PROTOCOL

An online **P**arenting **I**ntervention to **P**revent affective disorders in high-risk **A**dolescents: The PIPA Trial

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This protocol has regard for current HRA guidance and content.

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CONTACT NAMES AND NUMBERS

Sponsor	**University of Warwick** Gibbet Hill Road Coventry CV4 7AL Email: sponsors@warwick.ac.uk	**Chief Investigator**	**Associate Professor Andrew Thompson** University of Warwick Coventry CV4 7AL Email: andrew.d.thompson@warwick.ac.uk
Senior Project Manager	**Emma Withers** Warwick Clinical Trials Unit University of Warwick Gibbet Hill Road Coventry CV4 7AL Tel: 02476574656 Fax: 02476151586 Email: emma.withers@warwick.ac.uk	**Trial Manager**	**Kerry Raynes** Warwick Clinical Trials Unit University of Warwick Gibbet Hill Road Coventry CV4 7AL Tel: 02476528046 Fax: 02476151586 Email: k.raynes@warwick.ac.uk
Co-Investigator & Senior Research Fellow	**Dr Charlotte Connor** Warwick Clinical Trials Unit University of Warwick Gibbet Hill Road Coventry CV4 7AL Tel: 02476575078 Fax: 02476151586 Email: charlotte.connor@warwick.ac.uk	**Research Associate**	**Nicole De Valliere** Warwick Clinical Trials Unit University of Warwick Gibbet Hill Road Coventry CV4 7AL Tel: 02476574316 Fax: 02476151586 Email: nicole.de-valliere@warwick.ac.uk
Co-Investigator & Trial Statistician	**Professor Jane Warwick** Warwick Clinical Trials Unit University of Warwick Gibbet Hill Road Coventry CV4 7AL Fax: 02476151586 Email: j.warwick@warwick.ac.uk	**Co-Investigator**	**Professor Maximillian Birchwood** Professor of Youth Mental Health Division of Mental Health and Wellbeing University of Warwick Gibbet Hill Road Coventry CV4 7AL Email: m.j.birchwood@warwick.ac.uk
Co-Investigator & Health Economist	**Professor Stavros Petrou** Professor of Health Economics Nuffield Department of Primary Health Care Sciences University of Oxford Radcliffe Observatory Quarter Woodstock Road Oxford OX2 6GG Email: stavros.petrou@phc.ox.ac.uk	**Health Economics Research Fellow**	**Kamran Khan** University of Warwick Gibbet Hill Road Coventry CV4 7AL Tel: 02476575078 Fax: 02476151586 Email: k.a.khan@warwick.ac.uk
Co-Investigator	**Dr Paul Patterson** Public Health Programme Lead Forward Thinking Birmingham Birmingham Children's Hospital First floor - 1 Printing House Street Birmingham B4 6NH Tel: 07393 001851 Email: paul.patterson2@nhs.net	**Co-Investigator**	**Professor Sarah Stewart-Brown** Professor of Public Health University of Warwick Gibbet Hill Road Coventry CV4 7AL Email: sarah.stewart-brown@warwick.ac.uk

Trial Statistician	**James Griffin** Statistician Warwick Clinical Trials Unit Gibbet Hill Road Coventry CV4 7AL Tel: 02476151347 Fax: 0247615186 Email: james.griffin@warwick.ac.uk

Specialist Collaborator	**Associate Professor Marie Yap** Monash University Wellington Road Clayton VIC 3800 Australia Email: marie.yap@monash.edu	**Specialist Collaborator**	**Associate Professor Glenn Melvin** Faculty of Medicine Nursing of Health Sciences Monash University Wellington Road Clayton VIC 3800 Australia Email: glenn.melvin@monash.edu
Trial Steering Committee	**Chair: Professor David Daley** Professor of Psychological Intervention and Behaviour Change University of Nottingham Jubilee Campus Wollaton Road Nottingham NG8 1BB Email: david.daley@nottingham.ac.uk	**Trial Steering Committee**	**Independent Member: Anna Robinson** New Start Programme Lead Birmingham Education Partnership The Arch Unit G4-G5 48-52 Floodgate Street Digbeth Birmingham B5 5SL Email: anna.robinson@bep.education
Trial Steering Committee	**Statistician: Dr Mona Kanaan** Department of Health Sciences University of York Seebohm Rowntree Building Heslington York YO10 5DD Email: mona.kanaan@york.ac.uk	**Trial Steering Committee**	**Health Economist: Dr Barbara Barrett** Health Economist King's College London Strand London WC2R 2LS Email: barbara.m.barrett@kcl.ac.uk
Trial Steering Committee	**Lay Member: Layne Boyden**		
Data Monitoring Committee	**Chair: Professor Cathy Creswell** Professor of Clinical Psychology Psychology Department University of Oxford Oxford OX2 6GG Email: cathy.creswell@psych.ox.ac.uk	**Data Monitoring Committee**	**Statistician: Dr Adam Brentnall** Centre for Cancer Prevention, Queen Mary University of London, Wolfson Institute of Preventive Medicine, Charterhouse Square, London, E1 4NS Email: a.brentnall@qmul.ac.uk
Data Monitoring Committee	**Independent Member: Sajda Butt** Parenting / Training Expert MHFA England & SB Training & Consultancy Email: sajdabutt@googlemail.com		

Quality Assurance	**Warwick Clinical Trials Unit** University of Warwick Gibbet Hill Road Coventry CV4 7AL Email: wctuqa@warwick.ac.uk

Core Trial Management Group	Professor Andrew Thompson Professor Jane Warwick Emma Withers Kerry Raynes Dr Charlotte Connor Nicole De Valliere James Griffin Professor Stavros Petrou Kamran Khan Professor Maximillian Birchwood	**Wider Trial Management Group**	Professor Andrew Thompson Professor Jane Warwick Emma Withers Kerry Raynes Dr Charlotte Connor Nicole De Valliere James Griffin Professor Stavros Petrou Kamran Khan Dr Marie Yap Professor Maximillian Birchwood Professor Sarah Stewart-Brown Dr Glenn Melvin Dr Paul Patterson

General Trial Enquiries	Warwick Clinical Trials Unit (WCTU) University of Warwick Gibbet Hill Road Coventry CV4 7AL Tel: 02476528046 Fax: 02476151586 Email: pipa@warwick.ac.uk

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TRIAL SUMMARY

Trial Title	*An online Parenting Intervention to Prevent affective disorders in high-risk Adolescents: The PIPA Trial*
Short title	*PIPA*
Clinical Phase	*Phase III*
Trial Design	*Prospective, parallel group intention-to-treat RCT with families randomised to the Partners in Parenting personalised programme or standard educational package (control) group in a 1:1 ratio.*
Trial Participants	*Parents of young people (aged 11-15 years at trial entry)* *(Parents include all carers, non-biological parents, grandparents, and legal guardians).* *Young people aged 11-15 at trial entry.*
Sample size	*433 family dyads*
Intervention Duration	*Up to 9 weeks*
Follow-up Duration	*15 months post-randomisation (approximately 12 months post-intervention)*
Trial Period	*From 1st March 2019 to 30th November 2022*
Recruitment Period	*8 months*
Objectives Primary	*To undertake a RCT to evaluate the effect of the personalised programme on parent-reported severity of depressive symptoms in young people at high-risk of developing affective disorders.*
Secondary	*To evaluate the effect of the personalised programme on parenting, parental self-efficacy and parental wellbeing in parents of young people at high-risk of developing affective disorders.* *To evaluate the effect of the personalised programme on severity of depressive symptoms, emotion regulation skills, anxiety symptoms, parent attachment, emotional and behavioural difficulties and incidence of depression in young people at high-risk of developing affective disorders.* *To evaluate the cost and cost-effectiveness of the personalised programme for prevention of affective disorders in young people at high-risk based on measures of their health utility, health related quality of life and resource use.* *To undertake a process evaluation to investigate program acceptability, uptake, barriers and potential mechanisms of effectiveness of the parenting intervention and their effects in specific populations, including ethnic heritage and socio-demographic profile.*

List of abbreviations/GLOSSARY

Abbreviation	**Explanation**
ARC	Applied Research Collaboration
BEP	Birmingham Education Partnership
BSREC	Biomedical & Scientific Research Ethics Committee
CAS-8	Children's Anxiety Scale-8 items
CHU-9D	Child Health Utility – 9 Dimensions
CI	Chief Investigator
CLAHRC	West Midlands Collaboration for Leadership in Applied Health Research
CONSORT	*Con*solidated *S*tandards *o*f *R*eporting *T*rials
CRF	Case Report Form
CTU	Clinical Trials Unit
DAWBA	Development and Well-Being Assessment
DERS-SF	Difficulties in Emotion Regulation Scale – Short Form
DMC	Data Monitoring Committee
eCRF	Electronic Case Report Form
EQ5D	European quality of Life - 5 Dimensions
GCP	Good Clinical Practice
ICER	Incremental cost-effectiveness ratio
IPA	Interpretive Phenomenological Analysis
IPPA	Inventory of Parent and Peer Attachment
ISRCTN	International Standard Randomised Controlled Trial Number
NIHR	National Institute for Health Research
PPI	Patient & Public Involvement
PIPA	Parenting Intervention to Prevent affective disorders in high-risk Adolescents
PR	Parent Reported
PRADAS	Parenting to Reduce Adolescent Depression and Anxiety Scale
PSES	Parenting Self-Efficacy Scale
QoL	Quality of Life
QALYS	Quality Adjusted Life Years
RCT	Randomised Controlled Trial
Rx	Randomisation
SDQ	Strengths and Difficulties Questionnaire
SMFQ	Short Mood and Feelings Questionnaire

SOP	Standard Operating Procedure
SR	Self-reported
SWEMWBS	Short Warwick-Edinburgh Mental Well-being Scale
TMG	Trial Management Group
TSC	Trial Steering Committee
UoW	University of Warwick
WCTU	Warwick Clinical Trials Unit
WP	Work Package
YP	Young Person

1. BACKGROUND

1.1 Epidemiology and burden of the condition

Depression in young people is a global public health problem (Whiteford, Ferrari, Degenhardt, Feigin, & Vos, 2015). In the UK, it is projected that annual total costs for depression will be over £10 billion by 2019, with costs highest in younger groups (McCrone, Dhanasiri, & Patel, 2008). An increasing focus on prevention is evident with policy documents, such as the Royal College of Psychiatrists "No Health Without Public Mental Health" and the "Five Year Forward View for Mental Health", advocating public mental health approaches especially with regard to children and young people (Royal College of Psychiatrists, 2010; The Mental Health Taskforce, 2016). A recent UK government green paper has also highlighted the importance of the prevention of mental health problems in Young People (Department of Education & Department of Health, 2017).

1.2 Existing knowledge

Roughly half of all lifetime mental disorders start by mid-teens and three-quarters by mid-20s (Kessler et al., 2007). Early onset depressive disorders, especially if untreated, tend to become chronic or relapsing, increase suicide risk, and lead to a wide range of psychosocial and vocational impairments (Last, Hansen, & Franco, 1997; Lawrence et al., 2015; Rao et al., 1995). Although intervention efforts for these disorders continue to progress, a large proportion of the burden of disease is still unable to be averted even with optimal treatment (Andrews, Issakidis, Sanderson, Corry, & Lapsley, 2004). Of particular concern is that even when depressive symptoms are sub threshold, young people may experience greater functional impairment, suicidality (Balázs et al., 2013) and an elevated risk of developing an affective disorder (Klein, Shankman, Lewinsohn, & Seeley, 2009; Shankman et al., 2009). As the incidence of depression rises sharply during adolescence, this is a particularly opportune time to target preventive efforts. Hence, there is an urgent need for an effective, integrated approach to prevent depression during this time (Patel, Flisher, Hetrick, & McGorry, 2007).

Strategic settings for targeting preventive interventions for youth depression include the family, school, media, and the internet. We focus here on the family setting, particularly with parents, for a variety of reasons. Firstly, parents, carers and families are extremely important in the lives of young people, particularly in terms of their emotional wellbeing and mental health. Various national surveys have found that parents are typically the main source of help-seeking for young people experiencing mental health difficulties (Jorm, Wright, & Morgan, 2007; Yap, Reavley, & Jorm, 2013). Secondly, parents are intrinsically motivated to take action for their child's well-being, and may possess the wisdom and life experience to help them appreciate the value of prevention (Cairns, Yap, Pilkington, & Jorm, 2014). Thirdly, most young people still live with their parents (or at least one parent) and this proximity affords parents the opportunities to notice significant changes in their child's mental health and behaviour. As argued by proponents of family process (Schleider & Weisz, 2017) and family system (Restifo & Bogels, 2009) models, this proximity underscores the importance of parents in the development and maintenance of youth internalising problems. Fourthly, international policies and action plans related to mental health have recognised the importance of upskilling parents for the goal of prevention and promotion of youth mental and emotional well-being (Department of Education & Department of Health, 2017; European Commission, 2014; National Prevention Council, 2011; The Commonwealth of Australia., 2009; World Health Organisation, 2013).

There is now robust evidence delineating risk and protective factors for depressive disorders in young people (Beesdo, Knappe, & Pine, 2009; Cairns et al., 2014). Importantly, some of these factors are within parents' control or influence, and are potentially modifiable (Sandler, Schoenfelder, Wolchik, & MacKinnon, 2011). These include factors that involve the family system (e.g. inter-parental conflict; Yap, Pilkington, Ryan, & Jorm, 2014), can be detected early by parents (e.g. behaviourally inhibited temperament; Beesdo

et al., 2009), or are directly socialised or modelled by parents (e.g. parental responses to child emotions; Schwartz et al., 2012). Specifically, our recent meta-analysis identified a sound evidence base for three protective parental factors (warmth, autonomy granting, and monitoring) and three risk factors for depression (inter-parental conflict, over-involvement, and aversiveness; Yap, Pilkington, Ryan, & Jorm, 2014). Other factors that do not yet have sufficient evidence demonstrating parental influence have also been endorsed by international experts as potentially modifiable by parents (e.g. healthy sleep, diet, and physical activity; Yap, Pilkington, Ryan, Kelly & Jorm, 2014). Hence, research on risk and protective factors underscores the important role parents can play in prevention. However, findings from a national survey of Australian parents revealed that parents' knowledge about what they can do to reduce their child's risk of depression is less than optimal (Yap & Jorm, 2011), highlighting a need to equip parents through more effective translation of evidence into preventive resources. More locally Birmingham Education Partnership NewStart programme also revealed the lack of resource available to engage with parents of young people around mental health problems.

1.2.1 Limitations of existing prevention programmes for depression in young people

There is now a plethora of preventive interventions for depression in young people, (largely psychological in nature). These are often directly *targeted towards young people themselves*, with evidence of continued efficacy at 12 months post-intervention (Merry et al., 2011). Due to often being implemented in schools, many of these programmes include a minimal parent component. Most are also limited to teaching parents the skills that the young people are being taught (Patel, Flisher, Hetrick, & McGorry, 2007; Stockings et al., 2016). Notably, many programmes fail to adequately address modifiable risk and protective parenting factors for depression in young people.

In contrast, our Australian collaborator Yap and colleagues demonstrated through a recent meta-analysis that preventive interventions targeting parents *primarily,* can produce lasting benefits for internalising, depression and anxiety outcomes in young people (Yap, et al., under review). The meta-analysis included RCTs of preventive parenting programmes only if parents received the *majority* of the intervention. Notably, they found remarkably long-term effects on anxiety in young people (up to 11 years post intervention) and depression (up to 5.5 years) symptoms and diagnoses. Moreover, although very few RCTs assessed long-term diagnostic outcomes, pooled effects for anxiety diagnoses indicated a promising number-needed-to-treat (NNT) of 10, and for depression diagnoses the NNT (albeit marginally significant) was 11; these are similar to the NNT for the prevention of cases of depression using programmes targeting young people directly, at short-term follow-up (NNT=11; Merry et al., 2011). Preventive parenting interventions can be *universal* (i.e. delivered to all parents regardless of risk); *selective* (targeting parents whose children have known risk factors); or *indicated* (targeting parents whose children show signs or symptoms of emerging disorders; Mrazek & Haggerty, 1994). In Yap and colleagues' review (Yap, et al., under review), there was no evidence that type of prevention (universal, selective, or indicated) moderated intervention effects. However, most programmes (47 out of 50) were designed for parents of *pre-adolescent children*; only 3 (with mixed evidence) were appropriate for parents of young people aged 12 and over. Moreover, most existing parenting programmes are *limited in their public health benefit* because they involve trained professionals and are expensive to disseminate widely in the community. Finally, many programmes are not well-used even when available due to various barriers, e.g. scheduling difficulties, privacy concerns (Heinrichs, Bertram, Kuschel, & Hahlweg, 2005). Hence, there is a largely untapped potential of preventive programmes for parents of *young people*.

1.2.2 Potential of a web-based parenting intervention

With the increasing reach of the internet, the use of web-based media has been recommended as one key way to increase participation rates in preventive interventions (Cuijpers, van Straten, Warmerdam, & van Rooy, 2010). For example, in the UK in 2017, 98% of households with young people had internet access (Statistical Bulletin, 2017). The internet has become a popular source of information on parenting and

young people's mental health amongst parents (Lawrence et al., 2015; Metzler, Sanders, Rusby, & Crowley, 2012), and a recent survey has confirmed that tailored online parenting programmes for parents of young people are viewed favourably (Yap, Martin, & Jorm, 2017). However, based on Yap and colleagues' recent systematic review (Yap, et al., under review) and a search of major clinical trial registries, *there is currently no widely-accessible, tailored web-based parenting intervention to prevent depression in young people.* Yet, web-based interventions may hold great promise because they have the potential to overcome the aforementioned barriers inherent in existing face-to-face programmes, due to their anonymity, flexibility and accessibility; Implementation fidelity may also be enhanced by computerised delivery (Andrews, Cuijpers, Craske, McEvoy, & Titov, 2010). Online interventions have now demonstrated effectiveness (Andrews et al., 2010) and cost-effectiveness (Donker et al., 2015) for treating depression. Promising evidence is also emerging for online prevention programmes targeting young people directly (Calear & Christensen, 2010), as well as parents of younger children (Love et al., 2016; Morgan et al., 2017). Whilst the potential efficacy of web-based prevention programmes that target parents of young people remains largely unknown, such programmes would comprise a promising public health approach to preventing depression in young people that is potentially lower in cost per individual than existing programmes (Lee et al., 2016).

An important limitation of existing preventive interventions for internalising disorders in young people is that they typically focus on a limited number of parenting risk or protective factors for depression in young people (Restifo & Bogels, 2009; Schleider & Weisz, 2016; Yap et al., 2016). This narrow-focus means that programmes may not adequately address the full range of modifiable parenting factors for depression in young people and their relevance for individual families. The capacity of digital technology to automatically tailor a web-based intervention for individual users offers a potential solution to this limitation. Automated tailoring is beneficial when it involves screening each parent across all evidence-based risk and protective factors. This tailoring can therefore ensure a more thorough coverage of areas that may be important to target in the intervention. In doing so, the programme has greater breadth without imposing unnecessary burden on parents (due to the inclusion of less-relevant topics). Importantly, a tailored web-based intervention provides some personalisation of the programme for the parent without requiring the costly involvement of trained professionals, hence increasing the intervention's perceived relevance (Kreuter, Farrell, Olevitch, & Brennan, 2000), effectiveness (Wildeboer, Kelders, & van Gemert-Pijnen, 2016), and potential for scalability and sustainability (Kreuter et al., 2000).

To fill this critical gap in preventing depression in young people, our Australian collaborators developed a new web-based parenting programme that is individually tailored to need. Individual parents are assessed in nine modifiable parental domains, previously endorsed by research evidence (Yap, Pilkington, Ryan, & Jorm, 2014) and international experts (Yap, Pilkington, Ryan, Kelly, & Jorm, 2014),to identify specific risk or protective factors and tailor the programme. In their RCT with 359 family dyads, they found greater improvement in parenting in the personalised programme group (Cohen's d=0.51), compared to an active-control. Among young people with elevated depressive symptoms at baseline (n=105), the personalised programme group showed greater symptom reduction.

1.3 Need for a trial

The trial aims to adapt the Partners in Parenting website and resources and test whether the personalised programme prevents depression in young people. The programme was extensively piloted and found to be effective in Australia, as outlined in section 1.2. There is clear political imperative to improve young people's mental health with an emphasis on prevention, but there are few scalable evidence-based preventive approaches. The recent UK government green paper "Transforming Children and Young People's Mental Health Provision" specifically cites early intervention strategies. "This guidance will recommend that local authorities commission parenting programmes for which there is a good evidence

base" (Department of Education & Department of Health, 2017). We feel, therefore, it is propitious to thoroughly test an intervention that has proven effective in Australia, in a UK setting using robust RCT methodology.

1.4 Ethical considerations

The trial will be conducted in full conformance with the principles of the Declaration of Helsinki and Good Clinical Practice (GCP) guidelines. It will also comply with all applicable UK legislation and Warwick Standard Operating Procedures (SOPs). All data will be stored securely and held in accordance with Data Protection Act 2018 and the General Data Protection Regulation.

There are potential ethical issues regarding unintended consequences. There is a potential risk that identifying a young person at risk due to scoring high on the screening tool may cause them and/or their parents distress. There is previous literature to suggest this is unlikely in this population (Gould, et al., 2005; Jorm, Kelly, & Morgan, 2007). Nonetheless, we will continually monitor for signs of distress in the young person/parent that is likely to be associated with screening, identification or participation in the trial. Formal monitoring of all data will be done monthly through the management group and six-monthly through the trial steering and data monitoring committees. The trial's Senior Research Fellow and Research Associate will be available to respond to any concerns raised by participants throughout the trial.

Other ethical issues are those of consent and data protection. Electronic informed consent from parents will be necessary as the young people will all be under the age of 16 years. Electronic assent will also be obtained from the young person themselves at the start of the trial. Parents/young people will be informed that, even once consented, they will be able to withdraw from the trial at any point and given clear instructions on how to do so. Full ethical approval will be applied for through the University of Warwick Biomedical and Scientific Research Ethics Committee (BSREC).

Plain English will be used in all communication with young people and their families in order to normalise the outcome of the screening and facilitate opportunities for participants to discuss any concerns with the research team.

1.5 CONSORT

The trial will be reported in line with the CONSORT (*Con*solidated *S*tandards *o*f *R*eporting *T*rials) statement (Moher, Schulz, & Altman, 2001).

2. TRIAL DESIGN

2.1 Trial summary and flow diagram

The PIPA trial is a two-arm, randomised controlled trial to modify the Partners in Parenting website and resources to a UK context and assess whether the personalised programme reduces the risk of affective disorders in young people at high risk. Families will be randomised 1:1 between the personalised programme and standard educational package.

The trial will have three linked work packages (WPs):

WP1: Adaptation of the Australian Partners in Parenting website and resources (personalised programme and standard educational package) for a UK sample based on focus groups of parents, young people and teachers (stakeholders).
WP2: An internal pilot randomised controlled trial (RCT) of the UK versions of the personalised programme versus standard educational package with *a priori* stop-go progression criteria (Avery et al., 2017).
WP3: A definitive RCT and economic evaluation of the UK versions of personalised programme versus standard educational package over the 15-month post-randomisation period, which will continue seamlessly from the internal pilot, if progression criteria are met.

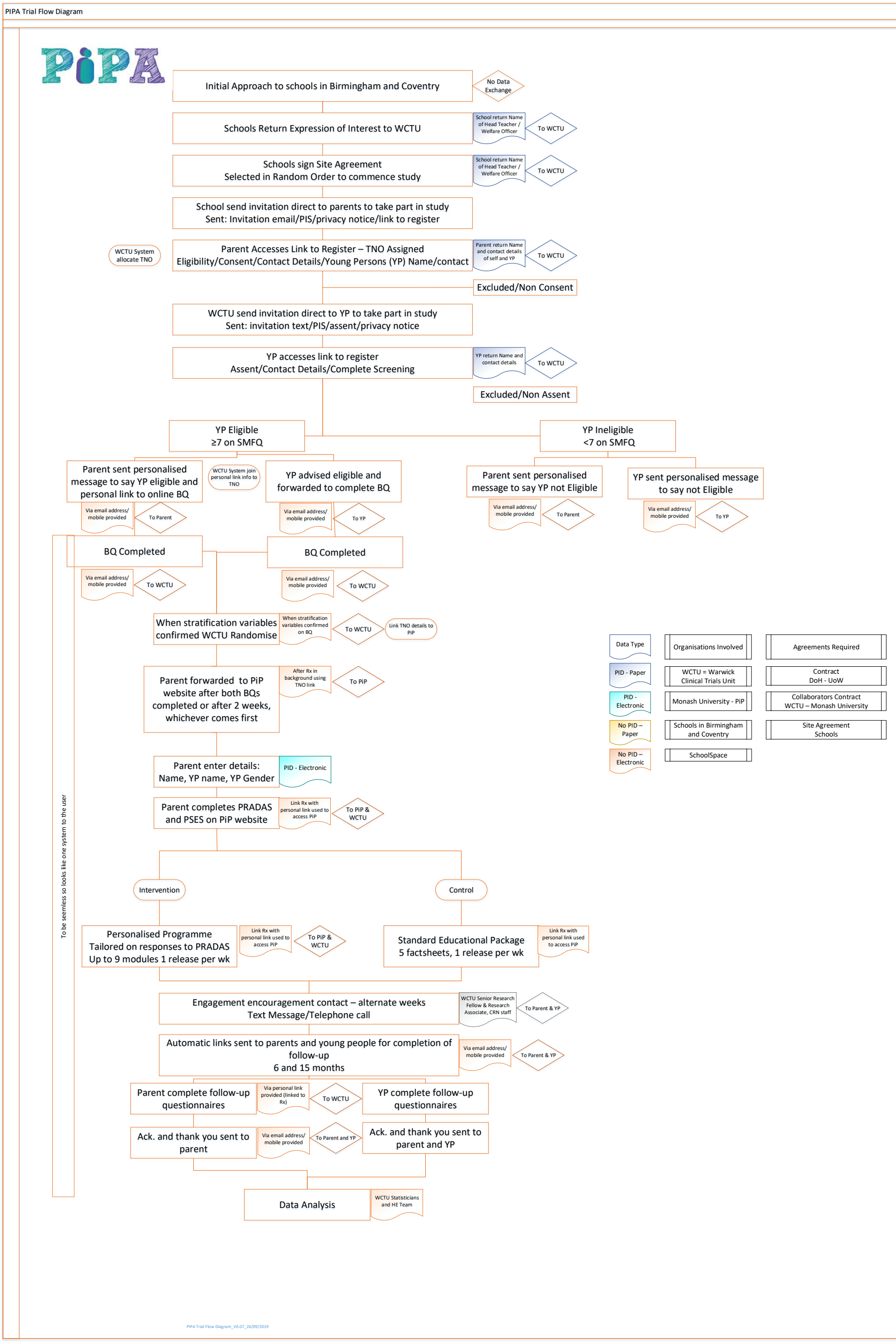

Figure 1 Trial Flow Diagram

2.2 Aims and objectives

2.2.1 Primary objective

To evaluate the effect of the personalised programme on parent-reported severity of depressive symptoms in young people at high-risk of developing affective disorders.

2.2.2 Secondary objectives

To evaluate the effect of the personalised programme on parenting, parental self-efficacy, parental wellbeing, quality of life and attachment in parents of young people at high-risk of developing affective disorders.

To evaluate the effect of the personalised programme on self-reported severity of depressive symptoms, emotion regulation skills, anxiety symptoms, attachment, emotional and behavioural difficulties, quality of life and incidence of depression in young people at high-risk of developing affective disorders.

To evaluate the cost and cost-effectiveness of the personalised programme for prevention of affective disorders in young people at high-risk.

2.3 Outcome measures

2.3.1 Primary outcome

- The primary outcome will be change in parent-reported depressive symptoms (SMFQ-PR score) between entry to the trial and 15 months post-randomisation.

2.3.2 Secondary outcomes

- Change in young people's self-reported depressive symptoms (SMFQ SR score) between entry to the trial and 15 months post-randomisation.
- Change in parenting behaviour (PRADAS score) between entry to the trial and 15 months post-randomisation.
- Change in parenting self-efficacy (PSES score) between entry to the trial and 15 months post-randomisation.
- Change in young people's resilience (DERS-SF score) between entry to the trial and 15 months post-randomisation.
- Change in mental wellbeing of parents (SWEMWBS score) between entry to the trial and 15 months post-randomisation.
- Change in young people's anxiety (CAS-8 score) between entry to the trial and 15 months post-randomisation.
- Change in young people's parent-reported emotional and behavioural difficulties (SDQ PR score) between entry to the trial and 15 months post-randomisation.
- Change in young people's self-reported emotional and behavioural difficulties (SDQ SR score) between entry to the trial and 15 months post-randomisation.

- Change in parent-reported parent attachment (IPPA PR) between entry to the trial and 15 months post-randomisation.
- Change in self-reported parent attachment (IPPA SR) between entry to the trial and 15 months post-randomisation.
- Change in number of cases of depression (depression component of the DAWBA) between entry to the trial and 15 months post-randomisation.
- Change in health-related quality of life as measured by Childhood Health Utility (CHU-9D), EQ-5D-5L, EQ-5D-5L-Y and EQ-5D-5L-Y proxy between entry to the trial and 15 months post-randomisation.
- Difference in quality adjusted life years (QALYs) derived from the health-related quality of life measures between entry to the trial and 15 months post-randomisation.
- Broader resource utilisation via participant online questionnaires will be used to calculate costs incurred between entry to the trial and 15 months post-randomisation.
- Cost-effectiveness results will be expressed in terms of the incremental cost-effectiveness ratio (ICER) and calculated as the difference in mean costs divided by the difference in mean QALYs between the trial comparators.

Further details of the trial scales to be used to assess outcomes are given in section 3.1.

2.4 Eligibility criteria

Families are eligible to be included in the trial if they meet the following criteria:

2.4.1 Inclusion criteria

Parent

1. Age ≥ 18 years
2. Provision of informed consent. Parents may include carers, non-biological parents, grandparents, and legal guardians.
3. Sufficient literacy levels to understand and engage with content delivered visually in English.
4. Has access to the internet and a personal email account (for email communication) and mobile phone number (phone and text messaging communication).

Young person

1. Age 11-15 years.
2. Attending a school taking part in the trial.

3. Parent has given written informed consent to participate in the trial.
4. Confirmed assent to participate in the trial.
5. Has a reading age of 11+ years.
6. Scoring 7 or above on the SMFQ.
7. Has access to a mobile phone for text messaging communication and the internet for questionnaire completion.
8. Lives with their participating parent.

2.4.2 Exclusion criteria

1. Parents being unable to access the PIPA database and the Partners in Parenting website.
2. Previous failed screening or randomisation in the present trial.
3. Participation in a parenting intervention in the last 90 days.
4. Parent and/or young person already taking part or have previously taken part in the PIPA trial from the household you wish to join from.

Participants will be confirming their own eligibility for the trial, with some data checks conducted by the WCTU trial team.

2.5 Sampling Frame

Recruitment of schools
We will approach secondary schools in Coventry and Birmingham. Should take up be less than 55%, we will broaden the net to include secondary schools in the surrounding areas (other areas of the West Midlands, Worcestershire, Staffordshire, etc.).

Recruitment of young people and their parents
Recruited schools will distribute information to all parents of young people in Years 7-10 (aged 11-15 years at trial entry), explaining the trial and inviting participation. Parents interested in participating in the trial will be asked to register for the trial and provide consent for their own and their child's participation on the dedicated trial database. We will ask them to provide the best contact details for their child.

All students in Years 7-10 with parental consent will be approached for assent and will then be asked to complete an initial screen using the SMFQ (Angold, Costello, & Messer, 1995). Screening will be done at a time deemed suitable by the individuals, online via the PIPA trial database. Information to aid participants to complete the screening will be included alongside a help number for any technical issues. Screening data will only be accessible by the research team using assigned logins and passwords. This will allow the research team to view the status of screening sessions. Data will be saved in encrypted files and, following closure of screening, will be held securely by the PIPA trial research team. All data will be treated in confidence and will not be disclosed or used for any unrelated purposes (except by prior agreement with the participant or to address specified risks to the participant, researcher or others). If the PIPA trial research team become concerned about the safety of a young person participating in the trial they will inform the parent or relevant authorities.

Young people who score 7 or above on the SMFQ will then be invited, via an automated message, to participate in the RCT with their nominated parent. Based on SMFQ data collected from a large UK population sample, we expect about 20% of students to score in this range. Families of young people

scoring below 7 on the SMFQ, expected to represent about 80% of the pre-screened sample, will not be part of the RCT. These families will receive a message, generated automatically, to inform them that they are not eligible.

A recruitment strategy for schools is attached as an appendix (see Appendix 1).

2.6 Informed Consent

Informed consent will be obtained remotely from the participating parents and assent obtained from the young person prior to completing the screening questionnaire.

2.7 Allocation to trial arm and withdrawals

Once consent has been received from the parent and assent from the young person, the young person will complete screening for the trial. Screened positive families will be sent links to baseline assessments and will be allocated to a trial arm using a fully automated minimisation procedure within the dedicated PIPA trial database, produced by WCTU. Allocation will be in 1:1 ratio between intervention (personalised programme) or active-control (standard educational package) condition. If the family are eligible the parent/carer will be directed to Partners in Parenting Website to complete the Parenting to Reduce Adolescent Depression and Anxiety Scale (PRADAS) scale and Parenting Self-Efficacy Scale (PSES) and then forwarded to the appropriate part of the Partners in Parenting website (either personalised programme or standard educational package) once their baseline assessments have been completed. Young participants will not be told their parent's allocation, but may be able to infer this based on any resulting changes to parenting. The minimisation procedure will have a random element and ensure balance of age group, school, gender of young person, gender of primary parent and number of parents participating between the trial arms. Multiple parents will be encouraged to participate but only one will self-select to complete all of the trial outcome measures. Screened negative families will receive an automated message upon completion of the trial screening.

Participants may withdraw from the trial interventions and/or the trial at any time without prejudice. Unless a participant explicitly withdraws their consent, they will be followed-up wherever possible and data collected as per the protocol until the end of the trial. Should a participant decide to withdraw, a withdrawal form will be completed by the PIPA trial team, with the option for participants to volunteer a reason as to why they wish to leave the trial. All data up to the point of withdrawal will be kept by the trial team unless a participant requests otherwise in which case the team will delete what is possible to be deleted.

If a parent chooses to withdraw, they can either withdraw from the intervention or withdraw from the trial completely. If the parent chooses to withdraw completely, this will also withdraw the young person. The young person will be notified if the parent chooses to withdraw completely.

If a young person chooses to withdraw, they can either withdraw from completing questionnaires or withdraw from the trial completely. If the young person chooses to withdraw completely, this will also withdraw the parent. The parent will be notified if the young person chooses to withdraw completely.

2.8 Trial interventions

2.8.1 Trial interventions

The project has three linked work packages (WPs).

2.8.1.1 **WP1 (Months 1-18): Adaptation of Partners in Parenting website and resources (personalised programme and standard education package) to UK context**

WP1 will be the adaptation phase of the Partners in Parenting website and resources including the (personalised programme, which was co-designed with Australian parents and young people and has been the subject of an RCT in Australia (Yap, et al., 2017)). We will recruit six focus groups of teachers, parents, and young people from diverse ethnic and sociodemographic backgrounds. Teachers and parents will be given access to the original (Australian version) of the personalised programme for review and they will work with the team to make changes to language used (e.g. idioms), and any other minor adaptations to improve accessibility and engagement, taking into account diversity issues. We will subsequently ask parents to beta test the adapted (new UK) version including feedback on usability issues of the Partners in Parenting website and accessing the materials on various platforms (tablet and phone). We plan to adapt the Partners in Parenting website to allow parents to access resources using a variety of technologies. Parents will also review the standard educational package that will be offered to the control group, to ensure its relevance in the UK context. At the end of WP1, we will have adapted the Partners in Parenting website and resources for use in the PIPA trial.

2.8.1.2 **WP2 (Month 19-22): Internal Pilot**

We will conduct a four month internal pilot of the definitive RCT protocol, to establish the feasibility of the full PIPA trial. The trial protocol is detailed in WP3 below.
The progression criteria to the full trial will be set *a priori* and take place four months from trial commencement and are based on recruitment, retention and adherence (please see section 6.4).

2.8.1.3 **WP3 (Month 23-45): Definitive RCT**

i). Intervention group: The Partners in Parenting personalised programme

The personalised programme aims to increase parental protective factors and decrease parental risk factors associated with depression in young people. The change in parenting factors (proximal outcome and direct target of the intervention) increases resilience in young people (specifically, their emotion regulation skills) and in turn reduces the risk for affective disorders in young people in the longer-term (Sandler, Ingram, Wolchik, Tein, & Winslow, 2015; Sandler, Schoenfelder, Wolchik, & MacKinnon, 2011). Improved parenting skills are expected to increase parents' sense of efficacy about their parenting, which will in turn maintain their positive parenting skills (Glatz & Buchanan, 2015). See **logic model figure** below:

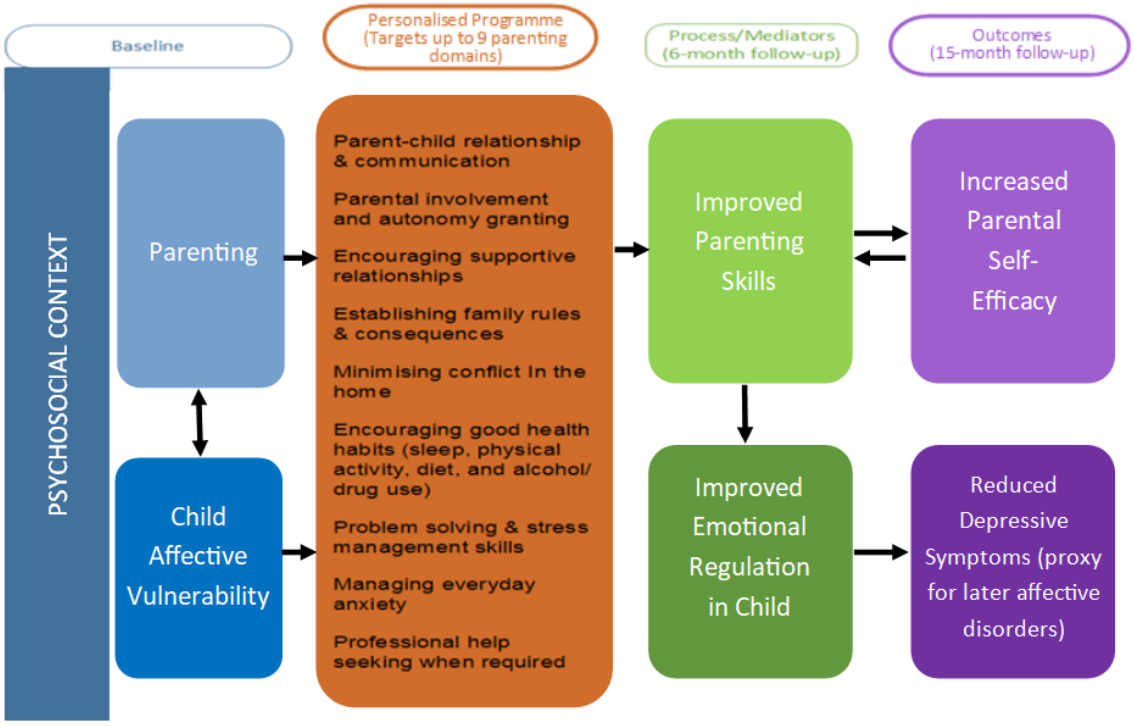

Figure 2: The PIPA trial logic model.

The personalised programme assesses each parent in up to nine modifiable parental domains that have been endorsed by research evidence (Yap, Pilkington, Ryan, & Jorm, 2014) and international experts (Yap, Pilkington, Ryan, Kelly, & Jorm, 2014) as important risk or protective factors, in order to identify the areas of parenting requiring improvement. The programme is then automatically personalised to each parent, ensuring that all areas for improvement (i.e. all risk and protective factors relevant to that parent) are targeted. The personalised programme comprises two individually tailored components:

> **(1)** An automated feedback report highlighting areas of strength and how parents can improve, will be provided immediately after parents complete an online measure assessing their current parenting practices (Cardamone-Breen, Jorm, Lawrence, Mackinnon, & Yap, 2017);
> **(2)** An interactive programme comprising up to nine modules, with a different combination of modules specifically recommended for each parent based on identified areas for improvement (Yap, et al., 2017).

After receiving their recommended modules, parents can further personalise their programme by deselecting recommended modules and/or selecting additional modules. They then confirm their selection and commence their personalised programme.

The nine modules cover the nine parenting domains derived from the evidence-based (Yap, Pilkington, Ryan, & Jorm, 2014) and international expert-endorsed (Yap, Pilkington, Ryan, Kelly, & Jorm, 2014) parenting guidelines developed by our Australian collaborators, titled *How to prevent depression and anxiety in your teenager: Strategies for parents* (Parenting Strategies Program, 2013). When parents log in to their personalised dashboard on the Partners in Parenting website, they see their modules and any goals

they have set, as well as their progress. Modules include illustrations, audio clips, vignettes, goal-setting exercises, and an end-of-module quiz with immediate feedback to consolidate learning. Module topics are shown in the logic model (Figure 1). Each module takes 15-20 minutes to complete, and one module per week is unlocked for parents, in a set order. Follow-up questionnaires will be completed at six and 15 months post-randomisation.

The personalised programme was designed to fulfil the principles of the evidence-based Persuasive Systems Design (Oinas-Kukkonen & Harjumaa, 2009) model (using technology to influence behaviour change), which was found in a recent meta-analysis to be associated with greater programme adherence (Kelders, Kok, Ossebaard, & Van Gemert-Pijnen, 2012). These principles include tailoring (e.g. feedback messages and module recommendations are tailored to each parent's strengths and weaknesses); personalisation (e.g. all communications are personalised to the parent); and self-monitoring (e.g. parents monitor their weekly goals on a personalised dashboard). The personalised programme is designed to be completed online, wherever it is convenient for the parent.

ii) Control group: The Partners in Parenting standard educational package

Parents in the control arm will be provided with a standardised package of online educational materials about development of young people and wellbeing. Each week for five weeks, parents will receive an automated email inviting them to access their factsheet for that week (to match the expected mean number of modules received by the intervention group). To mirror the experience of intervention group parents accessing each module on the trial website, control group parents will access each factsheet by logging in to their personalised dashboard. The factsheets provide general information to parents (without tailored, actionable strategies) and are designed to represent a selection of resources that are available to parents as part of the current UK health promotion approach for wellbeing of young people. The materials will be adapted from highly credible existing resources such as that provided on the Raising Children Network website (Raising Children Network). Minor adaptations will be made to the language (e.g. idioms) following consultations with focus group parents as part of WP1. The topics of the five factsheets are as follows: 1) Teen development: An overview; 2) The teenager's developing brain; 3) The teenager's changing body; 4) Resilience; and 5) Happy teenagers and teenage wellbeing. We have chosen to use an active control in order to engage parents and to aid retention in their allocated group for the duration of the trial. Follow-up questionnaires will be completed at six and 15 months post-randomisation.

Both the personalised programme and standard educational package will be delivered automatically by the Partners in Parenting website.

iii) Adherence: All RCT parent participants will receive fortnightly check-in calls from a research staff member while they are completing their allocated programme (intervention or control) to encourage adherence with the interventions. Research staff will be trained to make these calls following a standard script (i.e. a standard list of questions and prompts). In the alternating weeks when parents do not receive a check-in call, they will receive reminder text/email messages, to maintain the personal support and accountability. The aims of these contact attempts are to address any trial-related questions that arise, encourage parents to progress through their allocated intervention each week until completion, and enhance intervention adherence. Participants may withdraw from receiving these phone calls if they wish. If a participant is not engaging with the intervention, the trial team will pause the phone calls after four weeks of trying to make contact and only restart if the parent continues with their intervention in the three months following randomisation.
Based on research evidence that participant incentives can increase rate of completion of research assessments (Morgan, Rapee, & Bayer, 2017), we will be reimbursing parents and young people for completion of the baseline and both follow-up assessments. This will be a family payment of £25 and will be in acknowledgement of time commitments required to complete research assessments and does not

provide an excessive incentive. This will be in the form of a voucher. For follow-up, please see section 3.1.

2.8.2 Compliance/contamination

Participants will only have access to their randomised intervention. Participants will be allocated personal usernames and logins, enabling access only to the appropriate resources. The number of modules completed (relative to those selected), when these were completed and the time taken to complete the modules will be recorded. This information will provide information on the level of completion and adherence to selected modules at the end of the trial. Participants completing 2/3 of their selected modules will be considered compliant. These will vary as they are based on individual need, which is determined by their responses to the baseline PRADAS questionnaire, as well as their personal preferences in selecting which modules to lock into their personalised programme. The number of factsheets accessed will be recorded to evaluate the level of completion.

2.9 Process Evaluation

We will employ process evaluation at different stages throughout the trial to ensure we have a clear understanding of participation and trial functioning at each stage. Recruitment of sufficient eligible participants and engagement with the trial are clearly priorities for success of any intervention trial and we will monitor recruitment iteratively at every stage of the trial.

Additionally at adaptation stage (WP1) we will examine:

- Recording of any adaptations necessary to language and idioms within the Partners in Parenting website resources to ensure they are appropriate to the local population and ensure our recruitment materials and promotional information materials reflect these adaptations.

At pilot stage (WP2) we will consider:

- Recruitment patterns; including reasons for non-participation. All potential participants will be asked to complete a consent/assent form which will be automatically received electronically by the PIPA trial team. The consent form will include an option to document why potential participants do not wish to enter the trial. This in turn would allow us to address modifiable barriers to engagement. These consent forms will be held electronically at WCTU, following WCTU Data Management and Security SOPs.

At full trial stage (WP3):

- Groups of parents and school staff will be invited to attend separate focus groups to aid the trial team in evaluating the effectiveness of the trial and intervention and gain insight into coordination of the trial and further implementation of the programme. Topics will be generalised and findings from the focus groups will form the structure of the interviews with family dyads. The focus groups will be recorded and transcribed. These will be analysed by researchers trained in focus groups implementation.
- All parents will complete a predesigned satisfaction and acceptability question at the completion of the intervention and the trial.
- We also plan to recruit approximately 30 family dyads (from both the control and intervention groups) to complete a 30-minute interview to determine the effectiveness of the parenting intervention they were offered and its effects on specific populations, including ethnic heritage and socio-demographic profile at 4-months post-randomisation. Findings from the focus groups will inform a topic guide to investigate individual experience of the intervention and trial, suitability and acceptability of the intervention, its effectiveness and perceived changes in behaviours based on the intervention content. We will purposively sample from parents who both fully engaged with the personalised programme or the standard education package and also those who were less engaged (based on the number of recommended modules completed). Open-ended interviews will be recorded and transcribed by researchers trained in qualitative interviewing and analysis and will be guided by a standard Customer Satisfaction Survey utilising

a Likert type scale (Excellent, Very Good, Good, Fair, Poor), with clearly worded questions (e.g. How did you rate the support you received before, during and after the Intervention? How confident are you that the Intervention will help reduce risk of depression in your son/daughter?"; "How confident would you be in recommending the Intervention to others who are dealing with the same things as you and your family?"). The questions focus directly on experience, suitability, acceptability and effectiveness of the intervention and resilience in young people. Interviews will also provide options for further comments by interviewees, providing a rich source of qualitative data to inform the process evaluation.

Qualitative analysis of transcripts will be conducted using Framework analysis methodology, a well-used deductive qualitative method designed for large data sets and research that is applied or policy driven. This methodology is ideally suited to studies such as ours, which has pre-set aims and objectives (acceptability, suitability and effectiveness) and is recommended for studies in which qualitative interviews are conducted by a team of several researchers. Analysis will identify key ideas and emergent themes, develop a thematic framework and index significant themes, including disconfirming evidence, with regard to the acceptability, suitability and effectiveness of the interventions. In addition, we will implement a series of small focus groups with parents and school staff to capture process evaluation information on contextual issues, implementation processes and mechanisms of change. These will be analysed employing Interpretive Phenomenological Analysis (IPA) to amplify understanding of the wider utility and impact of the trial in an iterative fashion.

Data from the Partners in Parenting website will be obtained detailing which modules are recommended, selected and completed, the time and date each module is completed, which goals are completed within the modules and answers to quiz questions throughout the intervention period. The number of times parents access each module will also be collected.

2.10 Blinding

2.10.1 Methods for ensuring blinding

Allocation concealment will be maintained by using Warwick CTU's centralised randomisation service. All stratification data will be collected prior to participants being randomised.

This trial is entirely delivered online and no intervention will be delivered by the researchers. Once they have started their intervention, the participants are of course aware of their allocation. We will request that parents and young people in the trial do not discuss the Partners in Parenting website content with other parents or students at the schools or more widely through parenting networks until the end of the intervention. All outcomes are self-reported, by the parents and/or young people participating in the trial.

The core TMG, comprising of the Chief Investigator, Statistician, Senior Research Fellow, Research Associate, Health Economist, Senior Project Manager and Trial Manager, will not be blinded to the allocations. The DMC will have access to unblinded, aggregate, comparative data. All other investigators will be blinded to the allocations.

2.10.2 Unblinding the trial

Intervention codes will not be broken for the planned analyses of data until all decisions on the evaluability of the data from each individual participant have been made and documented.

2.11 End of trial

The end of the trial is defined as the end of the grant and will be 30th November 2022.

The trial will be stopped prematurely if;

- Mandated by the Ethics Committee
- Following recommendations from the Data Monitoring Committee (DMC)
- The pre-determined stop go criteria set for the pilot phase of the trial are not met
- Funding for the trial ceases

The sponsor and CI reserve the right to terminate the research on safety grounds at any time. Before terminating the research, the sponsor and investigators will ensure that a review of the overall benefit-risk analysis confirms the balance to be no longer acceptable. Should termination be necessary, both parties will arrange the relevant procedures which include informing the Biomedical and Scientific Research Ethics Committee. On termination of the research, the sponsor and investigators will ensure that adequate consideration is given to the protection of enrolled participants' interests.

The Biomedical and Scientific Research Ethics Committee will be notified in writing when the trial has been concluded.

3. METHODS AND ASSESSMENTS

3.1 Trial scales

Anacronym	Brief description
SMFQ PR	*Short Mood and Feelings Questionnaire (SMFQ; Angold, Costello, & Messer, 1995), (parent report). To measure parent-reported depressive symptoms in adolescents.*
SMFQ SR	Short Mood and Feelings Questionnaire (SMFQ), (young person report). To measure depressive symptoms assessed by self-report of young people.
PRADAS	*Parenting to Reduce Adolescent Depression and Anxiety Scale (PRADAS; Cardamone-Breen, Jorm, Lawrence, Mackinnon, & Yap, 2017) developed and validated by the intervention developers in Australia. To evaluate parenting behaviour.*
PSES	*Parenting Self-Efficacy Scale (PSES; Nicolas, Jorm , Cardamone-Breen, Lawrence & Yap, 2019), developed and validated by the intervention developers in Australia. To measure parental self-efficacy.*

DERS-SF	*Difficulties in Emotion Regulation Scale – short form (DERS-SF; Kaufman, et al., 2015), (young person-report). To measure resilience of young people.*
SWEMWBS	*Short Warwick Edinburgh Mental Wellbeing Scale (short WEMWBS; Clarke et al., 2011; Tennant et al., 2007), (parent). To measure mental wellbeing of parents.*
CAS-8	*Children's Anxiety Scale – 8 items (CAS-8; Spence et al., 2014) (young person-report). To measures anxiety in young people.*
SDQ PR; SDQ SR	*Strength and Difficulties Questionnaire (SDQ; Goodman, 1997; Goodman, Meltzer, & Bailey, 1998) (parent and young person report). To assess emotional and behavioural difficulties of young people.*
IPPA PR; IPPA SR	*Inventory of Parent and Peer Attachment (IPPA; McElhaney et al., 2008; JP Allen, pers. comm., 2013) (parent and young person completed).* To assess attachment of young people to parents and peers.
DAWBA	*Development and Well-Being Assessment depression component (DAWBA; Last, Henley, Norman, Goodman, & Ford, 2014). To identify likely cases of adolescent depression.*
CHU-9D; EQ-5D-5L-Y; EQ-5D-5L; EQ-5D-5L-Y proxy	*Preference based Health-related quality of life measures in the young person (Child Health Utility-9D; CHU-9D; Stevens, 2009; Stevens, 2010), EQ-5D-5L-Y; (Ravens-Sieberer et al., 2010) and parent (EQ-5D-5L and EQ-5D-5L-Y proxy; (Herdman et al., 2011).*

3.2 Schedule of delivery of intervention and data collection

Table 1. Assessments and time points for participants.

Assessment	**1**		**2**		**3**	
Assessment Window	**Baseline**		**6 month**		**15 month (approx. 12 months post intervention completion)**	
	P/C	**YP**	**P/C**	**YP**	**P/C**	**YP**
Pre-entry into trial						
Participant details	✓					
Inclusion/exclusion criteria	✓					

Assessment	1		2		3	
Assessment Window	**Baseline**		**6 month**		**15 month (approx. 12 months post intervention completion)**	
	P/C	**YP**	**P/C**	**YP**	**P/C**	**YP**
Informed consent	✓					
Assent		✓				
Screening		✓*				
Background & Medical History	✓					
SMFQ	✓	✓*	✓	✓	✓	✓
PRADAS	✓		✓		✓	
IPPA	✓	✓	✓	✓	✓	✓
PSES	✓		✓		✓	
DERS-SF		✓		✓		✓
Short WEMWBS	✓		✓		✓	
CAS-8		✓		✓		✓
SDQ	✓	✓	✓	✓	✓	✓
DAWBA		✓				✓
CHU-9D		✓		✓		✓
EQ5D-5L-Y		✓		✓		✓
EQ5D-5L	✓		✓		✓	
EQ5D-5L-Y proxy	✓		✓		✓	
Client service receipt inventory	✓		✓		✓	
Intervention satisfaction survey			✓		✓	

**SMFQ at baseline will be collected during screening for young person*

4. DUTY OF CARE

Any member of the PIPA research team to whom information is disclosed that raises concerns about the safety and wellbeing of a participant has a duty to report this to appropriate members of the study team. If appropriate study team members are unavailable then confidential advice may be sought from any suitably qualified clinician within Warwick CTU (for example, GP, physician, clinical psychologist). Participants scoring particularly high scores on the SMFQ scale and provide certain answers on the DAWBA will also raise concerns and trigger an automated alert to be sent to appropriate members of the trial team. The trial team will inform the Chief Investigator, or delegate, who will be involved in the escalation process.

The Trial Co-ordinating Centre will escalate such events, as appropriate, as soon as possible.

Examples of the types of disclosure that might raise safety concerns and warrant reporting under this duty of care are as follows;

- Serious self-harm
- Suicide attempt
- Significant suicidal thoughts
- Suicide
- Abuse

Examples of events that would not typically raise safety concerns and do not need to be reported are;

- Planned hospitalisation, e.g. operations
- Accidents and hospitalisation unrelated to the trial intervention, e.g. broken bones
- Illnesses unrelated to the trial intervention

This duty of care applies to all trial participants (i.e. the young person **and** their parent) for the duration of the trial.

All concerns raised will be handled discretely and sensitively, and will typically lead to a member of the PIPA trial team or WCTU Clinician contacting the parent or school to signpost to appropriate mental health or other services including General Practitioners. This information will be stated in the participant information leaflets.

4.1 Responsibilities

Trial Manager:

1. Critical Data checks for events requiring follow-up when participants submit questionnaires.
2. Highlight to CI or delegated trial team member any details of possible events, who will then use medical judgement in assessing whether follow-up is required.
3. Ensuring that all safety concerns are recorded and reported to the Sponsor as soon as possible and provide further follow-up information when available.

Trial Management Group:

1. To monitor duty of care to participants within the trial.
2. To monitor protocol non-compliances and any CAPAs that may arise as a result of this.

Chief Investigator (CI) / delegate or independent clinical reviewer:

1. Clinical oversight of the safety of participants in the trial, including an ongoing review of the risk / benefit.
2. Using medical judgement in assessing whether follow-up is required by the trial team upon receipt of an event.
3. Review of events in accordance with the trial risk assessment and protocol as detailed in the Trial Monitoring Plan.

Sponsor:

The University of Warwick will act as research sponsor for the study, with oversight being provided by Warwick Clinical Trials Unit. Warwick Clinical Trials Unit will report into each meeting of the Sponsorship and Oversight Committee for oversight purposes.

Trial Steering Committee (TSC):

In accordance with the Trial Terms of Reference for the TSC, periodically reviewing safety data and liaising with the DMC regarding safety issues.

Data Monitoring Committee (DMC):

In accordance with the Trial Terms of Reference for the DMC, unblinded safety data to determine patterns and trends of events, or identify safety issues, which may not be apparent on an individual case basis, will be periodically reviewed.

Charters will be in place for TSC and DMC members.

4.2 Notification of deaths

Notification of death forms will be completed by the trial team upon receipt of this knowledge. Upon receipt of a notification of death, the other half of the family dyad will be withdrawn from the trial.

Only deaths that are assessed to be caused by the trial intervention will be reported. The Chief Investigator, or nominated WCTU clinician, will make this assessment within seven calendar days of receipt of the notification of death. Once assessed, this report will be sent to the sponsor, if deemed necessary, within one working day.

4.3 Reporting urgent safety measures

If any urgent safety measures are taken the CI/delegate shall act immediately and in any event no later than three calendar days from the date the measures are taken, give written notice to BSREC and Sponsor of the measures taken and the circumstances giving rise to those measures.

5. DATA MANAGEMENT

Personal data collected during the trial will be handled and stored in accordance with the 2018 Data Protection Act.

Where possible, participants will be identified by a unique trial identification number, and their initials in order to maintain anonymity. In some instances, such as making phone calls to participants, this will not be possible. Handling of personal data by the PIPA trial team will be clearly documented in the participant information sheet and consent obtained.

Participant trial identification numbers will be generated by the WCTU programming team prior to randomisation. This trial identification number will be the identifier on all data recorded throughout the trial.

Personal identifying information will be held securely at WCTU, when received in response to invitation. This will include a copy of the participants' personal contact details that will be needed to communicate confirmation of randomisation allocation, send links to follow up questionnaires and may be used for follow-up in a duty of care situation (see section 4). Personal identifying information will be kept until the end of the trial, when they will no longer be needed, and will be disposed of in accordance with WCTU SOPs. Personal identifying information for negatively screened participants and participants who wish to

withdraw previous data will be deleted at the end of the recruitment phase of the trial. This will enable the trial team to prevent re-screening and re-entry and to effectively manage any duty of care situations which may arise. This will be made clear in the participant information sheet.

5.1 Data collection and management

Electronic Case Report Forms (eCRFs) will be developed to collect all required trial data. These will be completed by the participants and submitted to the PIPA trial team's database at Warwick Clinical Trials Unit, where the trial team will be able to access them. A member of the trial team will perform critical data checks on receipt of reports produced by the Programming Team at WCTU. The CRFs will be programmed with validations on each question to ensure that there are no spurious data. Where appropriate, the database will also ensure that compulsory questions are not missed by participants. An electronic link will be sent to participants for follow-up questionnaires at six and 15 months. If participants do not respond to the link, a reminder will be sent from the trial website for them to complete the CRF.

Follow-ups are classed as 'closed cases' when either an online CRF is not completed by the participant after they have been chased for return, or if they have advised that they wish to withdraw.

5.2 Database

The trial database will be developed by the Programming Team at WCTU and all specifications (i.e. database variables, validation checks, screens) will be agreed between the programmer and appropriate trial staff.

Data required to personalise and describe the intervention will be collected and stored on the Partners in Parenting website (Google Cloud Platform, owned by Monash University), along with information collected on the intervention, such as the number of modules completed or factsheets accessed. All other data will be collected and stored in the PIPA trial database (University of Warwick).

All PIPA data collected by WCTU will be stored in a SQL Server database hosted by the University of Warwick in a secure data centre. Servers are hosted in a virtual cloud built using VMWare vCloud product suite utilising clusters of Esxi hosts evenly stretched over 2 data centres located in 2 separate physical locations across the main University of Warwick site campus. This provides a highly available hosting environment with auto failover capabilities, protecting against server, storage, network and datacentre level failures. SQL Server databases are backed up daily with transaction logs shipped to a separate server every 10 minutes. All virtual machines are backed up nightly to the University's central backup system with retention schedules for up to 2 years. Data will be retained for at least 10 years after the trial's completion, in accordance with University of Warwick Research Data Management Policy. All databases and backups are encrypted to the Advanced Encryption Standard (AES) using a 256-bit key.

Access to the data will be restricted to those with a valid right to access the information by applying logical security rules consisting of user identification (authentication), application roles (authorisation) and device identification. These measures are enforced to ensure that only appropriate users with the required authority can obtain access to the system.

All baseline PRADAS and data collected through the Partners in Parenting website will be stored immediately after generation using Google Cloud Platform, via the European Data Centre. This will be programmed and maintained by staff at Monash University. This provides reliable and secure, medium-term storage for research data. All data will be encrypted and backed up regularly. Passwords generated for the database by parents and the trial team will not be stored in the database. Access to the data will be

restricted to those with a valid right to access the information. Trial staff at Monash University and Australian-based programmers follow Australia's privacy law framework which is regulated by the federal Privacy Act 1988, in addition to Australia's Victorian privacy legislation. Pseudonymised data will be transferred to Warwick University during the life of the trial and stored in the same way as Warwick University's trial data.

5.3 Data storage

All essential documentation and trial records will be stored by WCTU in conformance with the applicable requirements and SOPs and access to stored information will be restricted to authorised personnel. Data will be stored on University secure servers. Trial related documents will be made available for internal monitoring and audit activities.

5.4 Data access and quality assurance

All electronic participant-identifiable information will be held on a secure, password-protected database accessible only to essential personnel. This will have oversight from the Trial Manager and Senior Project Manager. Paper forms with participant-information will be held in secure, locked filing cabinets within a restricted area of WCTU. For quality assurance, the data and results will be monitored. A full data management plan will be produced by the Trial Manager and Statistician to outline the data monitoring checks required.

5.5 Data Shared with Third Parties

Any data transfer would be in accordance with WCTU SOPs and require data sharing/processing agreements to be in place.

5.6 Archiving

Trial documentation and data will be archived in accordance with WCTU SOPs.

6. STATISTICAL ANALYSIS

6.1 Sample size justification

In a large pilot RCT in Australia, the effect size of the personalised programme on parent-reported depressive symptoms in young people with elevated self-reported SMFQ scores at baseline was 0.35 (Cohen's D, n=105).

Assuming the correlation between pre- and post- intervention SMFQ scores is 0.5, with 346 families participating this trial, we would have 90% power to detect a difference of 0.35 in the primary outcome between the trial arms at the 5% level. To allow 20% losses to follow up, the recruitment target is 433 families. This should also ensure sufficient numbers in specific sub-groups, for example young people from low socioeconomic status and/or BME backgrounds.

6.2 Statistical analysis

6.2.1 Statistical policies

All analyses will be performed on an intention-to-treat basis. The baseline characteristics of the trial group will be presented using descriptive statistical methods. Continuous variables that follow an approximately normal (or symmetric) distribution will be summarised using means and standard deviations. Continuous variables that are skewed will be summarised using the median and inter-quartile range. Categorical data will be summarised using frequencies and percentages. Distributional assumptions will be checked and outliers identified using graphical methods (such as histograms and box-plots). All scales will be scored according to the appropriate manual.

6.2.2 Statistical analysis plan

A detailed statistical analysis plan (SAP) will be developed by the trial statisticians early in the trial, and circulated to the TMG, TSC and (if appropriate) DMC before finalising.

6.2.3 Summary of baseline data and flow of participants

A CONSORT diagram will be produced, showing participant flow through the trial, including numbers screened, number recruited and randomised, numbers withdrawn and numbers available for the analysis at each follow up.

6.2.4 Summary of primary and secondary outcomes

Mental health and wellbeing, as assessed by the relevant primary and secondary outcomes, will be summarised at baseline, six and 15 months post randomisation and the mean and 95% confidence intervals presented graphically, overall and by intervention group, over time.

6.2.5 Primary analysis

The primary endpoint is change in parent-reported SMFQ score between entry to the trial and 15 months post-randomisation. We will test the hypothesis that there is no difference in this between the control and intervention groups using a linear mixed model with school as a random effect and age group and number of participating parents (1 or 2) as a fixed effect. The estimate of intervention effect from the model will be presented with corresponding 95% confidence intervals. The number of cases of depression or anxiety disorders in young people up to 15 months will be reported (overall and by intervention group) and appropriate models (adjusted, as above) used to assess any difference between the intervention arms.

6.2.6 Secondary analysis

Similar appropriate linear mixed models, adjusted as above, will be developed to assess the impact of the intervention on each of the secondary outcome scales.

6.2.7 Subgroup analyses

Analysis of the primary outcome will be repeated separately in the following subgroups and estimates of the intervention effects and 95% confidence intervals presented in a Forest plot.

1. school location (inner city vs not inner city)
2. parents' highest education level (a surrogate for socioeconomic status)
3. ethnicity of parents
4. ethnicity of young people

6.3 Adjustment

All linear mixed models will be adjusted by the design variables (school, age group, gender of young person, gender of primary (participating) parent and number of parents participating).

6.4 Interim analysis and criteria for the premature termination of the trial

The study will have a pilot phase to establish the feasibility of the full PIPA trial. The stop-go decision will be made by the TMG, following consultation with the TSC and DMC four months from trial commencement using the following stop-go criteria as a guide:

1) Recruitment: Recruitment of at least 128 family dyads (i.e. at least 65% of planned) and;
2) Intervention adherence: Beyond 3 months post randomisation parents will have completed 50% of their recommended chosen modules (to be assessed in the subset of participants who have reached 3 months post randomisation time point by the end of month 4, which is expected to be 20 dyads).

There are no pre-planned interim analyses or formal rules for the full PIPA trial. The DMC will review the emerging trial data and external evidence on an ongoing basis and may recommend early stopping, if appropriate.

6.5 Subject population

The ITT (intention to treat) population will comprise all subjects who were randomised into the trial, regardless of whether they received trial intervention.

The compliance population will comprise all subjects who were randomised and received at least 2/3 of their selected modules.

6.6 Procedure(s) to account for missing or spurious data

Imputation of missing elements of individual scales using multiple imputation will be considered if appropriate (>10% of overall scores are missing, ≤ 80% of individual elements are not missing, missing at random assumption holds).

6.7 Other statistical considerations

Any deviations from the statistical analysis plan will be reported.

6.8 Health Economic Evaluation

In order to provide decision-makers with the best available evidence on whether or not local authorities should commission the personalised programme, it is important that evidence around its cost-effectiveness is also provided. This economic evaluation will aim to identify, measure and value the costs and

consequences of this online parenting intervention, and to synthesise the evidence using metrics amenable to cost-effectiveness based decision-making.

A prospective economic evaluation, conducted from the recommended NHS and personal social services perspective, will be integrated into the trial and documented in a Health Economics Analysis Plan (National Institute for Health and Care Excellence, 2013). Primary research methods will be followed to estimate the costs of delivering the personalised programme, including programme development, web maintenance, participant monitoring activities, and any follow-up/management. Broader resource utilisation will be captured through bespoke participant online questionnaires administered at baseline, and at six and 15 months post-randomisation. Unit costs for health and social care resources will be derived from local and national sources and estimated in line with best practice. Primary research using established accounting methods may also be required to estimate unit costs.

Young person health-related quality of life will be measured at baseline and at each follow-up point using the Child Health Utility-9D; CHU-9D (Stevens, 2009; Stevens, 2010), the EQ-5D-5L-Y (Ravens-Sieberer et al., 2010) and the proxy EQ-5D-5L-Y, whilst parental health-related quality of life will be measured at baseline and at each follow-up point using the EuroQol EQ-5D-5L (Herdman et al., 2011). Responses to the multi-attribute utility measures will be converted into health utilities using established utility algorithms for the purposes of family dyad quality-adjusted life year (QALY) estimation. The results of the economic evaluation will primarily be expressed in terms of incremental cost per QALY gained. We shall use non-parametric bootstrap estimation to derive 95% confidence intervals for mean cost differences between the trial groups and to calculate 95% confidence intervals for incremental cost effectiveness ratios (Barber & Thompson, 2000).

A series of sensitivity analyses will be undertaken to explore the implications of uncertainty surrounding the incremental cost-effectiveness ratios and to consider the broader issue of the generalisability of the trial results. For each sensitivity analysis, cost-effectiveness acceptability curves will be constructed using the net benefits approach (Stinnett & Mullahy, 1998). More extensive economic modelling using decision-analytic methods will extend the time horizon of the economic evaluation, drawing on best available information from the literature together with stakeholder consultations to supplement the trial data. Parameter uncertainty in the decision-analytic model will be explored using probabilistic sensitivity analysis. Longer term costs and consequences will be discounted to present values using discount rates recommended for technology appraisal in the United Kingdom (National Institute for Health and Care Excellence, 2013).

7. TRIAL ORGANISATION AND OVERSIGHT

7.1 Sponsor and governance arrangements

The University of Warwick will act as Sponsor for the trial. University policies and SOPs will be adhered to.

7.2 Ethical approval

Ethical approval will be sought through the University of Warwick Biomedical & Scientific Research Ethics Committee (BSREC).

Any protocol amendments will be dealt with in accordance with WCTU SOPs.

7.3 Trial Registration

This trial is registered with an International Standard Randomised Controlled Trial Number (ISRCTN) Register.

7.4 Notification of serious breaches to GCP and/or trial protocol

A "serious breach" is a breach which is likely to effect to a significant degree –

(a) the safety or physical or mental integrity of the participants of the trial; or
(b) the scientific value of the trial

The sponsor will be notified immediately of any case where the above definition applies during the trial conduct phase.

The sponsor of a clinical trial will notify the licensing authority in writing of any serious breach of

(a) the conditions and principles of GCP in connection with that trial; or
(b) the protocol relating to that trial, as amended from time to time, within 7 days of becoming aware of that breach

The PIPA TMG will be responsible for oversight of Protocol deviations and violations.

7.5 Indemnity

The University of Warwick provides indemnity for any harm caused to participants by the design of the research protocol.

7.6 Trial timetable and milestones

	2019				2020				2021				2022			
Task	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Pre-commencement																
Ethics permission for WP 1																
Staff recruitment																
Work package 1: Adaptation & Feasibility																
Staff training																
Recruitment of parents, young people and teachers																
Focus group consultations																
Pilot pre- and post-intervention assessments																
Programming of dedicated trial website (including adaptations to intervention)																
Ethics permission for WP2 and 3																
Work packages 2 & 3: RCT																
School and parent recruitment																

Participant screening																
Pre-intervention assessments																
Post-intervention assessments																
12-month follow-up assessments																
Data processing & analysis																
Output preparation & presentations																
Dissemination event																

7.7 Administration

The trial co-ordination will be based at WCTU, University of Warwick.

7.8 Trial Management Group (TMG)

The Trial Management Group, consisting of the project staff and co-investigators involved in the day-to-day running of the trial, will meet regularly throughout the project. Significant issues arising from management meetings will be referred to the Trial Steering Committee or Investigators, as appropriate.

7.9 Trial Steering Committee (TSC)

The trial will be guided by a group of respected and experienced personnel and trialists as well as at least one 'lay' representative. The TSC will have an independent Chairperson. Meetings will be held at regular intervals determined by need but not less than once a year. Routine business is conducted by email and post. Most of these meetings will take place via online meetings.

The first meeting of the TSC will be a joint meeting with the DMC to outline the trial.

The Steering Committee, in the development of this protocol and throughout the trial will take responsibility for:

- Major decisions such as a need to change the protocol for any reason
- Monitoring and supervising the progress of the trial
- Reviewing relevant information from other sources
- Considering recommendations from the DMC
- Informing and advising on all aspects of the trial

The membership of the TSC is shown on page 3.

The full remit and responsibilities of the TSC will be documented in the Committee Charter which will be signed by all members.

7.10 Data Monitoring Committee (DMC)

The DMC will consist of independent experts with relevant clinical research, and statistical experience. The first meeting of the DMC will be a joint meeting with the TSC to outline the trial. The DMC will then meet regularly thereafter. Confidential reports containing recruitment, protocol compliance, safety data and interim assessments of outcomes will be reviewed by the DMC. The DMC will advise the TSC as to whether there is evidence or reason why the trial should be amended or terminated.

The membership of the DMC is shown on page 3.

Committee meetings will also be attended by the Chief Investigator and Trial Manager, or delegate (for non-confidential parts of the DMC meetings) and the Trial Statistician.

The full remit and responsibilities of the DMC will be documented in the Committee Charter which will be signed by all members.

7.11 Essential Documentation

A Trial Master File will be set up according to Warwick SOPs and held securely at the coordinating centre.

The coordinating centre will provide Investigator Site Files to all recruiting schools involved in the trial.

7.12 Financial Support

The trial has been funded by a grant from National Institute for Health Research (NIHR).

7.13 Intellectual Property

The PIPA trial will generate new Intellectual Property (IP) as we are adapting the Partners in Parenting website and resources for use in the United Kingdom. Any IP generated under the PIPA trial in the United Kingdom will be owned by the University of Warwick and Monash University in accordance with their collaboration agreement dated 5 June 2019. Any Foreground IP and Arising Know-How (except non-severable Foreground IP and Know How relating to the Partners in Parenting website) will be owned by University of Warwick. All non-severable Foreground IP and Know How relating to the Partners in Parenting website will be owned by Monash University. Decisions on how this IP might be exploited in future, will be agreed by the collaborators and implemented in accordance with legal requirements.

8. MONITORING, AUDIT AND INSPECTION

- A Trial Risk Assessment will be conducted by the Trial Manager, Senior Project Manager, Trial Statistician, Chief Investigator (or delegated representative) and WCTU Quality Assurance Team.
- A Trial Monitoring Plan will be developed and agreed by the Trial Management Group (TMG) and TSC based on the trial risk assessment.
- A data management plan will be developed and agreed by the TMG.
- The trial will be audited by WCTU's Quality Assurance team as per WCTU SOPs.

9. PARTNER COLLABORATION

There are a number of key partners in this research project;

1) Monash University and authors of the Partners in Parenting website and resources: We have an established partnership with Associate Professors Yap and Melvin. The two universities have a clear and established alliance on which this partnership will be further fostered and a collaborative agreement is in place. We will work closely with our partners at Monash to develop the interventions for a UK setting and draw on the expertise of their RCT, which has established the evidence base for development of the interventions.

2) Birmingham Education Partnership (BEP): BEP is both a charity and a company (not for profit) that is focussed on school improvement. Their key activities include an in-depth understanding of the needs and strengths of all Birmingham schools, supporting those that are at risk, or those already struggling. They work through training, brokering and signposting, especially with Birmingham's teaching schools in systematic school improvement. BEP also champions peer review and the sharing of good practice. We have worked closely with BEP previously and they have been

instrumental in helping us to recruit schools to participate in our research.

3) Applied Research Collaboration [ARC (formerly CLAHRC)]: The NIHR ARC West Midlands is funded by the National Institute of Health Research with matched funds provided by local health and social services. ARC aims to create lasting and effective partnerships across health and social care organisations, and universities (Birmingham, Keele and Warwick) in order to improve care services across the West Midlands. The work builds on research conducted by both the NIHR Collaboration for Leadership in Applied Health Research and Care (CLAHRC) for West Midlands and the CLAHRC Birmingham and Black Country pilot.

4) Children Services Directorate at Coventry City Council: Coventry City Council run public health services for young people in the Coventry area including schools, and we have developed links with a number of key professionals including Dr Sue Frossell, Public Health consultant who has an interest in young people's mental health and wellbeing, and who is a collaborator on the project.

10. PATIENT AND PUBLIC INVOLVEMENT (PPI)

We will have substantial patient and public involvement in the feasibility phase of this trial. Lay members will be involved in focus groups to ensure that the intervention adaptations are suitable for UK participants. They will also be involved in ensuring that the online CRFs are suitable and accessible. There will also be a lay member on the TSC.

11. DISSEMINATION AND PUBLICATION

The results of the trial will be reported first to trial collaborators. A protocol paper will be published in an open access journal. An authorship agreement will be developed and authorship order on all subsequent publications will be determined by author input. Publications will be made available to the NIHR Journal library. The main report will be drafted by the trial co-ordinating team, and the final version will be agreed by the Trial Steering Committee before submission for publication, on behalf of the collaboration. A summary of the results of the trial will be made available to all participating schools and disseminated to them via presentation or short report.

The success of the trial depends on the collaboration of schools, schools networks and education authorities. Equal credit will be given to those who have wholeheartedly collaborated in the trial.

The trial will be reported in accordance with the Consolidated Standards of Reporting Trials (CONSORT) guidelines (www.consort-statement.org).

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Appendix 1

Recruitment Strategy

June – December 2019

- Identification of schools in Birmingham
- Identification of schools in Coventry
- Initial meeting with existing contracts (Birmingham Education Partnership & Coventry City Council), Headteacher consortiums in Birmingham & Coventry, Independent school consortiums in Birmingham & Coventry, Mental well-being leads, school governors, Headteacher conference
- Acquisition of expressions of interest and creation of shared research database of interested schools

January 2020 onwards

- Recruitment of schools
- Identification of school 'champion' within each interested school to assist with parent engagement/event planning and recruitment
- Identification of a parent/carer/Parent Teacher Association member/governor 'champion' to assist with dissemination about trial and recruitment
- Attendance at school events to engage with parents, describe the study and recruit - including monitoring of those who decline (reason and numbers approached)
- Presentations at Parent Teacher Association meetings
- Presentations to students
- Presentations to parents/carers
- Distribution of emails/letter/flyers/texts to engage with parents/carers and recruit (guided by schools)

September 2020

- Start of participant recruitment