A multicentre cluster randomised controlled trial to evaluate the effectiveness and cost-effectiveness of a school-based peer-led drug prevention intervention (The FRANK friends study)

VERSION 1_3 19/07/2019

Sponsor:	Cardiff University, 30-36 Newport Road, Cardiff, CF24 0DE.
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ISRCTN/ ClinicalTrials.gov ref:	TBC

SIGNATURE PAGE

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the trial in compliance with the approved protocol and will adhere to the principles outlined in the relevant trial regulations, GCP guidelines, and CTR's SOPs.

I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation without the prior written consent of the Sponsor. I also confirm that I will make the findings of the trial publicly available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the trial will be given; and that any discrepancies from the trial as planned in this protocol will be explained.

Director	TBC	
Name: Kerry Hood	**Signature**	**Date**
Chief Investigator:		
Name: James White	**Signature**	**Date 31/05/2019**

General Information This protocol describes the FRANK friends study and provides information about the procedures for entering participants into the trial. Every care has been taken in drafting this protocol; however, corrections or amendments may be necessary. These will be circulated to the known Investigators in the trial. Problems relating to the trial should be referred, in the first instance, to the CTR.

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Trial Co-ordination:

The FRANK friends study is being coordinated by the Centre for Trials Research (CTR), Cardiff University, a Clinical Research Collaboration (UKCRC) registered trials unit and the University of Bristol. This protocol has been developed by the FRANK friends Trial Management Group (TMG). For **all queries** please contact the FRANK friends team through

the main trial email addresses. Any inquiries will be directed through the Trial Manager(s) via the trial emails to either the Chief Investigator or a Co-Investigators.

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Glossary of abbreviations

AE	Adverse Event
ASSIST	A Stop Smoking in Schools Trial
CF	Consent Form
CI	Chief Investigator
CRF	Case Report Form
CRO	Contract Research Organisation
CTR	Centre for Trials Research

CTU	Clinical Trials Unit
CU	Cardiff University
DECIPHer	Centre for the Development and Evaluation of Complex Interventions for Public Health Improvement
Eu-DAP	European Drug Abuse Prevention Trial
FSM	Free School Meal
GAfREC	Governance Arrangements for NHS Research Ethics Committees
GCP	Good Clinical Practice
HE	Health Economics
IC	Informed consent
IDMC	Independent Data Monitoring Committee
IEC	Independent Ethics Committee
IRAS	Integrated Research Approval System
ISRCTN	International Standard Randomised Controlled Trial Number
NIHR	National Institute for Health Research
PHR	Public Health Research
PHW	Public Health Wales
PIS	Participant Information Sheet
QA	Quality Assurance
R&D	Research and Development
RCT	Randomised Controlled Trial
REC	Research Ethics Committee
SAP	Statistical Analysis Plan
SOP	Standard Operating Procedure
TM	Trial Manager
TMF	Trial Master File
TMG	Trial Management Group
TS	Trial Statistician
TSC	Trial Steering Committee
UKCRC	United Kingdom Clinical Research Collaboration

1 Amendment History

The following amendments and/or administrative changes have been made to this protocol since the implementation of the first approved version.

Amendment No.	Protocol version no.	Date issued	Summary of changes made since previous version
1	1.1	09/07/2019	Added sub-group analysis by having had an opportunity to use drugs.
2	1.2	18/07/2019	Remove £20 incentive for returning diary.
3	1.3	19/07/2019	Change the lay summary to note the 24-month follow-up will occur post randomisation not after the intervention is delivered. Minor typographical changes.

2 Synopsis

Short title	The FRANK friends study
CTR Internal ref. no.	739
Funder and ref.	National Institute for Health Research (NIHR) Public Health Research Programme (PHR). PHR - 12/3060/03.
Trial design	Parallel-group, multicentre, two-arm, cluster RCT, with process and economic evaluations.
Trial participants	School students in Year 9 (aged 13-14)
Planned sample size	5655 students
Planned number of sites	48 schools (24 intervention) across South Wales and the West of England
Inclusion criteria	Students in UK Year 9 (aged 13-14)
Exclusion criteria	Schools which are fee paying, special schools (e.g. for those with learning disabilities), pupil referral units, have less than 60 students in Year 9, likely to be closed or merged during the trial, not within a 90 minute travel time by car from the trial centres, and those that received the FRANK friends intervention in the pilot.
Intervention period	Peer supporters are asked to have informal conversations with their peers on drugs and log a record of these conversations in a pro-forma diary over a 10 week period.
Follow-up duration	24-month follow-up
Planned trial period	01/03/2019 to 30/06/2022 (40 months)
Primary objective	To investigate whether the FRANK friends intervention prevents the use of any illicit drug compared to usual practice at the 24-month follow-up.
Secondary objectives	To investigate whether the FRANK friends intervention at 24-months follow-up, compared to usual practice: 1. Prevents the use of any illicit drug over the past 12 months, past month and week; 2. Prevents the use of specific illicit drugs (ever, past 12 months, month and week; outcomes section 5.3 details each illicit drug); 3. Reduces the use of any illicit drug over the past 12 months, past month and week;

	4. Reduces the use of specific illicit drugs (past 12 months, month and week; section 5.3 details each illicit drug); 5. Prevents cannabis dependency; 6. Prevents smoking (lifetime and weekly smoking status); 7. Reduces the frequency of alcohol consumption (past 12 months, month and week); 8. Prevents alcohol use disorder; 9. Improves health related quality of life. A process evaluation (secondary objective 10) and economic evaluation (secondary objective 11) will also be conducted.
Primary outcomes	Use of any illicit drug, assessed by self-report questionnaire, 24-months post randomisation. The outcome will be modelled as a binary outcome (0 = never used; 1 = any lifetime use).
Secondary outcomes	1. Use of any illicit drug over the over the past 12 months, month and week (secondary objective 1): assessed by asking whether any of the drugs students indicate they have tried were used within each time frame. 2. Any use, past 12-months, past month and past weekly use of specific drugs (secondary objective 2): assessed by asking whether each drug was used within each time frame. 3. Reduces how frequently users have taken any illicit drugs ever, in the past 12 months, month and week (secondary objective 3). 4. Reduces how frequently users have taken specific illicit drugs ever, in the past 12 months, month and week (secondary objective 4). 5. Screening positive for cannabis dependence (secondary objective 5): assessed using the six item Cannabis Abuse Screen Test validated in adolescents (CAST). 6. Any smoking and weekly smoking (secondary objective 6): assessed using questions used in the ASSIST trial. Weekly smoking defined as usually smoking ≥ one cigarette a week. 7. Reduces the frequency of alcohol consumption in the in the past 12 months, month and week (secondary objective 7). 8. Screening positive for a DSM-5 alcohol use disorder (secondary objective 8). 9. Health related quality of life (CHU9D; secondary objective 9).

Intervention	FRANK friends is a peer-led drug prevention intervention to prevent drug use in UK year 9 secondary school children. FRANK friends aims to diffuse information from www.talktofrank.com via secondary school students' social networks in UK Year 9 (aged 13-14). FRANK friends has five stages: 1. Nomination of peer supporters; 2. Recruitment of peer supporters; 3. Training of peer supporters; 4. Intervention period of 10 weeks during which peer supporters initiate conversations with their peers in school; 5. Acknowledgment of peer supporters' contribution.

3 Trial summary & schema

3.1 Trial flow diagram

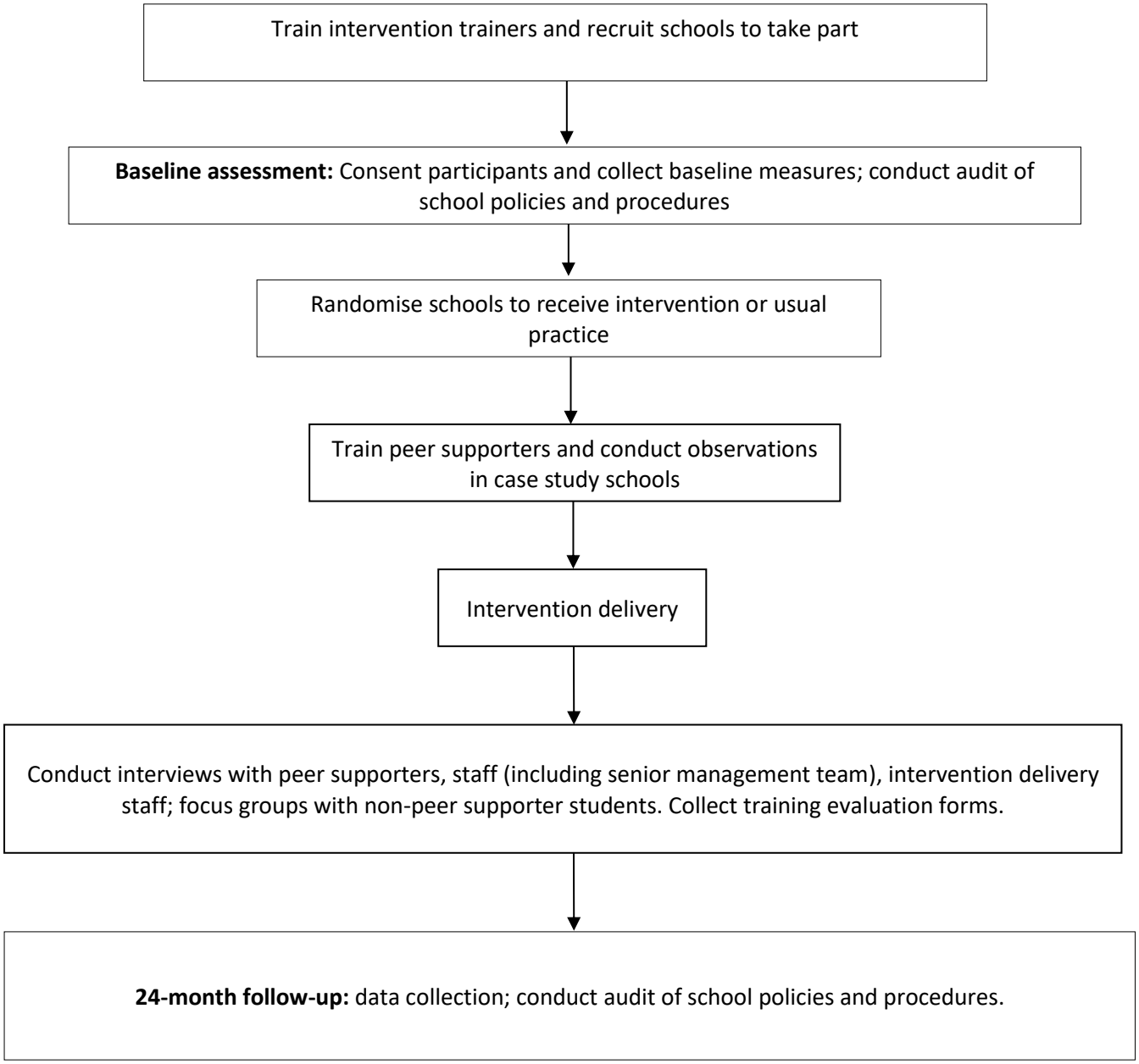

Figure 1. Trial flow diagram

3.2 Trial lay summary

Background: The latest UK data indicate that 37% of 15 year olds have ever tried an illicit drug. There are short as well as long-term effects on health arising from illicit drug use

amongst young people. Schools provide a systematic and efficient way of reaching a large number of people every year. Studies evaluating school-based drug prevention interventions have found few prevent or reduce student drug use, with only a handful taking place in the UK. In response, an effective school-based peer-led smoking prevention intervention (ASSIST) that has been delivered to around 120,000 UK students was adapted to deliver information from the UK national drug education website: www.talktofrank.com. In interviews and focus groups in the pilot study of this intervention, students, teachers, and parents, all thought the intervention was acceptable, easy to deliver and could have promising effects on drug use. The pilot study was too small to evaluate whether FRANK friends could prevent drug use, so we are now conducting a larger trial to evaluate effects on illicit drug use will be conducted.

The trial: This trial will introduce and evaluate FRANK friends (the "intervention") which is a school-based peer-led drug prevention intervention. In each school, students in UK year 9 (aged 13-14) will be asked to nominate fellow students who they think are influential. Students in receipt of the top 17.5% of nominations are asked to become peer supporters. Those who agree receive 2-days training out of school on the effects and risks associated with specific drugs, minimising potential harms, and the law using material taken from www.talktofrank.com. Peer supporters practise communication skills including, listening, negotiation, and how to talk with their peer group about drugs. They are then asked to have conversations about the harms of drug use with their peers over a 10-week period and record them in a diary. During these 10-weeks peer supporters receive four follow-up visits from trainers at school to provide support. There will be 48 schools in the trial and they will be randomly split into two groups, twenty-four schools will receive the intervention, and twenty-four will form a comparison group, and will continue with usual practice, the trial will include approximately 5655 students.

Methods: Before the intervention is delivered, questionnaire data will be collected from all students in year 9. In these questionnaires the use of drugs ever, in the past year, and in the past month will be measured as well as lifetime and weekly smoking, and quality of life. These things will be measured again 24 months after schools have been randomly split into two groups. The researchers will be looking to see if there are positive changes in student drug use, and whether these changes are greater within schools that received the intervention compared to schools that did not. Interviews with peer supporters, other students and trainers will also be conducted and training sessions will be observed to explore what happened during the training, how people feel about the intervention, and in what ways it has, or has not been useful. Finally, the cost of the intervention will be

calculated, and weighed up against any benefits in terms of student drug use, to see if it provides good value for money.

Findings will be presented to people who are involved in drug prevention in the UK (e.g. parents, public health teams, teachers, charities (e.g. Off the Record, Bristol Drugs Project, policy-makers) as well as at scientific conferences. If effective, avenues for delivering the intervention to other schools across the UK will be explored.

4 Background

Illicit drug use in UK adolescents is among the highest in Europe.(1), (2) Despite significant declines since the 1990s, the latest 2016 Smoking Drinking and Drug Use (SDDU) survey in England reports the lifetime prevalence of drug use in 11-15 year olds is 24% (or 21% after removing nitrous oxide and novel psychoactive substances added in 2016),(3) up from 15% in 2014.(4) In the 2015 Scottish Schools Adolescent Lifestyle and Substance Use Survey (SALSUS)(5) the prevalence of drug use in the past month among 15 year olds was 11% compared to 18% in the 2016 SDDU. There is some uncertainty about whether the increase in England between 2014 and 2016 reflects a real population level change,(3) but across surveys drug use increases rapidly in early adolescence. In the 2016 SDDU, lifetime prevalence at 11, 13 and 15 years of age was 11%, 21% and 37% respectively.(3) Of those who have used in the last year at age 15, 40% solely used cannabis but 24% used ≥2 drugs including one class A drug comprising amphetamines (if prepared for injection), ecstasy, cocaine, crack, heroin, LSD, magic mushrooms and methadone.

Drug use increases the risk of poor physical and mental health. Around 10% of cannabis users will become dependent upon it,(6) and regular users have poorer verbal learning, memory, and attention,(7) respiratory functioning(8), and are more likely to have a psychotic experience compared with never users. (9) Administration in placebo controlled RCTs of delta-9-tetrahydrocannabinol (THC), the main active compound in cannabis, can induce short-lived transient psychotic-like experiences,(10) and epidemiological studies suggest that cannabis use is associated with an increased risk of schizophrenia.(11) In the UK, 75% of 11-18 years olds receiving specialist drug treatment, primarily do so for cannabis use with a median age at first treatment of 16.(12) The annual economic costs of illicit drug use to the NHS have been estimated to be £488 million.(13)

Illicit drug use may also indirectly affect health by limiting educational attainment and limiting opportunities for employment. For example, lifetime cannabis use is associated with a 2 point lower Maths GCSE score, 48% increased risk of not attaining ≥5 GCSEs, and a three-fold increased risk of leaving school, or having no qualifications, compared to never users.(14) Around 10% of permanent and 3.3% of temporary exclusions in state-funded secondary schools in England are drug and alcohol related.(15) Opportunities for employment may also be limited by a conviction for possession of a controlled drug. In the UK in 2014/15, there were 142 guilty verdicts for drug offences in 10-14 year olds (5.5% of all indictable offences), increasing to 2,480 (17.2%) among 15-17 year olds.(16) These offences and convictions are subject to disclosure under the Rehabilitation of Offenders Act 1974.

4.1 Existing research

A number of school-based interventions have focused on preventing student drug use. Three systematic reviews have found these interventions are associated with modest improvements in knowledge about drugs, but few had an impact on drug use after 12 months.(17)(18)(19) The latest Cochrane systematic review of universal school-based interventions to prevent illicit drug use (comprising 51 randomised control trials (RCTs), 2 in the UK) found those that attempted to increase social competences (i.e. teaching self-management, social skills, problem-solving) and those based on social influence theories (i.e. correcting overestimates of drug prevalence) had the largest effects on drug use.(17) One NIHR funded systematic review found Positive Youth Development interventions had little effect on illicit drug use.(20) Another review of school-based peer-led interventions found a small protective effect on cannabis use (3 RCTs) at ≥12 months, suggesting peer-led approaches may be promising.(19) In the RCTs evaluating school-based peer-led drug prevention interventions, the Towards No Drug Abuse Network RCT found iatrogenic effects in a sub-group of students whose friends already used alcohol, tobacco and drugs.(21) In the peer-led arm of the EU-Dap trial, there were very low levels of implementation, with only 8% of centres implementing all seven sessions, and 71% not conducting any meetings at all.(22) This suggests that while peer-led approaches are promising, modifications are needed to avoid iatrogenic effects and improve implementation.

These systematic reviews highlight methodological weaknesses in the existing evidence base. These include: small sample sizes, potential contamination,(21) inadequate reporting of randomisation,(17) a failure to account for clustering,(17) (19) a lack of registered protocols and independent evaluation.(23) The lack of registered protocols is a particular problem with substance misuse prevention interventions, as it is often unclear which

outcome measure and what time point forms the basis of the primary effectiveness analysis, leading to concerns of outcome switching.

4.2 Rationale for current trial

In response to these gaps, three years of preparatory research with students, teachers, parents, public health practitioners and commissioners, funded by the NIHR PHR programme was undertaken. In partnership with stakeholders, an effective school-based peer-led smoking prevention intervention (ASSIST) (24) was adapted to deliver information from the UKs national drug education website Talk to FRANK (www.talktofrank.com). ASSIST is based on diffusion of innovations theory and aims to diffuse and sustain non-smoking norms via secondary school students' social networks in year 8 (aged 12-13).(24) Talk to FRANK (www.talktofrank.com) provides up-to-date, youth-friendly information on the legality and effects of drugs; an A-Z guide of drugs; and support for younger people or concerned others via instant messaging, confidential 24 hour telephone, email or text service. In partnership with stakeholders, FRANK friends was developed and prototyped to be a school-based peer-led intervention to prevent illicit drug use in UK year 9 students (aged 13 to 14).(25) Next, a pilot cluster RCT (cRCT) of FRANK friends was conducted with young people in UK year 9 (13-14 years) in 12 schools across south Wales to assess the acceptability of the intervention and trial methods. All criteria required to progress to a full-scale cRCT of FRANK friends were met.

5 Trial objectives/endpoints and outcome measures

The aim of the proposed research is to evaluate the effectiveness and cost-effectiveness of the FRANK friends intervention to prevent and reduce illicit drug use, using a cluster RCT design with embedded process and economic evaluations.

5.1 Primary objectives

To investigate whether the FRANK friends intervention prevents the use of any illicit drug compared to usual practice at the 24-month follow-up.

5.2 Secondary objectives

To investigate whether the FRANK friends intervention at 24-months follow-up, compared to usual practice:

1. Prevents the use of any illicit drug over the past 12 months, past month and week;
2. Prevents the use of specific illicit drugs (ever, past 12 months, month and week; outcomes section 5.3 details each illicit drug);

3. Reduces the use of any illicit drug over the past 12 months, past month and week;
4. Reduces the use of specific illicit drugs (past 12 months, month and week; section 5.3 details each illicit drug);
5. Prevents cannabis dependency;
6. Prevents smoking (lifetime and weekly smoking status);
7. Reduces the frequency of alcohol consumption (past 12 months, month and week);
8. Prevents alcohol use disorder;
9. Improves health related quality of life.

A process evaluation (secondary objective 10) and economic evaluation (secondary objective 11) will also be conducted.

5.3 Primary outcomes measure(s)

The primary outcome will be use of any illicit drug, assessed by self-report questionnaire, 24-months post randomisation. This is measured by asking students if they have ever tried: cannabis, cannabidiol products, nitrous oxide, poppers, glues, gases or aerosols, cocaine, amphetamines, ecstasy, steroids, mephedrone, synthetic cannabinoids, synthetic drugs which mimic ecstasy, other novel psychoactive substances (NPS), crack, heroin, ketamine, tranquilisers, methadone, LSD or hallucinogenic mushrooms. Street and common brand names (for NPS) will be provided for all. An open response category is provided that will be categorised. The outcome will be modelled as binary outcome (0 = never used; 1 = any lifetime use).

5.4 Secondary outcomes measure(s)

Secondary outcomes will be assessed at baseline and the 24-month follow-up. These secondary outcomes are mapped to the secondary objectives described in section 5.2.

- Use of any illicit drug over the over the past 12 months, month and week *(secondary objective 1):* assessed by asking whether any of the drugs students indicate they have tried were used within each time frame.
- Any use, past 12-month, past month and past weekly use of specific drugs (secondary objective 2): assessed by asking whether each drug was used within each time frame.
- Reduces the use of any *(secondary objective 3)* and specific illicit drugs *(secondary objective 4):* how frequently users have taken drugs ever, in the past 12 months, month and week.
- Screening positive for cannabis dependence *(secondary objective 5):* assessed using the six item Cannabis Abuse Screen Test validated in adolescents (CAST)(26).

- Any smoking and weekly smoking *(secondary objective 6):* assessed using questions used in the ASSIST trial(24). Weekly smoking defined as usually smoking ≥ one cigarette a week.
- Reduces the frequency of alcohol consumption in the in the past 12 months, month and week *(secondary objective 7)*.
- Screening positive for a DSM-5 alcohol use disorder *(secondary objective 8)*(27).
- Health related quality of life (CHU9D*; secondary objective 9*) (28).

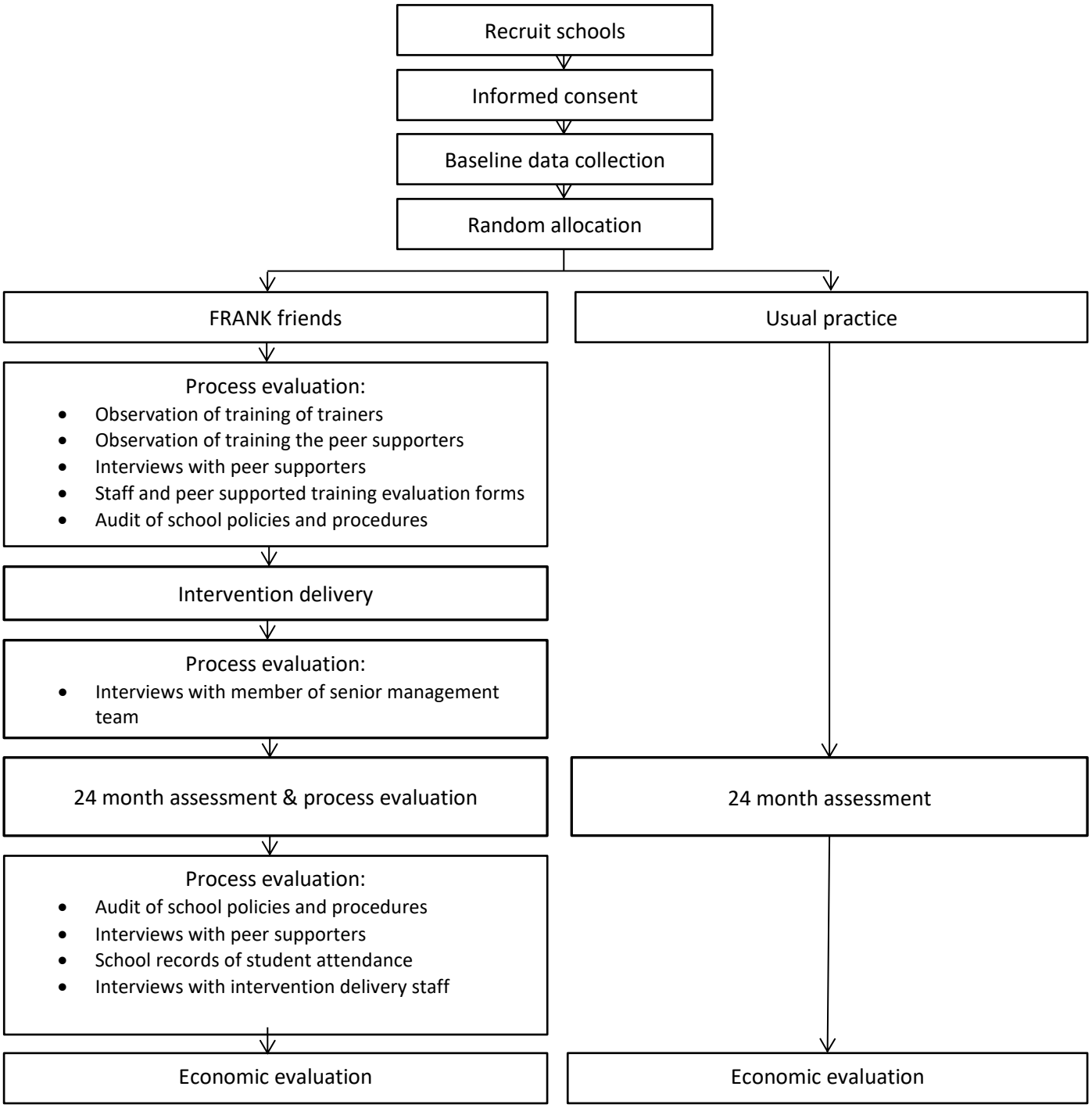

Figure 2. Trial schema diagram

6 Trial design and setting

This is a parallel-group, multicentre, two-arm, cluster RCT, with process and economic evaluations. Clusters (schools) will be randomised to receive either the 10-week FRANK friends intervention in addition to usual practice or usual practice alone. The effectiveness and cost-effectiveness of FRANK friends will be assessed 24-months after randomisation. The trial will be conducted in two geographical areas (the West of England and South Wales), which will enable exploration of the generalisability of the findings.

6.1 Risk assessment

A Trial Risk Assessment has been completed to identify the potential hazards associated with the trial and to assess the likelihood of those hazards occurring and resulting in harm. A copy of the trial risk assessment may be requested from the CTR, Cardiff Trial Manager. The trial is low risk.

Participant risks: Potential risks of the intervention to participants are minimal. Some individuals might find aspects of intervention content or research upsetting if they, or a significant other, have experienced a problem in relation to drug use. Trial managers will work with schools to ensure a system is in place to enable appropriate support to be provided in such circumstances. Any potential for harmful effects due to the intervention itself will be explored via the collection and analysis of qualitative data to explore unintended consequences.

Societal risks: As with any health intervention, there is a risk of widening health inequalities if the students that are exposed to the intervention are at a lower risk of drug use. We propose to examine the effect of FRANK friends on socioeconomic inequalities in illicit drug use operating at the parental and school-level.

7 School and Participant selection

School and participants are eligible for the trial if they meet all of the following inclusion criteria and none of the exclusion criteria apply. All queries about school and participant eligibility should be directed to the Trial Manager(s) before the sign a memorandum of understanding.

7.1 Inclusion criteria

Students in UK Year 9 (aged 13-14)

7.2 Exclusion criteria

Fee paying schools, special schools (e.g. for those with learning disabilities), pupil referral units and those that received the FRANK friends intervention in the pilot. Any school likely to be closed or merged with another school during the trial period, schools with less than 60 students in Year 9 (following the exclusion criteria applied in the ASSIST RCT), and not within a 90-minute travel time by car from the University of Bristol and CTR, Cardiff.

8 School recruitment

8.1 School identification

The trial will be conducted in two geographical areas (South Wales and the West of England), which will enable exploration of the generalisability of the findings. All state secondary schools within a one and half hours travel time from the recruiting centres based in CTR Cardiff and the University of Bristol will be eligible for inclusion in the sampling frame. 48 schools will be included (24 from each geographical area).

A list of eligible secondary schools will be obtained (one for Wales and one for England). These will be anonymised and an ID, area, and the proportion of students with the school that are entitled to receive free school meals (FSM) (based on the latest available figures) retained and passed to the trial statistician (TS) who will be blinded to any identifiable information. All schools will be organised into the two geographical areas and stratified according to the median FSM entitlement for that country. Within each strata the order of schools will be randomly shuffled. IDs will be passed on to TMs so schools can be identified. Initially the first listed schools within each stratum will be selected. If schools decline or do not respond, TMs will select the next school(s) listed within each stratum until all are recruited.

Eligible schools will be approached via a relevant senior manager (deputy head, head of pastoral care), identified with the help of the Schools Health Research Network in Wales and Public Health leads for schools in local authorities in England, and invited to participate in the FRANK friends study. Schools will be emailed or posted a project information sheet, reply envelope and form indicating if they wish to participate. If necessary, non-responders will be followed up with a reminder and then by a phone call by the Trial Manager(s). All interested schools will be visited by the Trial Manager for that geographical area and a contact from the intervention delivery team to discuss the trial in more detail and agree a research contract including signing a memorandum of understanding (MoU) describing the roles, responsibilities, timeline of intervention delivery, and assessments before taking part in

the FRANK friends study. The MoU will be signed by a member of the senior leadership team, ideally the headteacher, with an additional contact teacher also listed. Forty-eight schools (24 in each area), will be sampled from those eligible, using stratified random sampling to ensure a range of free school meal (FSM) eligibility in the final sample. Any schools that decline before randomisation will be replaced by the next randomly selected school from the same stratum and geographical area. All students in year 9 (aged 13-14) at these schools will be approached to take part.

8.2 Informed consent

Following the recruitment of schools, information sheets will be posted to parents, asking them to return a form to opt them out of participation if they do not want their child to take part. Informed consent or assent will be obtained from all participants who agree to take part in the trial (consent from adults and assent from children). At the beginning of data collections, it will be made clear that student participation is optional. Each school participating in the trial will be asked to identify a named individual who can provide support to any students who become upset or distressed. Any member of the research team and all fieldworkers visiting a school will be required to have a Disclosure and Barring check. All work will be carried out in accordance with General Data Protection Regulation 2018 and the UK Data Protection legislation 2018.

Student information sheets will be provided to schools to distribute to students 1-2 weeks before the baseline data collection. At the baseline data collection, students will be asked to read the information sheet and provide written assent. Time will be allocated at the baseline data collection for students to read the information sheet and ask questions before being asked to sign the Assent Form. Assent will be taken by a member of the research team or a field worker. Completed assent forms will be collected and kept at the recruiting centre (University of Bristol for West of England schools; CTR Cardiff for South Wales schools). Participants will be able to keep the information sheet which will provide details of who to contact if they require further information or support on their or others drug use. The right of the participant to refuse to participate without giving reasons, or whose parents/carers opt them out of the trial will be respected. For those students who opted out/declined to participate alternative arrangements will be provided to allow them to remain in the data collection environment to avoid embarrassment.

8.3 Randomisation

Randomisation will be completed at school-level. Randomisation will be coordinated centrally by the CTR. The randomisation schedule will be stratified and will be prepared and held by an independent statistician within the CTR. Within each of the two countries, schools will be organised into the two FSM strata. Each school will be assigned an ID number, after which an independent statistician will randomly allocate schools within each stratum to one of two arms using random block allocations. Block sizes of 2, 4 and 6 will be used. Further detail on this will be included in the unblinded randomisation protocol.

9 Withdrawal & losses to follow-up

9.1 Withdrawal

Schools and participants will have the right to withdraw consent for participation in any aspect of the FRANK friends study at any time. Participants' care from any services will not be affected at any time by declining to participate or withdrawing from the trial. If a participant initially consents but subsequently withdraws from the trial, a clear distinction will be made as to what aspect of the trial the participant is withdrawing from. Whilst it is possible to withdraw any data collected as part of the research it is only possible for peer supporters to withdraw from attending training to be a FRANK friends peer supporter. As these are informal peer-led interventions, it is not possible for participants to withdraw from receiving the intervention as this would require no contact with any trained peer supporters. In all instances, schools and participants who consent and subsequently withdraw should complete a withdrawal form or the withdrawal form should be completed on the participant's behalf by the Cardiff or Bristol Trial Manager(s) based on information provided by the participant. Withdrawal forms from West of England schools should be sent to the Trial Manager(s) and kept in the site file at the University of Bristol. Withdrawals from South Wales schools should be sent to the Trial Manager(s) in the CTR. Any queries relating to potential withdrawal of a school or participant should be forwarded to the Trial Manager(s) immediately.

9.2 Lost to follow-up

The outcome measurements will be assessed at two time points. Baseline measures will be assessed prior to randomisation of schools into the two trial arms (control and intervention conditions, 24 schools [clusters] in each, see section 13.3, sample size). A second set of measurements will take place 24-months post randomisation as per the baseline protocol. Following the protocols used in previous trials multiple absentee sessions to minimise

attrition will be carried out. (24) All schools, whether intervention of control will be incentivised to remain in the trial by offering a payment of £1000 at the end of the trial.

10 Trial Intervention

10.1 The FRANK friends intervention

FRANK friends is a peer-led drug prevention intervention to prevent drug use in UK year 9 secondary school children. FRANK friends has been developed over a 31-month NIHR PHR funded study (PHR - 12/3060/03) comprising intervention development, prototyping and a pilot cRCT.

Based on diffusion of innovations theory,(30) FRANK friends aims to diffuse information from www.talktofrank.com via secondary school students' social networks in UK Year 9 (aged 13-14). Following methods developed in the ASSIST intervention and found to be acceptable in the pilot study, FRANK friends has five stages:

1. Nomination of peer supporters: Students in UK year 9 are asked to identify influential peers using three questions, "Who do you respect in year 9 at your school?", "Who are good leaders in sports or other groups activities in year 9 at your school?", and "Who do you look up to in year 9 at your school?" The 17.5% of Year 9 students receiving the most peer nominations are invited to a recruitment meeting;
2. Recruitment of peer supporters: A meeting is held with nominees to explain the role of a peer supporter and answer questions. Parental consent is sought for participation in a training course;
3. Training of peer supporters: A 2-day training course is held out of school, facilitated by an intervention delivery team. Trainers are typically experienced in youth work and/ or health-promotion and employed by the NHS, third-sector charities, or local government. Trainers provide information on the effects and risks associated with specific drugs, minimising potential harms, and the law from Talk to FRANK. Peer supporters practise communication skills including, listening, negotiation, how to talk with their peer group about drugs, and how to access www.talktofrank.com by computer or smartphone. Methods used to achieve these aims include participatory learning activities such as role plays, student-led research, small group work and discussion, and games;
4. Intervention period: Peer supporters are asked to have informal conversations with their peers on drugs, when travelling to and from school, in breaks, at lunchtime, and after school in their free time, and log a record of these conversations in a pro-forma diary. Over the 10-week period four follow-up school visits are made by intervention

delivery staff to meet with peer supporters to provide support, trouble shooting, and monitor peer supporters' diaries;

5. Acknowledgment of peer supporters' contribution: At the end of the intervention peer supporters receive a certificate.

All staff who train FRANK friends peer supporters will receive two days training by members of the research team who trained staff in the pilot. Training protocols are based on those used in the ASSIST 'train the trainer' model. (31)

In England, funding for FRANK friends intervention delivery staff will come from the NIHRs West of England Clinical Research Network (CRN) and commissioners in local government. FRANK friends will be delivered in England by the West of England CRN staff. In Wales, funding for intervention delivery will come from Public Health Wales (PHW), based in the NHS, and be delivered by existing staff who work in smoking prevention.

The comparison schools will continue with usual practice which may or may not involve drug education. The details of any drug education, including other relevant interventions, will be examined as part of the process evaluation (see section 15).

11 Trial procedures

The outcome measurements will be assessed at two time points. Baseline measures will be assessed prior to randomisation of schools into the two trial arms (control and intervention conditions, 24 schools [clusters] in each, see section 13.3, sample size). A second set of measurements will take place 24-months post randomisation as per the baseline protocol.

11.1 Data collections

Students will be in UK year 9 (aged 13-14 years) at baseline and complete paper self-report questionnaires under 'exam conditions' in a classroom or school hall. School staff will be asked to be present but not help students to ensure anonymity. Fieldworkers will be on hand to provide support to students who require help. Completed paper questionnaires will be transported to CTR by the Trial Manager(s) or couriered. Data from questionnaires will be stored in anonymised form, using participant identification numbers. Participant identification numbers and corresponding participant names will be held in separate files. Both files will be stored in secure password protected folders.

12 Safety reporting

Definitions

Term	Definition
Adverse Event (AE)	Any untoward medical occurrence in a participant or clinical trial participant administered a medicinal product/ intervention and which are not necessarily caused by or related to that product
Serious Adverse Event (SAE)	Any adverse event that - • Results in death • Is life-threatening* • Required hospitalisation or prolongation of existing hospitalisation** • Results in persistent or significant disability or incapacity • Consists of a congenital anomaly or birth defect • Other medically important condition***

***Note:** The term 'life-threatening' in the definition of serious refers to an event in which the trial 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.

**** Note:** Hospitalisation is defined as an inpatient admission, regardless of the length of stay, even if the hospitalisation is a precautionary measure for continued observation. Pre-planned hospitalisation (e.g. for pre-existing conditions which have not worsened, or elective procedures) do not constitute an SAE.

***** Note:** other events that may not result in death, are not life-threatening, or do not require hospitalisation, may be considered as an SAE when, judged by the Chief Investigator to jeopardise the participant and may require medical, psychological or surgical intervention to prevent one of the outcomes listed above. Examples within this trial, may include a young person revealing incidences of self-harm, sexual abuse, and grooming by being provided drugs.

No adverse events arising from the intervention are expected. All intervention materials will be based on information from www.talktofrank.com and as a result are in line with the current, widely publicised UK governmental guidelines. CTR standard operating procedures for managing and reporting any serious adverse events (SAE) will be followed, which reflect those outlined in Good Clinical Practice (GCP) guidance. Adverse events which do not fall into the GCP categories of an SAE are defined as non-serious and will not be collected. The chief investigator will review SAEs examining the link with the intervention and sign all SAE reports. Once an SAE is received at the CTR, it will be sent to the Chief Investigator (or their delegate) for an assessment of expectedness. Only reports of related and unexpected Serious Adverse

Events (SAEs) should be submitted to the REC and TSC. These should be sent within 15 days of the chief investigator becoming aware of the event. If the chief investigator deems the SAE to be related to the intervention they will be reported to the sponsor (Cardiff University) within 24 hours of the trial team becoming aware of an event. In the pilot study no problems with the FRANK friends intervention or, questionnaires, were encountered in the pilot study, and there were not any AEs or SAEs reported.

Expected AE/SAE: There are no expected AE's/SAE's. Any planned treatments received by participants at the start of the trial will not be considered as AE's/SAE's.

Related AE/SAE: There are no AE's/SAE's expected to be related specifically to the trial interventions. The Chief Investigator (or delegate) will however make an assessment of causality in relation to the intervention for all SAEs reported according to the SAE working guidance document.

Trial Specific SAE Reporting requirements

For the purposes of this trial the following events will also be considered SAEs and must be captured on the SAE form and reported to the CTR with 24 hours of knowledge of the event:

- incidences of self-harm;
- sexual abuse;
- grooming by being provided drugs.

For the purposes of this trial the following events will not require reporting as SAEs:

- Any planned treatments received by participants at the start of the trial.

12.1 Reporting procedures

The CI (or delegate from the trial team) should sign and date the SAE reports to acknowledge that he/she has performed the seriousness and causality assessments. A completed SAE form for all events requiring immediate reporting should be submitted via email or phone to the CTR within 24 hours of knowledge of the event (see box below for email address and telephone number). A separate form must be used to report each event, irrespective of whether or not the events had the same date of onset. The participant will be identified only by their participant identifying number, partial date of birth (mm/yy) and initials. The participant's name should not be used on any correspondence. It is also required that sites respond to and clarify any queries raised on any reported SAEs and report any additional information as and when it becomes available through to the resolution of the event.

Additionally, the CTR may request additional information relating to any SAEs and the site should provide as much information as is available to them in order to resolve these queries.

An SAE form is not considered as complete unless the following details are provided:

- Full participant trial number
- Details of the Adverse Event
- A completed assessment of the seriousness, and causality as performed by the CI (or another on the delegation log).

If any of these details are missing, the school/individual will be contacted and the information should be provided by the school/individual to the CTR within 24 hours.

Serious Adverse Event (SAE) email address:

frank-friends-wales@cardiff.ac.uk

SAE Telephone number:

Sarah Rawlinson (029 206 87272)

Serious adverse events should be reported from time of signature of informed consent until the end of the 24-month follow-up has been completed.

13 Statistical considerations

13.1 Randomisation

Clusters (schools) will be randomised in a 1:1 ratio to receive either the 10-week FRANK friends intervention in addition to usual practice or usual practice. Within each trial area (the West of England and South Wales), schools will be stratified on the percentage of students in receipt of FSM to ensure balance across arms on parental socioeconomic disadvantage. Randomisation of the schools will occur after all schools have been recruited and they will be informed of their allocation after baseline data have been collected. All schools will be assigned an ID number, after which an independent CTR statistician, will randomly allocate recruited schools to Intervention or Control using computer generated random number block allocations. The independent CTU statistician will allocate Intervention or Usual practice to

ID numbers and inform the designated intervention delivery team member in each area so that delivery of intervention can start as soon as a school's baseline data collection has been completed. Schools in both arms will continue with their usual educational activities with regards to drugs education.

13.2 Blinding

All parties will be blind to allocation during the baseline data collection. It is not possible for FRANK friends study participants (students), teachers, trial managers, the intervention delivery team or researchers involved in the process evaluation to be blind to intervention status. However, fieldworkers at outcome data collections will remain blind to intervention status as will the statistician analysing the primary and secondary outcome data and the health economists undertaking the economic analysis. If school allocation becomes apparent during interactions with schools we will record this. Potential risks of the intervention to participants are minimal but in the case where unblinding is necessary, the allocation schedule will be available to the researchers either electronically via the independent CTR statistician's copy.

13.3 Sample size

The latest population-level prevalence study from the 2016 SDDU survey indicates the lifetime prevalence of drug use at the 24-month follow-up (among 15 year olds) will be 37%.(3) This is a 13% increase from the previous survey in 2014.(4) There is some uncertainty around this estimate as it is not in line with other comparable surveys (lifetime prevalence in 15 year olds in 2015 SALSUS was 19%).(5) Table 1 shows the required sample size based on prevalence in the usual practice group ranging between 19% and 37%. A 25% relative reduction in prevalence approximates to the pooled odds ratio of 0.70 for cannabis use found in a systematic review peer-led drug prevention programs (19) and the effect of FRANK friends compared with usual practice found in the pilot cRCT,(31) demonstrating that such an effect size is plausible and consistent with effect sizes seen in the literature. The potential population level reach of the intervention, coupled with the ability to repeat delivery every year, suggests that a reduction of this magnitude would be of public health importance.

The trial will take account of clustering. In the pilot cRCT the intracluster correlation (ICC) for the comparison between FRANK friends and usual practice was 0.003 at the 18-month

follow-up. Assuming 122 students per school, an ICC of 0.01 (to be conservative), coefficient of variation of sample size of 0.28, and 13.7% rate of attrition (based on the pilot data plus 1 additional school in case of drop out) if we use the 2014 prevalence rate of 24%, a trial involving 48 schools would provide 90% power at a 5% significance level (Table 1). Using the 2016 SDDU prevalence rate of 37% in usual practice, 36 schools is required. To ensure we are adequately powered, we propose to recruit 48 schools, as 88% power can be achieved if we find the 2016 SDDU prevalence rate and the ICC is larger at 0.02. If prevalence is closer to the SALUS rate of 19%,(5) we will have 84% power based on a ICC of 0.01. Applying the parameters from the pilot cRCT, a trial involving 48 schools would also provide 88% power to detect a difference of 12.0% vs. 8.7% in the secondary outcome of monthly drug use by 15 years of age.

Table 1. Sample size calculations (number of schools) to detect a difference in lifetime illicit drug use at 15 years of age [a] (bold figures indicate variations in parameters with main sample size calculation at top)

Power	Effect size [a]	Prevalence [b]	ICC [c]	N schools [d]	N students
90	24.0 vs. 18.1%	24.0%	0.01	48 (24 intervention)	5655
90	37.0 vs. 29.1%	**37.0%**	0.01	36 (18 intervention)	4242
90	19.0 vs. 14.1%	**19.0%**	0.01	56 (28 intervention)	6786
88	37.0 vs. 29.1%	37.0%	**0.02**	48 (24 intervention)	5655
90	24.0 vs. 18.1% [a]	24.0%	**0.003**	32 (16 intervention)	3676

[a] Based on OR from FRANK friends vs. usual practice in pilot cRCT(31) and MacArthur meta-analysis of peer-led drug prevention interventions.(19) [b] Smoking drinking and drug use study among young people in England: lifetime illicit drug use prevalence age 15 in 2014 (4) 2016 (3); 2015 Scottish Schools Adolescent Lifestyle and Substance Use Survey (SALSUS).(5) [c] ICC from model comparing FRANK friends vs. usual practice in pilot cRCT(31); [d] Inflated for 13.7% student dropout (based on pilot cRCT) (31) plus one extra 1 school.

13.4 Procedures for reporting deviation(s) from the original SAP

These will be submitted as substantial amendments where applicable and recorded in subsequent versions of the protocol and SAP.

14 Analysis

14.1 Main analysis

A detailed statistical analysis plan will be written prior to analysis. The reporting of findings will be in accordance with the CONSORT guidelines for cluster RCTs (29) and SPIRIT recommendations for reporting trials of interventions.(32) Statistical analysis will be performed in R or Stata (version 13 or higher).

All analyses will be intention to treat (i.e. students will be analyzed in the groups to which they were randomised, regardless of adherence to the intervention) and missing outcome data will not be replaced. Statistical tests and confidence intervals (CI) will be two-sided. Between-group comparisons will be presented with 95% confidence intervals wherever possible. As the trial includes a reasonable number of clusters, the analysis will be based on the individual student, allowing for clustering between students within school using robust standard errors. All analyses will control for baseline outcomes (if applicable), school level stratification variables (proportion of children eligible for FSM: country-specific median, geographical area) and student characteristics (age, gender, parental employment status).

Primary outcome: Multilevel logistic regression models will be used to compare the lifetime use of illicit drugs at 24 months by arm, and results presented as odds ratios and 95% CIs. Intra-cluster correlations (ICCs) alongside 95% CIs will also be reported**.**

Secondary outcomes: Multilevel linear (continuous outcomes) and logistic (binary outcomes) regression models will be used to compare secondary outcomes.

Sub-group analyses: Primary sub-group analyses will investigate the effect of the intervention on the frequency of any and specific drug use in a sub-group who report ever having used drugs at baseline. To examine the effect of the intervention on inequalities intervention effects in the following sub-groups: 1) school-level FSM entitlement above versus below country level median), 2) student-level FSM eligible versus not eligible, 3) parental employment status, and 4) gender. We will also estimate intervention effects in the following sub-groups to examine the impact of context and the hypothesized mechanisms of action: 5) geographical area, 6) peer supporter status, and 7) having had an opportunity to use drugs. Interactions between the trial arm and these variables will be modelled. We will also estimate the proportion of drug use which is recanted (where baseline lifetime drug users respond they have never used at follow-up) as a measure of reliability. The results of these exploratory analyses will be presented using confidence intervals.

Missing data: Baseline characteristics of students who have complete primary outcome data and those who do not will be compared. Multiple imputation will be performed to assess the impact of missing outcome data using MICE (Multivariate Imputation by Chained Equations) implemented using the ICE routine in Stata. Imputation models will include outcomes, intervention arm, stratifying variables and a main school effect to allow for clustering, as well as any appropriate baseline covariates. The main analyses will be repeated on the imputed datasets. Another sensitivity analysis will be conducted assuming all those lost to follow-up have used drugs.

Process outcomes: Multilevel linear and logistic regression models will be used to compare the hypothesised mediators of change outlined in our logic model (see appendix 1) at the 24-month follow-up. For the primary outcome, an interaction term will be fitted between allocation and ever having visited www.talktofrank.com, the perceived prevalence of drug use in the year group (anyone has used vs. no-one), having a conversation with school friends about drugs (ever vs. never), and ever receiving a drug offer.

15 Process evaluation

Informed by the Medical Research Council's guidance(33), an embedded process evaluation will be conducted. The process evaluation will explore the following issues:

- Fidelity during the training and intervention delivery. Drawing on Caroll et al's multicomponent model for measuring fidelity, (34) and tools developed in the pilot, [33] adherence to the intervention manual will be examined, as well as the extent to which training is standardised, and variations in quality of delivery across different schools and geographical areas.
- Intervention reach and reception. The proportion of students who report a conversation about drug related harms or harm minimisation in each arm will be compared. The receipt of the intervention and extent to which key intervention messages are evident with students who are and are not peer supporters will be examined.
- Contamination. Schools' activities related to drug use will be audited and interviews conducted with school staff to examine any changes to usual practice that might result due to participation in the trial.
- Acceptability of the intervention: to students who are and are not peer supporters, staff within schools including members of the senior management team, and public health practitioners who have delivered the intervention.

- Mechanisms of action, specifically whether the intervention worked as hypothesised in the logic model (see appendix 1) and whether this varied across trial centres and schools.

Table 2 summarises the data to be collected and issues addressed. In-depth qualitative data will be collected from four 'case study schools' which receive the intervention where more extensive evaluation will be undertaken at each centre (West of England and South Wales) using structured observations of training, interviews with trainees', and interviews with teachers on the senior management team.

Table 2. Summary of the process evaluation

Data source, method, sampling and timescale	**Key areas covered**	**Issues addressed**
Structured observation of training of trainers and peer supporters training (2 observations of training of trainers, 6 observations of peer supporter training (mix of the full 2 days and 4 follow-ups)).	Trainees' responses, adherence to manual.	Intervention fidelity, acceptability
10 interviews with peer supporters (or pairs of peer supporters) and 6 interviews with trainers in each case study school, ~ 1 month of being trained with 5 occurring ~ 1 month of end of 10-week intervention delivery. [a]	Trainees' experience of the training, contextual barriers and facilitators, impact on them and others.	Acceptability, mechanisms of change, reach, fidelity, sustainability
6 focus groups, with a random sample of nonpeer supporter students in each case study school ~1 month after 10-week intervention period.	Awareness of and exposure to the intervention, perception of intervention, impact on them and wider school life.	Reach, acceptability, fidelity, mechanisms of change.
Intervention delivery staff (trainers) and peer supporter training evaluation forms. Attendance registers of training and follow-up sessions to examine proportion of peer supporters who attend all sessions. All intervention schools.	Trainees' response, adherence to intervention, receipt of training.	Intervention fidelity, acceptability
Questionnaire at 24-month follow-up to students in all schools.	Exposure to the intervention, whether students report a	Intervention reach, acceptability,

	conversation about harms\ harm minimisation.	mechanisms of change, contamination.
Audit of school policies and procedures at baseline and the 24-month follow-up. Questionnaires with school PSHE leads. All schools.	Relevant drug prevention policies or practices for dealing with drug use.	Contamination, mechanisms of change, sustainability.
Interviews with member of senior management team (SMT) in all four case study schools ~6 months of end of 10-week intervention period. [a]	Awareness of and experience to the intervention, perception of intervention.	Intervention sustainability, acceptability, mechanism of change.
School records of student attendance in all schools at 24-month follow-up.	Whether any students moved from intervention to control schools.	Contamination.

[a] Or until data saturation is reached.

15.1 Qualitative analysis

A detailed qualitative analysis plan will be written prior to analysis. Qualitative data will be analysed using an approach which allows for both a deductive and inductive coding.(35) Data will be initially coded using an a priori coding scheme aligned with the process evaluation objectives as a means of organising the data for subsequent interpretation. Any unexpected themes emerging from the data which do not fit the coding scheme will also be coded. A thematic content analysis of the qualitative data will be undertaken, in which emergent themes will be identified and organised into an analytic framework. Transcripts of focus groups and interviews will be entered into the software package NVivo, which will be used as a data management tool, permitting quick access to data that falls within each theme.

16 Cost effectiveness analysis

A Health Economic Analysis Plan will be written prior to analysis. The economic analysis will consist of a cost consequences analysis (CCA) based on results within the duration of the trial and a cost effectiveness analysis where between group differences in the trial are extrapolated to the longer term. The costs of FRANK friends and usual practice arm of standard drug education will be estimated using information on all staff training (e.g. number,

duration and salary grade), including any expenses incurred by trainers, trainees and schools (e.g. teaching cover, travel and venue hire).

- *Within Trial Analysis*: Within the trial, an estimate the incremental net costs of FRANK friends (compared to the usual practice arm) will be completed according to the difference in outcome measures at the 24-month follow-up. We will estimate the incremental cost for primary and secondary outcomes. In the CCA, results will be presented in terms of health care, criminal justice costs and academic achievement. (36) Health related quality of life using the CHU9D (28) will be assessed, as well as a paediatric quality of life scale, to calculate Quality Adjusted Life Years in each trial arm. As the staff training peer supporters will be recruited from the NHS in Wales and local government in England a sub-group analysis by country to explore the economic impact of different models of delivery will be completed.
- *Long term analysis:* The health gains and cost savings associated with FRANK friends may occur beyond the time horizon of the trial leading to an underestimate of cost-effectiveness. Existing health economic models will be identified that link the outcomes in the trial to longer term costs and quality of life to extrapolate effects of the intervention beyond the trial period. In the absence of an appropriate health economic model, guidelines for best practice in economics modelling will be constructed.(37) Analyses where productivity losses are included/excluded to assess the impact on decision making will be conducted. Costs and effects will be discounted at the prevailing recommended rate (currently 1.5% per annum on both costs and effects). Probabilistic sensitivity analysis will be conducted to investigate the impact of uncertain parameters including the discount rate for public health interventions.

17 Data management

All data (including source data) will be entered and transcribed by the project staff using a secure data management system at CTR, a UKCRC-registered trials unit. Completed questionnaires will be transported or couriered to CTR by Trial Manager(s) and stored in a locked cabinet. Data from questionnaires will be stored in anonymised form, using participant identification numbers. Participant identification numbers and corresponding participant names will be held in separate files. Both files will be stored in secure password protected folders.

18 Protocol/GCP non-compliance

The CI will report any non-compliance to the trial protocol or the conditions and principles of Good Clinical Practice to the CTR in writing as soon as they become aware of it.

19 End of trial definition

The end of the trial will be considered as the date on which the last participant has completed their follow-up assessment or qualitative component. The sponsor will notify the main REC of the end of the trial within 90 days of its completion or within 15 days if the trial is terminated early.

20 Archiving

The TMF containing essential documents will be archived at an approved external storage facility for a minimum of 15 years. The CTR will archive the TMF on behalf of the Sponsor. Essential documents pertaining to the trial shall not be destroyed without permission from the Sponsor. Archiving and access to archive will be managed in accordance with the Standard Operating Procedures of the CTR.

21 Regulatory considerations

21.1 Ethical and governance approval

Ethical approval for the trial will be obtained from the School for Social Sciences (SOCSI) Ethics Committee at Cardiff University prior to commencement. The FRANK friends intervention is low risk and ethical approval was received in the pilot study and for previous work of this nature and so no ethical concerns are anticipated.

22 Safety Reporting

22.1 Questionnaire participants

There is a small chance that completing the questionnaires may trigger feelings of distress among students. Information containing sources of help will therefore be distributed during completion. If a participant becomes visibly upset while completing a questionnaire a trial team member present will:

- Remind them they do not have to complete the questionnaire;
- Check if they are upset because of the questionnaire;
- Advise them to talk to someone and remind them about the sources of help sheet;

- In the case of students, ensure the teacher is aware the individual has become upset;
- Note the incident on a data collection record form.

Trial administrators at each centre will check all questionnaires and log receipt after each data collection. If the administrator finds that a student writes something on their questionnaire indicating they are at risk of serious physical or emotional harm the CI or Cardiff/Bristol Trial Manager will be informed and they will contact the Child Protection Officer at the school to report the concern. While it is not possible to pre-empt all the comments that may indicate serious harm, comments describing actual self-harm or suicidal behaviour, suicidal plans, emotional, physical or sexual abuse, neglect, persistent or extreme bullying and risk of radicalisation will be passed on. Definitions of what constitutes physical, sexual and emotional abuse, neglect and bullying will be based on National Society for the Prevention of Cruelty to Children (NSPCC) guidance.

All work will be carried out in accordance with guidelines laid down by the Economic and Social Research Council (ESRC) the Data Protection Act 1998, and the latest Directive on GCP (2005/28/EC).

23 Data protection

The CTR will act to preserve participant confidentiality and will not disclose or reproduce any information by which participants could be identified, except where specific consent is obtained. Data will be stored in a secure manner and will be registered in accordance with the General Data Protection Regulation 2016. The data custodian for this trial is Cardiff University.

24 Indemnity

The Chief Investigator, local Investigators and coordinating centre do not hold insurance against claims for compensation for injury caused by participation in a trial and they cannot offer any indemnity.

25 Trial sponsorship

Cardiff University will act as Sponsor for the trial. Delegated responsibilities will be assigned to the sites taking part in this trial.

26 Funding

The trial is funded by the National Institute for Health Research Public Health Research Programme. The grant awarded is £1,465,055.20.

27 Trial management

27.1 TMG (Trial Management Group)

The TMG will consist of the Chief Investigator (chair), co-applicants, the FRANK friends Senior Trial Manager, Trial Manager(s) from CTR Cardiff and the University of Bristol, Data Manager, and Trial Administrator(s). The role of the TMG will be to assist in the trial set up by providing specialist advice, input to and comments on the trial procedures and documents (information sheets, protocol etc). They will also advise on the promotion and the running of the trial and deal with any issues that arise. The group will meet, either face-to-face or using audio-conferencing facilities, at least quarterly throughout the course of the trial and if necessary, additional/more frequent meetings may occur particularly at crucial time points during the trial, for example during the set-up phase. TMG members will be required to sign up to the remit and conditions as set out in the TMG Charter.

27.2 TSC (Trial Steering Committee)

The TSC will meet every 12 months and include the chief investigator, Bristol lead, an independent chair, and independent external members including: a representative from Public Health Wales, a statistician, an addiction specialist, an expert in adolescent substance misuse and a teacher. The TSC will act as an independent strategic oversight body to ensure transparency and that relevant milestones are being met and will report back to the NIHR PHR Programme.

27.3 Project team

This group will consist of the chief investigator, FRANK friends Trial Manager(s) and co-ordinating team within CTR Cardiff and the University of Bristol who will meet weekly to discuss the day to day issues that arise from the trial.

27.4 DMC (Data Monitoring Committee)

Given the low risk nature of the trial, and the fact that there are no interim data collections scheduled, we will ask the TSC to act as DMC.

28 Quality Control and Assurance

28.1 Audits and inspections

The trial may be inspected and audited by Cardiff University under their remit as Sponsor.

29 Publication Policy

A publication policy will be drafted and approved by the TMG. It will state principles for publication, describe a process for developing output, contain a map of intended outputs and specify a timeline for delivery. The publication policy will respect the rights of all contributors to be adequately represented in outputs (e.g. authorship and acknowledgments) and the trial to be appropriately acknowledged. Authorship of parallel studies initiated outside of the TMG will be according to the individuals involved in the project but must acknowledge the contribution of the TMG and the Trial Coordination Centre.

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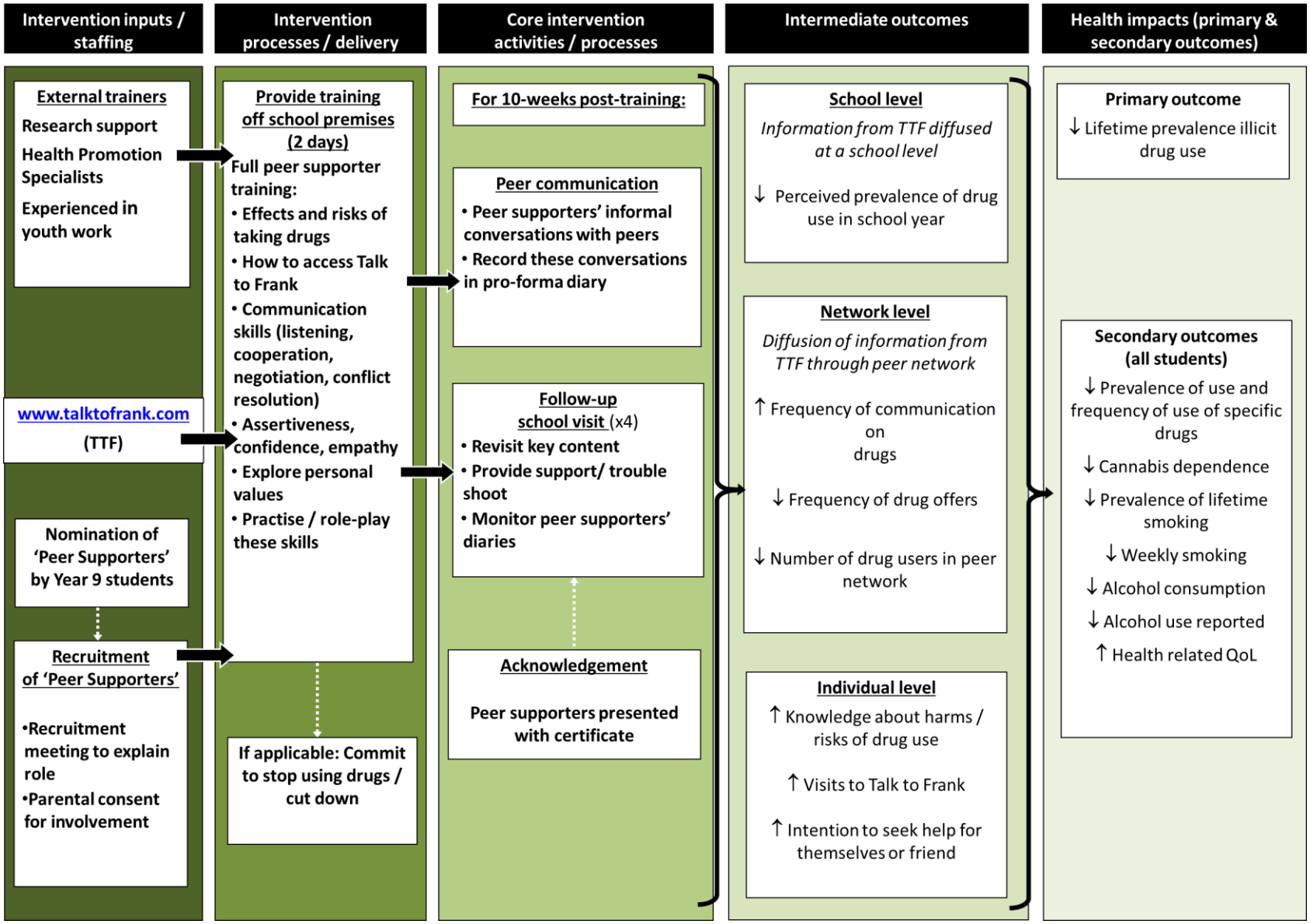

Figure 3. FRANK friends logic model