iris+
Enhanced Identification
and Referral to Improve Safety

A primary care system-level training and support programme for the secondary prevention of domestic violence and abuse: a multicentre cluster randomised trial with economic and process evaluation.

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Calan Domestic Violence Services Website: https://www.calandvs.org.uk	Domestic abuse agency, service delivery partner
Fortalice Ltd 43 Bradford Street, Bolton, BL2 1HT Email: info@fortalice.co.uk	Domestic abuse agency, service delivery partner
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GLOSSARY OF ABBREVIATIONS

AE	Adverse Event
BNSSG ICB	Bristol, North Somerset and South Gloucestershire Integrated Care Board
BTC	Bristol Trials Centre
CAPC	Centre for Academic Primary Care
CI	Chief Investigator
CRF	Case Report Form
cRCT	Cluster Randomised Controlled Trial
CRN	Clinical Research Networks
CTU	Clinical Trials Unit
CYP	Children or Young People/Person
DH	Department of Health
DVA	Domestic violence and abuse
DMEC	Data Monitoring and Ethics Committee
DSA	Data Sharing Agreement
GCP	Good Clinical Practice
GDPR	General Data Protection Regulation
HCP	Primary health care professional
HERMES	Health professionals responding to men for safety study
HRA	Health Research Authority
HRQoL	Health Related Quality of Life
ICB	Integrated Care Board
ICC	Interclass correlation coefficient
ICF	Informed Consent Form
IRIS	Identification and Referral to Improve Safety
IRIS+	Enhanced Identification and Referral to Improve Safety
ISF	Investigator Site File
ISRCTN	International Standard Randomised Controlled Trials Number
M-DASC	Modified Domestic Abuse and Safeguarding Children Scale
mNCA	Model Agreement for Non-Commercial Research
NHS R&D	National Health Service Research & Development
NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health and Care Research
OID	Organisation Information Documents

CI	Chief Investigator
PIL	Participant Information Leaflet
PHR	Public Health Research
PPI	Patient and Public Involvement
PPI&E	Patient and Public Involvement and Engagement
QALY	Quality Adjusted Life Years
RCT	Randomised Controlled Trial
R&D	Research and Development
RDN	Research Delivery Networks (previously CRN)
RDSF	Research Data Facility Storage
REC	Research Ethics Committee
REDCap	Research Electronic Data Capture
REPROVIDE	Reaching Everyone: Programme of Research on Violence in diverse Domestic Environments
SAE	Serious Adverse Event
SOP	Standard Operating Procedure
SUSAR	Suspected Unexpected Serious Adverse Reaction
TMF	Trial Master File
TMG	Trial Management Group
TRE	Trusted Research Environment
TSC	Trial Steering Committee
UHBW	University Hospitals Bristol and Weston NHS Foundation Trust
UoB	University of Bristol
WHO	World Health Organisation

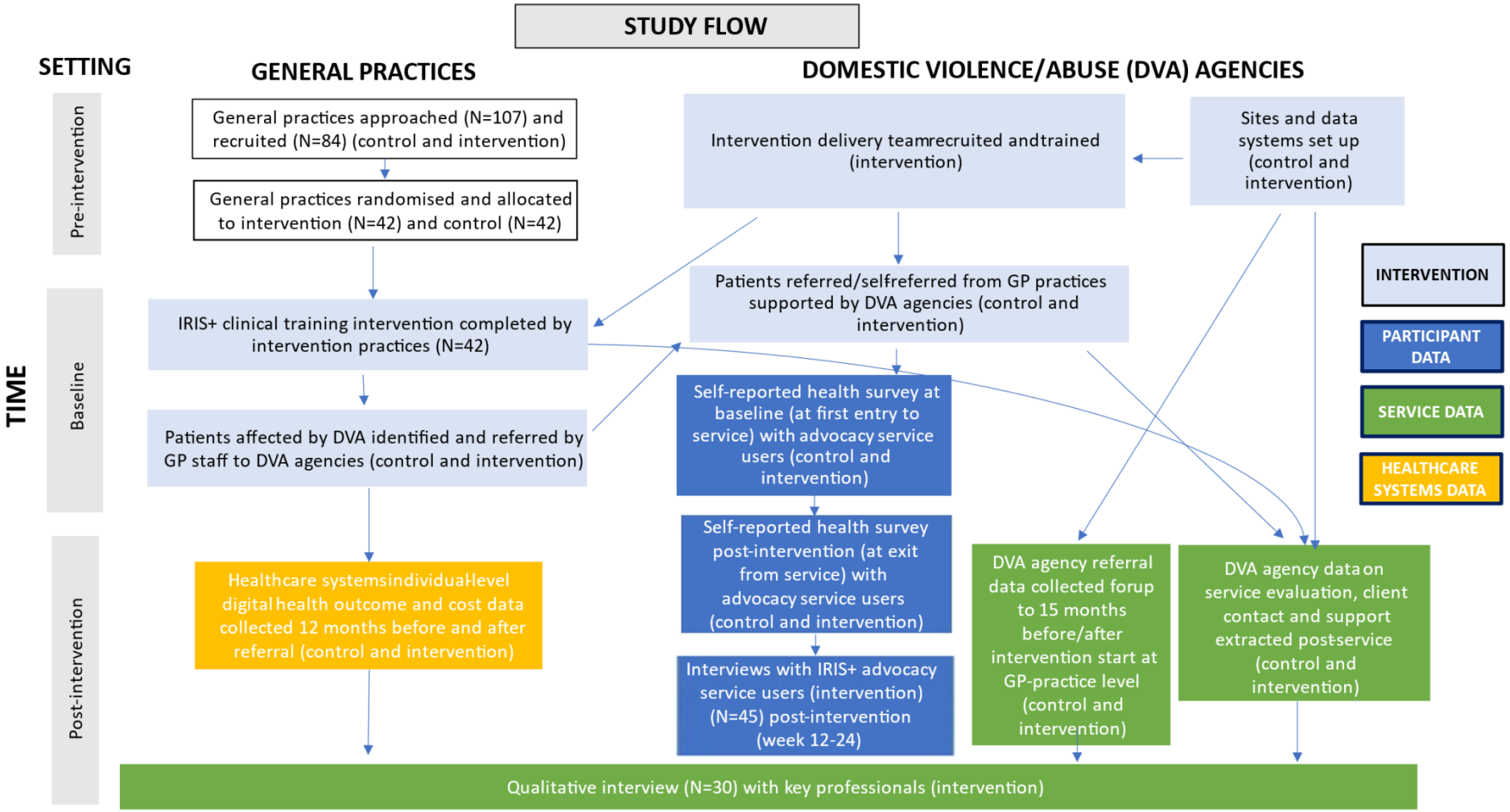
TRIAL SUMMARY

Trial Title	A primary care system-level training and support programme for the secondary prevention of domestic violence and abuse: a multicentre cluster randomised trial with economic and process evaluation
Short title	IRIS+ RCT
Chief Investigator	Dr Eszter Szilassy
Sponsor	University of Bristol
Funder	NIHR Public Health Research Programme
Trial Design	A multicentre cluster randomised trial with economic and process evaluation
Trial Participants	1. cRCT: GP practices 2. Post-intervention interview study: (i) DVA advocacy service users: female and male adults and children and young people (CYP) referred or self-referred from GP practices participating and supported by the IRIS+ service at the DVA agencies (ii) Clinical leads, service providers, local commissioners, and local authority staff facilitating the delivery of IRIS+ and/or working on local DVA and public health strategy (key professionals involved with the delivery of IRIS+ intervention).
Sample size	1. cRCT: 84 GP practices 2. Post-intervention interview study: (i) Approximately 45 interviews with a sub-sample of IRIS+ service users (approx. 15 women, 15 men, 15 children and young people (CYP)) (ii) Approximately 30 interviews with clinical leads, service providers, commissioners
Number of centres	Three; comprising of general practices in Bolton, South Gloucestershire/Bristol and Swansea Bay areas
Intervention	IRIS+ training and advocacy support intervention
Control	IRIS training and advocacy support intervention (usual care)
Intervention treatment duration	Following the two-hour IRIS+ clinical training session, which builds on the IRIS training (see below) that all intervention practices must have previously received, the IRIS+ patient referral pathway will be available for patient referrals for each intervention practice for a period of 12-15 months. Advocacy support for referred patients at the DVA agencies will be needs-led and will take circa 3 months. Advocacy support will be available at the DVA agencies for a total period of up to 18 months (12-15 months plus three months after the last patient referral to allow sufficient time for advocacy support for patients referred at the end of the practice referral period).
Control duration	Following the (two two-hour) IRIS clinical training that all control practices must have already received, the IRIS referral pathway will be available for patient referrals for at least a total of 18 months (possibly beyond given that the IRIS service is a commissioned programme at the trial centres). Advocacy support for referred patients at the DVA agencies will be needs-led and will take circa 3 months.
Inclusion criteria	1. cRCT (GP practices): General practices participating (or eligible to participate) in the IRIS programme at the time of recruitment. 2. Post-intervention interview study: (i) DVA advocacy service users: female and male adults referred or self-referred from GP practices participating

	and by the IRIS+ service at the DVA agencies. CYP between the ages of 13-16 referred or self-referred from GP practices participating and supported by the DVA agencies (who have been in direct contact with the IRIS+ CYP worker) (ii) Key professionals involved with the delivery and facilitation of the IRIS+ intervention
Exclusion criteria	Exclusion criteria for cRCT (GP practices): General practices not participating (or not eligible to participate) in the IRIS programme at the time of recruitment. Exclusion criteria for interview participants: Adults (>16 years of age): (i) deemed by the advocate educator or researcher to be put at greater risk if they participate; (ii) with mental health symptoms that will prevent them from research engagement; (iii) adult safeguarding concerns that may compromise the safety of the participant; (iv) incapacitated at time of seeking consent; (v) unable to understand written information in English in order to be able to give informed consent and undergo an interview if approached. Children: (i) Children under 13; (ii) parent or carer or advocate educator or researcher believe that a child's involvement is likely to cause distress or upset, increase the risk of DVA, or any form of child maltreatment; (iii) there are child or adult safeguarding concerns that may compromise the safety of the child/adult participants; (iv) unable to understand written information in English in order to be able to give informed consent and undergo an interview if approached; (v) CYP who do not have capacity to understand or consent to the research process.
Primary objective	Evaluate the effectiveness of the IRIS+ intervention for men and CYP compared to IRIS in terms of the rate of referral from general practice, or self-referral, to a specialist DVA agency providing advocacy support. Research question: Is the IRIS+ intervention effective with regards to referring men and children affected by DVA from primary care for specialist DVA advocacy support?
Primary outcome	Co-primary outcomes: (i) Referral rate, per general practice, of adult males to DVA agencies out of the population expected to have been exposed to, or perpetrating DVA. (ii) Referral rate, per general practice, of CYP to DVA agencies out of the population expected to have been exposed to DVA.

Secondary objectives	1. Evaluate the effectiveness of the IRIS+ intervention for women compared to IRIS in terms of the rate of referral from general practice, or self-referral, to a specialist DVA agency providing advocacy support. Research question: Is the IRIS+ intervention effective with regards to referring women affected by DVA from primary care for specialist DVA advocacy support? 2. Estimate the intervention's cost-effectiveness compared to IRIS. Research question: What is the cost-effectiveness of the IRIS+ intervention compared to IRIS from a societal and health sector (NHS) perspective? 3. Assess the impact of IRIS+ on women, men and children's physical health, mental health, wellbeing (diagnosis, prescribing) from healthcare systems data. Assess patient-reported health-outcomes, HRQoL (Health Related Quality of Life), and DVA exposure of adult and child DVA advocacy service users compared to IRIS. Research questions: What is the impact of IRIS+ on women, men and children's health-outcomes compared to IRIS? 4. Gain insights into the process through which the complex IRIS+ intervention reaches DVA advocacy service users through the different contexts of implementation; and explore the extent to which variations in area contextual factors facilitate or impede implementation, effectiveness and reach. Research question: How does IRIS+ gain traction and reach DVA advocacy service users through different contexts of implementation; and how do differences in delivery and area contextual factors affect and explain the IRIS+ intervention's implementation, effectiveness and reach?
Secondary outcomes	(i) Referral rate, per general practice, of females to DVA agencies out of the population expected to have been exposed to, or perpetrating DVA. (ii) Cost-effectiveness of IRIS+ (within trial [short-term] and modelling [long-term]) (iii) Physical health and mental health (diagnosis, prescribing) (iv) Adult and CYP self-reported health-outcomes, HRQoL for service-user participants supported by DVA agencies, and adult DVA exposure (v) Implementation scalability, mechanism of impact and reach (vi) Service delivery
Study duration	Funding start date: 1 May 2024 Anticipated duration: 44 months Anticipated end date: 31 Dec 2027

TRIAL FLOWCHART



1 BACKGROUND AND JUSTIFICATION

1.1 Background

Domestic violence and abuse (DVA) is a major public health challenge (1-4). It is associated with a wide range of long-term physical and mental health conditions in victims, perpetrators, and their children (5-10) resulting in increased use of health services (11) and vast social and economic costs (12, 13). Lifetime population prevalence is consistently higher for people seeking health care (14), including primary care (15), even though DVA often remains hidden from clinicians. The annual cost to the UK economy of DVA in 2017 was £66 billion (£2.3 billion in health services) (13).

Over the past decade, UK primary care has started to respond to DVA, with training of general practice teams in the identification, support and referral of women affected by DVA. The leading service model is IRIS (Identification & Referral to Improve Safety), a widely commissioned evidence-based training and advocacy support programme for women survivors. Success in identifying women is growing, but men survivors and children/young people (CYP) exposed to DVA are rarely identified in primary care and referred for specialist support. The mental and physical health impact across CYP's life-course (9, 10) and on men survivors (16-19) thus remains neglected with a persistent gap between the health impact of DVA and interventions to prevent or mitigate that impact.

Benefits of IRIS for identifying and referring female survivors (20) are well-established through a landmark trial (21) and a subsequent interrupted-time-series evaluation that reported effective (22, 23) and cost-effective implementation (24) and a positive social return on investment (25). Small studies have explored women's experiences of IRIS (20, 26) and service evaluations have recorded its benefits (27, 28). Primary care can provide a safe and confidential place for disclosure and enquiry about abuse and a crucial link to further support from the specialist DVA sector.

Primary care is a key location for interventions to prevent DVA and improve health outcomes for men and children. It is well-placed to provide a pathway for specialist support to *all* patients affected by DVA. Yet, despite the specific call for evidence from the NICE evidence reviews (21) and international guidelines (29) on integrated healthcare responses for men and CYP, the effectiveness and cost-effectiveness of interventions for men (30), and CYP (31, 32) remain uncertain.

Recognising the needs of a wider range of patient groups and to address these gaps, we collaborated with IRISi (UK social enterprise) and other partners in the DVA sector to develop and pilot IRIS+ in England and Wales. IRIS+ is an adapted multi-sectoral IRIS programme responding to the diverse needs of all patient groups. Building on the IRIS training and advocacy support programme, IRIS+ offers a coordinated whole-systems approach for DVA training and advocacy interventions. IRIS+ adds to IRIS by expanding the clinical focus, patient care pathways and specialist advocacy support to men and children. While the IRIS programme focuses on the needs of female survivors of DVA, IRIS+ -without diminishing the focus on women- also responds to the needs of men experiencing or perpetrating DVA, and CYP living with DVA and/or experiencing it in their own relationships.

1.2 Justification

We tested the feasibility and potential cost-effectiveness of the IRIS+ Programme. The study showed that the IRIS+ training and support intervention was acceptable to clinicians, service providers and patients, and was feasible to implement in English and Welsh urban areas in both IRIS-trained and non-IRIS trained general practices. Our findings demonstrated that completion of clinical training and working within the IRIS+ referral and support structure improved clinicians' preparedness to respond to the needs of all patient groups. This translated to high rates of referrals for all patient groups, including men and CYP. The study also found evidence for good patient engagement with specialist support. Women, men and children participating in the study reported positive impact of support, including improved physical and mental health, wellbeing and confidence (33).

Although the feasibility study demonstrated acceptability, feasibility (33) and potential cost-effectiveness (34), there remains uncertainty about the effectiveness, actual cost-effectiveness and scalability of the intervention. Uncertainty also remains about broader health outcomes for women beyond referral to voluntary sector DVA advocacy support, and outcomes for men and CYP.

The current study will address a gap in understanding the link between referrals to DVA specialist service support and effectiveness in terms of health-outcomes and health-related quality of life (HRQoL). It will also measure actual intervention costs and costs to healthcare settings compared to IRIS. Implementation scalability, effectiveness, cost-effectiveness and impact will be tested in different contexts to ensure generalisability. The evidence from this trial will reduce uncertainty about effectiveness of service integration and of a whole family approach, contributing directly to better outcomes for families affected by DVA.

Learning from our IRIS cRCT (21), from the IRIS+ feasibility study (33), and from close collaboration with DVA service providers and with our PPI&E (Patient and Public Involvement and Engagement) groups, informed the design of the current trial. If the trial shows improved referral and health outcomes, and downstream benefit for survivors and CYP through cost-effectiveness analysis, this will form a strong basis for commissioning. The study will also inform policy and practice by generating evidence about the extent to which local variations in different implementation contexts facilitate or impede effectiveness and reach.

Evidence generated by this research, regardless of the effectiveness of the intervention, will address a substantial evidence gap in understanding DVA interventions for women, men, and CYP. This will benefit those designing future interventions, service-users and those involved in the delivery and commissioning of DVA interventions, including staff working for health and social care services.

2 TRIAL AIMS AND OBJECTIVES

2.1 Main research question

Is the IRIS+ intervention effective, cost-effective and scalable with regards to referring adults and children affected by DVA from primary care for specialist advocacy support?

2.2 Aim

Compare the effectiveness and cost-effectiveness of IRIS+, with IRIS as the comparator, for women, men and CYP in three centres in England and Wales with differential prior engagement in IRIS, corresponding to typical implementation contexts.

2.3 Objectives and research questions

2.3.1 Primary objectives

Evaluate the effectiveness of the IRIS+ intervention for men and CYP compared to IRIS in terms of the rate of referral from general practice, or self-referral, to a specialist DVA agency providing advocacy support. (Co-primary outcomes i-ii)

Research question: Is the IRIS+ intervention effective with regards to referring men and children affected by DVA from primary care for specialist DVA advocacy support?

2.3.2 Secondary objectives

1. Evaluate the effectiveness of the IRIS+ intervention for women compared to IRIS in terms of the rate of referral from general practice, or self-referral, to a specialist DVA agency providing advocacy support. (Secondary outcome i)

   Research question: Is the IRIS+ intervention effective with regards to referring women affected by DVA from primary care for specialist DVA advocacy support?

2. Estimate the intervention's cost-effectiveness compared to IRIS. (Secondary outcome ii)

   Research question: What is the cost-effectiveness of the IRIS+ intervention compared to IRIS from a societal and health sector (NHS) perspective?

3. Assess the impact of IRIS+ on women, men and children's physical health, mental health, wellbeing (diagnosis, prescribing) from healthcare systems data. Assess patient-reported health-outcomes, HRQoL, and DVA exposure of adult and child DVA advocacy service users compared to IRIS. (Secondary outcomes iii-iv)

   Research questions: What is the impact of IRIS+ on women, men and children's health-outcomes compared to IRIS?

4. Gain insights into the process through which the complex IRIS+ intervention reaches DVA advocacy service users through the different contexts of implementation; and explore the extent to which variations in area contextual factors facilitate or impede implementation, effectiveness and reach. (Secondary outcomes v-vi)

   Research question: How does IRIS+ gain traction and reach DVA advocacy service users through different contexts of implementation; and how do differences in delivery and area contextual factors affect and explain the IRIS+ intervention's implementation, effectiveness and reach?

3 OUTCOME MEASURES

3.1 Co-primary outcome measures

i. Referral rate, per general practice, of adult males to DVA agencies out of the population expected to have been exposed to, or perpetrating DVA.
ii. Referral rate, per general practice, of CYP to DVA agencies out of the population expected to have been exposed to DVA.

3.2 Secondary outcome measures

i. Referral rate, per general practice, of females to DVA agencies out of the population expected to have been exposed to, or perpetrating DVA.
ii. Cost-effectiveness of IRIS+ (within trial [short-term] and modelling [long-term])
iii. Physical health and mental health (diagnosis, prescribing)
iv. Adult and CYP self-reported health outcomes, DVA exposure and HRQoL for service-user participants supported by DVA agencies
v. Implementation scalability, mechanism of impact and reach
vi. Service delivery

4 TRIAL DESIGN AND SETTING

4.1 Trial design

IRIS+ is a multicentre, cluster randomised controlled trial (cRCT) across three geographical areas with economic and mixed-method process evaluation using a collaborative evaluation approach (35, 36). The IRIS+ cRCT is informed by the design of the IRIS trial (21), where the intervention was implemented within primary care teams.

4.2 Trial setting

We will test IRIS+ in geographically, socioeconomically and organisationally different sites and in different implementation contexts corresponding to different levels of prior engagement in IRIS to maximise generalisability of study findings.

4.2.1 Sites

GP practices within the geographical boundaries of the centres.

4.2.2 Centres

Our study centres are:

1. Bolton (England): established IRIS site since 2015 (long standing prior engagement with IRIS)
2. South Gloucestershire/Bristol (England): established IRIS site since 2013/2010 (long standing prior engagement with IRIS)
3. Swansea (Wales): recent IRIS site since 2020. The site has a combination of more recently trained and untrained practices allowing testing in a variety of contexts (more recent and no prior engagement with IRIS).

Third sector DVA organisations

1. Bolton (England): Fortalice Ltd
2. South Gloucestershire/Bristol (England): Next Link
3. Swansea Bay (Wales): Calan DVS

5 INCLUSION AND EXCLUSION CRITERIA

5.1 Inclusion criteria

Inclusion criteria for GP practices (cRCT): General practices participating (or eligible to participate) in the IRIS programme (commissioned in the local authority/health board area) at the time of recruitment.

Inclusion criteria for post-intervention interview participants (part of mixed-method study):

(i) DVA advocacy service users: female and male adults referred or self-referred from GP practices participating and supported by the IRIS+ service at the DVA agencies. CYP between the ages of 13-16 referred or self-referred from GP practices participating and supported by the DVA agencies (who have been in direct contact with the IRIS+ CYP worker) and whose non-perpetrating parent or carer agrees for the child to take part and who consent in their own right

(ii) Key professionals involved with the delivery and facilitation of the IRIS+ intervention

5.2 Exclusion criteria

Exclusion criteria for GP practices (cRCT): General practices not participating (or not eligible to participate) in the IRIS programme at the time of recruitment.

Exclusion criteria for post-intervention interview participants (part of mixed-method study):

Adults (>16 years of age):

(i) deemed by the advocate educator or researcher to be put at greater risk if they participate;

(ii) with mental health symptoms that will prevent them from research engagement;

(iii) adult safeguarding concerns that may compromise the safety of the child/adult participants;

(iv) incapacitated at time of seeking consent;

(v) unable to understand written information in English in order to be able to give informed consent and undergo an interview if approached.

Children:

(i) Children under 13;

(ii) parent or carer or advocate educator or researcher believe that a child's involvement is likely to cause distress or upset, increase the risk of DVA, or any form of child maltreatment;

(iii) there are child or adult safeguarding concerns that may compromise the safety of the child/adult participants;

(iv) unable to understand written information in English in order to be able to give informed consent and undergo an interview if approached;

(v) CYP who do not have capacity to understand or consent to the research process.

6 TRIAL PROCEDURES

6.1 Sample size - cRCT

84 general practices

6.2 Sample size calculation - cRCT

Calculation based on number of referrals during the seven-practice pilot (29 men and 44 children, over 18-months), interclass correlation coefficient (ICC) of 0.03 based on our teams' previous experience of primary care-based CRTs (Eldridge) and patterns in these coefficients for primary care studies (37), coefficient of variation of cluster size of 0.57 (based on actual list sizes of 107 general practices in Bolton from England (38) and Swansea and previous site Powys in Wales (39)), with an alpha of 0.025 to adjust for two co-primary outcomes (men and CYP referrals, primary objective) with power of 90%. Average *child* population of 1535 per practice (20% child population of actual list sizes of 107 general practices in Bolton and Swansea and Powys), lifetime prevalence of DVA of 12% (40), 4 intervention referrals per practice per 12-months (44 children from seven practices over 18-months in IRIS+ feasibility study) and an intervention to control rate ratio of 5.5 (30% of the referral rate ratio of 18.58 for women in IRIS trial (21)). Gives 40 practices per group. Average *adult male* population of 3009 per practice (49% males out of 80% adult population actual list sizes of 107 general practices in Bolton and Swansea and Powys), DVA perpetration over the past 12-months in men of 4.52% (18), 3 referrals per intervention practice per 12-months (29 men from seven practices over 18-months in IRIS+ feasibility study), and an intervention to control rate ratio of 10 (50% of the referral rate ratio of 18.58 for women in IRIS trial (21)). Gives 37 practices per group.

We assumed that there would be more children than women referred in the control groups (0.73) and fewer men (0.3) based on our co-applicants' knowledge of the current rates of referral within IRIS. We need to estimate the denominator using known practice list sizes, due to known under-reporting of DVA at general practice level. This was calculated assuming the recruitment centres were Bolton, Swansea Bay and Powys as in the funding application. However, the centres are now Bolton, Swansea Bay and South Gloucestershire/Bristol. Given the large sampling errors on ICCs (41, 42), we have used patterns in ICCs (81) and experience, rather than specific ICC values from previous studies to estimate our ICC. Further, for binary outcomes, the likely maximum value of an ICC is related to the prevalence of the binary outcome (42)**.** The likely maximum value of an ICC becomes smaller the more extreme the prevalence is. For a 5% prevalence, the likely maximum ICC value is around 0.05 but observed ICCs for this prevalence tend to be smaller. For example, in the IRIS trial (21) where the rates for the primary outcome were around 5%, the ICC was only 0.0008. Our specified ICC of 0.03 for the more extreme rates in the proposed trial is thus conservative. Our observed ICC is likely to be smaller. With an ICC of 0.01 we would have near 100% power to detect our clinically important difference for both men and children. Even with a more conservative ICC of 0.04 we would have 81% power for men, 74% power for children.

The sample size is inflated to account for attrition of general practices or participants, with two extra general practices per group randomised (N = 42). The randomisation is at general practice-level and practices are unlikely to drop out, as both the intervention and control programmes are low burden, with training only implemented once after randomisation. Some practices may merge in the lifetime of the study, however they normally retain location. Since the practice-level intervention will take place at the beginning of the study, practice mergers are unlikely to affect recruitment and intervention delivery.

6.3 Post-intervention interview study with adult and CYP service users and key professionals:

(i) Approximately 45 interviews with a sub-sample of IRIS+ service users (approx. 15 women, 15 men, 15 children and young people (CYP))
(ii) Approximately 30 interviews with key professionals involved with the delivery and facilitation of the IRIS+ intervention (clinical leads, service providers, commissioners)

6.4 Sample size calculation – Post-intervention interview study

The sample size for the interviews was estimated based on our pilot study. Based on our pilot, we anticipate that approximately 45 post-intervention interviews with IRIS+ advocacy support service users (15 women, 15 men, 15 CYP) and approximately 30 interviews with key professionals will be required. Actual sample size will be determined by information power (43) with continuous assessment as data collection progresses. We will use purposeful sampling to maximise heterogeneity in terms of (i) key service user participants' characteristics relevant to intervention impact and reach (site, age, gender, etc) (special attention will be on ensuring ethnic diversity due to anticipated language-based selection and self-selection criteria and bias) and (ii) key professional participants' characteristics relevant to implementation and reach (site, sector/industry, role, gender, etc.).

6.5 Recruitment, consent and randomisation for cRCT

6.5.1 General practice recruitment

We will aim to recruit a total of 84 general practices from the three areas.

All eligible general practices in Bolton (N=49), South Gloucestershire/Bristol (N=57) and in the Swansea Bay area (N=46) will be approached to participate in the study. This will be done using a number of different approaches. Initially each practice will receive an email invitation from the Research Delivery Network, in England and Health and Care Research Wales, in Wales. This will also include advertising the study via GP bulletins and their websites.

Alongside this, general practices will receive an invitation email/letter to participate from IRISi and the DVA services, including details of the study. IRIS advocate educators and clinical leads who have contact with general practices will also share information about the study. The study will be advertised on the DVA services social media platforms.

General practices who are interested will be asked to complete an expressions of interest form. Interested practices will receive a phone call/e-mail from the study team with further information and will be sent an information leaflet. Practices wishing to have further details or clarification, will be offered a conversation by the research team to explain the study in more detail.

6.5.2 General practice consent

Since the study involves randomisation at the practice level, acceptance and understanding of participation by all the key stakeholders at the practice (and a commitment to organisational and procedural change) will be vital. Practices therefore will be given time to discuss and consider participation. Those still interested will consent on a first come first served basis through signing the mNCA (Model Agreement for Non-Commercial Research) which is signed off by the Sponsor. The relevant (intervention or control) OID (Organisation Information Document) will be completed post-randomisation once the site knows which group they have been allocated to.

Since this is a cluster randomised trial, and all patients within one practice will be treated in the same way, consent will be obtained from practices. Use of routine non-identifiable digital healthcare systems data does not require patient consent.

6.5.3 General practice randomisation

All eligible and consenting GP practices will be randomised using a 1:1 allocation ratio to the intervention or usual care group based on randomisation procedure. The randomisation procedure will be:

1. stratified by centre (Bolton, South Gloucestershire/Bristol, Swansea Bay)
2. within centre, further stratified by level of prior engagement with IRIS (more recent and no prior engagement with IRIS)
3. minimised on practice size (small (< 6500), medium (6501 - 9999) and large (≥ 10000).

Randomisation will be carried out through an online randomisation system designed and administered by a third-party secure internet-based randomisation system (Sealed Envelope Ltd; www.sealedenvelope.com). Randomisation will be carried out by an unblinded member of the research team (e.g. Trial Coordinator) as it will not be possible to maintain blinding for those team members as they will be involved in arranging the training for the intervention sites. It will also not be possible for the GP practices to be blinded to group allocation for the same reason.

6.6 Recruitment and consent for post-intervention interviews

6.6.1 Adult and CYP service user recruitment

A small sub-sample of IRIS+ advocacy support service users who consented to be contacted at exit from the service will be recruited by a researcher to participate in an in-depth semi-structured post-intervention interview.

Service users supported by the DVA agency will be given information about the study by advocate educators. A minimum standard of English will be required from service users (as judged by the advocate educators) in order to be able to understand the written English of the information leaflet and the consent form. Those who give their consent (via the advocate educator) to be contacted by a researcher for a post-intervention interview (via parental/carer consent to be contacted for CYP- see below), will be invited by a researcher (via phone call, email or text/WhatsApp message) to participate in a post-intervention semi-structured in-depth face-to-face or phone/online interview with a researcher following their last support session. PPI groups and partner organisations will review recruitment materials and will advise on recruitment.

6.6.2 Adult and CYP service user consent

DVA agencies routinely seek consent from all individuals entering the service including individuals referred or self-referred from participating practices. This consent procedure includes seeking consent for sharing any personal data, such as NHS numbers. Consent will be obtained by the Advocate Educator during their initial meeting(s) with the service user. Personal data (including NHS numbers) will only be shared by the DVA agencies with the unblinded members of the research team (e.g. Trial Coordinator, Trial Statistician) if the service user has provided consent. Use of routine non-identifiable DVA agency data (i.e. on referrals) does not require consent.

For the post-intervention interviews we will ensure that all participants are fully informed about the study, have an opportunity to discuss participation and are given time to read the information leaflet and consider participation and what is involved. We will ensure that appropriate DVA support is available to participants (specialist services already support participants in the study sites).

The researcher will seek written, or if that is not possible (for remote/phone interviews), audio-recorded verbal consent from service users (adults and CYP) for the post-intervention interviews. For CYP, both parental/carer and CYP (in their own right) consent will be sought (see details below).

Consent procedure for children: In the first instance the IRIS+ support worker will provide the parent/carer service user with information about the post-intervention interviews and will seek parent/carer written consent for the IRIS+ support worker to securely pass their details onto a

researcher and for the researcher to contact the parent/carer to discuss the child's possible involvement in a research interview.

The researcher will then make contact with the parent/carer to discuss the possibility of the child's involvement in the research and will provide the parent/carer and the child with comprehensive information leaflets about the study. The parent/carer and their child will be given at least one week to read the information leaflets and to consider whether or not the child wants to take part in the study. If the parent/carer consents then a suitable time and safe place will be arranged to meet (or phone/online if this is what the child/young person prefers) the child/young person and seek their consent for the interview.

Children and young people's consent or assent will be sought. Assent or consent will be sought depending on the age and understanding of the child. In line with HRA guidance, (44) consent will be sought from a child or young person if they are 'Gillick competent'.

Competency is assessed on a case-by-case basis and depends on the age, understanding and maturity of the child or young person. This will depend on 'their capacity to understand the specific circumstances and details of the research being proposed, which in turn will relate to the complexity of the research itself' (https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/research-involving-children/)

Whether a child is competent to understand the research and the advantages or disadvantages of participation will be assessed by the researcher in conjunction with the consenting safe parent/carer and, where appropriate, the IRIS+ children's worker.

Children/young people's assent to take part in research will be sought where the child or young person is not considered to be Gillick Competent. Assent is the agreement of, or affirmation by, a child/young person to take part in research. In these cases, parents/carers would be providing their informed consent on behalf of the child/young person for the research to take place. Seeking assent from children and young people who are not Gillick competent provides a means of including children in the decision-making process and providing them with information about the research which matches their capacity.

If a child does not consent or assent to an interview being undertaken, then this will be fully respected.

In line with HRA guidance, parent/carer consent will not be sought for young people aged 16 or over. Young people aged 16 or over will be asked for their consent to be contacted by the researcher by the children's worker and/or IRIS+ support worker. If the young person consents, the researcher will then make contact with them following the protocol for adult IRIS+ service users set out earlier.

6.6.3 Key professional recruitment

Key professionals involved with the delivery and facilitation of the IRIS+ intervention will be recruited by a researcher to participate in an in-depth semi-structured interview.

Key professionals will be identified throughout the intervention set up and delivery by the research team, in collaboration with partner organisations delivering the intervention. PPI groups and partner organisations will review recruitment materials and will advise on recruitment. Potential participants will be contacted by a researcher (via phone call or email) to participate in a post-intervention interview.

6.6.4 Key professional consent

The researcher will seek written, or if that is not possible (for remote/phone interviews), audio-recorded verbal consent before interviews. We will ensure that all participants are fully informed about the study, have an opportunity to discuss participation and are given time to read the information leaflet and consider participation and what is involved. We will ensure that appropriate DVA support is available to participants (specialist services already exist in the study sites).

All recruitment and consent procedures will comply with the HRA's Participant Information Quality Standards (45).

6.7 Method and schedule of data collection

See Appendix 1 and Appendix 3

6.7.1 GP referral data collection

Referrals of men and CYP (co-primary outcomes i-ii) and referrals of women (secondary outcome i) to specialist DVA services will be routinely collected by DVA agencies and will be extracted by DVA agency staff from DVA agency data systems for 15 months before and up to 15 months following the clinical training session (first clinical training session if training is delivered in two or more sessions) in intervention practices (See Data collection timeline in Appendix 1.), and a matched date for control practices. Matching will be done by pairing intervention and control practices by practice size, site and clinical training time, due to the potential of secular trends. Data report on referrals will be shared quarterly with research team.

The 12-15 months follow-up period for the referral data (from the date of the clinical training at each general practice) is based on IRIS implementation (89), and IRIS+ pilot findings and accounts for time that may be needed for clinicians in intervention practices to embed the new DVA identification process and the referral route for children and men in their practice (any late joiners may have a shorter embedding period, but will have a minimum of 12 months for patient referrals). The matched referral period will be staggered for control practices to synchronise with the start dates for intervention practices to avoid bias due to secular trends in referral.

6.7.2 Individual-level healthcare systems digital data extraction

Individual-level healthcare systems female, male and CYP digital data (secondary outcomes ii-iii) will be extracted for 12 months before, and 12 months after referral. Data collection will be facilitated by service users' NHS numbers (provided to DVA agencies by GP practices at the time of referral) who will match NHS numbers to their service user IDs. The trial statistician will then merge these data with EQ-5D, randomisation data, GP practice demographics, service user demographics and referral data, which will be securely provided to data providers such as SAIL Databank, Wales and Graphnet CareCentric, England. The data providers will merge, using NHS numbers, with data held on healthcare use, and physical and mental health (diagnosis, prescribing).

6.7.3 Medical notes review for DVA identification

We intend to extract identification data (secondary outcome iii) from a small subsample of GP practices (control and intervention), as part of the process evaluation. This will be subject to securing extra funding/capacity for this work. Non-identifiable data will be extracted from the GP electronic medical records for a period of 12 months after the delivery of the IRIS+ training intervention (matched date for control practices) to review clinical DVA identifications during the study period. We will search for specific codes relating to DVA victimisation or perpetration event or disclosure. Cases identified will be checked by a practice team member (assisted by a researcher blinded to data) for DVA relevance and for the action taken by the clinician. No identifiable information on-(or off-) site will be accessed by research team.

6.7.4 Individual-level self-reported DVA advocacy service user data collection

Individual-level self-reported DVA advocacy service user data (secondary outcomes ii; iv) on adult and CYP health- and service support outcomes (including relevant EQ-5Ds) will be routinely collected by DVA agencies as part of routine service monitoring between baseline and last meeting/session (case closure, circa 3 months). HRQoL for women (EQ-5D-3L) will be collected for individuals referred/self-referred from both intervention and control practices. HRQoL for men (EQ-5D-3L) and CYP (EQ-5D-Y) will be

collected for individuals referred/self-referred from intervention practices. HRQoL for men and CYP from control practices will only be collected for those who self-refer. The EQ-5D-Y and child health outcome will be collected by the CYP worker with the child as part of routine service monitoring.

Routinely collected service monitoring and evaluation data (secondary outcome vi) DVA advocacy service user feedback, service user contact, type and length of support, and basic demographics will be routinely collected by DVA agencies as part of routine service monitoring and extracted by DVA agency staff from the agencies' case management systems. Data report will be shared quarterly with the research team. Personal data (including NHS numbers) will only be shared if the service user has provided consent.

6.7.5 Post-intervention service user and key professional interview data collection

Qualitative data on DVA advocacy service user experiences of receiving support and outcomes will be collected by a researcher in post-intervention in-depth semi-structured face-to-face or phone/online interviews. If the service user participant has a minimum standard of English, as judged by the advocate educator (able to understand the written English of the information leaflet and consent form), but requests that they conduct the interview in the language of their choice, and if an interpreter is acceptable to them to be present, the research team will aim to support this. Given the highly sensitive nature of these interviews, the specific arrangements for this will be explored on a case-by-case basis pre-interview, as working with a translator as an intermediary may compromise the rapport between the researcher and the participant, and may pose a safety risk to interview participants (46).

Implementation scalability, impact mechanism and reach data (secondary outcome v) - in addition to post-intervention semi-structured in-depth interviews with adults and CYP, and routine training, service monitoring and evaluation data, will be collected with key professionals involved in the organisation and delivery of the intervention, using semi-structured face-to-face or phone/online interviews conducted by a researcher.

The research team will write reflexive notes throughout the study process about experiences of implementation to add further insight to the interviews.

6.8 Withdrawal from the trial

GP practices can choose to withdraw for any reason at any time during their involvement in the trial. The CI can also decide to withdraw GP practices if circumstances require at any time during the trial. Although it is the practice's right to withdraw without giving a reason, it is a GCP requirement that a reason be sought and recorded if given. In the event of any form of withdrawal, data obtained up to this point (including data linked with patients referred until this point) will be retained for analysis, as advised in the PIL.

Individual interview participants can choose to withdraw for any reason at any time during their involvement in the trial. The CI can also decide to withdraw interview participants if circumstances require at any time during the trial. Although it is the participant's right to withdraw without giving a reason, it is a GCP requirement that a reason be sought and recorded if given.

In the event of any form of withdrawal and unless interview participants indicate otherwise, data obtained up to this point will be retained for analysis, as advised in the PIL.

6.9 Trial stopping rules

The trial may be prematurely discontinued by the Sponsor, CI, Regulatory Authority or Funder based on new safety information or for other clinical or administrative reasons given by the Data Monitoring and Ethics Committee (DMEC), regulatory authority or ethics committee concerned.

The trial may also be prematurely discontinued due to lack of recruitment or upon advice from the TSC, who will advise on whether to continue or discontinue the trial and make a recommendation to the

Funder. If the trial is prematurely discontinued, no new participants will be recruited, and a decision on data collection on active participants and routine data will be made in discussion with the TSC/DMEC and Sponsor.

6.10 End of Trial

The end of the trial will be after we have collected all data, received the final data extractions and have resolved data queries.

7 INTERVENTION

7.1 The intervention and its components

The IRIS+ (intervention) and IRIS (control) programmes are targeted at primary health care clinicians and all patients for IRIS+; and women for IRIS attending general practices. The IRIS programme is targeted at women only and for IRIS+ it will be targeted at women, men and CYP affected by parental DVA and/or experiencing it in their own relationships. Given that IRIS+ is a system-level intervention sitting both within primary care and the voluntary sector, it is placed to reach all people, regardless of age, gender or sexuality, including disadvantaged, marginalised and vulnerable populations.

The IRIS+ programme is a collaboration between the DVA and health sectors, expanding the population scope of IRIS (47). IRIS+ is a complex intervention comprising the following components:

- clinical training to primary care teams on DVA among women, men and CYP and separate non-clinical training for admin staff;
- direct referral pathway for affected women, men and CYP to a local DVA agency;
- specialist 1:1 advocacy support by DVA agency for female and male survivors and for CYP living with DVA and/or experiencing it in their own relationships;
- risk assessment and signposting/referral to a local perpetrator group programme for adult male perpetrators.

The DVA advocacy is an integral part of the intervention. The perpetrator group programme is linked to the intervention via a direct referral pathway or signposting, but is not part of the intervention (advocate educators can make direct referrals to a perpetrator programme or perpetrators may self-refer to the program). The theoretical framework of the intervention is based on educational outreach, adult learning theory, normalisation process theory and peer influence (48-50). It was developed using the MRC framework for complex interventions (36, 51). The clinical training, the availability of a direct referral pathway, the specialist advocacy support, and signposting build on and expand the IRIS training and advocacy support programme. It comprises linked components at general practice and DVA agency level.

At the general practice level, the intervention is designed to engage clinicians by improving the identification and management of female and male adult patients who experience or perpetrate DVA, and CYP living with DVA or experiencing it in their own relationships.

The two-hour (or locally tailored) face-to-face or online interactive clinical training intervention (and brief online or face to face reinforcement session) consolidates and improves clinicians' knowledge of DVA and health, particularly in terms of engagement with men who are victims and/or perpetrators, and direct engagement with CYP affected by DVA. It also improves clinicians' understanding of how the experiences of abuse may differ for those from diverse communities and how experiences of intersectionality may lead to additional barriers to disclosure. The clinical training and referral pathway enable clinicians to identify and refer female, male and CYP patients for specialist advocacy support; safely and accurately record DVA in electronic medical records; manage ongoing relationships with affected patients, including safely managing ongoing relationships with members of the same family. Training will take place in general practices or in external venues or remotely.

The intervention includes a password-protected updated online IRIS+ resources for clinicians working in intervention practices, supplementing and consolidating training with key parts of the clinician training and practical information. Patient- and clinician-facing publicity materials (waiting room posters, patient cards, etc) are also part of the intervention.

At DVA agency level, the intervention includes DVA advocacy support for all adults provided by the named advocate educators. CYP are supported by the named CYP workers. The advocate educators and the CYP workers are based in the local voluntary sector DVA agencies (Fortalice and Calan). The advocate educators co-deliver the clinical training with the IRIS+ clinical lead. The advocate educators and the CYP workers receive referrals from clinicians working at the intervention practices and provide DVA advocacy to referred adults and CYP face-to-face or remotely. (Appendix 2: IRIS+ intervention flowchart).

IRIS+ is free of charge, does not have a referral threshold, and patients registered with an IRIS+ general practice can self-refer to the service, therefore those who do not directly engage with clinicians in general practice may still be able to receive DVA advocacy.

IRISi will coordinate setting up and access to the IRIS+ training intervention, and training resources, (starting with training for trainers).

7.2 Intervention in relation to IRIS (control intervention)

The key difference between IRIS and IRIS+ for CYP and men are the strengthened clinical training, the availability of a direct referral pathway, the availability of specialist advocacy support, and the availability of a local group perpetrator programme.

With regards to clinician response to CYP, the difference is the additional training component on CYP in IRIS+, enabling clinicians to proactively ask and identify CYP living with DVA and/or experiencing it in their own relationships directly (and indirectly via their parents). With regards to the specialist advocacy support response to CYP, the difference is the additional CYP worker role and capacity in the DVA support agency providing dedicated direct specialist support to CYP. The additional clinician training, the direct referral pathway and the specialist support resource for CYP are expected to generate higher identification and referral rates and more direct engagement with CYP by both clinicians and specialist service providers. It is expected that better clinical and specialist service engagement with CYP will lead to improved health and wellbeing outcomes for CYP (and, in turn, their parents).

With regards to clinician response to men, the difference from IRIS is the additional training component on male survivors and perpetrators enabling clinicians to proactively ask and identify men. With regards to the specialist advocacy support response to men, the difference is the additional male worker role and capacity in the DVA support agency providing dedicated specialist support to male survivors and risk assessment and signposting to male perpetrators. It is expected that better clinical and specialist service engagement with men will lead to improved health and wellbeing outcomes for both male survivors and partners of perpetrators. In terms of programme mechanisms for perpetrators, clinicians and advocate educators are not trained or expected to bring about change in perpetrator behaviour (specialist work with male perpetrators takes place outside the IRIS+ intervention), but the advocate educators will signpost referred men to perpetrator programmes and the train-the-trainer event and the clinical training includes reference to the model of change for male perpetrators.

7.3 Intervention delivery

Following the two-hour IRIS+ clinical training session, which builds on the IRIS training (see below) that all intervention practices must have previously received, the IRIS+ patient referral pathway will be available for patient referrals for each intervention practice for a period of 15 months (with an assumed up to three months of embedding. See ‘referral window’ in Data collection timeline in Appendix 1). Any late joiners may have a shorter embedding period, but will have a minimum of 12 months for patient referrals. Advocacy support for referred patients at the DVA agencies will be needs-led and will take circa 3 months. Advocacy support will be available at the DVA agencies for a total period of up to 18 months (up to 15 plus up to three months after the last patient referral to allow sufficient time for advocacy support for patients referred at the end of the practice referral period).

7.4 Control intervention

Control practices will continue to participate in the evidence-based IRIS programme (21, 47) (or if not yet IRIS-trained and allocated to control, they will start their participation in the IRIS programme), and will receive the ongoing support and reinforcement of that programme as their usual practice. Following the (two two-hour) IRIS clinical training that all control practices must have already received, the IRIS referral pathway will be available for patient referrals for the whole duration of the IRIS+ intervention (possibly beyond given that the IRIS service is a commissioned programme at the trial centres). Advocacy support for referred patients at the DVA agencies will be needs-led and will take circa 3 months.

8 SAFETY REPORTING

All adverse event reporting will be in accordance with the UHBW 'research safety reporting policy'. The trust handles safety reporting on behalf of University of Bristol as Sponsor under a service level agreement.

8.1 Operational definitions

Tables 1, 2, 3 list the definitions and classifications that will apply to all safety reporting in this trial.

Table 1: Definitions of adverse events and definition

Term	Definition
Adverse Event (AE)	Any unfavourable and unintended sign or symptom that develops or worsens during trial participation, whether or not it is considered to be related to the trial intervention. In all instances, it will be up to the CI (or appropriate delegate, e.g. clinician) to determine whether the person's change in health is related to the trial.
Serious Adverse Event (SAE)	A serious adverse event is any untoward medical occurrence that: • results in death • is life-threatening • requires inpatient hospitalisation or prolongation of existing hospitalisation • results in persistent or significant disability/incapacity • consists of a congenital anomaly or birth defect Other 'important medical events' may also be considered serious if they jeopardise the participant or require an intervention to prevent one of the above consequences. [a] *"Life-threatening" in the definition of "serious" refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.* [B] *"Hospitalisation" is defined as an unplanned overnight stay. Note, however, that the patient must be formally admitted – waiting in outpatients or an Emergency Department would not count as hospitalisation (even though this can sometimes be overnight). Prolongation of an existing hospitalisation qualifies as a SAE. Planned hospital stays would not be counted as SAEs, nor would stays in hospital for "social reasons" (e.g. respite care, the fact that there is no-one at home to care for the patient). Also, if patients had a day-case operation, this would not qualify as hospitalisation. However, if a planned operation was brought forward because of worsening symptoms, this would be considered as an SAE. Hospitalisations for the purpose of the intervention are an exception to SAE reporting unless complications occur.*

Table 2: Classification of Severity

Mild event	An event that is easily tolerated by the participant, causing minimal discomfort and not interfering with everyday activities.
Moderate event	An event that is sufficiently discomforting to interfere with normal everyday activities.
Severe event	An event that prevents normal everyday activities.

Table 4: Classification of Expectedness

Expected	Reaction could be predicted/is foreseeable.
Unexpected	Reaction was unanticipated.

Table 3: Classification of Relatedness

Not related	Temporal relationship of the onset of the event, relative to administration of the intervention, is not reasonable or another cause can by itself explain the occurrence of the event.
Unlikely to be related	Temporal relationship of the onset of the event, relative to administration of the intervention, is unlikely and it is likely there is another cause which can by itself explain the occurrence of the event.
Possibly related	Temporal relationship of the onset of the event, relative to administration of the intervention, is reasonable but the event could have been due to another, equally likely cause.
Probably related	Temporal relationship of the onset of the event, relative to administration of the intervention, is reasonable and the event is more likely explained by the intervention than any other cause.
Definitely related	Temporal relationship of the onset of the event, relative to administration of the intervention, is reasonable and there is no other cause to explain the event, or a re-challenge (if feasible) is positive.

8.2 Identification of (S)AEs

As a cluster-randomised trial, in which GP practices are randomised and not individual patients, we do not have direct access to information pertaining to adverse events (AEs) and serious adverse events (SAEs) for patients and service users who may be affected by the intervention or study related procedures in any of the trial practices. We acknowledge that the risks in this population for AEs and SAEs is high, however, we will not be consenting referred patients using the IRIS+ service (service user participants) to collect data or access data from their case notes/records, therefore we will not be able to collect in-depth safety data on these service user participants. It will be the DVA agencies delivering the intervention who may become aware of events as part of their service. They will follow their organisational safety procedures, and they will keep case records, will report, monitor and support service users in accordance with their safeguarding and safety guidelines.

For service user participants at the DVA agencies, there will be a distinction between identification and reporting of AEs and SAEs collected routinely and reported to the research team quarterly from DVA agencies, and AEs and SAEs reported directly from participants who consent to the post-intervention interview in the intervention arm only.

We are requesting quarterly reports from the DVA agencies as part of our data collection (see section Method and schedule of data collection). These reports will include routinely collected data from service users from both intervention and control GP practices. These reports will also include any deaths or suicide attempts for monitoring by the DMEC. The sponsor will also be sent this information with the understanding that there will be no classification for any events and therefore there will be no expedited reporting for this trial population.

Individual-level safety reporting will only be possible for the post-intervention interview aspect of the trial for those service user participants in the intervention arm only who are consented for interview at the end of their support period (post-intervention) with the DVA agencies. We anticipate that some AEs may be identified during interview. The researcher will report any AEs that occur should they become aware, as below.

8.3 Safety reporting period

Quarterly reports from DVA agencies

Data on deaths and attempted suicides will be collected for the duration of the IRIS+ service delivery at DVA agencies (for 18 months post IRIS+ clinical training) and will be reported quarterly to the research team.

Post-intervention interview (S)AEs

Data on potential adverse events which may have occurred whilst the participant was receiving the intervention from the DVA agencies, will be collected at the time of post-intervention interviews. It is understood that these events are being collected retrospectively and likely that the event has since been resolved. Therefore, individual participants will not be followed up post-interview. Data collection period for all interviews will be between 3-24 months post IRIS+ clinical training.

8.4 Classification of (S)AEs

Post-intervention interview

Where possible and reasonable, the researcher will ask further questions to help classify if the event was serious, expected and related as per the trial's safety SOP.

8.5 Expected events

A list of events that can be expected during this trial or within this patient population can be found below.

The following events are classified as expected during this trial:

- Suicide attempts
- Self-harm
- Hospitalisation due to DVA incident

8.6 Recording and reporting AEs and SAEs

For post-intervention service user interview participants only, AEs and SAEs will be collected at interview and will be reported to our DMEC and sponsor as per safety reporting requirements.

Only non-serious AEs that are assessed as being **possibly, probably or definitely related to the intervention and/or study procedures**, should be recorded using the IRIS+ non-Serious Adverse Events Log.

All SAEs should be recorded. SAEs will require expedited reporting to the Sponsor if they are (i) fatal AND assessed as expected, or (ii) assessed as unexpected AND assessed as being possibly, probably or definitely related to the intervention and/or study procedures. The PI, or appropriate delegate, should complete these assessments.

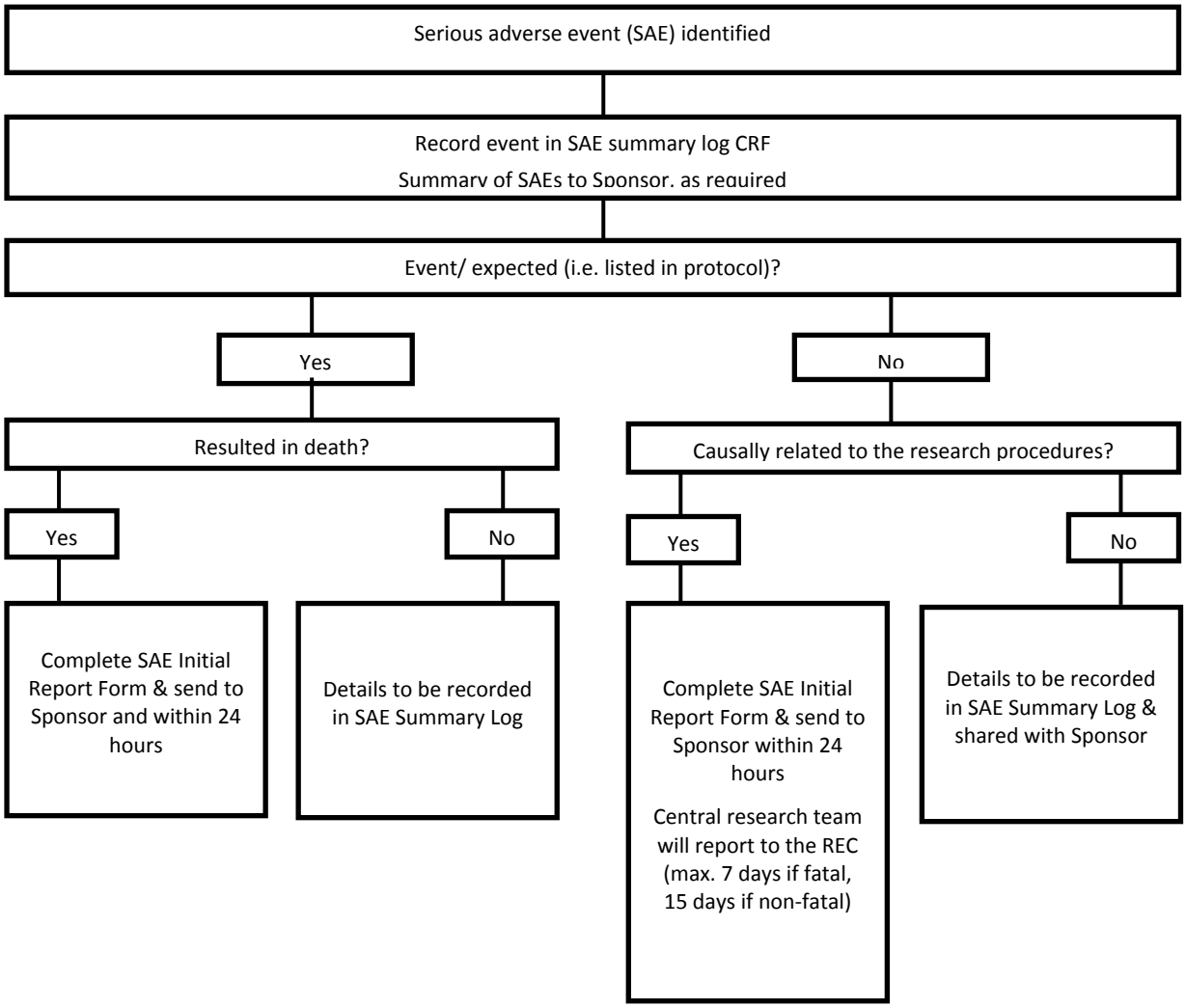
For SAEs that require expedited reporting, a full SAE Initial Report Form should be completed. The initial report may be provided orally but a written SAE Initial Report Form must be completed within 24 hours of staff becoming aware of the event.

For SAEs which are unexpected and related, the research team will report these to the REC within 15 days (non-fatal) or within 7 days (fatal) of staff becoming aware of the event.

8.7 Follow-up of AEs and SAEs

We do not anticipate following up (S)AEs which have occurred retrospectively which are divulged at interview. However, during the post-intervention interview, should the researcher feel there is cause for concern, they will follow the safety SOP which may include referring back to the DVA agency to take forward the support of the individual, as appropriate.

Figure 1 Overview of safety reporting requirements for AEs assessed as being serious (SAEs).



8.8 Urgent safety measures

Due to the population involved in this trial, the DVA agencies will follow their local procedures should they suspect a service user is at immediate risk of harm. As the only research participants involved in this trial would be those who consent to take part in the post-intervention interview, any USMs will only relate to those participants either at a trial procedure level or individual level.

In line with UHBW Research Safety Reporting procedures, the Sponsor and investigator may take appropriate urgent safety measures to protect research participants from an immediate hazard to their health and safety.

The CI will notify the REC immediately where possible, and no later than three days from the date the measures are taken, and the circumstances giving rise to those measures. The Sponsor will then follow-up with written notification within three days of the action being taken, i.e. in the form of an

amendment, describing the event, the measures taken and justification for the measures taken. NHS R&D offices will be notified in accordance with local policies/procedures. The DMEC will be asked to review information relating to USM and report recommendations to relevant parties.

8.9 Monitoring and assessment of serious/adverse events

All adverse event reporting will be in accordance with the UHBW Bristol 'Research Safety Reporting Policy'. The trust handles Safety Reporting on behalf of University of Bristol (UoB) as Sponsor under a Service Level Agreement.

8.10 Safety data review

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

In accordance with the Trial Terms of Reference, the DMEC will report its periodic review of safety data to the TSC.

8.11 Notification of deaths

All DVA agency service user deaths will be reported quarterly to the sponsor irrespective of whether the death is related to participation in the study. This information will be passed to the sponsor by the trial team.

9 DATA ANALYSIS

The effectiveness of the IRIS+ intervention will be assessed through analysis of the primary objective, and secondary objectives 1 and 3, with cost-effectiveness assessed through the economic evaluation; secondary objective 2.

All quantitative data will be collected and managed using REDCap electronic data capture tools (52, 53) hosted at the University of Bristol. Quantitative data analysis will be carried out in Stata (54). No interim comparative between-group analysis is planned before the end of the trial follow-up period. All cRCT data will be reported according to the CONSORT extension for cRCTs (55). To investigate the effect of missing data on treatment effect estimates for the co-primary outcomes, economic evaluation and patient-reported outcomes we will explore the use of appropriate methods to account for missing data (56). This may include methods assuming data are Missing At Random (MAR) (for example, multiple imputation using chained equations and predictive mean matching), and sensitivity to the MAR assumption. All qualitative data will be stored and analysed in NVivo (57).

9.1 Analysis of GP referral data

Number of referrals of men and CYP to specialist DVA services, out of the population expected to have been exposed to, or perpetrating DVA.

The population will be calculated using the numbers of males/CYP registered in each general practice multiplied by the estimated proportion of those experiencing DVA, 0.12 CYP, or perpetrating, 0.0452 males. These are the same proportions used the sample size calculation.

Each co-primary outcome will be analysed separately by population using an appropriate mixed-effects random-intercept regression model for rate data, adjusted for baseline referrals over the 15 months before intervention, allocation, and stratification centre (Bolton, South Gloucestershire/Bristol, Swansea Bay) as a random effect. Consideration will be given to a model that appropriately estimates when there are true zero rate outcomes, which may be reported for control practices. If estimable within this model, the stratification variable of, more recent and no prior engagement with IRIS, and minimisation variable of practice size (small (<6500), medium (6501-9999) and large (≥ 10000) will also be included. The alpha value of the regression model will be 2.5% to account for the two co-primary outcomes.

Subgroup analyses will be carried out to investigate whether there is a differential effect of intervention within centre (Bolton, South Gloucestershire/Bristol, Swansea Bay), different levels of prior engagement in the IRIS programme (more recent and no prior engagement with IRIS), and by socioeconomic disadvantage (general practice postcode index of multiple deprivation). This will use a similar regression model to the primary analysis, but will include the subgroup variable as an interaction with allocation, with other appropriate model adjustments as required.

We aim to carry out sensitivity analyses using the number of patients identified in healthcare systems digital data as experiencing, or perpetrating DVA as the population.

Number of referrals of women to specialist DVA services will be analysed using an appropriate mixed-effect regression model for rate data, calculated and adjusted as described for the co-primary outcomes. The estimated proportion of those experiencing DVA is 0.169. We aim to carry out sensitivity analyses using the number of patients identified in healthcare systems digital data as experiencing, or perpetrating DVA as the population.

9.2 Health economics analysis

The primary economic analysis will be an economic evaluation alongside the trial using a health-sector perspective (NHS). Resources in relationship to the intervention will be recorded by partner agencies at centre level and include salary of advocacy workers (including CYP worker), travel, recruitment, equipment for advocate educator (laptop and telephone), cost of publicity materials distributed at general practices, cost of clinical lead (time apportioned to delivering the intervention), central management costs for the partner agency, cost of onward referral from partner agency to another service where appropriate and IRISi fee. Cost of the control arm will include similar items, but not include CYP worker as well as costs in relation to supporting men. The IRISi fee for established areas is expected to be smaller. Thus, for this and other reasons, it is expected that intervention costs will vary by centre. Resource per eligible patient will be calculated using micro-costing (58). Resource use within healthcare settings for DVA-referred patients will be measured using healthcare systems digital data (Wales: SAIL Databank; England: Graphnet CareCentric) and will include community-based NHS visits, including GP and nurse visits; inpatient and day-case hospital admissions, A&E and outpatient visits and medication prescribing. The use of SAIL Databank and Graphnet CareCentric will enable costing to secondary and tertiary healthcare services, as well as primary care services. These data will be analysed within each data providers' Trusted Research Environment (TRE), and will not be extracted as microdata, but will instead be extracted in summary reports. These data cannot be combined across TREs, and therefore only aggregated results by sites (Bolton, South Gloucestershire/Bristol, Swansea Bay) will be combined and reported. Healthcare costs will be based on NHS reference costs, personal social services research unit costs (59, 60) and British National Formulary (61) whenever possible. The cost associated with each resource use item will be calculated by multiplying the units of resource used in the 12-month period after referral, by its unit cost. The within trial economic evaluation will use 12-months (short-term) as period for analysis.

Quality adjusted life-years (QALYs) accumulated will be calculated from the UK preference-based utility scores using the area-under-the-curve approach: assuming a linear change between the time points (baseline – support complete [3 months] – 12-months). Cost and QALY estimates will be jointly determined in regression analysis, further adjusted by randomisation variables, and baseline scores for QALYs, using seemingly unrelated regressions. The same stratification and minimisation variables used in the statistical analysis will be used for consistency. Although data on costs will be obtained from healthcare systems digital data, patterns of missing data in the domains of the EQ-5D will be examined. As well as a cost per QALY gained (cost-utility) analysis, we will also estimate the cost per life-years (cost-effectiveness analysis).

The secondary economic analysis will primarily take a societal perspective and will include a cost-utility analysis comparing IRIS+ with usual care (IRIS). The cost-effectiveness modelling will consist of a Markov model, using ten years as period of analysis, consistent with other studies (50, 74) and in line with the understanding that this is the potential lifetime effect of the intervention. The economic modelling will focus on cost-utility (cost per QALY gained) as recommended by NICE (62). The adoption of a societal perspective for the long-term modelling is justified by the fact that in DVA, a large proportion of the costs fall outside healthcare. Given that the intervention is already multi-sectorial (health care + third sector specialist support services), the societal approach is appropriate as base case. However, a secondary analysis will use a health services and personal social services (NHS+PSS) perspective, as recommended by NICE (62). For IRIS practices (control), HRQoL improvements can only be measured for men and CYP if they self-refer into support services. Should there be no self-referrals of men and CYP in the IRIS arm, the model will consider that no improvement was obtained, as there will be no men and CYP receiving advocacy support, and there is no published evidence that suggests identification alone increases HRQoL. Cost-effectiveness will be assessed by evaluating the incremental cost-effectiveness ratio and comparing this with £20,000 and £30,000 per QALY thresholds (63). A probabilistic sensitivity analysis will be conducted to assess methodological, parameter uncertainties in both forms of economic analysis. Structural uncertainties will be assessed exploring different scenarios.

Consideration will be given to spill-over effects. It is likely that this would affect both intervention and control groups in a similar fashion. As a result of spill-over effects, benefits measured in this study may be underestimated, providing a conservative approach that does not *a priori* favour the intervention.

GP-reported healthcare use and cost differences will be explored, particularly in terms of acute care needs and mental health needs, using regression models appropriate for the outcome, adjusted as described for the co-primary outcomes. To address substitution effects, a difference-in-difference analysis will be carried out comparing changes over-time for healthcare use (including mental health) and wellbeing (including prescribing) for women referred into IRIS+ (intervention) and IRIS (control). Healthcare systems digital data for 12 months before and after referral will be used. Costs may also be included as a relevant outcome. Duration of harms, patterns in prescribing and severity of diagnosis will be explored and estimated between treatment groups, and population groups (women, men, children), using regression analysis. A before-and-after time-series analysis should enable the modelling of downstream benefits of the intervention for men and children.

We will explore differences in socio-economic and contextual characteristics for those referred into specialist services that decide not to engage. Understanding of populations not identified but at risk will rely on comparisons with relevant national surveys that identify exposure to violence (e.g. Crime Survey for England & Wales, National Study of Health and Wellbeing). Understanding the needs of those not identified through the intervention will also be explored during interviews with key professionals through discussion of the limits of implementation reach and impact.

Adults and CYP service-user self-reported and routinely collected service data (baseline and post-intervention) on health-outcomes, and DVA exposure will be analysed using regression models appropriate for the outcome, adjusted by length of time supported by the DVA agency, and other covariates as described for the co-primary outcomes.

9.3 Process evaluation

Post-intervention in-depth qualitative interviews will be audio-recorded, transcribed verbatim, coded and analysed thematically using Framework analysis (64) to articulate contrasting perspectives, context and unintended consequences of intervention and then juxtaposed with the trial results. Analysis will be informed by reflexive notes about the implementation process from study team members. The qualitative research team will develop the initial coding frame based on anticipated (from the literature and the logic model) and emergent themes (from the data). It will be tested in pilot interviews and subsequently revised. The qualitative research team will then identify themes within elements of the analysis framework, and these will be revised and interpreted through research team discussions. A member of the research team will independently code a proportion of the data. Discrepancies in coding will be adjudicated by a third member of the research team. To assess the mechanisms of implementation and reach, service evaluation, monitoring, GP DVA identification (from a small subsample of practices-subject to further funding) and DVA agency data will be analysed using Stata. The process evaluation will triangulate quantitative and qualitative data to identify associations between the intervention, outcomes, and context. This will inform refinement of the logic model. Building on evidence about the real-world implementation of the IRIS model (22-24), an approach to scalable and sustainable implementation of IRIS+ will be developed by IRISi in collaboration with the research team.

Discussions with IRISi, our partner organisations and PPI groups will support interpretation of data. Their expertise will inform the refinement of the logic model, the understanding of the barriers and enablers of the intervention and the identification of any unintended consequences.

10 DATA MANAGEMENT

10.1 Data protection

All study data will be collected, processed and stored in compliance with the UK General Data Protection Regulation 2018 (GDPR) and the UK Data Protection Act 2018.

10.2 Data handling

For the trial, research data will be transferred electronically from the DVA agency (service use data) to the Trial team at the Bristol Trials Centre (BTC) at the University of Bristol (UoB). The pseudonymised data (i.e with NHS number) transfer will be via a secure email, such as CJSM (Criminal Justice Secure Email) or Egress. Large files can be transferred via the University of Bristol's secure data transfer system, 'Fluff'.

The BTC Systems Team will merge the data from the above DVA agencies on a UoB server and allocate a trial ID number per service user. Research data will then be transferred onto a REDCap database. REDCap is a secure, web-based electronic data capture system designed for the collection of research data. The system has been developed and supported by Vanderbilt University. The BTC, has set up its own infrastructure so that all systems are hosted at and supported by UoB. Only Systems Team members, the Trial Statistician, Trial Health Economist, Trial Coordinator and Trial Administrator will be unblinded to be able see patient identifiers e.g. NHS numbers.

Standard operating procedures (SOPs) for database use, are available and regularly maintained by BTC. The database is password protected, accessible only to necessary IRIS+ study and BTC staff.

As detailed in Section 6.7.2, NHS number and specific data will be securely provided to data providers by the trial statistician. Data held by healthcare systems data providers such as SAIL Databank, Wales and Graphnet CareCentric, England) will not be transferred, but held and analysed in each providers' TRE. We will aim to access data from NHS Bristol, North Somerset and South Gloucestershire Integrated Care Board (BNSSG ICB) once their TRE goes live (pending appropriate negotiation). Any necessary data required for outcome analysis will be imported into the TRE and matched on NHS number by the relevant organisation.

For the interview study, we will use encrypted, University-owned audio recording devices to collect interview data. Participants will be asked to consent to this prior to participating. Any data that is used for analysis will be anonymised appropriately.

10.3 Data storage

The raw data from the DVA agencies will be stored on a secure location on the Bristol Medical School (BRMS) secure drive at the UoB. A specific folder location will be created for the raw transferred data to be stored in. Only the BTC Systems Team, Trial Statistician and Trial coordinator will have permission to access this folder. All trial documentation will be retained in a secure location during the conduct of the trial and for 25 years after the end of the study, when any patient identifiable records will be destroyed by confidential means.

Medical notes review files, reflective notes and all audio-recording files of the qualitative interviews will be retained in a secure location during the conduct of the study and for 25 years after the end of the trial, when these files will be deleted. All hard copies of participants' contact details and transcripts will be stored securely. Transcripts will be stored separately from participants' contact/personal details. This will all comply with BTC SOPs.

10.4 Access to data

For monitoring purposes, the CI will allow monitors from the Sponsor or delegate, persons responsible for the audit, representative of the REC and other Regulatory Authorities to have direct access to data/documents.

The Trial operations team and Data Manager (in collaboration with the CI) will manage the access rights to the data set. The access rights will be reviewed annually to ensure they remain appropriate and to ensure personnel updates have been accounted for.

Where data has been obtained through data linkage with external registries, the relevant data sharing agreements will be observed (which may restrict some further data sharing).

10.5 Archiving

This trial will be sponsored by the University of Bristol who are also the data custodian. Research data will be kept for at least 25 years after the end of the trial. Data will be kept at the University of Bristol for this time and, at the end of the archiving period, will be destroyed by confidential means with the exception of a final trial dataset which will be made available for data-sharing purposes.

Where trial related information is documented in the medical records, these records will be identified by a label bearing the name and duration of the trial and clearly stating the 'do not destroy before' date. Where electronic records are in use, local site policy will be followed.

An archiving plan will be developed for all trial materials storage in accordance with the BTC archiving policy. All audio-recording files will be retained in a secure location during the conduct of the trial and for 25 years after the end of the trial, when these files will be deleted. The CI (or delegate) will provide oversight of all data destruction.

Data held at the University of Bristol will conform to the University of Bristol Data Security Policy and be held in compliance with the UK General Data Protection Regulation (GDPR), tailored by the Data Protection Act 2018.

11 TRIAL MANAGEMENT

A Trial Steering Committee (TSC) and Data Monitoring Committee (DMEC) will be established in conjunction with a Trial Management Group (TMG) to provide oversight of the trial on behalf of the funder.

11.1 Host: NHS Bristol, North Somerset and South Gloucestershire (BNSSG) ICB

NHS Bristol, North Somerset and South Gloucestershire (BNSSG) Integrated Care Board (ICB) is the host organisation. They will ensure NHS engagement and their Research Team will support the project. The Host will be responsible for delivering the contract, including financial obligations and will work with the Sponsor to monitor and manage supplier contracts.

11.2 Sponsor: University of Bristol

The University of Bristol has agreed to be the Trial Sponsor and will ensure the study meets its contractual, legal, insurance, financial and regulatory obligations, including reporting of Safety Events.

11.3 Trial Management: Bristol Trials Centre

Trial management will be coordinated by the Bristol Trials Centre. They will develop, test and maintain the study database, monitor, conduct and deliver the study. The trial will be overseen by and conform to the Bristol Trials Centre's standard operating procedures.

11.4 Trial Management Group (TMG)

The TMG will comprise of all investigators, including the PPI co-applicant. The TMG have responsibility for the day-to-day management of the trial, including trial design and delivery, budget, data analyses and publication and will report to the TSC. The TMG will meet on a regular basis with a core working group of staff having frequent progress meetings.

11.5 Data Monitoring and Ethics Committee (DMEC)

The Data Monitoring and Ethics Committee will meet once prior to recruitment of the first participant (GP practice) and convene prior to the TSC meeting to review all adverse event data and any other ethical aspects that arise and report to the TSC. The DMEC will comprise of fully independent members, including a chairperson, statistician and relevant experts in the clinical and academic field of this research. The CI, trial coordinator, clinical/data linkage lead, health economics lead and statistics lead will attend the open session only, with the study statistician attending both open and closed sessions.

11.6 Trial Steering Committee (TSC)

Membership, responsibilities, and reporting mechanisms of the TSC will be formalised in a TSC charter. The TSC will make recommendations/key decisions during the trial to the TMG and minutes will be sent to the funder. The TSC will comprise of independent members and some non-independent members (not below 75% level of independence). Members will including a chairperson, statistician, relevant experts in the clinical and academic field of this research, and at least one PPI representative. The CI, lead statistician and trial coordinator will represent the TMG as non-independent members and any other TMG members will be agreed by the TSC chair.

The TSC and the DMEC will meet at least every six months, or more often as agreed at the first meeting.

12 PATIENT AND PUBLIC INVOLVEMENT AND ENGAGEMENT (PPI&E)

We will work with and expand our existing female (through VOICES) and male (through ManKind Initiative) survivor groups. Through our partner agencies (VOICES, Calan, Fortalice), we will recruit a diverse group of young people (aged 15-21) with lived experience to advise on specific aspects of intervention/study delivery.

Our team is committed to maximise the scope and depth of PPI&E across all study stages. We will meet with each group (or with individual members) biannually to: 1. Discuss aims and trial design, agree terms of reference, recruitment strategy, review/test study materials 2. Review progress and issues on recruitment, protocol deviation, participant safety, data security 3. Discuss analysis, interpretation, dissemination, help plan pathways to impact 4. Develop non-academic outputs targeted at service users, service providers, commissioners and the public. Discussion with our PPI groups will inform the understanding of the barriers and enablers of the intervention and the identification of any unintended consequences. We will also engage members between meetings on specific issues when their expertise is required. At least one member will join our TSC.

The CYP members will work closely with the research team to co-devise/test the CYP interview, comment on emerging findings, formulate recommendations, communicate findings (co-design infographics, write blog posts, etc). We will carefully consider the age, diversity of backgrounds, experiences and any vulnerabilities of CYP contributors to ensure their wellbeing and that there are mutual benefits of involvement. Our PPI co-app will be integral to supporting the group and delivering activities embedded in each study stage.

The study will be informed by the experiential knowledge of our public contributors about safety and the practicalities of taking part in research during difficult crises. We recognise that building and sustaining meaningful partnerships across multiple groups representing diverse communities can be challenging.

Contributors will receive appropriate training and support to enable them to meaningfully participate in methodology and data interpretation work. We will draw on the resources and training developed/provided by the Centre for Academic Primary Care (CAPC) PPI team and our public involvement partnerships.

13 MONITORING

The trial will be monitored and audited in accordance with the Sponsor's policy, which is consistent with the UK Policy Framework for Health and Social Care Research. All trial related documents will be made

available on request for monitoring and audit by the Sponsor, the relevant REC and other licensing bodies.

13.1 Protocol compliance

There will be no prospective, planned deviations or waivers to the protocol. Accidental protocol breaches will be documented and reported to the Trial Coordinator, CI and Sponsor immediately. Information about protocol breaches will also be included in routine reports to the TMG, TSC and DMEC. In the event of systematic protocol deviations, investigation and remedial action will be taken in liaison with the CI, Sponsor, TSC, DMEC and the TMG.

All protocol breaches will be reported to the Sponsor as soon as possible after they occur/are identified. The Sponsor will determine whether it constitutes a serious breach, requiring onward reporting to the REC.

14 ETHICAL AND REGULATORY CONSIDERATIONS

14.1 Governance and legislation

This trial will be conducted in accordance with:

- Good Clinical Practice (GCP)
- UK Policy Framework for Health and Social Care Research
- Data Protection Act 2018
- General Data Protection Regulation

Service Level Agreements (SLA) will be in place with the three service provider DVA agencies (Fortalice Ltd., Next Link and Calan DVS). These are contractual agreements and will include details of roles, responsibilities and data requirements for the DVA agencies implementing the IRIS+ advocacy service.

Each GP practice will have an OID agreement. Before any practice can refer patients into the trial, the CI or designee will obtain confirmation of capacity and capability (or equivalent organisation approval) for each site in-line with HRA processes along with other documentation required for the sponsor to grant sites with a greenlight letter.

For all amendments, the CI or designee will confirm with the Sponsor and relevant RDNs that permissions are ongoing prior to implementation.

The protocol will be registered with ISRCTN and published in an open access journal. GCP training will be carried out by certain staff members depending on their delegated responsibilities within the trial, the level of training required will be determined according to the NIHR Delegation and Training Decision Aid. Informed consent to participate in the trial will be sought and obtained according to GCP guidelines.

The study team has extensive experience working in the field of adversity and DVA, and all are acutely aware of ethical and safety issues raised by this research. We will give full account of these risks and will put appropriate measures and procedures in place to prevent and mitigate these risks.

14.2 Research Ethics Committee (REC) review

We will follow the Ottawa statement on the ethical design and conduct of cRCTs (65) and the WHO ethical and safety recommendations for intervention research on violence against women (66). We will apply learning from our prior research on health care responses to DVA. Before the start of the trial, approval will be obtained from the Health Research Authority (HRA) (which includes review by an NHS Research Ethics Committee) for the trial protocol, participant consent forms and other participant-facing documents.

14.3 Amendments

Any amendments to the protocol or other trial related participant facing documents will be approved by the Funder and the Sponsor before being submitted to the REC/HRA for approval prior to implementation.

It is the Sponsor's responsibility to decide whether an amendment is substantial or non-substantial for the purposes of submission to the MHRA and/or REC, in accordance with the legislation and HRA processes. All amendments will be documented on the HRA amendment tool regardless of substantiality.

14.4 Peer review

The proposal for this trial has been peer-reviewed through the NIHR PHR peer-review process, which includes independent expert and lay reviewers.

14.5 Data quality

The quality of the trial data will be monitored throughout the trial and data completeness will be reported to the DMEC and TSC, and any cause for concern over data quality will be highlighted and an action plan put in place.

14.6 Financial and other competing interests

The research team and all CI must disclose any ownership interests that may be related to products, services, or interventions considered for use in the trial or that may be significantly affected by the trial. Competing interests will be reported in all publications and in the final report.

14.7 Indemnity

The trial is sponsored by the University of Bristol. The University has Public Liability insurance to cover the liability of the University to research participants. This is detailed in the certificate of insurance.

14.8 Access to the final trial dataset

Anonymous research data will be stored securely and kept for future analysis. Members of the TMG will develop a data sharing policy consistent with UoB policy. Data will be kept anonymously on research data facility storage (RDSF). Requests for access to data will follow the RDSF process on their website. https://www.bristol.ac.uk/acrc/research-data-storage-facility

The data sharing agreement will cover limitations of use, transfer to third parties, data storage and acknowledgements. The person applying for use of the data will be scrutinised for appropriate eligibility by the trial operations team (in collaboration with the CI). Given the highly sensitive nature of DVA research, we will adopt trauma-informed data sharing approaches, still consistent with open science.

15 DISSEMINATION PLAN

A plan for disseminating the trial results will be developed by the TMG. We will comply with the NIHR's threaded publication approach to publishing full accounts of NIHR-funded research. We will report our findings across a series of research articles, complemented by an overall synopsis that draws together all the strands of the project.

We will produce two types of outputs: academic and public outputs on effectiveness, cost-effectiveness and reach, and guidance about the implementation of the IRIS+ intervention and intellectual property of the IRIS+ model. Academic outputs will include: peer-reviewed journal articles of the study protocol, trial effectiveness and cost-effectiveness, and process evaluation findings; presentations at local, national, and international meetings and conferences, including at DVA conferences and national primary care conferences; webinars with policy makers and practitioners in areas local to participating general practices to present interim and final findings; policy briefings for local and national policy makers; Public-facing outputs will include blogposts, news stories and accessible digital summaries of findings co-produced with our PPI groups; webinars/presentations (developed with our PPI groups) for the public including survivors of DVA.

If the trial shows effectiveness and cost-effectiveness, we will work with IRISi to scale up the intervention and develop evidence-based commissioning guidance which will be a vehicle for intervention scaling-up. We will collaborate with our partners with commissioning expertise and the ICB to enable regional commissioning. We will work with the University of Bristol Research Development and contracts team in consultation with IRISi on the IRIS+ intellectual property. The IRIS+ training materials will be part of a commissionable program.

This research follows the principles of co-production, in which those who will benefit from the work are involved throughout. Across the programme we will develop collaborative relationships with policymakers, practitioners and people with lived experience of DVA to shape the direction, delivery and dissemination of our research. This will be facilitated by our PPI groups and through policy stakeholder meeting with commissioners and policy-makers.

We will disseminate our findings through existing IRISi networks of individuals and organisations implementing and commissioning IRIS and through our existing networks in the DVA sector. In collaboration with our PPI groups and the University of Bristol's communication team, we will create a user-friendly study website [https://irisplustrial.bristol.ac.uk/] hosted at the University of Bristol, to publicise blogposts, public-facing news stories, and webinars. We will develop blogs and news stories on other websites including IRISi. We will use Bluesky and LinkedIn to share outputs. Our Communication Officer in Centre for Academic Primary Care and colleagues at PolicyBristol, a University of Bristol team that aims to enhance the influence and impact of research on policy and practice at the local, national and international level, will support this work.

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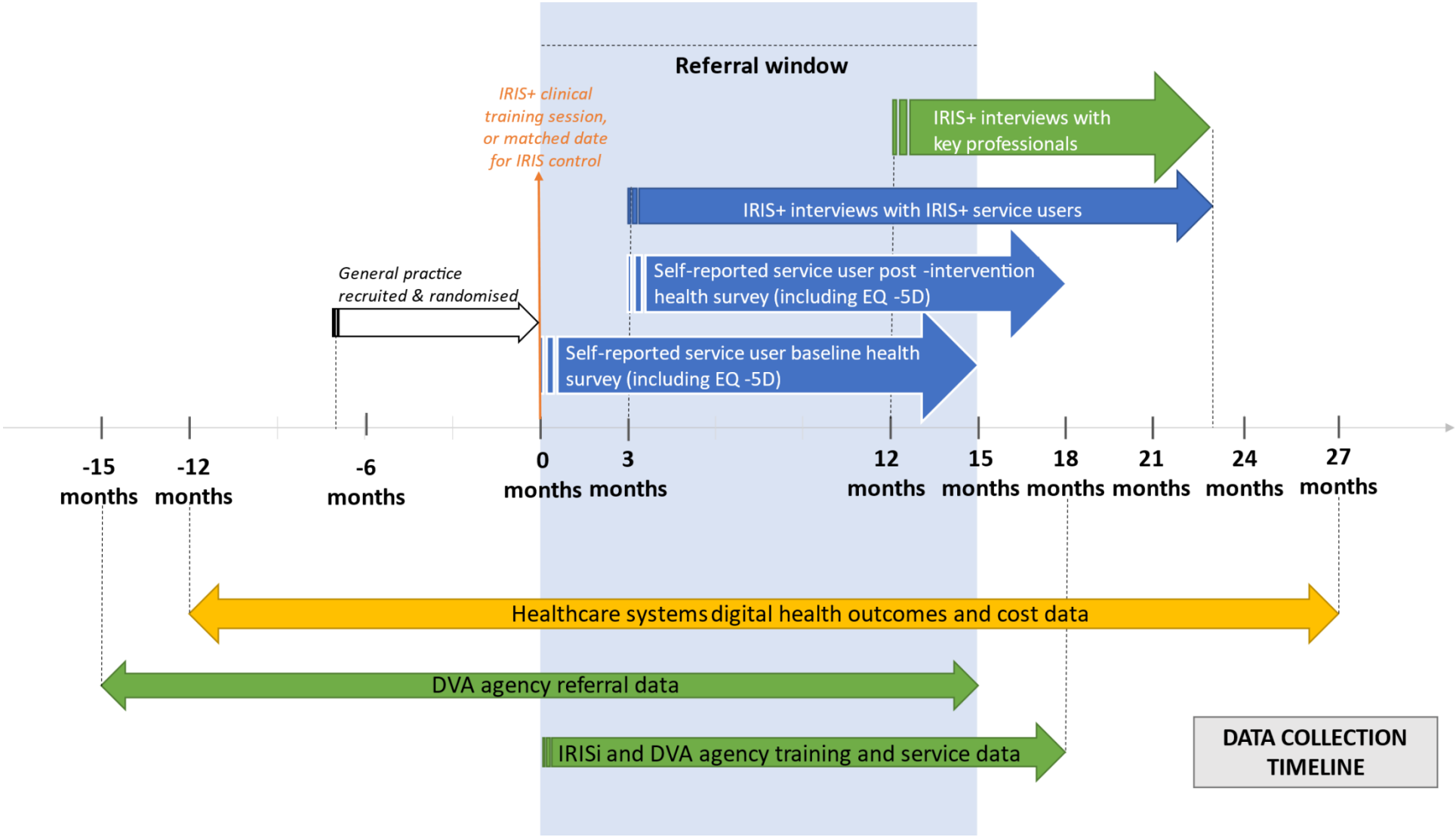
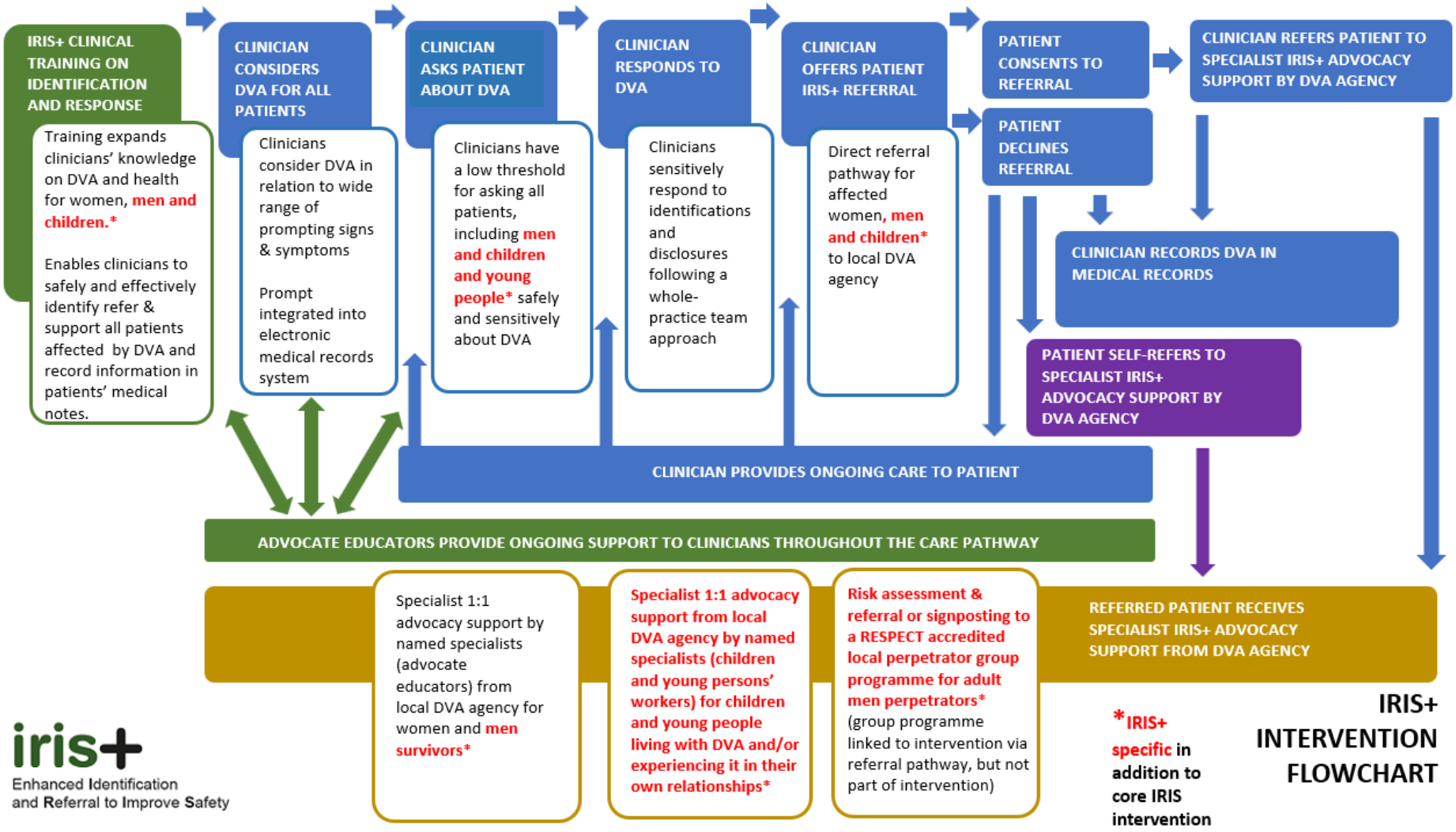
APPENDICES

APPENDIX 1 – DATA COLLECTION TIMELINE



Appendix 2: IRIS+ Intervention flowchart



Appendix 3: Method and schedule of assessment and consent procedure per outcomes

OUTCOME	METHOD OF ASSESSMENT	SCHEDULE OF ASSESSMENT	CONSENT PROCEDURE
Co-primary outcomes			
(i) Referral rate, per general practice, of adult males to DVA agencies out of the population expected to have been exposed to, or perpetrating DVA	Extracted from DVA agency data systems' routine data by DVA agency staff	15 months before and following the clinical training session in intervention practices, and a matched date for control practices	Extraction of routine non-identifiable DVA agency data does not require consent
(ii) Referral rate, per general practice, of CYP to DVA agencies out of the population expected to have been exposed to DVA			
Secondary outcomes			
(i) Referral rate, per general practice, of females to DVA agencies out of the population expected to have been exposed to, or perpetrating DVA	Extracted from DVA agency data systems' routine data by DVA agency staff	15 months before and following the clinical training session in intervention practices, and a matched date for control practices	Extraction of routine non-identifiable DVA agency data does not require consent
(ii) Cost-effectiveness of IRIS+ (within trial [short-term] and modelling [long-term])	Individual-level healthcare systems female, male and CYP digital data collection will be facilitated by NHS numbers extracted by general practices provided to DVA agencies, who will match this information to their own routinely collected service user IDs. The trial statistician will then merge these data with EQ-5D, randomisation data, GP practice demographics, service user demographics and referral data, which will be securely provided to data providers such as SAIL Databank, Wales and Graphnet CareCentric, England. The digital data providers will merge, using NHS numbers, with data held on healthcare use, and physical and mental health (diagnosis, prescribing). These data will be analysed within each data providers Trusted	Collected for 12 months before, and 12 months after referral	Use of routine non-identifiable digital health data does not require consent. DVA agencies routinely seek consent from all individuals entering the service from participating practices, including seeking consent for sharing any personal data, such as NHS numbers. Consent is obtained by the Advocate Educator during their initial meeting(s) with the service user. Personal data (including NHS numbers) will only be shared by the DVA agencies with the unblinded members of the research team if the service user has provided consent.

	Research Environment (TREs), and will only be extracted in summary reports. These data cannot be combined across TREs, and therefore only aggregated results by sites (Swansea, Bolton, Bristol) will be combined and reported.		
	Individual-level self-reported DVA advocacy service user data on adult and CYP health- and service support outcomes will be extracted from DVA agency data systems' routine data by DVA agency staff	Health outcomes collected at baseline and at case closure (circa 3 months after referral). Service support outcomes collected at baseline, during the advocacy service intervention, and at case closure (circa 3 months after referral).	DVA agencies consent as above. Use of routine non-identifiable digital health data does not require consent
(iii) Physical health and mental health (diagnosis, prescribing)	Individual-level healthcare systems female, male and CYP digital data collection will be facilitated by NHS numbers provided to DVA agencies at the time of referral by general practices and matched to routinely collected healthcare systems digital data on healthcare use, and physical and mental health (diagnosis, prescribing) held by data providers such as SAIL Databank, Wales and Graphnet CareCentric, England.	Collected for 12 months before, and 12 months after referral	Use of routine non-identifiable digital health data does not require consent
	In addition, we also intend to review and extract DVA identification data from medical notes from a small subsample of GP practices (medical notes review) as part of the process evaluation. This will be subject to securing extra funding for this work.	Collected for 12 months before, and 12 months after IRIS+ clinical training (matched date for control practices)	

(iv) Adult and CYP self-reported health-outcomes, HRQoL for service-user participants supported by DVA agencies, and adult DVA exposure	Individual-level self-reported DVA advocacy service user data on adult and CYP health- and service support outcomes will be extracted from DVA agency data systems' routine data by DVA agency staff	Health outcomes collected at baseline and at case closure (circa 3 months after referral). Service support outcomes collected at baseline, during the advocacy service intervention, and at case closure (circa 3 months after referral).	DVA agencies consent as above.
	Data collected by a researcher in post-intervention in-depth semi-structured face-to-face or phone/online interviews	Collected post-intervention (within 3 months after case closure)	Information about the study will be handed out to DVA advocacy service users by the advocate educator. Those who consent to be contacted by a researcher for an interview (via parental consent for CYP) will be invited and consented to participate in the interview study by a researcher. Consent will be written consent. If written consent is not possible (for remote/telephone interviews) we will take and audio-record verbal consent.
(v) Implementation scalability, mechanism of impact and reach	Data collected by a researcher in post-intervention in-depth semi-structured face-to-face or phone/online interviews	In addition to post-intervention semi-structured in-depth interviews with adults and CYP as specified above (iv), and routine training, service monitoring and evaluation data, as specified below (vi) – data will be collected by a researcher in semi-structured face-to-face or phone/online interviews with key professionals involved with the delivery and facilitation of the IRIS+ intervention (between 12-23 months post clinical training/first referral)	Service users, as above. Key professionals will be invited and consented to participate in the interview study by a researcher. Consent will be written consent. If written consent is not possible (for remote/telephone interviews) we will take and audio-record verbal consent.
(vi) Service delivery	Extracted DVA agency data systems' routine data	Post-intervention (18 months post clinical training/first referral)	Use of routine non-identifiable DVA agency data does not require consent

Appendix 4: Amendment History

Record of protocol version numbers and amendments:

Version		Notes
Number	**Date**	