs during a critical period of central nervous system development, with the first 1000 days of life the most dynamic and rapid period of brain development, setting the foundation for all future neural development.[12, 13] This period of brain development is particularly vulnerable to adverse environmental events and exposures, including preterm birth. The VPT infant is often critically ill and requiring invasive interventions in the neonatal intensive care unit (NICU). Together with their early illness, this care environment, whilst necessary to support life, can disrupt brain maturation. Further, the NICU environment can alter the parent-infant relationship, infant sensorimotor experiences, and offers limited opportunities for social, motor, cognitive and language interactions.[14-16] Parents are more likely to experience higher anxiety and depression after preterm birth than peers who have babies born at term,[10, 17, 18] which contributes to an altered parent-child relationship and increases the risk for poorer developmental outcomes for VPT children.[5, 19] Very preterm birth alone carries heavy healthcare costs in the newborn period, but longer-term costs are much higher when children have developmental or health problems.[20] Averting

these long-term sequelae for VPT infants through early intervention has potential economic benefits in health and education.[9] While medical advances continue to improve neonatal care,[21] clinical rehabilitation for these high-risk infants has not kept pace with advances in basic science and developmental theory to improve outcomes for infants and their parents.[22-24]

In a Cochrane review of early developmental interventions post hospital discharge, our team demonstrated that early intervention had a moderate effect on cognitive development (standardised mean difference [SMD] = 0.32, 95% confidence interval [CI] 0.16, 0.47) but a smaller effect on motor development (SMD = 0.10, 95% CI 0.01, 0.19) up to 3 years of age compared with usual care.[25] A recent systematic review of interventions commencing in the NICU found that parent-delivered motor interventions were more effective than other early developmental interventions in improving motor and cognitive outcomes in the short term.[26] Neurorehabilitation and neuroplasticity research supports high repetitions of task specific activities to enhance learning and establish neural pathways in infants.[24, 27] It has also been shown that intense interventions that involve parents are more effective at promoting neurodevelopmental outcomes than low intensity interventions that focus only on the therapist and infant.[28, 29] Given that VPT infants are at high risk of motor, cognitive and behavioural impairments, there is an even greater need for high repetitions and intensity to enhance learning in infants born VPT, and thus interventions must engage parents to achieve a high dose.[29]

The provision of high-intensity intervention during a time of maximum neuroplasticity, as supported by the basic science and theoretical literature,[12,36] is not currently available to VPT infants in Australia and in many countries internationally. Our research has shown that the majority of preterm infants do not receive timely early intervention, and those with higher

family social risk (socio-economic disadvantage) are less likely to receive intervention.[30] Further barriers to accessing effective early intervention for preterm infants and their families include a 'wait and see' approach rather than a preventative model, lack of access to appropriately trained health professionals (particularly for rural, remote and/or socioeconomic disadvantaged families), provision of generic interventions rather than targeting the needs of the individual infant and family, limited funding for services, and lack of communications between families and health professionals.[30, 31] Consequently, many preterm infants do not receive intervention during a critical developmental window for promoting functional neural pathways and improving future function.[32]

Two promising interventions for preterm infants and their families that have been recently trialled by our team include "SPEEDI" and "e-prem". SPEEDI (Supporting Play Exploration and Early Development Intervention) is a face to face early intervention program, developed by author SD and colleagues in Virginia, USA, and has been trialled in two pilot randomised controlled trials (RCTs) (one in the USA[33, 34] and one in Australia[35]). Although both SPEEDI pilot studies were underpowered for determining efficacy, there was a trend for infants in the SPEEDI group to have better motor, cognitive and language scores on the Bayley-III at 4 (Australian pilot) and 6 (USA pilot) months' corrected age compared to those in the control group. Both studies determined the SPEEDI intervention was feasible to deliver. A protocol paper for a larger trial evaluating the efficacy of SPEEDI was published in 2020.[36]

e-prem was developed by authors KT, PJA and AJS based on their research on early intervention for preterm infants and is an adaptation of the VIBeS Plus program.[37] e-prem involves initial face to face intervention followed by a web-based intervention, with age-based online modules completed over the first year of life, supported by clinicians via telephone. In a pilot RCT of e-prem compared with usual care, 100 preterm infants were

followed up at 24 months' corrected age. Parent-infant interaction was assessed using the Emotional Availability Scale (EAS) at 24 months' CA. Parents in the intervention group scored higher than those in the control group (reflecting more optimal outcomes) on maternal structuring (mean difference = 0.72, 95% confidence interval [CI] = 0.21, 1.22), and children in the intervention group scored higher than those in the control group on child responsiveness (coefficient = 0.58, 95% CI = 0.03, 1.13), and child involvement (coefficient = 0.62, 95% CI = 0.09, 1.15).[38]

With advances in digital technologies and improved accessibility, telehealth (defined as the use of information and communication technologies to provide clinical services from a distance) has made it possible for therapeutic interventions to be delivered straight to families in their home.[39] Utilising this improved accessibility, together with the results of our previous research, we have consolidated the SPEEDI and e-prem intervention programs, and developed an innovative approach to early intervention to enhance neurodevelopment called TEDI-Prem (Telehealth for Early Developmental Intervention in babies born very preterm). We now plan to test the efficacy of the TEDI-Prem intervention in a randomised trial.

AIMS

The primary aim of this RCT is to determine the efficacy of TEDI-Prem plus usual care compared with usual care alone to improve motor outcomes at 12 months' corrected age (CA) in children born VPT. Secondary aims are outlined in Box 1.

Box 1: Secondary aims

To determine the efficacy of TEDI-Prem plus usual care compared with usual care alone to improve:

1. motor outcomes at 24 months' CA for infants born VPT
2. cognitive, language, behaviour and quality of life at 12 and 24 months' CA for infants born VPT
3. parent well-being (anxiety and depression), quality of life, and self-efficacy at 12 and 24 months' CA for parents of infants born VPT
4. parent-infant interaction at 12 and 24-months' CA between infants born VPT and their primary caregiver
5. healthcare utilisation at 12 and 24 months' CA for infants born VPT
6. cost-effectiveness over 24 months

METHODS AND ANALYSIS

Study design

A multicentre, pragmatic, parallel group, RCT designed according to SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) guidelines,[40] the principles of Good Clinical Practices, and in adherence to the National Statement and Australian Code for Responsible Research Conduct.

Study setting

Trial recruitment will be undertaken in the neonatal intensive care unit (NICU) or special care nursery (SCN) of five hospitals in the state of Victoria, Australia, including The Royal Women's, The Royal Children's, Monash Children's, Joan Kirner Women's and Children's,

and the Northern Hospitals. These centres are chosen as they encompass five of the six main sites of care for VPT infants in Victoria.

Participants

VPT infants and their parent/s (at least one parent must participate in the trial) from Victoria, Australia. Throughout this protocol, the term 'parent' will be used to refer to any individual who provides primary care to the infant (e.g. grandparent, foster carer). Inclusion and exclusion criteria are outlined in box 2.

Box 2: Eligibility for inclusion in the randomised controlled trial

Inclusion criteria

- Infant born <32 weeks' gestation.
- Infant medically stable and not ventilator-dependent at recruitment (minimum age for enrolment 32 weeks' and maximum 40 weeks' postmenstrual age).
- Have one parent who speaks and can read English (as the video content and intervention materials are in English).
- Able to participate in an early intervention program for a 12-month period.
- Able to attend primary outcome assessment at 12 months' CA.

Exclusion criteria

- Infant with a diagnosis of a congenital abnormality known to affect neurodevelopment, who require specific intervention, such as infants with Trisomy 21.
- Families who are planning to move overseas/interstate prior to the primary outcome assessment at 12 months' CA.

- Parents not wanting to engage in telehealth intervention.

Sample Size Calculation

The primary outcome is the Bayley-4[41] Motor Composite score at 12 months' CA, which has a mean of 100 and standard deviation of 15. Whilst there is no reported minimum clinically important improvement on the Bayley-4, a difference of 5 points represents a SMD of 1/3 between groups, and is considered clinically important and consistent with previous RCTs in the field that have changed clinical practice.[4] In order to achieve 90% power to identify a SMD of 1/3 based on a two-sided t-test with a 5% significance level, we require 190 participants per group assuming that the observations are independent. Given that our sample will be children born <32 weeks we would expect approximately 20% to be multiple births. Assuming an intra-class correlation coefficient of 0.2 between multiple births, this equates to a design effect of 1.04, hence we need to recruit 198 per group to have 190 effective participants. Allowing for 15% loss to follow-up (conservative estimate – previous studies by our team have >90% follow-up), we aim to randomise a total of 466 infants over 32 months.

Recruitment

Eligible infants will be identified by a member of the research team at the participating sites while infants are in the NICU or SCN. With approval from the infant's clinical team, when the infant is considered medically stable, is not ventilator dependent (can be on continuous positive airway pressure [CPAP]), and is between 30-40 weeks' gestation, parents of eligible infants will be approached by a member of the research team and provided with the Participant Information and Consent Form for the trial (see online supplementary material 1). In the event that COVID-19 precautions prohibit the research team entering the NICU or SCN at a participating site, a clinical team member will approach families to introduce the

study and gain verbal consent for a research team member to contact them to explain the study in more detail. The research team member will give a verbal explanation of the trial, including a description of the trial processes, the voluntary nature of the trial and that a decision to participate, or not, will not affect the standard clinical care they and their infant receives. See Figure 1 for an overview of participant recruitment and follow-up.

Data collection, management, and access

Data for this trial will be collected and entered using electronic data collection forms which will be completed by the parent and researchers and entered via The University of Melbourne's REDCap database system. All data will be de-identified, with all participants allocated a unique trial identification number. Intervention sessions will be recorded using Zoom Video Communications Inc (ZOOM). All files containing private or confidential data will be stored only in locations accessible to designated members of the research team on secure networks which are backed up nightly.

Baseline data collection

Perinatal information: Data on the birth history and neonatal course (e.g. gestational age, birthweight, sex, multiple birth status, cranial ultrasound findings, proven or suspected necrotising enterocolitis, maternal antenatal corticosteroid administration, postnatal corticosteroid use and use of oxygen at discharge from hospital) will be collected by the research team members from medical files and the hospital neonatal database. Prior to randomisation, consenting parents will be asked to complete baseline questionnaires to obtain the following information:

Social risk: The Social Risk Index which assesses six aspects of social status including family structure, education of primary caregiver, primary income earner occupation, primary income earner employment status, language spoken at home, and maternal age at birth will be used to assess social risk.[42]

Parenting self-efficacy: The Karitane Parenting Confidence Scale is a reliable and valid measure for assessing parent confidence in 15 task-specific areas including confidence in feeding, settling and decision making.[43] This will also be collected at 12 and 24 months' CA.

Parent depression, anxiety and stress: The DASS-21 evaluates severity of symptoms associated with depression, anxiety and stress, and categorises results as mild, moderate or severe.[44] This will also be collected at 12 and 24 months' CA for all participants, and at 3 and 6 months' CA for parents in the intervention group.

Parent Quality of Life: The Short-Form Six-Dimension Quality of Life (SF-6D) instrument will be used to facilitate the estimation of quality adjusted life years (QALY) and to inform the cost-effectiveness of the intervention.[45] This will also be completed at 12 and 24 months' CA.

Use of therapy services: A purpose-built questionnaire will be used to measure access to therapy services for the child. This will also be administered at 3, 6, 12, 18 and 24 months' CA to monitor access to early interventions services (see online supplementary material 2).

Randomisation

Following completion of all baseline questionnaires, infant participants will be randomised to the TEDI-Prem intervention or usual care group in a 1:1 ratio when the infant is ≥ 32 weeks' gestation and medically stable. Randomisation will be computer generated using block randomisation with variable block sizes and stratified by site of recruitment and multiple birth. Infants from multiple births will be randomised to the same group due to the nature of the intervention. Randomisation will be conducted using a web-based randomisation program to ensure allocation concealment. Following randomisation, parents will be notified of group allocation by a research team member. All participants will be gifted four age-appropriate toys at the baseline assessment as a thank you for their participation in the trial, and will receive a support services information letter with contact and referral information of different support options in the community.

Trial intervention

In addition to usual care, participants randomised to the intervention arm will receive the TEDI-Prem intervention program which will start whilst the infant is in the hospital. See Table 1 for an overview of how TEDI-Prem differs to usual care. The intervention program is a collaboration between a physiotherapist/occupational therapist (TEDI-Prem therapist) and the parent. It consists of thirteen 45-60-minute sessions delivered across three phases, from infant randomisation up until 12 months' CA. Due to the nature of the intervention, the participants and TEDI-Prem therapists will not be blinded to the trial intervention.

As per the SPEEDI study,[34] the TEDI-Prem intervention uses a perception action model of development whereby an infant's motor activity supports their attempts to explore and engage with their environment, allowing the infant to receive and interpret important

information and solve problems by linking the mind and body in a cycle that supports development across multiple domains.[46]

The TEDI-Prem intervention content and strategies were developed to address the deficits commonly seen in infants born preterm and their parents, and include using self-calming strategies and environmental support to enhance parent-infant interaction, with large doses of practice to support postural control and learning, visual motor, and object interactions in the first few months of the intervention, along with psychosocial education to support parent mental health and well-being. The TEDI-Prem therapist uses the key strategies outlined in Box 2 to address the principles of the program and increase the infant's opportunities for movement.

Box 2: TEDI-Prem Key Strategies

1) Providing graded postural support;
2) Observing spontaneous movement in response to support;
3) Varying postural support to encourage different opportunities and sensory-motor exploration;
4) Varying positions with minimal support to encourage variable, infant-directed movement; and
5) Providing opportunities to visualise, track, and manipulate objects.

As parents deliver the intervention rather than a therapist, higher intensity of intervention can be provided to drive neuroplasticity. Throughout the TEDI-Prem intervention program, parents learn the necessary skills to scaffold their infant's learning. In phase one of the program, there is a strong focus on guiding parents to understand behavioural cues and how

to identify ideal times for play and interaction with their infant. Enhanced parental capacity for engagement and self-efficacy allows parents to transition into providing activities that support their infant's developmental function (phase two and three) and provide opportunities for early problem solving, and is also likely to have a positive impact on parental well-being.[22] In phases two and three of the program, parents are encouraged to provide environmental enrichment through positioning, presenting toys, and social engagement, while supporting the infant's self-directed movements and interactions without imposing movement.

The use of video-based telehealth sessions will allow therapists to assess the infant and coach the family on intervention strategies individualised to their infant and home environment. The novel intervention is grounded in neurorehabilitation theory and combines a model of care where there is continuity of care from the hospital into the community environment by utilising telehealth and web-based education modules which can be adapted according to the needs of the individual infant and family.

There are several resources used to support the intervention sessions including a series of parent education handouts with accompanying worksheets and parent education videos, and an 'Activities for Home Play' booklet and accompanying parent education videos. The parent education handouts cover a variety of topics including psychosocial education to support parent mental health and well-being, education on infant development, including language and communication, and education on parent-infant relationships and sensitive parenting behaviours (see supplemental material 3 for list of parent education handouts). The accompanying parent education videos support and reinforce the content provided in the parent education handouts and feature parents reflecting on and sharing their experiences of

having a baby born prematurely. The 'Activities for Home Play' booklet includes illustrations and written instructions on the developmental play goals and intervention activities the parent and TEDI-Prem therapist will work on throughout phase two and three of the program. The accompanying parent education videos demonstrate examples of the TEDI-Prem principles and intervention activities described in the booklet. Parents will be encouraged to use the toys gifted to them at the commencement of the trial during the intervention activities. Compliance and dosage will be assessed by parent report during each TEDI-Prem session.

The parent education handouts and accompanying educational videos made available to parents at each phase will be individualised to ensure it is relevant to the infant's family structure and supports the needs of the parent as they change and/or evolve throughout the program. The TEDI-Prem therapist will make relevant resources available to parents after each intervention session via email and access to a secure, password protected video sharing platform. New content will be provided during each phase of the program and content from previous phases will be reviewed as required. The 'Activities for Home Play' booklet will be introduced and provided to parents at the end of phase one in preparation for use in phase two, when the infant is discharged home. During the intervention sessions, the TEDI-Prem therapist will view the 'Activities for Home Play' booklet's accompanying educational videos with the parent – selecting videos based on the developmental needs and progression of the individual infant.

Table 1: TIDier Checklist: How TEDI-Prem differs to usual care

Item	TEDI-Prem	Usual care
Brief name	Telehealth for Early Developmental Intervention in babies born very preterm.	NA

Why	Coaching of parents to deliver intensive early motor, cognitive and language training to enhance neuroplasticity and parent education and support to improve parent mental health and well-being	Developmental monitoring with referral to intervention when impairments are identified
Materials	Enrich environments with novel toys to entice infants to actively and intensively practice and persist with problem solving demands. Parents adapt environment to support infant based upon behaviour. Parent education handouts and accompanying videos support parent mental health and well-being and learning and implementation of program principles	Materials not used (toys will be given to all participants, however, instructions not given)
Who	Physiotherapist/occupational therapist (>5 years experience in paediatrics) acts as a coach for the parent to work with their infant. Therapists complete 12 hours of online training modules and participate in a 3-day training workshop prior to trial commencement.	Referral to a physiotherapist, speech pathologist or occupational therapist, as needed
How/ Where	Hospital (face to face) and home based in infant's natural environment at time of intervention (via telehealth)	Face to face hospital or outpatient based as needed
When /How much	13 sessions over 3 phases: **Phase 1:** From group randomisation to infant hospital discharge home. 4 x 30-45-minute sessions face to face in hospital. If infants are transferred to another hospital or discharged home during phase 1, sessions are delivered via telehealth. Phase 1 focuses on building reciprocal engagement and parents reviewing and implementing key principles. **Phase 2:** From discharge home to 6 months' corrected age. 6 x 45–60-minute sessions via telehealth. Phase 2 focuses on the parent providing daily opportunities for advancing motor, cognitive, and social skills in play (20 minutes per day, 5 times per week). **Phase 3:** From 6 – 12 months' corrected age. 3 x 45–60-minute sessions. Phase 3 focuses on scaffolding the needs of each family to enhance independence. This may include integration into local services as needed.	- Depends on the parents' natural interaction patterns - May be limited one-on-one play, use of toys, or support of variable movements - Community–based early intervention if referred as part of usual care
Tailoring	Intervention commences early in life and is tailored to infant's environment, developmental stage and parents' skills levels.	Intervention only delivered if impairment identified and often has

		long wait list.
How well	Therapists trained to deliver TEDI-Prem intervention. Sessions video recorded for fidelity checks	Data will be captured on interventions (age commenced, intensity and duration).

Key principles and fidelity

The key principles of the intervention are outlined in Table 2 and are the foundation from which the intervention content and strategies are delivered. These key principles will form the evaluation of the fidelity of the intervention and will be in part assessed on therapist adherence and measured by the frequency with which the intervention therapist demonstrates, talks about, or brainstorms with a parent about the TEDI-Prem principles and strategies. One of the four sessions in phase one and all sessions in phase two and three will be video recorded. TEDI-Prem therapists will complete a self-assessment of adherence using a fidelity checklist following each session. Author's SD and SB will randomly select three video recorded sessions (one from each phase) per participant to further assess therapist adherence and provide feedback and additional training and/or support as required.

Table 2: TEDI-Prem Key Principles

Principle 1: Education and support for parent mental health and well-being This principle aims to provide a protective influence for the development of very preterm infants. The TEDI-Prem therapist checks in with the parent regarding their emotional health during each of the TEDI-Prem sessions. A series of supporting educational handouts and videos are provided throughout the 12 month intervention program which focus on psycho-education and strengthening the parent-child relationship. Parent mental health is screened throughout the intervention program enabling more targeted intervention and assisting parents in accessing support services where indicated.
Principle 2: Cue based directed care and interactions Parents learn to read their infant's behavioural cues during caregiving, play, and social interaction. The parent learns to match their behaviour and interactions to meet the infant's

demonstrated readiness. This key principle encourages sensitive and responsive parenting behaviours and supports parents in identifying the infant's alert and active times for intervention, develop a routine for interaction, as well as following the infants lead on when to provide rest breaks. Parents are encouraged to use vocalisation along with social and motor interactions in response to the infant's cues.

Principle 3: Encourage self-directed movement

This principle allows the infant ample time to elicit self-directed movement, to make errors, and to correct these errors as independently as possible. Rather than aiming for a pre-determined 'correct pattern' of movement, the infant's own strategies for movement are supported to emerge.

Principle 4: Do not impose movement

When the infant requires assistance to transition between postures, to maintain postures, or to interact with objects, there is a focus on providing the least amount of assistance required and not imposing movement.

Principle 5: Provide a "just right" challenge

The 'just right challenge' is about matching the skill set required for an activity with the performance capacity of the infant engaged in the activity. Through scaffolding, that is, offering just the right help at just the right time in just the right way, the TEDI-Prem therapist teaches parents to determine and utilise the 'just right challenge' during all interactions. For infants to make continual gains in a safe, timely, and positive manner, it's important to know how much assistance they need to perform an activity and to understand ways to adapt the activity to place it at the cusp of an infant's developmental ability. This can involve altering the level of assistance provided, changing the infant's posture, modifying the environment, and adapting aspects of the task such as object placement. The parent learns how to provide graded postural support and observes their infant's spontaneous movement, social engagement, and vocalisations in response to the support to determine if the 'just right challenge' has been met.

Principle 6: Encourage socialisation and communication

Across postures and with varying level of postural support, parents encourage infants to focus on their face and engage in early social interaction including vocalisations and visual engagement. Infants learn to read their parents behavioural cues and develop an understanding of facial expressions and vocalisations as a form of communication. As infants fix on their parents faces, smile and/or vocalise, and parents respond in a timely and sensitive way, infants learn reciprocity and the value in making sound. This provides the building blocks of social engagement and early language and communication.

Principle 7: Encourage object interaction

Across a variety of positions and with graded postural support, infants are provided opportunities to see, feel, mouth, and hold objects that vary in weight, size, texture, hardness, and colour. Consideration of object placement motivates infants to move through different positions to interact with objects. This principle enables varied cognitive and movement opportunities as well as sensory inputs. Infants learn about cause and effect

and means end as they move their body and interact with objects and the world around them.
Principle 8: Provide opportunities for variable movement Varied exploratory movements are essential building blocks for learning any new postural skill. Trial and error with movement is essential in the learning process.
Principle 9: Guided participation This principle builds the foundation for intense early intervention and aims to support a less skilled person in developing a specific new practice. The basic processes of guided participation that are utilised in the intervention are: 1. Providing bridges from the known to the new; 2. Choosing and structuring learning activities; 3. Structuring responsibility in joint problem solving; and 4. Transferring responsibility for managing activities Using guided participation, the TEDI-Prem therapist assists parents in learning to read their infant's readiness cues for caregiving, interaction and play, and match their own interaction to the infant's readiness.

*Table adapted from SPEEDI Key Principles, as published previously.[34]

Outcome measures

At 12 and 24 months' CA, all infants will be assessed by an examiner who is blinded to group allocation. The outcome measures in this trial and their timing of collection are described in Table 3. An overview is provided in Figure 2 below.

Table 3: Primary and secondary outcome measures

Primary outcome
Infant motor composite score on the Bayley Scales of Infant and Toddler Development-4th edition (Bayley-4) at 12 months' CA.[47]
Secondary outcomes
Infant • Child cognition assessed using the Bayley-4 cognitive composite scores at 12 and 24 months' CA.[47] • Child language assessed using the Bayley-4 language composite score and receptive and expressive scaled scores at 12 and 24 months' CA.[47]

• Child motor development assessed using the Bayley-4 motor composite score at 24 months' CA.[47] • Child behaviour assessed using the Infant Toddler Social Emotional Assessment (ITSEA) at 12 and 24 months' CA.[48]
Parent • Parental depression and anxiety assessed using the Depression Anxiety Stress Scales (DASS-21) at 12 and 24 months' CA.[44] • Parenting self-efficacy assessed using the Karitane Parenting Confidence Scale (KPSE) at 12 and 24 months' CA.[49] • Parent-infant interaction assessed using the Emotional Availability Scale (EAS) at 12 and 24 months' CA.[50]
Cost-effectiveness of TEDI-Prem compared with usual care (to be published separately to the main trial results) • Costs assessed using cost of the intervention, children's health care utilisation and family productivity loss. • Quality adjusted life years (QALYs) assessed based on child and parent quality of life. • Child quality of life measured via parent report using the EuroQol Toddler and Infant Populations (EQ-TIPS) at 12 and 24 months' CA.[51] • Parent quality of life measured using the Assessment of Quality of Life (SF-6D) at 12 and 24 months' CA.[45] • Cost-effectiveness of the intervention compared with usual care assessed as cost per additional QALY gained.

Statistical analysis

The statistical analysis will be conducted by a statistician who will remain blinded until the end of the trial. Data will be analysed using the intention to treat principle and will include all participants according to their treatment allocation irrespective of whether they received any of the intervention (i.e. treating all intercurrent events using a treatment policy strategy). Sensitivity analysis will be conducted using a hypothetical strategy for adherence, where adherence will be defined as participating in at least 80% of TEDI-Prem intervention sessions for participants in the intervention group.

Mean differences between groups in the primary outcome will be examined using linear regression, fitted via generalised estimating equations to account for multiple births and adjusted for site. Differences between groups in secondary outcomes will be examined using linear regression for continuous outcomes and logistic regression for binary outcomes. All models will be fitted via generalised estimating equations to account for multiple births and adjusted for site.

Analyses will be repeated in subgroups according to social risk (high vs low), gestational age (extremely preterm vs very preterm) and later neurological diagnosis (yes vs none) at 12 months' CA via the inclusion of an interaction term in the regression models.

PATIENT AND PUBLIC INVOLVEMENT

We have included stakeholder involvement at several stages in the development of the trial. As part of our Centre for Research Excellence (CRE) in Newborn Medicine, we completed a Delphi study identifying the research priorities of parents with experience of newborn medicine.[52] Parents identified many questions as high-priority with primary areas related to supporting parental mental health, relationships between parents and neonatal clinical staff (including involvement in care and communication), bonding and the parent-child relationship, and addressing long-term impacts on child health and neurodevelopment. These consumer-identified research priorities were integrated into the design of the TEDI-Prem intervention program and its effect on outcomes in these areas will be evaluated.

In addition, members from the CRE in Newborn Medicine's Consumer Advisory Group (CAG) were actively involved in the development of the TEDI-Prem intervention program and the trial's research methods and design. Members of the CAG participated in a focus group where the consumer perspective on the appropriateness, acceptability and fit of our

study name, the interventions key principles (underlying mechanisms of change) and forms (activities embedded into the intervention that will be used to carry out key principles, including their timing and frequency) was provided. This feedback was incorporated into the study design and procedures outlined. Further, members of the CAG reviewed and approved various research materials to ensure they are easily accessible to consumers.

ETHICS AND DISSEMINATION

A Data Safety Monitoring Board (DSMB) will be established to review and evaluate study data on adverse safety events, study conduct and progress, and trial efficacy. The DSMB will monitor trial efficacy through a single interim analysis of the primary outcome once 50% of participants have completed their 12 month CA follow up. The Haybittle – Peto boundary stopping rule will be applied to the results of the interim analysis to decide if the trial should be stopped prematurely. If the interim analysis shows a p-value of equal to or less than 0.001 that a difference as extreme or more extreme than that found between treatments if the null hypothesis were true, then the trial will be stopped early. If additional psychological support for parental mental health is indicated, they will be provided with referral/information about appropriate support services, with their permission.

Trial findings will be disseminated through presentations at national and international conferences, publication in peer reviewed journals, as well as digital and print media. Results will be shared with all trial participants as well as other interested consumers (parents, health professionals, and service providers) through our partnerships with support groups of parents of children born preterm (on their social media and web-based platforms) and via the CRE in Newborn Medicine's professional links and networks. Consent from trial participants to be contacted for future follow-up studies will be sought.

DISCUSSION

This paper outlines the protocol for the trial of an early intervention program designed for VPT infants over the first year of life. The TEDI-Prem program commences in the hospital prior to discharge and provides an intervention delivered earlier than traditional health service models of early intervention for preterm children. We propose that providing targeted intervention to support the development of the parent-child interaction, an enriched environment, an infants' self-directed movement and their parent's well-being at an earlier age whilst in the hospital and across the first year will lead to improvements in neurodevelopment, parental mental health, and a cost-effective model of delivering early intervention services for VPT infants compared with usual care.

Figure 1: Participant flow chart

Figure 2: Outcome measures and timing of administration throughout the trial

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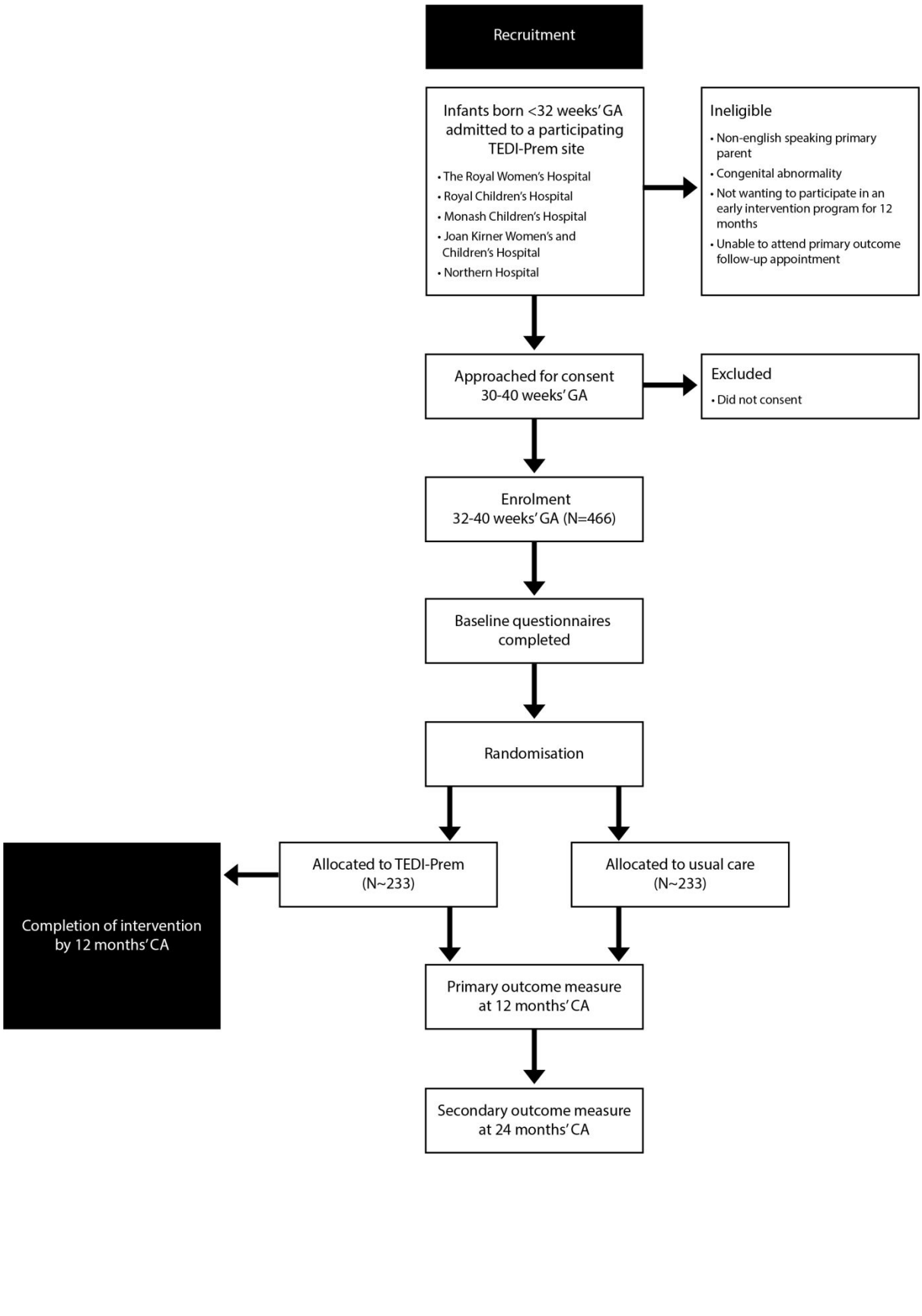

	Baseline	3mo CA	4mo CA	6mo CA	8mo CA	10mo CA	12mo CA	18mo CA	24mo CA
Perinatal data	☑						☑		
Bayley - 4							☑		☑
EAS							☑		☑
QUESTIONNAIRES									
Socio-demographics	☑						☑		☑
KPSE	☑						☑		☑
DASS-21	☑						☑		☑
ITSEA							☑		☑
EQ-TIPS							☑		☑
SF-6D	☑						☑		☑
Therapy services	☑	☑		☑			☑	☑	☑

Bayley-4: Bayley Scales of Infant and Toddler Development 4th Edition; EAS: Emotional Availability Scale; KPSE: Karitane Parenting Self Efficacy Scale; DASS-21: Depression Anxiety Stress Scales; ITSEA: Infant Toddler Social Emotional Assessment; EQ-TIPS: EuroQol Toddler and Infant Populations (EQ-TIPS) measure; SF-6D: Short Form Quality of Life.

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Participant Information Sheet/Consent Form - Parent/Guardian
[Insert site name]

Title:	The effect of telehealth for early intervention on neurodevelopmental outcomes of infants born very preterm and their parent's well-being: a randomised controlled trial (TEDI-Prem)
Short title:	TEDI-Prem: Telehealth for Early Developmental Intervention in babies born very preterm
Study sponsor:	The University of Melbourne
Coordinating Principal Investigator:	Professor Alicia Spittle
Principal Investigator:	[Insert site PI name]
Location:	[Insert location]

This is an invitation for you and your child (or children if you have given birth to twins or higher order multiples) to take part in a research study called TEDI-Prem because they were born less than 32 weeks' gestation.

This Participant Information and Consent Form tells you about the research study. It explains the tests and treatments involved. Knowing what is involved will help you decide if you want your child to take part in the research.

Please read this information carefully. Ask questions about anything that you don't understand or want to know more about. Before deciding whether or not your child can take part, you might want to talk about it with a relative, friend or your child's doctor or care team.

What is TEDI-Prem?

TEDI-Prem is a new early intervention program for babies born prematurely and their parents. TEDI-Prem stands for telehealth for early developmental intervention in babies born very preterm.

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What is the purpose ofthe TEDI-Prem study?

Children born less than 32 weeks' gestational age are at risk of developmental problems, and their parents are also at risk for anxiety and depression. We have developed the TEDI-Prem program to help babies with their development and support parent's mental health, but we need to know if the intervention works.

The aim of the study is to see if the intervention improves child development, particularly motor skills, as well as thinking and talking, and parent mental health. If we find that the intervention improves outcomes for children after premature birth, we hope to make it widely available across Australia.

Who is organising and funding the TEDI-Prem study?

This research is being conducted by The University of Melbourne and has been funded by the Medical Research Future Fund.

What does taking part in the TEDI-Prem study involve?

You and your child will be participating in a randomised controlled research study.
This means we will put people into two groups:
one group will receive the TEDI-Prem intervention in addition to usual care, and the other group will receive usual care only.

The results are compared to see if one of these is better. To try to make sure the groups are the same, each participant is put into a group by chance (random). Your child has an equal chance of being in either group. Neither you or the researchers can choose which group your child is put in. This research study has been designed to make sure the researchers interpret the results in a fair and appropriate way.

If you indicate that you want you and your child to participate, you will be asked to sign the consent form and we will collect some information from you and the medical record (such as your contact details, details about your child – including birth weight, medical complications and treatments).

Before you find out which group you're in you will be asked to complete some questionnaires. We will ask you about:

How you have been feeling and your mood, and about your family background and education

Information about your baby

These questionnaires will take about 5-10 minutes to complete

After you complete this information, your family will be randomly allocated to either the intervention or comparison group

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What does my child have to do?

Your child will need to do different things depending on whether they're randomly allocated to the intervention or comparison group.

All children will receive a follow-up assessment at 12 and 24 months of age (based on their original due date).

What if I'm randomly allocated to the comparison group?

Your child will continue to receive usual clinical care. This may include physiotherapy or occupational therapy services depending on your child's needs and the gestation they were born at. You will also be asked to complete some online questionnaires.

What if I'm randomly allocated to the intervention group?

You will participate in the TEDI-Prem program. The program starts in the neonatal nursery and continues until your child is 12 months' corrected age (12 months after their due date). During each session a physiotherapist or occupational therapist will provide movement and interaction activities designed to help your child's development. Each session will take about 45-60 minutes and we will video record the sessions. Only researchers involved with this study, and no others, are permitted to view these videos.

We will provide additional information about your child's development, parental wellbeing and relationships, and the intervention activities on a TEDI-Prem website. We will use website analytics on the use of the TEDI-Prem website by participants in the intervention group, including information such as the number of visits and time spent on the website. You will also be asked to complete some online questionnaires.

See the table on the next page for information about what's involved in the TEDI-Prem program

What's involved in the follow-up assessments?

We will invite you to bring your child into hospital for an assessment when they are 12 months and then at 24 months of age (based on their original due date). These two visits will include a developmental assessment to look at your child's thinking, language and motor development. This assessment will involve activities with your child such as looking at pictures, responding to questions, and playing with puzzles and balls, as well as a videoed play session with you. The visits will be at [insert hospital site name].

Other relevant information

We plan to recruit 466 children and their parents to participate in this research study from The Royal Children's Hospital, The Royal Women's Hospital, Monash Children's Hospital, Joan Kirner Women's and Children's Hospital and the Northern Hospital. The study will run for 5 years.

There are no additional costs associated with participation in this research study, nor will you be paid. You will be reimbursed for any parking expenses for attending the 12 and 24 months assessments. You will receive three toys for your child at enrolment along with a toy/book at 12 and 24 months.

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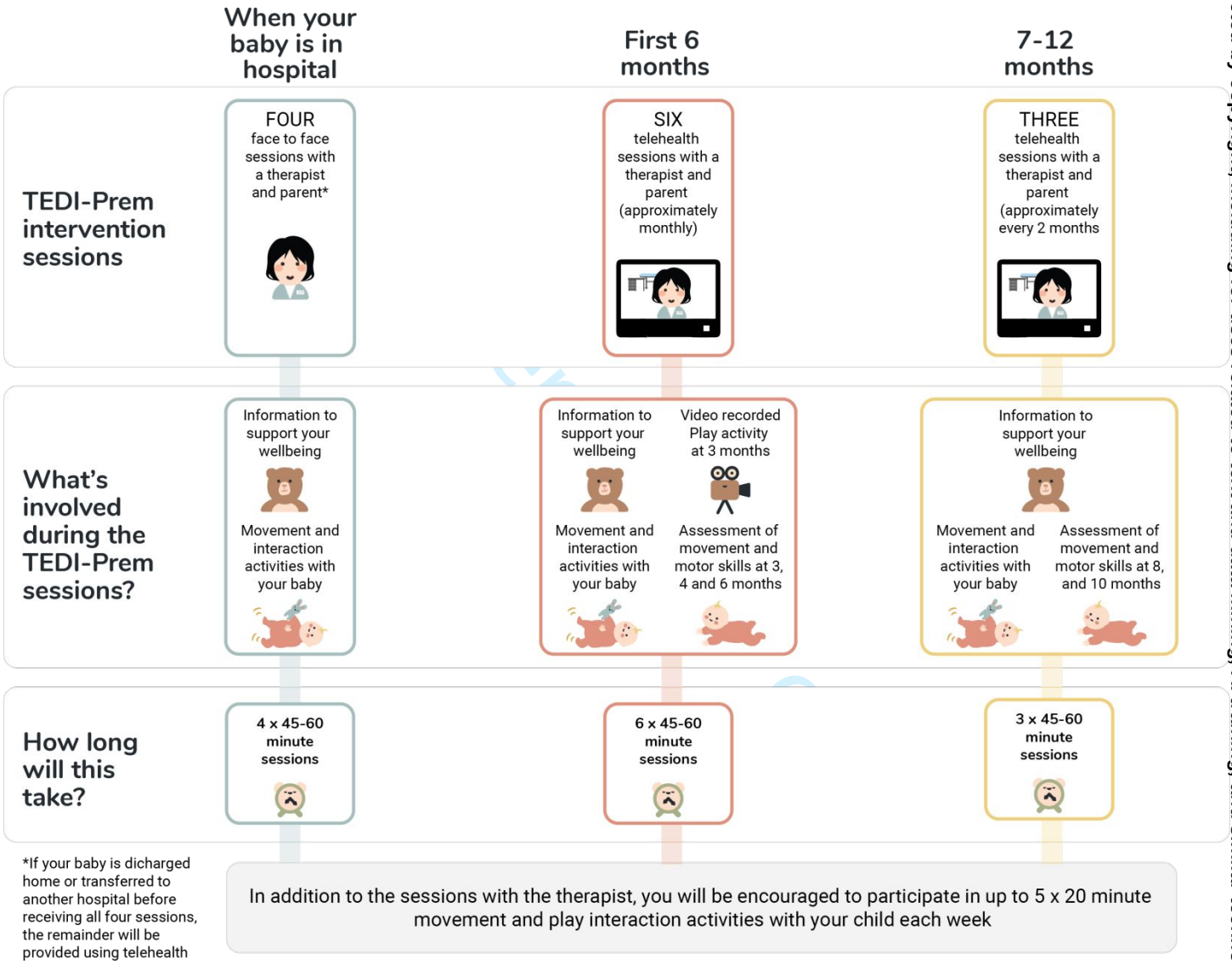
TEDI-Prem Intervention Program



What questionnaires will I be asked to complete?

Both groups will be asked to complete questionnaires across their child's first two years of life. See the table on the next page for more information about the questionnaires and how long they take.

Do we have to take part?

Participation in this research is voluntary. If you do not wish your child to take part, they do not have to. If you decide that they can take part and later change your mind, you are free to withdraw your child from the project at any stage.

Your decision that your child can or cannot take part, or that they can take part and then be withdrawn, will not affect their routine treatment, relationship with those treating them, or their relationship with [Institution].

What are the alternatives to participation?

You and your child do not have to take part in this research study to receive treatment and usual care at this hospital. Other options are available; these include accessing early intervention programs privately or through Medicare.

Are there benefits of taking part?

We cannot guarantee or promise that your child will receive any benefits from this research; however, possible benefits for the TEDI-Prem intervention group may include positive effects on your child's development and your wellbeing. For all families in the study, the assessments at 12 and 24 months will provide information about your child's development and if needed, referral for further intervention, and some parents may find this useful.

Are there possible risks or disadvantages of taking part?

We do not anticipate any risks or side-effects from participation in this study.

However, being involved in the TEDI-Prem intervention requires additional time for parents. If the assessments identify that your child may need further developmental support, this may be concerning for parents. Sometimes talking about or answering questions about your own wellbeing and family situation can be upsetting.

If you have become upset or distressed as a result of participation in the research, we can arrange appropriate support. This support may be provided by a qualified member of the research team, or a professional who is not in the team. If you have any concerns or questions related to the study please contact Professor Alicia Spittle Chief Investigator on (03) 9035 5340.

Can my child have other treatments during the study?

Yes. Participation in this research study will not influence whether you and your child can access other treatments or interventions.

What if I withdraw my child from the study?

You can withdraw your child from the study at any time. You just need to tell us so. You do not need to tell us why you are taking your child out of the study. If your child leaves the study, we will use the information we have collected about you and your child. If you do not want us to use this information, please tell us. If you do not want us to keep using you and your child's information, we will securely destroy it.

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TEDI-Prem Questionnaires completed online

3 months

Use of therapy services

This will take about 5 minutes

6 months

Use of therapy services

This will take about 5 minutes

12 months

Your wellbeing, parenting role & information about your family

Your health and your child's health

Use of therapy services

This will take about 20 minutes

18 months

Use of therapy services

This will take about 10 minutes

24 months

Your wellbeing, parenting role & information about your family

Your health and your child's health

Use of therapy services

This will take about 20 minutes

Every couple of months we will ask you how much time you and your child spent playing and interacting for the week

This will take about 5 minutes

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What happens when the study ends?

At the end of the study we will send you a letter that tells you what we found out in this research. This letter will be about the whole group of children who took part in the study and not your individual child.

How do I let you know that we want to take part?

If you decide you want your child to take part in the research study, you will be asked to sign the consent section. By signing it you are telling us that you:

- ☑ Understand what you have read
- ☑ Consent to you and your child taking part in the research study
- ☑ Consent for your child to have the tests and treatments that are described
- ☑ Consent to the use of the child's personal and health information as described

You will be given a copy of this Participant Information and Consent Form to keep.

Optional Consent

If your child takes part in this study we will ask you to think about consenting to a couple of extra things. These things are optional. The first one is about linking with your child's Medicare/PBS information. The second one is letting us use your child's information for future studies about children who were born preterm. You can say no to both of these things or to just one of them. If you say no, your child can still take part in the study.

The optional parts of the study are explained in more detail below.

A First optional consent: Medicare/PBS data linkage

We would like your permission to let us link to information collected by Services Australia. You will be asked to fill out a separate consent form authorising the study access to your child's complete Medicare Benefits Schedule and/or Pharmaceutical Benefits Scheme (MBS/PBS) data, as outlined in the attached consent form.

The information we collect from Medicare will help us to examine how TEDI-Prem affects healthcare use and costs. So we are able to do this, we will ask you to complete a Services Australia 'Authority to release personal Medicare and PBS claims information to a third party form'. The consent form is sent securely to Services Australia who holds this information confidentially.

B Second optional consent: Future research studies

We will collect a lot of information during this research study. However, there are still lots of things about the development of children who are born preterm that we do not understand. We could answer some of these questions in the future by using the information from this study in a different way. We would like you to consider letting us use your child's information in future research studies about children who are born preterm. We will only use the information in research studies that have been approved by a Human Research Ethics Committee.

If you agree to this we will use your child's information without contacting you.

What will happen to information about my child and I?

We will collect and use personal and health information about you and your child for research purposes. By signing the consent form you consent to the research staff collecting and using personal information about you and your child for the research project. Any information obtained in connection with this research project that can identify you or your child will remain confidential. It will be disclosed only with your permission, or as required by law.

We will store your and your child's information securely in the [department name] at [institution] and The University of Melbourne.

Information about you and your child may be obtained from their health records held at this and other health services, for the purpose of this research. By signing the consent form, you agree to the study team accessing health records if they are relevant to you and your child's participation in this research project.

Only the researchers involved with this study, [insert hospital site name] ethics committee, The Royal Children's Hospital Ethics committee and authorised University of Melbourne/Murdoch Children's Research Institute staff can have access to this information. We can disclose the information only with your permission except as required by law.

The stored information will be **re-identifiable.** This means that we will remove identifying information such as your child's name and give the information a special code number. Only the research team can match your child's name to their code number, if it is necessary to do so.

To advance science, medicine and public health, we may also need to share your child's **de-identified** data with other ethically approved research studies, biobanks, or medical journals. If we need to do this, we will remove identifying details such as your child's name, date of birth and address and give the data a special code number. Only the research team on this study will be able to match your child's name to their code number.

The information supplied by Services Australia will only be used for the purpose of this study. It is anticipated that the results of this research study will be published and or presented in a variety of forums. In any publication and/or presentation, information will be provided in such a way that you and your child cannot be identified, except with your permission.

Information about your child's participation in this research study may be recorded in their health records. You have the right to access and correct the information we collect and store about your child. This is in line with relevant Australian and/or Victorian privacy and other relevant laws. Please contact us if you would like to access this information.

As the child participants in this study are under 18 years old, we will keep their information at least until the youngest participant turns 25 years old. All information will be stored securely in locked filing cabinets at the [institute] and once all analyses have been performed, the data will be securely archived. Electronic information, including videos, will also be stored on a password- protected server and REDCap computer database at the University of Melbourne for 7 years after the youngest child in the study turns 18, after which time it may

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be destroyed or kept indefinitely. Only the study researchers will have access to the data.

You must be aware that the information collected about your child may at some point not be able to be identified once the identifying information has been removed. Access to information about you after this point will not be possible.

The Royal Children's Hospital and Murdoch Children's Research Institute are research partners. This means that the two organisations will always share research information with each other.

Who has reviewed the study?

All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC).

The ethical aspects of this research study have been approved by the HREC of The Royal Children's Hospital and [insert hospital site name].

This study will be carried out according to the National Statement on Ethical Conduct in Human Research (2007). This statement has been developed to protect the interests of people who agree to participate in human research studies.

Who do I contact if I have any questions or concerns?

If you would like more information about the study, please contact:

- [insert PI name], on (03) [insert phone number], [insert email]
- Professor Alicia Spittle,

.

Coordinating Principal Investigator on (03) 9345 5390.

If you have any questions or concerns about your rights as a participant in this study, or if you have any complaints you may contact: [insert institute details]

You can contact the Director of Research Ethics & Governance at The Royal Children's Hospital Melbourne if you:

- have any concerns or complaints about the study
- are worried about your rights as a research participant
- would like to speak to someone independent of the study.

The Director can be contacted by telephone on (03) 9345 5044.

If you have a privacy complaint in relation to the use of your MBS and/or PBS data you should contact the Office of the Australian Information Commissioner. You will be able to lodge a complaint with them.

Website: www.oaic.gov.au

Telephone: 1300 363 992

Email: enquiries@oaic.gov.au

Mail: GPO Box 5218, Sydney NSW 2001

Recruitment of Children Under 14

Where children under the age of 14 are being recruited, and are on two Medicare cards, both card numbers and the signatures of both primary card holders will need to be on the child's consent form. Data relating to a child's Medicare card will only be supplied where the primary card holder of that card has consented

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Consent Form - Parent/Guardian

Title:	The effect of telehealth for early intervention on neurodevelopmental outcomes of infants born very preterm and their parent's well-being: a randomised controlled trial (TEDI-Prem)
Short title:	TEDI-Prem: Telehealth for Early Developmental Intervention in babies born very preterm
Study sponsor:	The University of Melbourne
Coordinating Principal Investigator:	Professor Alicia Spittle
Principal Investigator:	[Insert site PI name]
Location:	[Insert location]

Declaration by Parent/Guardian

- I have read the Participant Information Sheet or someone has read it to me in a language that I understand.
- I understand the purposes, procedures and risks of the research described in the study.
- I give permission for my child's doctors, other health professionals, hospitals or laboratories outside this hospital to release information to The University of Melbourne and [insert hospital site name] concerning my child's medical condition and treatment for the purposes of this study. I understand that such information will remain confidential except as required by law.
- I have had an opportunity to ask questions and I am satisfied with the answers I have received.
- I freely agree to my child participating in this research study as described and understand that I am free to withdraw them at any time during the research project without affecting their future health care.
- I understand that I will be given a signed copy of this document to keep.

Optional consent

☐ I do	☐ I do not	consent to the storage and use of my child's and my information in future ethically-approved research studies related to preterm children
☐ I do	☐ I do not	consent to data linkage with my child's Medicare/PBS data

Name of Child _____

Name of Parent/Guardian _____

Signature of Parent/Guardian _____ Date _____

I have given a verbal explanation of the research study, its procedures and risks and I believe that the parent/ guardian has understood that explanation.

Name of Researcher _____

Signature _____ Date _____

Note: All parties signing the consent section must date their own signature

Online supplementary material 2: Therapy services questionnaire

TEDI-Prem would like to check in and see if your child received any of the following therapy services in the **last month**

1. Physiotherapy: yes/no,
   If yes, on average how often:
   ☐once per week
   ☐once a fortnight
   ☐once a month
   ☐less than once a month

2. Occupational therapy: yes/no,
   If yes, on average how often:
   ☐once per week
   ☐once a fortnight
   ☐once a month
   ☐less than once a month

3. Speech Pathology: yes/no,
   If yes, on average how often
   ☐once per week
   ☐once a fortnight
   ☐once a month
   ☐less than once a month

4. Other therapy: yes/no
   If yes, please describe: **comment box**
   On average how often:
   ☐once per week
   ☐once a fortnight
   ☐once a month
   ☐less than once a month

Online supplementary material 3: TEDI-Prem parent education handouts

You, your baby and the neonatal unit
Partners
Getting support as a parent
Coping tips for families
From sleep to play
Bonding with your baby
Your relationships
Supporting siblings
Signs of stress, anxiety and depression
Managing stress, anxiety and depression
Corrected age
Preparing to go home
Communication and language: term – 3 months
Play and the home environment
Looking after yourself as a parent
Toy ideas for early development
Play and interaction
Your relationship with your baby

Communication and language: 4-6 months
Child speech and language development
Communication and language: 7-9mths
Play and interaction and toys 6-12 months
Communication and language: 10-12mths
Discharge to home – my support plan
Five steps for assertive communication
My self care plan
My support plan

BMJ Open

A protocol for a multisite randomised controlled trial assessing the effect of the Telehealth for Early Developmental Intervention in babies born very preterm (TEDI-Prem) program on neurodevelopmental outcomes and parent well-being

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	Spittle, Alicia; University of Melbourne, Department of Physiotherapy; Murdoch Children's Research Institute, Clinical Sciences; The Royal Women's Hospital
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A protocol for a multisite randomised controlled trial assessing the effect of the Telehealth for Early Developmental Intervention in babies born very preterm (TEDI-Prem) program on neurodevelopmental outcomes and parent well-being

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The trial sponsor is responsible for the initiation, management and financing of the trial and carries the medico-legal responsibility associated with its conduct. The quality and integrity of the clinical trial data is also the responsibility of the trial sponsor.

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Trial Protocols

Abbreviations:
VPT: Very Preterm
TEDI-Prem: Telehealth for Early Developmental Intervention in babies born very preterm
CA: Corrected Age
NICU: Neonatal Intensive Care Unit
SCN: Special Care Nursery

Bayley-4: Bayley Scales of Infant and Toddler Development- 4th edition
KPSE: Karitane Parenting Confidence Scale
DASS-21: Depression Anxiety and Stress Scale 21
SF-6D: Short-Form Six-Dimension Quality of Life
EQ-TIPS: EuroQol Toddler and Infant Populations measure
ITSEA: Infant Toddler Social Emotional Assessment
EAS: Emotional Availability Scale
SMD: Standardised Mean Difference
CI: Confidence Interval
SPEEDI: Supporting Play Exploration and Early Development Intervention
RCT: Randomised Controlled Trial
SPIRIT: Standard Protocol Items: Recommendations for Interventional Trials
REDCap: Research Electronic Data Capture

Author's contributions
Stacey C Dusing, Peter J Anderson, Kim Dalziel, Anne E Holland, Rod W Hunt, Katherine J Lee, Angela Morgan, and Karli Treyvaud were involved in conception and design of the study. Abbey L Eeles and Alicia J Spittle were involved in the conception and design of the study, and initial manuscript preparation. All authors provided critical review of the protocol, approved the final version as submitted, and agree to be accountable for all aspects of the work. Alicia J Spittle are the guarantor.

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ABSTRACT

Introduction
Infants born very preterm (VPT, <32 weeks' gestation) are at increased risk for neurodevelopmental impairments including motor, cognitive and behavioural delay. Parents of infants born VPT also have poorer mental health outcomes compared with parents of infants born at term.

We have developed an intervention program called TEDI-Prem (Telehealth for Early Developmental Intervention in babies born very preterm) based on previous research. TEDI-Prem aims to improve neurodevelopmental outcomes and parental well-being in children born VPT. Here we present the protocol outlining a multicentre, pragmatic, parallel group, randomised controlled trial (RCT) to determine the efficacy of TEDI-Prem plus usual care, compared with usual care alone.

Methods and analysis
We will recruit 466 VPT infants from the neonatal units of five hospitals in Victoria, Australia. Participants will be randomised, stratified by site of recruitment and multiple birth, to TEDI-Prem plus usual care or usual care alone. The TEDI-Prem intervention program involves 13 sessions across three phases. Phase one commences in the neonatal unit with four face to face sessions with parent/s and a physiotherapist/occupational therapist. Once discharged from hospital, sessions across phase two and three (six and three sessions, respectively) continue via telehealth until infants are 12 months' corrected age (CA).

The primary outcome is the Bayley Scales of Infant and Toddler Development- 4th edition (Bayley-4) motor composite score at 12 months' CA. Secondary outcomes address other neurodevelopmental domains (Bayley-4 cognitive and language composite score; Infant Toddler Social Emotional Assessment), parental mental health (Depression Anxiety and Stress Scale 21), parent-child interaction (Emotional Availability Scale), and program cost effectiveness which encompasses parent quality of life (Short-Form Six-Dimension Quality of Life) and child quality of life (EuroQol Toddler and Infant Populations measure) at 12 and 24 months' CA.

Mean differences between groups will be examined using linear regression for continuous outcomes and logistic regression for binary outcomes. All models will be fitted via generalised estimating equations to account for multiple births and adjusted for hospital site.

Ethics and dissemination
This trial has Royal Children's Hospital Human Research and Ethics committee approval (HREC/67604/RCHM-2020) with specific site approval for all participating sites. Findings will be disseminated through peer-reviewed publications, conference presentations, digital and print media and to participants.

Registration details
This trial is registered with the Australian New Zealand Clinical Trials Registry (ACTRN12621000364875).

Strengths and limitations of this study

- We have adapted and combined two pilot-tested intervention programs targeted at very preterm infants and their families.

- The intervention sessions are delivered in hospital in Phase 1 and post-discharge in Phases 2 and 3 with face to face and telehealth modes utilised respectively. This increases access to intervention for families, including those who face barriers to service use such as living in regional or rural communities.
- This study will recruit a large sample size from 5 out of 6 Victorian neonatal intensive care units. The intervention is conducted in a high income setting and therefore may not be generalisable to low-middle income settings.

INTRODUCTION

Worldwide, over 2.5 million babies are born very preterm (VPT, <32 weeks' gestation) each year.[1] In Australia alone, there are approximately 5000 VPT births each year, and whilst most of these infants survive,[2] over 50% of VPT infants will have a neurodevelopmental impairment.[3, 4] The neurodevelopmental deficits resulting from early birth may compromise physical function, academic achievement and quality of life.[5-7] While survival rates are improving in children born VPT, the rates of neurodevelopmental impairments are not improving over time[8] and are associated with substantial economic costs.[9] Further, following the VPT birth, parents have higher rates of mental health problems than their peers with term-born infants, which is itself associated with poorer child outcomes.[10, 11]

Very preterm birth occurs during a critical period of central nervous system development, with the first 1000 days of life the most dynamic and rapid period of brain development, setting the foundation for all future neural development.[12, 13] This period of brain development is particularly vulnerable to adverse environmental events and exposures, including preterm birth. The VPT infant is often critically ill and requiring invasive interventions in the neonatal intensive care unit (NICU). Together with their early illness, this care environment, whilst necessary to support life, can disrupt brain maturation. Further, the NICU environment can alter the parent-infant relationship, infant sensorimotor experiences, and offers limited opportunities for social, motor, cognitive and language interactions.[14-16] Parents are more likely to experience higher anxiety and depression after preterm birth than peers who have babies born at term,[10, 17, 18] which contributes to an altered parent-child relationship and increases the risk for poorer developmental outcomes for VPT children.[5, 19] Very preterm birth alone carries heavy healthcare costs in the newborn period, but longer-term costs are much higher when children have developmental or health problems.[20] Averting

these long-term sequelae for VPT infants through early intervention has potential economic benefits in health and education.[9] While medical advances continue to improve neonatal care,[21] clinical rehabilitation for these high-risk infants has not kept pace with advances in basic science and developmental theory to improve outcomes for infants and their parents.[22-24]

In a Cochrane review of early developmental interventions post hospital discharge, our team demonstrated that early intervention had a moderate effect on cognitive development (standardised mean difference [SMD] = 0.32, 95% confidence interval [CI] 0.16, 0.47) but a smaller effect on motor development (SMD = 0.10, 95% CI 0.01, 0.19) up to 3 years of age compared with usual care.[25] A recent systematic review of interventions commencing in the NICU found that parent-delivered motor interventions were more effective than other early developmental interventions in improving motor and cognitive outcomes in the short term.[26] Neurorehabilitation and neuroplasticity research supports high repetitions of task specific activities to enhance learning and establish neural pathways in infants.[24, 27] It has also been shown that intense interventions that involve parents are more effective at promoting neurodevelopmental outcomes than low intensity interventions that focus only on the therapist and infant.[28,25] Given that VPT infants are at high risk of motor, cognitive and behavioural impairments, there is an even greater need for high repetitions and intensity to enhance learning in infants born VPT, and thus interventions must engage parents to achieve a high dose.[25]

The provision of high-intensity intervention during a time of maximum neuroplasticity, as supported by the basic science and theoretical literature,[12,36] is not currently available to VPT infants in Australia and in many countries internationally. Our research has shown that the majority of preterm infants do not receive timely early intervention, and those with higher

family social risk (socio-economic disadvantage) are less likely to receive intervention.[29] Further barriers to accessing effective early intervention for preterm infants and their families include a 'wait and see' approach rather than a preventative model, lack of access to appropriately trained health professionals (particularly for rural, remote and/or socioeconomic disadvantaged families), provision of generic interventions rather than targeting the needs of the individual infant and family, limited funding for services, and lack of communications between families and health professionals.[29, 30] Consequently, many preterm infants do not receive intervention during a critical developmental window for promoting functional neural pathways and improving future function.[31]

Two promising interventions for preterm infants and their families that have been recently trialled by our team include "SPEEDI" and "e-prem". SPEEDI (Supporting Play Exploration and Early Development Intervention) is a face to face early intervention program, developed by author SD and colleagues in Virginia, USA, and has been trialled in two pilot randomised controlled trials (RCTs) (one in the USA[32, 33] and one in Australia[34]). Although both SPEEDI pilot studies were underpowered for determining efficacy, there was a trend for infants in the SPEEDI group to have better motor, cognitive and language scores on the Bayley-III at 4 (Australian pilot) and 6 (USA pilot) months' corrected age compared to those in the control group. Both studies determined the SPEEDI intervention was feasible to deliver. A protocol paper for a larger trial evaluating the efficacy of SPEEDI was published in 2020.[35]

e-prem was developed by authors KT, PJA and AJS based on their research on early intervention for preterm infants and is an adaptation of the VIBeS Plus program.[36] e-prem involves initial face to face intervention followed by a web-based intervention, with age-based online modules completed over the first year of life, supported by clinicians via telephone. In a pilot RCT of e-prem compared with usual care, 100 preterm infants were

followed up at 24 months' corrected age. Parent-infant interaction was assessed using the Emotional Availability Scale (EAS) at 24 months' CA. Parents in the intervention group scored higher than those in the control group (reflecting more optimal outcomes) on maternal structuring (mean difference = 0.72, 95% confidence interval [CI] = 0.21, 1.22), and children in the intervention group scored higher than those in the control group on child responsiveness (coefficient = 0.58, 95% CI = 0.03, 1.13), and child involvement (coefficient = 0.62, 95% CI = 0.09, 1.15).[37]

With advances in digital technologies and improved accessibility, telehealth (defined as the use of information and communication technologies to provide clinical services from a distance) has made it possible for therapeutic interventions to be delivered straight to families in their home.[38] Telehealth has the added benefit of reducing the risk of exposure to other illnesses and infections; especially for patients who may have compromised or weakened immune systems such as those born very preterm.

The results of our previous research demonstrated that whilst utilising telehealth, e-prem alone did not appear to improve motor or cognitive outcomes in very preterm infants but showed an improvement in parent mental health and the parent-child relationship. SPEEDI showed preliminary evidence of effectiveness in improving neurodevelopmental outcomes but has not been delivered via telehealth and does not target parent mental health and wellbeing. In order to give the intervention the best chance of demonstrating effectiveness, we have consolidated the effective components from both previous interventions and developed an innovative approach to early intervention to enhance neurodevelopment called TEDI-Prem (Telehealth for Early Developmental Intervention in babies born very preterm). We now plan to test the efficacy of the TEDI-Prem intervention in a randomised trial.

AIMS

The primary aim of this RCT is to determine the efficacy of TEDI-Prem plus usual care compared with usual care alone to improve motor outcomes at 12 months' corrected age (CA) in children born VPT. Secondary aims are outlined in Box 1.

Box 1: Secondary aims

To determine the efficacy of TEDI-Prem plus usual care compared with usual care alone to improve:

1. motor outcomes at 24 months' CA for infants born VPT
2. cognitive, language, behaviour and quality of life at 12 and 24 months' CA for infants born VPT
3. parent well-being (anxiety and depression), quality of life, and self-efficacy at 12 and 24 months' CA for parents of infants born VPT
4. parent-infant interaction at 12 and 24-months' CA between infants born VPT and their primary caregiver
5. healthcare utilisation at 12 and 24 months' CA for infants born VPT
6. cost-effectiveness over 24 months

METHODS AND ANALYSIS

Study design

A multicentre, pragmatic, parallel group, RCT designed according to SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) guidelines,[39] the principles of Good Clinical Practices, the template for intervention description and replication (TIDieR)

checklist and guide (Table 1),[40] and in adherence to the National Statement and Australian Code for Responsible Research Conduct.

Study setting

Trial recruitment will be undertaken in the neonatal intensive care unit (NICU) or special care nursery (SCN) of five hospitals in the state of Victoria, Australia, including The Royal Women's, The Royal Children's, Monash Children's, Joan Kirner Women's and Children's, and the Northern Hospitals. These centres are chosen as they encompass five of the six main sites of care for VPT infants in Victoria.

Participants

VPT infants and their parent/s (at least one parent must participate in the trial) will be recruited from Victoria, Australia. Throughout this protocol, the term 'parent' will be used to refer to any individual who provides primary care to the infant (e.g. grandparent, foster carer). Inclusion and exclusion criteria are outlined in box 2.

Box 2: Eligibility for inclusion in the randomised controlled trial

Inclusion criteria

- Infant born <32 weeks' gestation.
- Infant medically stable and not ventilator-dependent at recruitment (minimum age for enrolment 32 weeks' and maximum 40 weeks' postmenstrual age).
- Have one parent who speaks and can read English (as the video content and intervention materials are in English).
- Able to participate in an early intervention program for a 12-month period.

- Able to attend primary outcome assessment at 12 months' CA.

Exclusion criteria

- Non-English speaking primary parent.
- Infant with a diagnosis of a congenital abnormality known to affect neurodevelopment, who require specific intervention, such as infants with Trisomy 21.
- Families who are planning to move overseas/interstate prior to the primary outcome assessment at 12 months' CA.
- Parents not wanting to engage in telehealth intervention.

Sample Size Calculation

The primary outcome is the Bayley-4[41] Motor Composite score at 12 months' CA, which has a mean of 100 and standard deviation of 15. Whilst there is no reported minimum clinically important improvement on the Bayley-4, a difference of 5 points represents a standardised mean difference (SMD) of 1/3 between groups, and is considered clinically important and consistent with previous RCTs in the field that have changed clinical practice.[4] In order to achieve 90% power to identify a SMD of 1/3 based on a two-sided t-test with a 5% significance level, we require 190 participants per group assuming that the observations are independent. Given that our sample will be children born <32 weeks we would expect approximately 20% to be multiple births. Assuming an intra-class correlation coefficient of 0.2 between multiple births, this equates to a design effect of 1.04, hence we need to recruit 198 per group to have 190 effective participants. Allowing for 15% loss to follow-up (conservative estimate – previous studies by our team have >90% follow-up), we aim to

randomise a total of 466 infants over 32 months. In an Australian pilot study of SPEEDI, >85% of eligible infants were recruited over a 3-month period at a single site (n=17 infants).[34] Over 700 infants are born VPT in Victoria each year and we are recruiting from four out of five Victorian NICUs, along with a large special care nursery, making our sample size target very achievable. Further, the fact that the intervention involves telerehabilitation will allow participants to be recruited without geographical limitations.

Recruitment

Eligible infants will be identified by a member of the research team at the participating sites while infants are in the NICU or SCN. With approval from the infant's clinical team, when the infant is considered medically stable, is not ventilator dependent (can be on continuous positive airway pressure [CPAP]), and is between 30-40 weeks' gestation, parents of eligible infants will be approached by a member of the research team and provided with the Participant Information and Consent Form for the trial (see online supplementary material 1). In the event that COVID-19 precautions prohibit the research team entering the NICU or SCN at a participating site, a clinical team member will approach families to introduce the study and gain verbal consent for a research team member to contact them to explain the study in more detail. The research team member will give a verbal explanation of the trial, including a description of the trial processes, the voluntary nature of the trial and that a decision to participate, or not, will not affect the standard clinical care they and their infant receives. See Figure 1 for an overview of participant recruitment and follow-up.

Data collection, management, and access

Data for this trial will be collected and entered using electronic data collection forms which will be completed by the parent and researchers and entered via The University of

Melbourne's Research Electronic Data Capture (REDCap)[42, 43] database system. All data will be de-identified, with all participants allocated a unique trial identification number. Intervention sessions will be recorded using Zoom Video Communications Inc (ZOOM). All files containing private or confidential data will be stored only in locations accessible to designated members of the research team on secure networks which are backed up nightly.

Baseline data collection

Perinatal information: Data on the birth history and neonatal course (e.g. gestational age, birthweight, sex, multiple birth status, cranial ultrasound findings, proven or suspected necrotising enterocolitis, maternal antenatal corticosteroid administration, postnatal corticosteroid use and use of oxygen at discharge from hospital) will be collected by the research team members from medical files and the hospital neonatal database. Prior to randomisation, consenting parents will be asked to complete baseline questionnaires to obtain the following information:

Social risk: The Social Risk Index which assesses six aspects of social status including family structure, education of primary caregiver, primary income earner occupation, primary income earner employment status, language spoken at home, and maternal age at birth will be used to assess social risk.[44]

Parenting self-efficacy: The Karitane Parenting Confidence Scale is a reliable and valid measure for assessing parent confidence in 15 task-specific areas including confidence in feeding, settling and decision making.[45] This will also be collected at 12 and 24 months' CA.

Parent depression, anxiety and stress: The DASS-21 evaluates severity of symptoms associated with depression, anxiety and stress, and categorises results as mild, moderate or severe.[46] This will also be collected at 12 and 24 months' CA for all participants, and at 3 and 6 months' CA for parents in the intervention group.

Parent Quality of Life: The Short-Form Six-Dimension Quality of Life (SF-6D) instrument will be used to facilitate the estimation of quality adjusted life years (QALY) and to inform the cost-effectiveness of the intervention.[47] This will also be completed at 12 and 24 months' CA.

Use of therapy services: A purpose-built questionnaire will be used to measure access to therapy services for the child. This will also be administered at 3, 6, 12, 18 and 24 months' CA to monitor access to early interventions services (see online supplementary material 2).

Randomisation

Following completion of all baseline questionnaires, infant participants will be randomised to the TEDI-Prem intervention or usual care group in a 1:1 ratio when the infant is ≥ 32 weeks' gestation and medically stable. Randomisation will be computer generated using block randomisation with variable block sizes and stratified by site of recruitment and multiple birth. Infants from multiple births will be randomised to the same group due to the nature of the intervention. Randomisation will be conducted using a web-based randomisation program to ensure allocation concealment. Following randomisation, parents will be

notified of group allocation by a research team member. All participants will be gifted four age-appropriate toys at the baseline assessment as a thank you for their participation in the trial, and will receive a support services information letter with contact and referral information of different support options in the community.

Trial intervention

In addition to usual care, participants randomised to the intervention arm will receive the TEDI-Prem intervention program which will start whilst the infant is in the hospital. See Table 1 for an overview of how TEDI-Prem differs to usual care. The intervention program is a collaboration between a physiotherapist/occupational therapist (TEDI-Prem therapist) and the parent. It consists of thirteen 45-60-minute sessions delivered across three phases, from infant randomisation up until 12 months' CA. Due to the nature of the intervention, the participants and TEDI-Prem therapists will not be blinded to the trial intervention. Four TEDI-Prem therapists will be involved in administering the intervention throughout the trial.

The novel intervention is grounded in neurorehabilitation and parent-child interaction theory and combines a model of care where there is continuity of care from the hospital into the community environment by utilising telehealth and web-based education modules which can be adapted according to the needs of the individual infant and family. As per the SPEEDI study,[33] the TEDI-Prem intervention uses a perception action model of development whereby an infant's motor activity supports their attempts to explore and engage with their environment, allowing the infant to receive and interpret important information and solve problems by linking the mind and body in a cycle that supports development across multiple

domains.[48] Further, the TEDI-Prem intervention utilises the theoretical approaches from e-prem which was designed to work with parents to support their mental health and relationship with their child to improve child development. Consistent with Bronfenbrenner's bioecological theory of development, the parent-child relationship provides the child's most proximal, strongest, and immediate environment for development[49] and many of the positive effects of early intervention programs for preterm children work through improving the parent-child relationship and parent adaptability.[50] Belsky's determinants of parenting model also highlights how factors such as parent mental health influence parenting.[51]

The TEDI-Prem intervention content and strategies were developed to address the deficits commonly seen in infants born preterm and their parents,[52-54] and include using self-calming strategies and environmental support to enhance parent-infant interaction, with large doses of practice to support postural control and learning, visual motor, and object interactions in the first few months of the intervention, along with psychosocial education to support parent mental health and well-being. The TEDI-Prem therapist uses the key strategies outlined in Box 3 to address the principles of the program and increase the infant's opportunities for movement.

Box 3: TEDI-Prem Key Strategies

1) Providing graded postural support;
2) Observing spontaneous movement in response to support;
3) Varying postural support to encourage different opportunities and sensory-motor exploration;
4) Varying positions with minimal support to encourage variable, infant-directed movement; and

5) Providing opportunities to visualise, track, and manipulate objects.

As parents deliver the intervention rather than a therapist, higher intensity of intervention can be provided to drive neuroplasticity. Throughout the TEDI-Prem intervention program, parents learn the necessary skills to scaffold their infant's learning. In phase one of the program, there is a strong focus on guiding parents to understand behavioural cues and how to identify ideal times for play and interaction with their infant. Enhanced parental capacity for engagement and self-efficacy allows parents to transition into providing activities that support their infant's developmental function (phase two and three) and provide opportunities for early problem solving, and is also likely to have a positive impact on parental well-being.[22] In phases two and three of the program, delivered via telehealth, parents are encouraged to complete five activities (watching people and toys, tummy time, holding head up, kicking play, and toy play with hands and legs in the middle), individualised to the infant's abilities, to support variable practice with developmental play, provide environmental enrichment through positioning, presenting toys, and social engagement, while supporting the infant's self-directed movements and interactions without imposing movement.

The use of video-based telehealth sessions will allow therapists to observe the infant and work with the family (through the use of guided participation) on intervention strategies individualised to their infant and home environment.

There are several resources used to support the intervention sessions including a series of parent education handouts and videos, and an 'Activities for Home Play' booklet. The parent education handouts cover a variety of topics including psychosocial education to support parent mental health and well-being, education on infant development, including language

and communication, and education on parent-infant relationships and sensitive parenting behaviours (see supplemental material 3 for list of parent education handouts). The parent education videos support and reinforce the content provided in the parent education handouts and demonstrate examples of the TEDI-Prem principles and five intervention activities. The 'Activities for Home Play' booklet includes illustrations and written instructions on the developmental play goals and intervention activities the parent and TEDI-Prem therapist will work on throughout phase two and three of the program. Parents will be encouraged to use the toys gifted to them at the commencement of the trial during the intervention activities. Compliance and dosage will be assessed by parent report during each TEDI-Prem session.

The parent education handouts and accompanying educational videos made available to parents at each phase will be individualised to ensure it is relevant to the infant's family structure and supports the needs of the parent as they change and/or evolve throughout the program. The TEDI-Prem therapist will make relevant resources available to parents after each intervention session via email and access to a secure, password protected video sharing platform. New content will be provided during each phase of the program and content from previous phases will be reviewed as required. The 'Activities for Home Play' booklet will be introduced and provided to parents at the end of phase one in preparation for use in phase two, when the infant is discharged home. During the intervention sessions, the TEDI-Prem therapist will view educational videos with the parent – selecting videos based on the developmental needs and progression of the individual infant. Figure 3 provides an overview of the TEDI-Prem intervention.

Table 1: TIDier Checklist: How TEDI-Prem differs to usual care

Item	TEDI-Prem	Usual care
Brief name	Telehealth for Early Developmental Intervention in babies born very preterm.	NA
Why	Use of guided participation to enable parents to deliver intensive early motor, cognitive and language training to enhance neuroplasticity and parent education and support to improve parent mental health and well-being	Developmental monitoring with referral to intervention when impairments are identified
Materials	Enrich environments with age appropriate, engaging toys to entice infants to actively and intensively practice and persist with problem solving demands. A grasping toy (ball), hand rattle, wrist/ankle rattle and book are given to all participants. Parents adapt environment to support infant based upon behaviour. Parent education handouts and accompanying videos support parent mental health and well-being and learning and implementation of program principles	Materials not used (toys will be given to all participants, however, instructions not given)
Who	Physiotherapist/occupational therapist (>5 years experience in paediatrics) uses participatory guidance to support the parent to work with their infant. Therapists complete 12 hours of online training modules which provides education on the theoretical underpinnings of the program, the methodology of the trial, and the intervention content. Further, therapists participate in a 3-day training workshop where a multidisciplinary team of Physiotherapists, Occupational Therapists, and Psychologists teach the intervention prior to trial commencement.	Referral to a physiotherapist, speech pathologist or occupational therapist, as needed
How/ Where	Hospital (face to face) and home based in infant's natural environment at time of intervention (via telehealth)	Face to face hospital or outpatient based as needed
When /How much	13 sessions over 3 phases:	- Depends on the parents' natural interaction patterns

	Phase 1: From group randomisation to infant hospital discharge home. 4 x 30-45-minute sessions face to face in hospital. If infants are transferred to another hospital or discharged home during phase 1, sessions are delivered via telehealth. Phase 1 focuses on building reciprocal engagement and parents reviewing and implementing key principles. **Phase 2:** From discharge home to 6 months' corrected age. 6 x 45–60-minute sessions via telehealth. Phase 2 focuses on the parent providing daily opportunities for advancing motor, cognitive, and social skills in play (20 minutes per day, 5 times per week). **Phase 3:** From 6 – 12 months' corrected age. 3 x 45–60-minute sessions via telehealth. Phase 3 focuses on scaffolding the needs of each family to enhance independence. This may include integration into local services as needed.	- May be limited one-on-one play, use of toys, or support of variable movements - Community–based early intervention if referred as part of usual care
Tailoring	Intervention commences early in life and is tailored to infant's environment, developmental stage and parents' skills levels.	Intervention only delivered if impairment identified and often has long wait list.
How well	Therapists trained to deliver TEDI-Prem intervention. One of the four sessions in phase one and all sessions in phase two and three will be video recorded for fidelity checks	Data will be captured on interventions (age commenced, intensity and duration).

Key principles and fidelity

The key principles of the intervention are outlined in Table 2 and are the foundation from which the intervention content and strategies are delivered. These key principles will form the evaluation of the fidelity of the intervention and will be in part assessed on therapist adherence and measured by the frequency with which the intervention therapist demonstrates, talks about, or brainstorms with a parent about the TEDI-Prem principles and strategies. One of the four sessions in phase one and all sessions in phase two and three will be video recorded. TEDI-Prem therapists will complete a self-assessment of adherence using a fidelity

checklist following each session. Author's SD and SB will randomly select three video recorded sessions (one from each phase) per participant to further assess therapist adherence and provide feedback and additional training and/or support as required.

Table 2: TEDI-Prem Key Principles

Principle 1: Education and support for parent mental health and well-being This principle aims to provide a protective influence for the development of very preterm infants. The TEDI-Prem therapist checks in with the parent regarding their emotional health during each of the TEDI-Prem sessions. A series of supporting educational handouts and videos are provided throughout the 12 month intervention program which focus on psycho-education and strengthening the parent-child relationship. Parent mental health is screened throughout the intervention program enabling more targeted intervention and assisting parents in accessing support services where indicated.
Principle 2: Cue based directed care and interactions Parents learn to read their infant's behavioural cues during caregiving, play, and social interaction. The parent learns to match their behaviour and interactions to meet the infant's demonstrated readiness. This key principle encourages sensitive and responsive parenting behaviours and supports parents in identifying the infant's alert and active times for intervention, develop a routine for interaction, as well as following the infants lead on when to provide rest breaks. Parents are encouraged to use vocalisation along with social and motor interactions in response to the infant's cues.
Principle 3: Guided participation This principle builds the foundation for intense early intervention and aims to support a less skilled person in developing a specific new practice. The basic processes of guided participation that are utilised in the intervention are: 1. Providing bridges from the known to the new; 2. Choosing and structuring learning activities; 3. Structuring responsibility in joint problem solving; and 4. Transferring responsibility for managing activities Using guided participation, the TEDI-Prem therapist assists parents in learning to read their infant's readiness cues for caregiving, interaction and play, and match their own interaction to the infant's readiness.
Principle 4: Encourage self-directed movement This principle allows the infant ample time to elicit self-directed movement, to make errors, and to correct these errors as independently as possible. Rather than aiming for a

pre-determined 'correct pattern' of movement, the infant's own strategies for movement are supported to emerge.
Principle 5: Do not impose movement When the infant requires assistance to transition between postures, to maintain postures, or to interact with objects, there is a focus on providing the least amount of assistance required and not imposing movement.
Principle 6: Provide a "just right" challenge The 'just right challenge' is about matching the skill set required for an activity with the performance capacity of the infant engaged in the activity. Through scaffolding, that is, offering just the right help at just the right time in just the right way, the TEDI-Prem therapist teaches parents to determine and utilise the 'just right challenge' during all interactions. For infants to make continual gains in a safe, timely, and positive manner, it's important to know how much assistance they need to perform an activity and to understand ways to adapt the activity to place it at the cusp of an infant's developmental ability. This can involve altering the level of assistance provided, changing the infant's posture, modifying the environment, and adapting aspects of the task such as object placement. The parent learns how to provide graded postural support and observes their infant's spontaneous movement, social engagement, and vocalisations in response to the support to determine if the 'just right challenge' has been met.
Principle 7: Encourage socialisation and communication Across postures and with varying level of postural support, parents encourage infants to focus on their face and engage in early social interaction including vocalisations and visual engagement. Infants learn to read their parents behavioural cues and develop an understanding of facial expressions and vocalisations as a form of communication. As infants fix on their parents faces, smile and/or vocalise, and parents respond in a timely and sensitive way, infants learn reciprocity and the value in making sound. This provides the building blocks of social engagement and early language and communication.
Principle 8: Encourage learning through object interaction Across a variety of positions and with graded postural support, infants are provided opportunities to see, feel, mouth, and hold objects that vary in weight, size, texture, hardness, and colour. Consideration of object placement motivates infants to move through different positions to interact with objects. This principle enables varied cognitive and movement opportunities as well as sensory inputs. Infants learn about object affordance, cause and effect, and means end as they move their body and interact with objects and the world around them.
Principle 9: Provide opportunities for variable movement Varied exploratory movements are essential building blocks for learning any new postural skill. Trial and error with movement is essential in the learning process.

*Table adapted from SPEEDI Key Principles, as published previously.[33]

Outcome measures

At 12 and 24 months' CA, all infants will be assessed by an examiner who is blinded to group allocation. The outcome measures in this trial and their timing of collection are described in Table 3. An overview is provided in Figure 2 below.

Table 3: Primary and secondary outcome measures

Primary outcome
Infant motor composite score on the Bayley Scales of Infant and Toddler Development-4th edition (Bayley-4) at 12 months' CA.[55]
Secondary outcomes
Infant • Child cognition assessed using the Bayley-4 cognitive composite scores at 12 and 24 months' CA.[55] • Child language assessed using the Bayley-4 language composite score and receptive and expressive scaled scores at 12 and 24 months' CA.[55] • Child motor development assessed using the Bayley-4 motor composite score at 24 months' CA.[55] • Child behaviour assessed using the Infant Toddler Social Emotional Assessment (ITSEA) at 12 and 24 months' CA.[56]
Parent • Parental depression and anxiety assessed using the Depression Anxiety Stress Scales (DASS-21) at 12 and 24 months' CA.[46] • Parenting self-efficacy assessed using the Karitane Parenting Confidence Scale (KPSE) at 12 and 24 months' CA.[57] • Parent-infant interaction assessed using the Emotional Availability Scale (EAS) at 12 and 24 months' CA.[58]
Cost-effectiveness of TEDI-Prem compared with usual care (to be published separately to the main trial results) • Costs assessed using cost of the intervention and children's health care utilisation. • Quality adjusted life years (QALYs) assessed based on child and parent quality of life. • Child quality of life measured via parent report using the EuroQol Toddler and Infant Populations (EQ-TIPS) at 12 and 24 months' CA.[59]

- Parent quality of life measured using the Assessment of Quality of Life (SF-6D) at 12 and 24 months' CA.[47]
- Cost-effectiveness of the intervention compared with usual care assessed as cost per additional QALY gained.

Statistical analysis

The statistical analysis will be conducted by a statistician who will remain blinded until the end of the trial. Data will be analysed using the intention to treat principle and will include all participants according to their treatment allocation irrespective of whether they received any of the intervention (e.g. treating all intercurrent events using a treatment policy strategy). Sensitivity analysis will be conducted using a hypothetical strategy for adherence, where adherence will be defined as participating in at least 80% of TEDI-Prem intervention sessions for participants in the intervention group.

Mean differences between groups in the primary outcome will be examined using linear regression, fitted via generalised estimating equations to account for multiple births and adjusted for site. Differences between groups in secondary outcomes will be examined using linear regression for continuous outcomes and logistic regression for binary outcomes. All models will be fitted via generalised estimating equations to account for multiple births and adjusted for site.

Analyses will be repeated in subgroups according to social risk (high vs low), gestational age (extremely preterm vs very preterm) and later neurological diagnosis (yes vs none) at 12 months' CA via the inclusion of an interaction term in the regression models.

PATIENT AND PUBLIC INVOLVEMENT

We have included stakeholder involvement at several stages in the development of the trial. As part of our Centre for Research Excellence (CRE) in Newborn Medicine, we completed a Delphi study identifying the research priorities of parents with experience of newborn medicine.[60] Parents identified many questions as high-priority with primary areas related to supporting parental mental health, relationships between parents and neonatal clinical staff (including involvement in care and communication), bonding and the parent-child relationship, and addressing long-term impacts on child health and neurodevelopment. These consumer-identified research priorities were integrated into the design of the TEDI-Prem intervention program and its effect on outcomes in these areas will be evaluated.

In addition, members from the CRE in Newborn Medicine's Consumer Advisory Group (CAG) were actively involved in the development of the TEDI-Prem intervention program and the trial's research methods and design. Members of the CAG participated in a focus group where the consumer perspective on the appropriateness, acceptability and fit of our study name, the interventions key principles (underlying mechanisms of change) and forms (activities embedded into the intervention that will be used to carry out key principles, including their timing and frequency) was provided. This feedback was incorporated into the study design and procedures outlined. Further, members of the CAG reviewed and approved various research materials to ensure they are easily accessible to consumers.

ETHICS AND DISSEMINATION

A Data Safety Monitoring Board (DSMB) will be established to review and evaluate study data on adverse safety events, study conduct and progress, and trial efficacy. The DSMB will monitor trial efficacy through a single interim analysis of the primary outcome once 50% of participants have completed their 12 month CA follow up. The Haybittle – Peto boundary stopping rule will be applied to the results of the interim analysis to decide if the trial should

be stopped prematurely. If the interim analysis shows a p-value of equal to or less than 0.001 that a difference as extreme or more extreme than that found between treatments if the null hypothesis were true, then the trial will be stopped early. If additional psychological support for parental mental health is indicated, they will be provided with referral/information about appropriate support services, with their permission.

Trial findings will be disseminated through presentations at national and international conferences, publication in peer reviewed journals, as well as digital and print media. Further, we will disseminate our research results to trial participants, individuals with lived experience of preterm birth, health professionals, and service providers. This will be accomplished through direct communication with participants, collaborations with preterm parent support groups using their social media and web platforms, the CRE in Newborn Medicine's professional networks, and conference presentations. If found to be effective, training courses on TEDI-Prem will be rolled out using this protocol including the online training for therapists. Consent from trial participants to be contacted for future follow-up studies will be sought.

DISCUSSION

This paper outlines the protocol for the trial of an early intervention program designed for VPT infants over the first year of life. Publication of protocols enhances the transparency of research and allows for replication. The TEDI-Prem program commences in the hospital prior to discharge and provides an intervention delivered earlier than traditional health service models of early intervention for preterm children. We propose that providing targeted intervention to support the development of the parent-child interaction, an enriched environment, an infants' self-directed movement and their parent's well-being at an earlier

age whilst in the hospital and across the first year will lead to improvements in neurodevelopment, parental mental health, and a cost-effective model of delivering early intervention services for VPT infants compared with usual care.

Figure 1: Participant flow chart

Figure 2: Outcome measures and timing of administration throughout the trial

Figure 3: TEDI-Prem intervention overview

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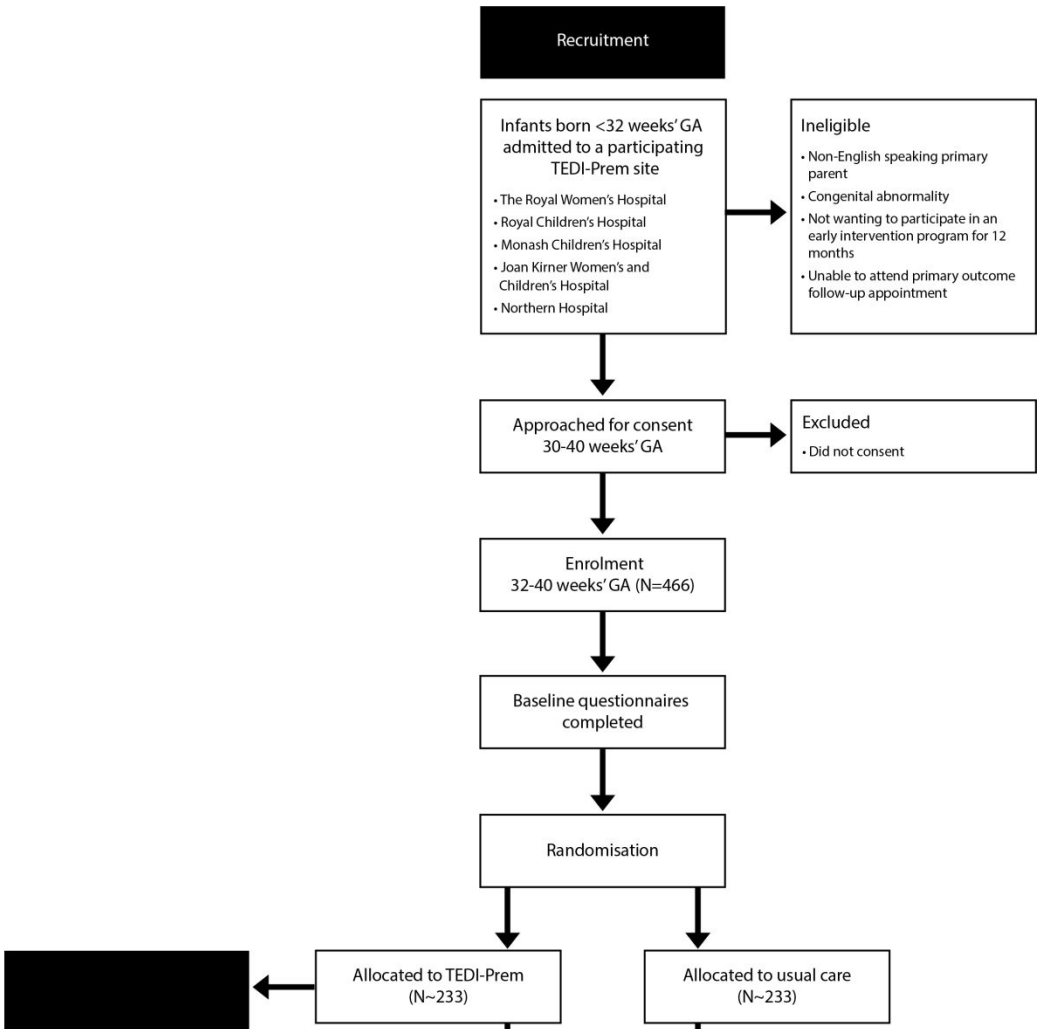
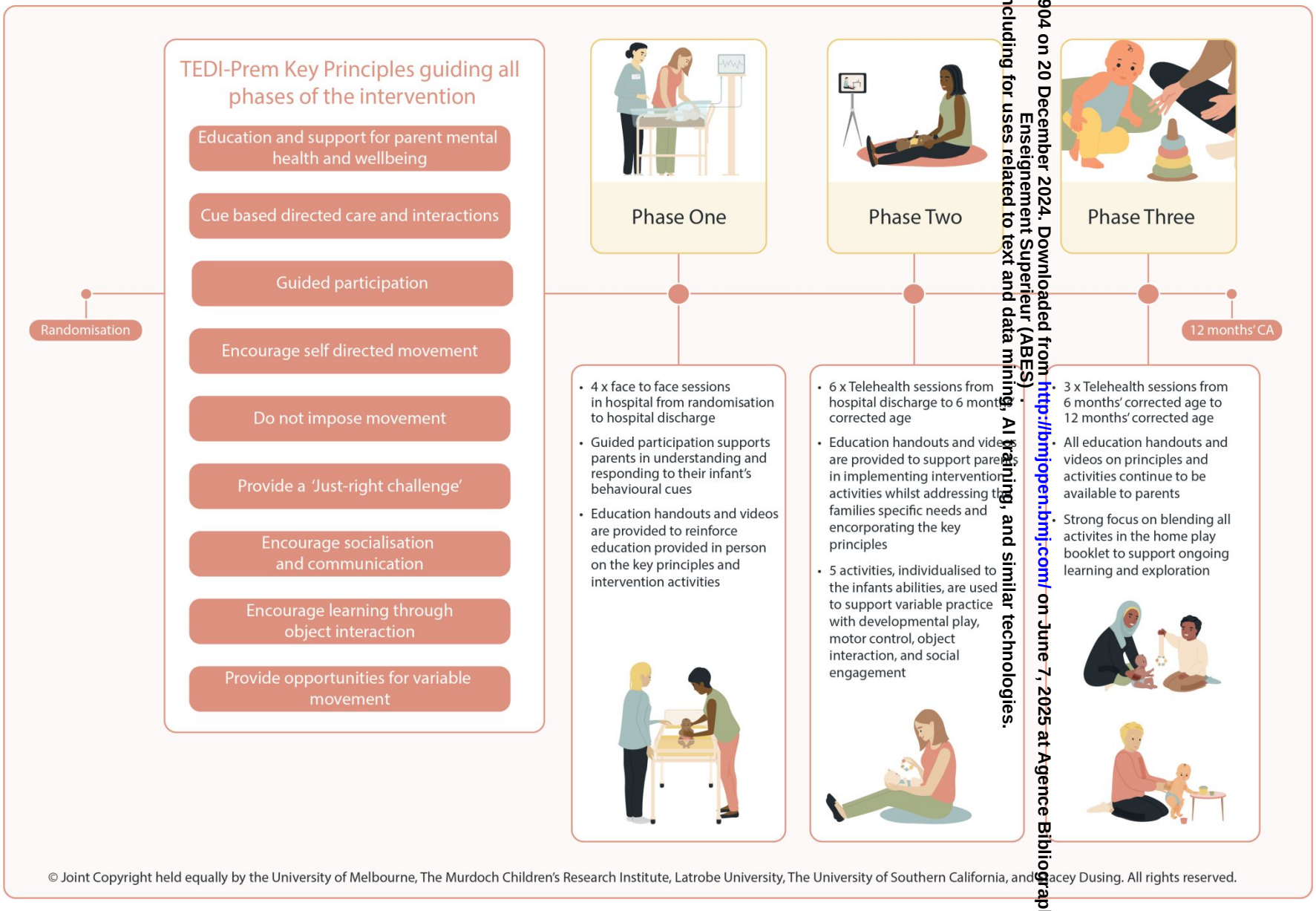


	Baseline	3mo CA	4mo CA	6mo CA	8mo CA	10mo CA	12mo CA	18mo CA	24mo CA
Perinatal data	☑						☑		
Bayley - 4							☑		☑
EAS							☑		☑
QUESTIONNAIRES									
Socio-demographics	☑						☑		☑
KPSE	☑						☑		☑
DASS-21	☑						☑		☑
ITSEA							☑		☑
EQ-TIPS							☑		☑
SF-6D	☑						☑		☑
Therapy services	☑	☑		☑			☑	☑	☑

Bayley-4: Bayley Scales of Infant and Toddler Development 4th Edition; EAS: Emotional Availability Scale; KPSE: Karitane Parenting Self Efficacy Scale; DASS-21: Depression Anxiety Stress Scales; ITSEA: Infant Toddler Social Emotional Assessment; EQ-TIPS: EuroQol Toddler and Infant Populations (EQ-TIPS) measure; SF-6D: Short Form Quality of Life.



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Participant Information Sheet/Consent Form - Parent/Guardian
[Insert site name]

Title:	The effect of telehealth for early intervention on neurodevelopmental outcomes of infants born very preterm and their parent's well-being: a randomised controlled trial (TEDI-Prem)
Short title:	TEDI-Prem: Telehealth for Early Developmental Intervention in babies born very preterm
Study sponsor:	The University of Melbourne
Coordinating Principal Investigator:	Professor Alicia Spittle
Principal Investigator:	[Insert site PI name]
Location:	[Insert location]

This is an invitation for you and your child (or children if you have given birth to twins or higher order multiples) to take part in a research study called TEDI-Prem because they were born less than 32 weeks' gestation.

This Participant Information and Consent Form tells you about the research study. It explains the tests and treatments involved. Knowing what is involved will help you decide if you want your child to take part in the research.

Please read this information carefully. Ask questions about anything that you don't understand or want to know more about. Before deciding whether or not your child can take part, you might want to talk about it with a relative, friend or your child's doctor or care team.

What is TEDI-Prem?

TEDI-Prem is a new early intervention program for babies born prematurely and their parents. TEDI-Prem stands for telehealth for early developmental intervention in babies born very preterm.

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What is the purpose ofthe TEDI-Prem study?

Children born less than 32 weeks' gestational age are at risk of developmental problems, and their parents are also at risk for anxiety and depression. We have developed the TEDI-Prem program to help babies with their development and support parent's mental health, but we need to know if the intervention works.

The aim of the study is to see if the intervention improves child development, particularly motor skills, as well as thinking and talking, and parent mental health. If we find that the intervention improves outcomes for children after premature birth, we hope to make it widely available across Australia.

Who is organising and funding the TEDI-Prem study?

This research is being conducted by The University of Melbourne and has been funded by the Medical Research Future Fund.

What does taking part in the TEDI-Prem study involve?

You and your child will be participating in a randomised controlled research study.
This means we will put people into two groups: **one group will receive the TEDI-Prem intervention in addition to usual care, and the other group will receive usual care only.**

The results are compared to see if one of these is better. To try to make sure the groups are the same, each participant is put into a group by chance (random). Your child has an equal chance of being in either group. Neither you or the researchers can choose which group your child is put in. This research study has been designed to make sure the researchers interpret the results in a fair and appropriate way.

If you indicate that you want you and your child to participate, you will be asked to sign the consent form and we will collect some information from you and the medical record (such as your contact details, details about your child – including birth weight, medical complications and treatments).

Before you find out which group you're in you will be asked to complete some questionnaires. We will ask you about:

How you have been feeling and your mood, and about your family background and education

Information about your baby

These questionnaires will take about 5-10 minutes to complete

After you complete this information, your family will be randomly allocated to either the intervention or comparison group

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What does my child have to do?

Your child will need to do different things depending on whether they're randomly allocated to the intervention or comparison group.

All children will receive a follow-up assessment at 12 and 24 months of age (based on their original due date).

What if I'm randomly allocated to the comparison group?

Your child will continue to receive usual clinical care. This may include physiotherapy or occupational therapy services depending on your child's needs and the gestation they were born at. You will also be asked to complete some online questionnaires.

What if I'm randomly allocated to the intervention group?

You will participate in the TEDI-Prem program. The program starts in the neonatal nursery and continues until your child is 12 months' corrected age (12 months after their due date). During each session a physiotherapist or occupational therapist will provide movement and interaction activities designed to help your child's development. Each session will take about 45-60 minutes and we will video record the sessions. Only researchers involved with this study, and no others, are permitted to view these videos.

We will provide additional information about your child's development, parental wellbeing and relationships, and the intervention activities via email. You will also be asked to complete some online questionnaires.

See the table on the next page for information about what's involved in the TEDI-Prem program

What's involved in the follow-up assessments?

We will invite you to bring your child into hospital for an assessment when they are 12 months and then at 24 months of age (based on their original due date). These two visits will include a developmental assessment to look at your child's thinking, language and motor development. This assessment will involve activities with your child such as looking at pictures, responding to questions, and playing with puzzles and balls, as well as a videoed play session with you. The visits will be at [insert hospital site name].

Other relevant information

We plan to recruit 466 children and their parents to participate in this research study from The Royal Children's Hospital, The Royal Women's Hospital, Monash Children's Hospital, Joan Kirner Women's and Children's Hospital and the Northern Hospital. The study will run for 7 years.

There are no additional costs associated with participation in this research study, nor will you be paid. You will be reimbursed for any parking expenses for attending the 12 and 24 months assessments. You will receive three toys for your child at enrolment along with a toy/book at 12 and 24 months.

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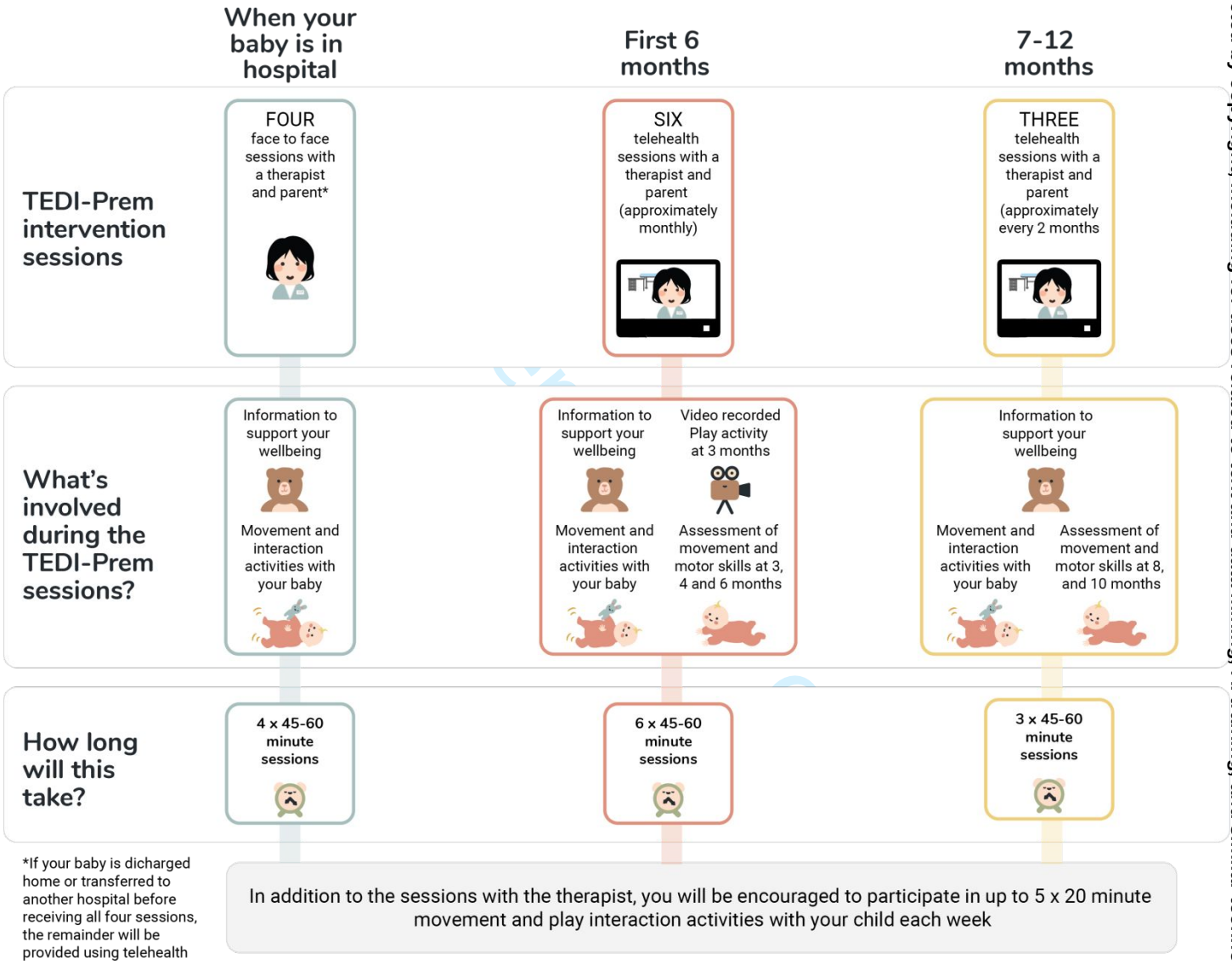
TEDI-Prem Intervention Program



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What questionnaires will I be asked to complete?

Both groups will be asked to complete questionnaires across their child's first two years of life. See the table on the next page for more information about the questionnaires and how long they take.

Do we have to take part?

Participation in this research is voluntary. If you do not wish your child to take part, they do not have to. If you decide that they can take part and later change your mind, you are free to withdraw your child from the project at any stage.

Your decision that your child can or cannot take part, or that they can take part and then be withdrawn, will not affect their routine treatment, relationship with those treating them, or their relationship with [Institution].

What are the alternatives to participation?

You and your child do not have to take part in this research study to receive treatment and usual care at this hospital. Other options are available; these include accessing early intervention programs privately or through Medicare.

Are there benefits of taking part?

We cannot guarantee or promise that your child will receive any benefits from this research; however, possible benefits for the TEDI-Prem intervention group may include positive effects on your child's development and your wellbeing. For all families in the study, the assessments at 12 and 24 months will provide information about your child's development and if needed, referral for further intervention, and some parents may find this useful.

Are there possible risks or disadvantages of taking part?

We do not anticipate any risks or side-effects from participation in this study.

However, being involved in the TEDI-Prem intervention requires additional time for parents. If the assessments identify that your child may need further developmental support, this may be concerning for parents. Sometimes talking about or answering questions about your own wellbeing and family situation can be upsetting.

If you have become upset or distressed as a result of participation in the research, we can arrange appropriate support. This support may be provided by a qualified member of the research team, or a professional who is not in the team. If you have any concerns or questions related to the study please contact Professor Alicia Spittle Chief Investigator on (03) 9035 5340.

Can my child have other treatments during the study?

Yes. Participation in this research study will not influence whether you and your child can access other treatments or interventions.

What if I withdraw my child from the study?

You can withdraw your child from the study at any time. You just need to tell us so. You do not need to tell us why you are taking your child out of the study. If your child leaves the study, we will use the information we have collected about you and your child. If you do not want us to use this information, please tell us. If you do not want us to keep using you and your child's information, we will securely destroy it.

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TEDI-Prem Questionnaires completed online

3 months

Use of therapy services

This will take about 5 minutes

6 months

Use of therapy services

This will take about 5 minutes

12 months

Your wellbeing, parenting role & information about your family

Your health and your child's health

Use of therapy services

This will take about 20 minutes

18 months

Use of therapy services

This will take about 10 minutes

24 months

Your wellbeing, parenting role & information about your family

Your health and your child's health

Use of therapy services

This will take about 20 minutes

Every couple of months we will ask you how much time you and your child spent playing and interacting for the week

This will take about 5 minutes

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What happens when the study ends?

At the end of the study we will send you a letter that tells you what we found out in this research. This letter will be about the whole group of children who took part in the study and not your individual child.

How do I let you know that we want to take part?

If you decide you want your child to take part in the research study, you will be asked to sign the consent section. By signing it you are telling us that you:

- Understand what you have read
- Consent to you and your child taking part in the research study
- Consent for your child to have the tests and treatments that are described
- Consent to the use of the child's personal and health information as described

You will be given a copy of this Participant Information and Consent Form to keep.

Optional Consent

If your child takes part in this study we will ask you to think about consenting to a couple of extra things. These things are optional. The first one is about linking with your child's Medicare/PBS information. The second one is allowing us to share the scores of any common assessments performed for the TEDI-Prem study with other services and or studies in which your child is enrolled or allowing us to obtain the scores of any common assessments performed by other services and or studies your child is enrolled in. The third one is letting us use your child's information for future studies about children who were born preterm. You can say no to all of these things or to just one of them. If you say no, your child can still take part in the study.

The optional parts of the study are explained in more detail below

- A First optional consent: Medicare/PBS data linkage

We would like your permission to let us link to information collected by Services Australia. You will be asked to fill out a separate consent form authorising the study access to your child's complete Medicare Benefits Schedule and/or Pharmaceutical Benefits Scheme (MBS/PBS) data, as outlined in the attached consent form.

The information we collect from Medicare will help us to examine how TEDI-Prem affects healthcare use and costs. So we are able to do this, we will ask you to complete a Services Australia 'Authority to release personal Medicare and PBS claims information to a third party form'. The consent form is sent securely to Services Australia who holds this information confidentially.

Second optional consent: Consent for sharing of common assessment scores between studies and ANZNN

If your child is co-enrolled in the TEDI-Prem study and another research study or they are eligible for a developmental follow up assessment through the Australian and New Zealand Neonatal Network (ANZNN), these studies or services may be collecting some of the same data to track your child's progress after birth. ANZNN is a collaborative network that monitors the care of infants who are born less than 28 weeks gestation or weighing less than 1kg. The assessments performed for the TEDI-Prem study that may have overlap with ANZNN or other studies in which your child is enrolled are as follows:

- The BAYLEY-4 Assessment - which is the main face to face developmental assessment completed at 12 and 24 months' corrected age by a qualified assessor.
- The ITSEA (Infant/Toddler Social Emotional Assessment) - a parent completed survey about your child's social and emotional development - how they behave and interact with others.
- EQ-TIPS: EuroQol Toddler and Infant Populations measure - a parent completed survey about a child's quality of life.

Where we have any of these assessments in common with ANZNN or other studies, we are requesting your permission to either a) share the scores of any assessments performed by TEDI-Prem with ANZNN and/or researchers of other studies in which your child is enrolled or alternatively b) request that ANZNN and/or another research study shares the scores of assessments performed by their team with our study.

Sharing this information will mean that you only need to do the assessment on one occasion, rather than having to complete the same assessment multiple times. It is important to note that we are requesting only to share the scores of the assessments between research teams and/or ANZNN.

Scores will be exchanged using worksheets that identify your child only by their de-identified study numbers from the relevant research studies.

However, the researchers will need to share two personal identifiers alongside the deidentified study numbers with the initial request for information. Sharing of these personal identifiers with the request is essential so that they can check that the scores being transferred belong to the correct child. The personal identifiers that will be shared will be limited to your child's unique medical record number and their date of birth. Personally identifiable information will only be electronically transferred through secure channels and will not be shared with third parties.

Third optional consent: Future research studies

We will collect a lot of information during this research study. However, there are still lots of things about the development of children who are born preterm that we do not understand. We could answer some of these questions in the future by using the information from this study in a different way. We would like you to consider letting us use your child's information in future research studies about children who are born preterm. We will only use the information in research studies that have been approved by a Human Research Ethics Committee. If you agree to this we will use your child's information without contacting you.

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What will happen to information about my child and I?

We will collect and use personal and health information about you and your child for research purposes. By signing the consent form you consent to the research staff collecting and using personal information about you and your child for the research project. Any information obtained in connection with this research project that can identify you or your child will remain confidential. It will be disclosed only with your permission, or as required by law.

We will store your and your child's information securely in the [department name] at [institution] and The University of Melbourne.

Information about you and your child may be obtained from their health records held at this and other health services, for the purpose of this research. By signing the consent form, you agree to the study team accessing health records if they are relevant to you and your child's participation in this research project.

Only the researchers involved with this study, [insert hospital site name] ethics committee, The Royal Children's Hospital Ethics committee and authorised University of Melbourne/Murdoch Children's Research Institute staff can have access to this information. We can disclose the information only with your permission except as required by law.

The stored information will be **re-identifiable.** This means that we will remove identifying information such as your child's name and give the information a special code number. Only the research team can match your child's name to their code number, if it is necessary to do so.

To advance science, medicine and public health, we may also need to share your child's **de-identified** data with other ethically approved research studies, biobanks, or medical journals. If we need to do this, we will remove identifying details such as your child's name, date of birth and address and give the data a special code number. Only the research team on this study will be able to match your child's name to their code number.

The information supplied by Services Australia will only be used for the purpose of this study. It is anticipated that the results of this research study will be published and or presented in a variety of forums. In any publication and/or presentation, information will be provided in such a way that you and your child cannot be identified, except with your permission.

Information about your child's participation in this research study may be recorded in their health records. You have the right to access and correct the information we collect and store about your child. This is in line with relevant Australian and/or Victorian privacy and other relevant laws. Please contact us if you would like to access this information.

As the child participants in this study are under 18 years old, we will keep their information at least until the youngest participant turns 25 years old. All information will be stored securely in locked filing cabinets at the [institute] and once all analyses have been performed, the data will be securely archived. Electronic information, including videos, will also be stored on a password- protected server and REDCap computer database at the University of Melbourne for 7 years after the youngest child in the study turns 18, after which time it may

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be destroyed or kept indefinitely. Only the study researchers will have access to the data.

You must be aware that the information collected about your child may at some point not be able to be identified once the identifying information has been removed. Access to information about you after this point will not be possible.

The Royal Children's Hospital and Murdoch Children's Research Institute are research partners. This means that the two organisations will always share research information with each other.

Who has reviewed the study?

All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC).

The ethical aspects of this research study have been approved by the HREC of The Royal Children's Hospital and [insert hospital site name].

This study will be carried out according to the National Statement on Ethical Conduct in Human Research (2007). This statement has been developed to protect the interests of people who agree to participate in human research studies.

Who do I contact if I have any questions or concerns?

If you would like more information about the study, please contact:

- [insert PI name], on (03) [insert phone number], [insert email]
- Professor Alicia Spittle, Coordinating Principal Investigator on (03) 9345 5390.

If you have any questions or concerns about your rights as a participant in this study, or if you have any complaints you may contact: [insert institute details]

You can contact the Director of Research Ethics & Governance at The Royal Children's Hospital Melbourne if you:

- have any concerns or complaints about the study
- are worried about your rights as a research participant
- would like to speak to someone independent of the study.

The Director can be contacted by telephone on (03) 9345 5044.

If you have a privacy complaint in relation to the use of your MBS and/or PBS data you should contact the Office of the Australian Information Commissioner. You will be able to lodge a complaint with them.

Website: www.oaic.gov.au
Telephone: 1300 363 992
Email: enquiries@oaic.gov.au
Mail: GPO Box 5218, Sydney NSW 2001

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Recruitment of Children Under 14

Where children under the age of 14 are being recruited, and are on two Medicare cards, both card numbers and the signatures of both primary card holders will need to be on the child's consent form. Data relating to a child's Medicare card will only be supplied where the primary card holder of that card has consented.

Consent Form - Parent/Guardian

Title:	The effect of telehealth for early intervention on neurodevelopmental outcomes of infants born very preterm and their parent's well-being: a randomised controlled trial (TEDI-Prem)
Short title:	TEDI-Prem: Telehealth for Early Developmental Intervention in babies born very preterm
Study sponsor:	The University of Melbourne
Coordinating Principal Investigator:	Professor Alicia Spittle
Principal Investigator:	[Insert site PI name]
Location:	[Insert location]

Declaration by Parent/Guardian

- I have read the Participant Information Sheet or someone has read it to me in a language that I understand.
- I understand the purposes, procedures and risks of the research described in the study.
- I give permission for my child's doctors, other health professionals, hospitals or laboratories outside this hospital to release information to The University of Melbourne and [insert hospital site name] concerning my child's medical condition and treatment for the purposes of this study. I understand that such information will remain confidential except as required by law.
- I have had an opportunity to ask questions and I am satisfied with the answers I have received.
- I freely agree to my child participating in this research study as described and understand that I am free to withdraw them at any time during the research project without affecting their future health care.
- I understand that I will be given a signed copy of this document to keep.

Optional consent

☐ I do	☐ I do not	consent to data linkage with my child's Medicare/PBS data
☐ I do	☐ I do not	consent for sharing of common assessment scores between other studies my child is enrolled in and/or the Australian and New Zealand Neonatal Network (ANZNN)
☐ I do	☐ I do not	consent to the storage and use of my child's and my information in future ethically-approved research studies related to preterm children

Name of Child _____

Name of Parent/Guardian _____

Signature of Parent/Guardian _____ Date _____

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I have given a verbal explanation of the research study, its procedures and risks and I believe that the parent/ guardian has understood that explanation.

Name of Researcher _____

Signature _____ Date _____

Note: All parties signing the consent section must date their own signature

Online supplementary material 2: Therapy services questionnaire

TEDI-Prem would like to check in and see if your child received any of the following therapy services in the **last month**

1. Physiotherapy: yes/no,
   If yes, on average how often:
   ☐once per week
   ☐once a fortnight
   ☐once a month
   ☐less than once a month

2. Occupational therapy: yes/no,
   If yes, on average how often:
   ☐once per week
   ☐once a fortnight
   ☐once a month
   ☐less than once a month

3. Speech Pathology: yes/no,
   If yes, on average how often
   ☐once per week
   ☐once a fortnight
   ☐once a month
   ☐less than once a month

4. Other therapy: yes/no
   If yes, please describe: **comment box**
   On average how often:
   ☐once per week
   ☐once a fortnight
   ☐once a month
   ☐less than once a month

Online supplementary material 3: TEDI-Prem parent education handouts

You, your baby and the neonatal unit
Partners
Getting support as a parent
Coping tips for families
From sleep to play
Bonding with your baby
Your relationships
Supporting siblings
Signs of stress, anxiety and depression
Managing stress, anxiety and depression
Corrected age
Preparing to go home
Communication and language: term – 3 months
Play and the home environment
Looking after yourself as a parent
Toy ideas for early development
Play and interaction
Your relationship with your baby

Communication and language: 4-6 months
Child speech and language development
Communication and language: 7-9mths
Play and interaction and toys 6-12 months
Communication and language: 10-12mths
Discharge to home – my support plan
Five steps for assertive communication
My self care plan
My support plan

Correction for 'Protocol for a multisite randomised controlled trial assessing the effect of the Telehealth for early developmental Intervention in babies born very preterm (TEDI-Prem) programme on neurodevelopmental outcomes and parent well-being'

Eeles AL, Spittle AJ, Dusing S, *et al*. Protocol for a multisite randomised controlled trial assessing the effect of the Telehealth for Early Developmental Intervention in babies born very preterm (TEDI-Prem) programme on neurodevelopmental outcomes and parent well-being. *BMJ Open* 2024;14:e086904. doi:10.1136/bmjopen-2024–086904

This article has been corrected since it was published online. The authorship has been updated from "Abbey L Eeles, Alicia J Spittle, Stacey Dusing, Peter J Anderson, Shaaron Brown, Kim Dalziel, Susan M Fehring, Gillian Henty, Anne E Holland, Huang, Rod W Hunt, Elizabeth Kozaris, Katherine Lee, Angela T Morgan, Rachel Schembri, Karli Treyvaud" to "Abbey L Eeles, Stacey C Dusing, Peter J Anderson, Shaaron Brown, Kim Dalziel, Susan M Fehring, Gillian Henty, Anne E Holland, Li Huang, Rod W Hunt, Elizabeth Kozaris, Katherine J Lee, Angela Morgan, Rachel Schembri, Karli Treyvaud, Alicia J Spittle".

BMJ Open 2025;**15**:e086904corr1. doi:10.1136/bmjopen-2024-086904corr1