Study Acronym: ASSIST+Frank

Full study title: Adapting and piloting the ASSIST model of informal peer-led intervention delivery to the Talk to Frank drug prevention programme in UK secondary schools (ASSIST+Frank): an intervention development, pilot and exploratory trial

Sponsor:	Cardiff University, 30-36 Newport Road, Cardiff, CF24 0DE.
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This protocol has been authorised by:

Name	**Role:**	**Signature**	**Date**
Dr J White	Chief Investigator		05/02/2014

General Information This protocol describes the ASSIST+Frank study and provides information about the procedures for entering schools and recruiting participants into the study. The protocol should not be used as a guide, or as an aide-memoire for the treatment of participants. Every care has been taken in drafting this protocol; however, corrections or amendments may be necessary. These will be circulated to the known co-applicants of the study. Problems relating to the study should be referred, in the first instance, to the study manager.

Compliance This study will adhere to the conditions and principles outlined in the EU Directive 2001/20/EC, EU Directive 2005/28/EC and the ICH Harmonised Tripartite Guideline for Good Clinical Practice (CPMP/ICH/135/95). It will be conducted in compliance with the protocol, the Research Governance Framework for Health and Social Care (Welsh Assembly Government November 2001 and Department of Health 2nd July 2005), the Data Protection Act 1998, Mental Capacity Act (2005), and other regulatory requirements as appropriate.

Funding The ASSIST+Frank study is being funded by the National Institute for Health Research (NIHR) Public Health Research Programme (PHR). Public Health Wales (PHW) fund the intervention costs relating to ASSIST in the ASSIST+Frank study, and intervention costs relating to Frank Friends/+Frank will be met by NISCHR NHS Excess Treatment Costs Scheme.

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Table of Contents

Glossary of abbreviations

ALPHA	Advice Leading to Public Health Advancement
ALSPAC	Avon Longitudinal Study of Parents and Children
ASSIST	A Stop Smoking in Schools Trial (used here to denote the intervention, rather than the trial)
CF	Consent Form
CI	Chief Investigator
CRF	Case Report Form
CRO	Contract Research Organisation
CTU	Clinical Trials Unit
CU	Cardiff University
DECIPHer	Centre for the Development and Evaluation of Complex Interventions for Public Health Improvement
EUCTD	European Union Clinical Trials Directive
Eu-DAP	European Drug Abuse Prevention Trial
ICH	International Conference on Harmonization
GCP	Good Clinical Practice
GAfREC	Governance Arrangements for NHS Research Ethics Committees
HE	Health Economics
HSE	Health Survey for England
IC	Informed consent
IDMC	Independent Data Monitoring Committee
IEC	Independent Ethics Committee
IRAS	Intergrated Research Approval System
ISRCTN	International Standard Randomised Controlled Trial Number
NIHR	National Institute for Health Research
NHS	National Health Service

NISCHR	National Institute for Social Care & Health Research
PI	Principal Investigator
PHR	Public Health Research
PPI	Patient and Public Involvement
PHW	Public Health Wales
PIS	Patient Information Sheet
R&D	Research and Development
RCT	Randomised Controlled Trial
REC	Research Ethics Committee
SEWTU	South East Wales Trials Unit
SMT	School Management Team
SOP	Standard Operating Procedure
TMF	Trial Master File
TMG	Trial Management Group
TND	Towards No Drug abuse
TSC	Trial Steering Committee
UKCRC	United Kingdom Clinical Research Collaboration

1 Amendment History

Amendment No.	Protocol version no.	Date issued	Author(s) of changes	Details of changes made

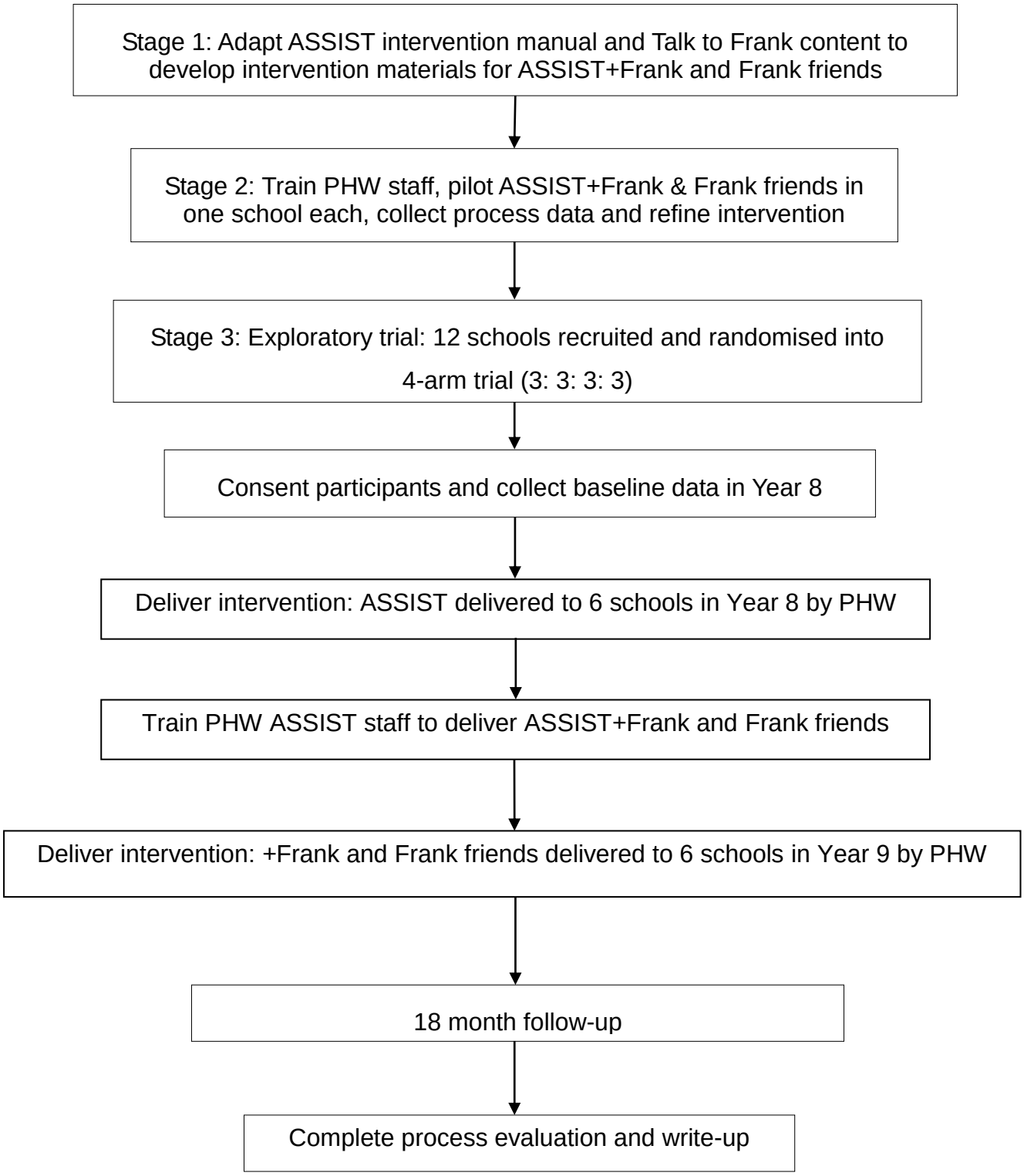
2 Synopsis

Full title	Adapting and piloting the ASSIST model of informal peer-led intervention delivery to the Talk to Frank drug prevention programme in UK secondary schools (ASSIST+Frank): an exploratory trial
Acronym	ASSIST+Frank
Study design	This project will have 3-stages: Stage 1: Development of training materials and an intervention manual for ASSIST+Frank and Frank friends; Stage 2: Piloting of ASSIST+Frank in one school and Frank friends in one school followed by a period of refinement of the interventions; Stage 3: Exploratory 4-arm trial with cluster randomisation (at the level of school) in 12 state secondary schools in South Wales with an embedded process evaluation.
Study participants	Students aged 12-13 (year 8) at baseline in state secondary schools.
Planned sample size	The total sample size of 12 schools for the exploratory trial is anticipated to equate to approximately 2040 students (assuming a 170 pupils in a year), which with a response rate of 80% will achieve a sample of 1632 students (408; 408; 408; 408 per arm). If the average year group had 150 students, we would expect 1800 to be sampled, and with an 80% response rate 1440 to participate, equating to 360 per arm.
Follow-up duration	18 months
Planned study period	1st March 2014 to 31st October 2016
Primary aim	To assess the feasibility and acceptability of delivering the ASSIST+Frank adjunct and Frank friends interventions to determine whether to proceed to a full-scale RCT.
Interventions	ASSIST is an informal peer-led smoking prevention intervention to diffuse and sustain non-smoking norms via secondary school students' social networks in year 8. ASSIST+Frank is an informal peer-led drug prevention adjunct to ASSIST designed to be delivered in year 9 in secondary schools to the year groups who have previously received ASSIST in year 8. Frank friends is a stand-alone, informal drug prevention intervention

	which aims to identify and recruit peer opinion leaders in year 9 to diffuse information via existing social networks and modify school norms regarding drug use and minimise the harms associated with drug use.

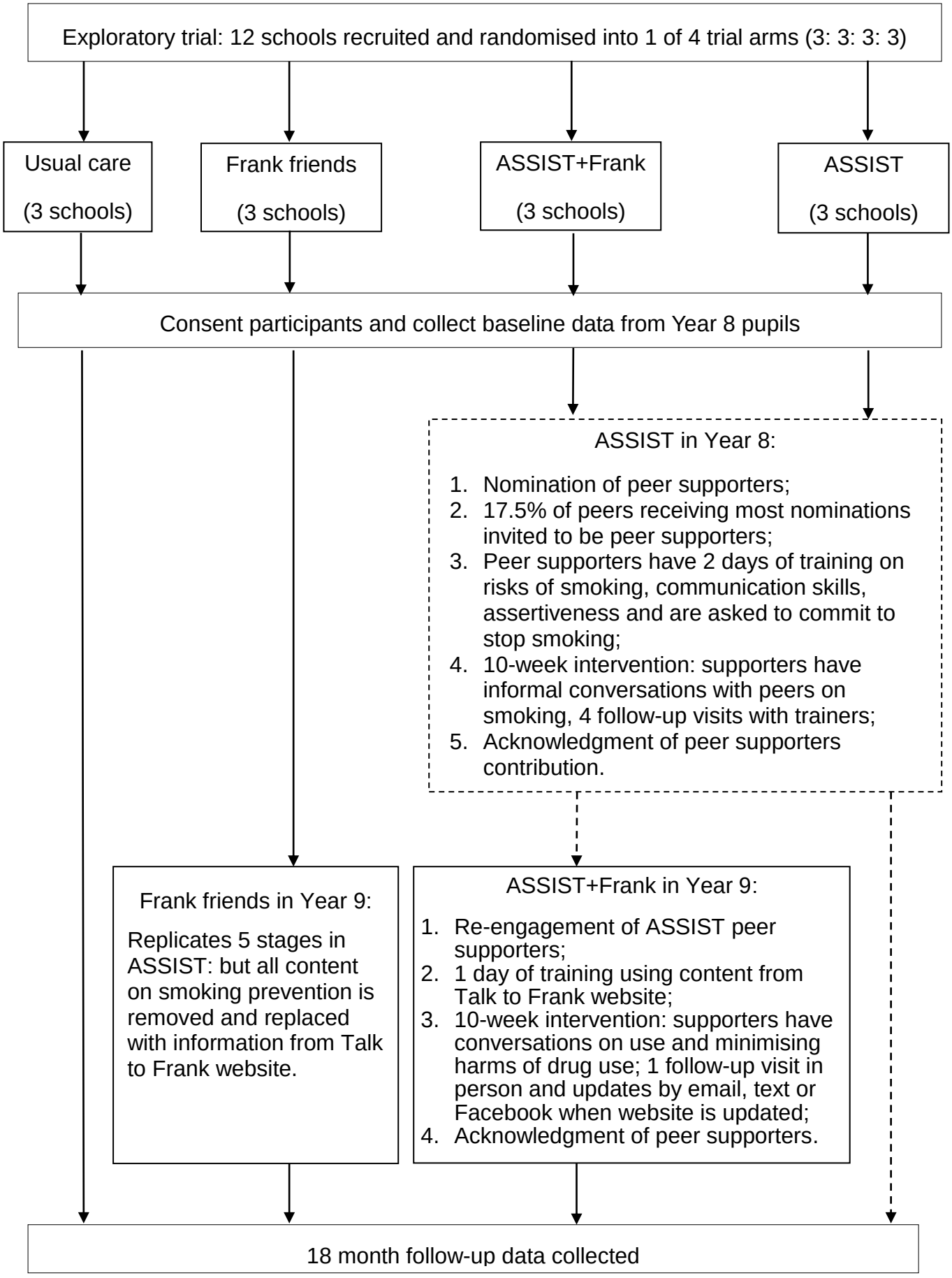
3 Trial/ summary & study schema

3.1 Study schema [a]



[a] Note: Stages will not take place in chronological order. ASSIST will be delivered in year 8 and the baseline data collection for the exploratory trial (stage 3) will take place before the piloting of ASSIST+Frank and Frank friends.

3.2 Participant flow diagram



3.3 Study summary

Background

School-based drug prevention interventions have historically focused on abstinence, been delivered by school teachers or law enforcement officers, and had limited effectiveness in terms of behaviour change. Informal school-based peer-support has been effective in preventing the uptake of smoking but evidence on the prevention of illicit drug use using peer support is inconclusive.

Aims

The primary aim of this project is to develop, pilot and assess the feasibility, acceptability and delivery of two new, informal peer-led interventions designed to prevent illicit drug use among secondary-school students, as well as to assess trial recruitment and retention rates. We will evaluate the effect of these peer-led drug and a peer-led smoking intervention on the: incidence of drug use (primary outcome); the frequency of use of any and specific drugs; cannabis dependence; incidence of smoking; smoking frequency; nicotine dependence; and alcohol use. These data will not provide any indication of effectiveness but will give an indication of trial feasibility, effect-sizes, and potential mechanisms of action to inform the design of a definitive phase three trial.

Design

Intervention development, piloting and cluster randomised controlled exploratory trial (MRC complex intervention phase II trial). Two drug prevention interventions (ASSIST+Frank and Frank friends) will be developed using the peer nomination and training manual from an existing effective peer-led smoking prevention intervention, ASSIST; content on drug misuse will come from the UK national drug education service, "Frank". (www.talktofrank.com). ASSIST+Frank and Frank friends will be piloted in one school each and be followed by a process evaluation and period of intervention refinement. A 4-arm cluster exploratory RCT (ASSIST in year 8 with ASSIST+Frank adjunct intervention in year 9; ASSIST in year 8 only; Frank friends in year 9 only; usual care comparison) will then be conducted, with an embedded process evaluation

Population

Students aged 12-14 in state secondary schools.

Outcome measures

Within the exploratory trial, a mixed methods process evaluation will be used to assess each intervention against pre-defined progression criteria (to be agreed by the Trial Steering Committee) based on: 1) the feasibility of delivering ASSIST+Frank and Frank friends; 2) the acceptability of ASSIST+Frank and Frank friends to peer supporters; 3) the acceptability of the interventions to school senior management teams, other school staff, and parents; and 4) acceptability of trial design and assessment methods. Numbers of schools and participants recruited and retained will be presented as well as data on intervention fidelity. The indicative primary effectiveness outcome will be the incidence of any drug use assessed 18 months post randomisation. Secondary outcomes include the frequency of use of any and specific drugs; cannabis dependence; smoking frequency; nicotine dependence; and changes in social networks of peer drug and tobacco use.

Duration and follow-up

Following the development, piloting and refinement of ASSIST+Frank and Frank friends participants in the exploratory trial will provide consent and complete a baseline self-report questionnaire. Students randomised into the ASSIST and ASSIST+Frank arms will receive ASSIST in year 8. Approximately 6 to 12 months after the delivery of ASSIST, during year 9, students will receive the ASSIST+Frank and Frank friends arms interventions. 18 months post randomisation participants will complete the follow up questionnaire to assess any change in drug use.

4 Introduction

4.1 Background

The NIHR commissioning brief PHR no 12/3060 noted that peer-support has been effective for alcohol and smoking but evidence on the prevention of illicit drug use using peer support is inconclusive. This led to a call to answer the research question: *"What is the effectiveness and cost effectiveness of using peer support to prevent illicit drug uptake and use in young people?"* We identified two systematic reviews (1)(2) and two RCTs not included in these

reviews (3)(4) which had used peers support to prevent drug misuse in young people and these informed the aims, objectives, design and methods of the study. These reviews and studies are summarised below.

Systematic reviews evaluating peer-led drug prevention interventions with adolescents: A Cochrane review of schools-based drug prevention interventions examined the effects of peer-led versus teacher-led interventions (1). Based on one RCT of the Life Skills programme, this review suggests that drug prevention in schools may be more effective when delivered by peers (5). This version of the Life Skills programme focused on fostering self-esteem, confidence and independent decision-making in addition to drugs education. Peer-leaders were aged 14-16, and either volunteered to participate, or were recruited via teacher-nomination. Following training, peer-leaders were asked to deliver a 20-session programme to 11-12 year old students at their school. After four months (5) and one year (6) fewer students reported using marijuana in the past month in the peer-led than control arm.

Mentoring to prevent illegal drug use: A separate 2011 Cochrane review of mentoring programmes to prevent drug use included 4 RCTs but a pooled effect was not estimated due to heterogeneity in drug use measures (2). Only one programme had a peer-led component relevant to a school-setting, involving older peers providing social support to youth 10-16 years of age. The 'Big Brothers Big Sisters Programme' was effective in preventing the uptake of any drug use among young people reporting never having used drugs at baseline (7).

RCTs of school-based drug prevention: Two RCTs were identified which included peer-led components within a drug prevention curriculum either to deliver additional sessions (4), or review teacher delivered content at each session (3). The European Drug Addiction Prevention (EU-DAP) study was a 4-arm RCT in 170 schools (N=7079, students 12-14 years of age) that examined the effectiveness of a 12-hour curriculum to reduce substance use across seven countries. The four arms were: a) teacher-delivered curriculum (TDC) only; b) TDC with seven additional peer-led sessions; c) TDC plus three workshops for parents; and d) a control. Schools were instructed to select same age peers either by teacher nomination or

student vote. After 18-months, multilevel models showed a weak effect on lifetime cannabis use (OR = 0.83; 95% CI = 0.65, 1.05; NNT = 34) and frequent cannabis use (≥ 3 occasions in past 30 days; OR = 0.74; 95% CI = 0.53, 1.00; NNT = 46) in students allocated to any active arm (i.e. a-c) versus the control arm. A null effect was reported for allocation to the peer-led and parent arm on cannabis use and results were not tabulated because programme implementation was very low in the peer-arm. Only 8% of centres implemented all seven peer-led sessions and 71% did not conduct any meetings at all. This suggests these estimates on effectiveness of the peer-led arm are unlikely to be precise. Also that interventions using formal peer-led delivery should undergo extensive piloting and testing to explore the acceptability and feasibility of delivering the intervention with peer-supporters.

A three-arm RCT of the Towards No Drug Abuse (TND) programme (8), examined the additional benefit of adding a peer-led review of intervention materials at the end of 12 sessions delivered by teachers (3). TND emphasises improving education on the risks of drug use, decision making and self-control. High-school classes (n= 840 students; mean age 16) were randomized to: a) standard TND curriculum; b) standard TND curriculum with a peer-led component (TND-Network); a control. Peer-leaders were those receiving the most nominations regarding "who would make the best leaders for a project in class". Groups were then created within each class by assigning students to a leader whom they had chosen, or to whom they were socio-metrically closest (9). Compared with controls, students in the TND arm did not report a significant change in their drug use, but those in the TND Network arm reported a reduction in the frequency of cannabis and cocaine use in the past month at a one year follow-up. An interaction between allocation to TND-Network vs. control arm and peer substance use (i.e. the average use of tobacco, alcohol, cannabis and cocaine reported by the five classmates nominated as friends) revealed that the intervention was most effective for students embedded in peer networks that did not engage in substance use. Those students with friends who had already used substances in the TND-network arm were more likely to increase their use suggesting the potential for harms via the diffusion of pro-drug norms in poorly designed peer-led interventions. However, contamination is a major methodological weakness in this trial which allocated classes (rather than year group or schools); therefore the effect of TND network in this comparison may have been diluted (3).

4.2 Rationale for current study

We only identified three RCTs using peer support to prevent illicit drug use with two positive (3)(6) and one non-significant result (4). Due to the low levels of intervention implementation in one trial (4), and a potentially harmful effect observed for high risk groups in another (3), these studies suggest that, while peer-led drug prevention interventions are promising, modifying the peer-led components may be warranted to optimise peer support for drug prevention with young people.

ASSIST is an effective, informal peer-led intervention for smoking prevention delivered in secondary schools (10). Based on diffusion of innovation theory (11) it purposively recruits 'influential' students aged 12-13 years (UK year 8) and trains them as ‘peer supporters’ to spread and sustain non-smoking norms through informal conversations with their peers. A cluster RCT in 59 schools (n=10,730) in 2001-2004 found that it reduced weekly smoking among students over a 2-year period; including smoking frequency among students who had ever smoked before (10).

We will develop an additional component of the ASSIST smoking prevention intervention to be delivered in year 9 when students are aged 13-14. The ASSIST+Frank adjunct intervention will involve one additional day of training of former ASSIST peer supporters to develop the skills to discuss drug use with their peer group. We will also develop a standalone drug prevention version of ASSIST to be delivered in year 9, Frank friends. Frank friends will replicate the ASSIST model of peer recruitment and training but replace content on the harms associated with smoking tobacco with information on drug use. In the +Frank and Frank friends interventions peer supporters will be educated on the harms associated with drug use and how to minimise the known harms amongst their friends. The drug use content will come from the Talk to Frank website (www.talktofrank.com). Talk to Frank is the UK national drug education service and provides up-to-date, youth-friendly information and advice on the risks and harms of drug use.

It is important to note that there are differences between the intervention we propose and the approaches used in the EU-Dap and TND-Network interventions. Firstly, the ASSIST model is an informal method of delivery which asks influential peers to talk about substance use behaviour (currently smoking) with friends during conversations in naturally occurring contexts, rather than via leading formal sessions in classrooms. Secondly, as well as standard education on the risks of drug use, Talk to Frank provides advice on minimising the harms

associated with drug use through multiple, interactive methods (e.g. text messaging, telephone, email, and anonymous web-chat) that may be better suited as an adjunct to peer communication than classroom-based advice.

An unpublished feasibility trial of a drug prevention intervention based on the ASSIST model (CASE+) found little change in intentions to use cannabis in 732 12-13 year old students (in six Scottish secondary schools) over a three month follow-up (12). However, there are a number of factors which limit the relevance of this trial to this study, a) no drug use data were collected, b) three month follow-up is not long enough to ascertain the likely effect over longer periods, and, c) intervention content was solely on cannabis use. The intervention added one extra day of education solely on cannabis use to the existing two days of training on smoking in ASSIST. A process evaluation indicated that although implementation fidelity and acceptability with school staff was high, the addition of the extra day of training on cannabis at the same time as the training on smoking had two unhelpful effects. First, the three-day training attempted to deliver too much information. This distracted students from engagement with key messages and reduced the time spent on developing the peer supporters' skills in having conversations with their friends. Second, the peer supporters rarely had conversations about cannabis, since given the choice of discussing smoking or cannabis use, it was easier for them to opt to focus on smoking, because there were few students experimenting with cannabis at age 12/13, and there was a sensitivity around discussing cannabis use as it is illegal. This study indicated that tackling both behaviours at the same time was problematic, and that peer supporters needed additional training and support to engage in conversations about cannabis as confidently as they were able to do around tobacco use.

The proposed ASSIST+Frank extension is quite different to CASE+, in that the ASSIST smoking prevention intervention will be implemented in year 8, with the additional drug focus and Talk to Frank materials (ASSIST+Frank) being introduced to those same peer supporters in year 9, one year later. A process evaluation following the piloting and an exploratory trial will explore whether the ASSIST+Frank and Frank friends intervention are acceptable and peer supporters are adequately informed and supported to disseminate the harm minimisation message from Talk to Frank. Exploratory analysis will also examine the relative effectiveness of these interventions in preventing and reducing drug use against a usual care control. An arm of ASSIST only schools will also be included in the exploratory

trial to examine the potential unintended beneficial effects of a smoking prevention intervention on drug use, in particular cannabis use which is typically used with tobacco.

5 Study aim and objectives

5.1 Primary aim

To assess the feasibility and acceptability of delivering the ASSIST+Frank adjunct and Frank friends interventions to determine whether to proceed to a full-scale RCT.

5.2 Study objectives:

- assess and refine the ASSIST logic model so that it is applicable to drug prevention;
- assess the acceptability of the intervention and evaluation to ASSIST+Frank and Frank friends trainers, students, parents, and school staff;
- explore the barriers and facilitators of implementing the interventions;
- explore the fidelity of intervention delivery by ASSIST+Frank and Frank friends trainers and peer supporters;
- explore whether the proposed outcome measures are suitable for assessing illicit drug use (primary outcome) and the secondary outcomes of interest;
- assess trial recruitment and retention rates;
- identify potential effect sizes that are likely to be detected as part of a definitive trial and an appropriate sample size;
- record the delivery costs and to pilot methods for assessing cost effectiveness;
- identify the structures, resources and partnerships necessary for a definitive trial to take place;
- to develop the protocol for a definitive trial and economic evaluation of the impact of ASSIST+Frank and Frank friends compared to usual advice provided in schools to reduce illicit drug use.

6 Study design

This proposed project has 3-stages (see above study schema on page 14):

Stage 1: Development of training materials and an intervention manual for ASSIST+Frank and Frank friends;

Stage 2: Piloting of ASSIST+Frank in one school and Frank friends in one school followed by a period of refinement of the interventions;

Stage 3: Exploratory 4-arm trial with cluster randomisation (at the level of school) in 12 state secondary schools in South Wales with an embedded process evaluation.

7 School and participant selection

Schools and participants are eligible for the trial if they meet all of the following inclusion criteria and none of the exclusion criteria. All queries about school eligibility should be directed to the ASSIST+Frank Study Manager (Kim Madden) before randomisation.

7.1 Inclusion criteria

Schools will be recruited and randomised if they are among the state secondary schools identified by Welsh Government and Public Health Wales as eligible to receive the ASSIST intervention in academic year 2013-2014. Students in year 8 in these schools in 2013-2014 will be eligible participants in baseline and follow-up data collections (baseline conducted in year 8; 18-month follow-up year 9).

8 Outcome measures

The primary aim of the exploratory trial will be to assess the feasibility and acceptability of delivering the ASSIST+Frank and Frank friends interventions as well as trial methods prior to a phase III definitive trial.

8.1 Progression criteria

Within the exploratory trial, a process evaluation will inform assessment against the following progression criteria (to be agreed in advance by the Trial Steering Committee):

Acceptability and feasibility of the interventions to school and intervention delivery staff

1. Was it feasible to implement the ASSIST+Frank intervention in (at least) 2 out of 3 intervention schools? This will be assessed according to whether: a) 75%+ of year 8 ASSIST peer supporters are recruited and re-trained as ASSIST+Frank peer supporters in year 9; b) 75%+ of year 9 students nominated are recruited and trained as Frank friends peer supporters and, c) PHW staff delivered the additional ASSIST+Frank training in full in all 3 intervention schools. This will be assessed via interviews and focus groups with peer supporters and PHW staff, as well as observations of peer supporter training.
2. Was it feasible to implement the Frank friends intervention in (at least) 2 out of 3 intervention schools? This will be assessed according to whether: a) PHW staff delivered the Frank friends training in full in all 3 schools. This will be assessed via interviews and focus groups with peer supporters and PHW staff, as well as observations of peer supporter training.

Acceptability of the intervention to peer supporters and fidelity

3. Was the intervention acceptable to students trained as ASSIST+Frank peer supporters? This will be assessed according to whether: a) 75%+ of ASSIST+Frank peer supporters report having at least 1 or more informal conversations with their peers at school about drug-related risks/harms; and b) 75%+ of ASSIST+Frank peer supporters report at least one contact with PHW staff, either via a follow-up visit and/or contact via email, text or Facebook. This will be assessed via interviews and focus groups with peer supporters and PHW staff, and analysis of documentary evidence (e.g. PHW log of attendance at follow-ups, etc.).
4. Was the intervention acceptable to students trained as Frank friends peer supporters? This will be assessed according to whether: a) 75%+ of Frank friends peer supporters report having at least 1 or more informal conversations with their peers at school about drug-related risks/harms; and b) 75%+ of Frank friends peer supporters report on-going contact with PHW staff throughout the year via a follow-up visit. This will

be assessed via interviews and focus groups with peer supporters and PHW staff, and analysis of documentary evidence (e.g. PHW log of attendance at follow-ups, etc.).

Acceptability of the intervention to school staff and parents

5. Was the ASSIST+Frank intervention acceptable to the majority of school senior management teams (SMT), other school staff, and parents? This will be assessed via interviews with SMT and focus groups with school staff and parents.
6. Was the Frank friends intervention acceptable to the majority of school senior management teams (SMT), other school staff, and parents? This will be assessed via interviews with SMT and focus groups with school staff and parents.

Acceptability of the trial design and assessment methods

7. Were the trial design and methods acceptable and feasible? This will be assessed according to whether: a) randomization occurred as planned and was acceptable to SMTs; b) a minimum of 5 out of 6 intervention schools and 2 out of 3 schools from the comparison arms participate up in the 18 month follow-up? and, c) the student survey response rates are acceptable at baseline (80%+) and follow-up (75%+).

8.2 Pilot primary outcome measure

Incidence of any illicit drug use assessed by self-report questionnaire 18 months after randomisation.

8.3 Pilot secondary outcome measures

Using the example questions proposed by the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) (14), those used in the ALSPAC study (15), the most recent Health and Social Care Information Centre report on Smoking, Drinking and Drug Use Among Young People in England, (16) and the Eu-Dap trial (17) we will evaluate the effect of the interventions on:

- Use of cannabis, cocaine, amphetamines, crack, ecstasy, aerosols, gas, glue, solvents, poppers, nitrus oxide, sedatives or sleeping Pills, LSD, magic mushrooms, ketamine,

steroids, methadrone, other prescription drugs, and opioids. Questions will assess use: ever (lifetime prevalence), over the 12 months, past 30 days and past week (15);

- Age of first experimentation with any drug;
- Cannabis use: age of first use; frequency of use; symptoms after use (e.g. anxiety, relaxation, paranoia); method of use (by itself, mixed with tobacco) (15); cannabis dependence: Cannabis Abuse Screen Test (CAST; (18) (19));
- Tobacco use: lifetime use; current use; use in past 12 months, past 30 days and past week; frequency of use; (taken from ASSIST trial (10) and Health Survey for England (20)); Heaviness of Smoking Index; Fagerstrom test of nicotine dependence (21);

We will also collect data on attitudinal and knowledge based precursors to drug use to explore potential mediators of the effect of ASSIST+Frank and Frank friends on drug use. These include the perceived prevalence of drug use within the year, knowledge on the harms of drug use, methods of help seeking, frequency of drug use offers, and attitudes towards heavy drug use and drug dependency, adolescent mental health (Short mood and feelings questionnaire (22)); school engagement (using the Beyond Blue 'School climate' scale (23)), and records on educational achievement. These intermediate outcomes will be used to explore potential mechanisms, such as drugs literacy, drug use norms and peer communication.

We will collect detailed information on social networks to map contacts between peer supporters and drug and non-drug using peers. We will collect data on: up to five best friends inside or outside school, boyfriends/ girlfriends; and explore changes in: the average level of drug use amongst school friends, drug use amongst peer-leaders and their peer groups, isolated students (with no nominations), and the number of friends in and outside of school, as well as the number of nominations sent and received. We will also collect data on the frequency of communication with peers on the harms or risks associated with drug use and the method of communication (face to face, the internet (including what websites), instant messaging via smart phone, texting) as responses may inform the design of future interventions.

9 Recruitment

9.1 Number of schools and participants

A total of 12 schools with approximately 1632 students will be recruited.

9.2 Recruitment process

The exploratory trial will be embedded within the 2013-2014 delivery of ASSIST by PHW. The Welsh Government provide PHW with a list of approximately 160 schools eligible for ASSIST, out of the 220 secondary schools in Wales. These schools are selected on the basis of the percentage of children in receipt of free school meals and those who have not received ASSIST in the past two years are prioritised. PHW has agreed that out of these 160 schools those eligible can be invited to participate in the exploratory trial (n=12). PHW will recruit schools for the ASSIST+Frank study at the same time as schools for the 2013-2014 roll-out of ASSIST. Eligible schools in the counties of Cardiff, Newport, Torfaen, Blaenau Gwent, Rhondda Cynon Taf, Merthyr, and Caerphilly will be sent a project information sheet, reply envelope and form indicating that if they wish to contact PHW or the CI. If necessary, non-responders will be followed up with a reminder and then by a phone call by the Study Manager. All interested schools will be visited by the CI or Study Manager to discuss the study in more detail and agree a research contract. Further schools will be sampled where the required number of schools is not obtained.

9.3 Informed consent

Schools

The head-teacher (or designated member of the school senior management team) will be asked to sign a formal commitment for their school to take part in the study. The commitment will describe the roles and responsibilities of the school and the research team during the research period at the school.

Teachers, parents and PHW staff

The ASSIST+Frank Study Manager will provide all adult participants with information on the study, explain the aims of the study and they will then be asked to give informed consent prior to participation in the research. They will be assured that if they decide not to participate, their decision will be handled confidentially. Written informed consent detailing the right to withdraw will be collected for all participants.

Student consent

Written consent will be sought from young people. Age-appropriate information sheets will be provided, together with verbal explanation by researchers. Parents who do not wish their child to participate will be able to 'opt-out'. Letters will be sent to parents/guardians to contact the school if they do not wish their child to participate in the trial. At the beginning of data collections, it will be made clear that participation by students is optional. Note that this 'opt-out' consent is acknowledged standard practice for school-based studies in the UK, used by members of our investigator team in school-based interventions in England (e.g. Pupil-led sex education in England (RIPPLE study) (24)), and the original ASSIST RCT held in 59 schools (N students = 10,730) in South Wales and Bristol (10)).

9.4 Registration

Participants' personal details will be collected on paper and stored electronically. This information will be stored separately from questionnaire data. All data will be handled according to the principles of the Data Protection Act (1998), for further details please see section 15.5.

9.5 Non-registration

Personal details of schools not selected for recruitment, or parents or students who decline to consent, will not be retained.

9.6 Randomisation

In the exploratory trial, randomisation of schools will occur after all schools have completed baseline data collection. Schools will be randomly assigned to one of the 4 arms with an assignment ratio of 3: 3: 3: 3. Allocation will be conducted by an independent SEWTU statistician, blind to the identity of schools, and minimised on: the percentage of pupils in receipt of free school meals and school size to balance the randomisation. Optimal allocation will be used to carry out the randomisation. Here a balance algorithm is used when pre-defined sequence generation is required or when all units are randomised jointly. Data on school size and free school meal entitlement will be collected at recruitment and used to balance the randomisation.

10 Withdrawal & loss to follow-up

Schools and participants will have the right to withdraw consent for participation in any aspect of the ASSIST+Frank study at any time. Participants' care from health services will not be affected at any time by declining to participate or withdrawing from the study.

If a participant initially consents but subsequently withdraws from the study, a clear distinction will be made as to what aspect of the study 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 an ASSIST, ASSIST+Frank or Franks 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 Study Manager based on information provided by the participant. This withdrawal form should be sent to the ASSIST+Frank Study Manager. Any queries relating to potential withdrawal of a school or participant should be forwarded to the Study Manager immediately.

In order to minimise loss to follow-up we will replicate the procedures trialled in the original evaluation of ASSIST of conducting repeated absentee visits to schools. Schools will also be paid £300 for staff cover for the data collections.

11 Intervention

The exploratory trial will have four arms.

11.1 Intervention arms

11.1.1 ASSIST

ASSIST is an informal peer-led smoking prevention intervention to diffuse and sustain non-smoking norms via secondary school students' social networks in year 8 (aged 12-13) (10). ASSIST has five stages:

1. Nomination of peer supporters: Students aged 12–13 years (UK year 8) are asked to identify influential peers using three questions, "Who do you respect in year 8 at your

school?", "Who are good leaders in sports or other groups activities in year 8 at your school?", and "Who do you look up to in year 8 at your school?" The 17.5% of year 8 pupils 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. Trainers make it clear that students who smoke can only be peer supporters if they commit to trying to stop smoking;
3. Training of peer supporters: The aims of the training are to: provide information about risks of smoking and benefits of remaining smoke-free; develop communication skills including, listening, cooperation and negotiation, and conflict resolution; enhance students' confidence, empathy, assertiveness, attitudes to risk-taking, and exploration of personal values and to role play having informal conversations about smoking with their peers. Training takes place at a venue outside school over 2-days by a team of external trainers experienced in youth work and health-promotion.
4. Intervention period: 10-week peer-led intervention where supporters have informal conversations with their peers on smoking, 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. Four follow-up school visits by trainers to meet with peer supporters and provide them with additional support and training and to review progress with the informal conversations;
5. Acknowledgment of peer supporters' contribution: All peer supporters are presented with a certificate; those who hand in their diary are also presented with a gift certificate.

11.1.2 ASSIST+Frank

The intervention manual for ASSIST+Frank has yet to be developed and will undergo extensive piloting. There may therefore be revisions to the outline below. At present it is anticipated that ASSIST+Frank will have four stages:

1. Reengagement of ASSIST peer supporters: ASSIST year 8 peer supporters will be invited in year 9 to continue and extend their role. Trainers will make it clear that students who take drugs can only be peer supporters if they commit to reduce and try to stop taking any drugs (in line with the ASSIST model);
2. Training of peer supporters: ASSIST+Frank peer supporters will revisit key exercises on communication skills including, listening, negotiation, and ways of giving information; new sessions will focus on: the effects and risks associated with specific drugs and minimising potential harms; how to talk with their peer group about drugs including

aspects of confidentiality and the law; how to access Talk to Frank website (www.talktofrank.com), by smartphone, or by text; and time will be devoted to answering questions. Training will be one full day on drug education and practising conversations and be delivered by the PHW ASSIST team who are experienced in youth work and health-promotion;

3. Intervention period: Peer supporters will be asked to have conversations with their peers on the risks of different drugs and log these interactions over 10-weeks. One follow-up visit will be made by two ASSIST+Frank trainers with further contact via by a preferred method (email, text and/or Facebook) when Talk to Frank is updated.
4. Acknowledgment of peer supporters' contribution: At the end of the intervention, supporters would receive a certificate with an additional gift voucher for those who handed in their diary.

11.1.3 Frank friends

The intervention manual for Frank friends has yet to be developed and will undergo extensive piloting. At present it is anticipated that Frank friends will have five stages:

1. Nomination of peer supporters: Students aged 13–14 years (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 pupils 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. Trainers make it clear that students who take drugs could only be peer supporters if they commit to reduce and try to stop taking any drugs;
3. Training of peer supporters: The aims of the training are to: provide information about the effects and risks associated with specific drugs and minimising potential harms; including the legal consequences; develop communication skills including, listening, cooperation and negotiation, and conflict resolution; enhance students' confidence, empathy, assertiveness, attitudes to risk-taking, and exploration of personal values. The trainers will also discuss the tobacco and alcohol use within this context. Training will be over 2 days on drug education and practising peer supporter skills by the PHW ASSIST team who are experienced in youth work and health-promotion.
4. Intervention period: 10-week peer-led intervention where supporters have informal conversations with their peers on the harms associated with different 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. Four follow-up school visits by trainers to meet with peer supporters;

5. Acknowledgment of peer supporters' contribution: All peer supporters are presented with a certificate; those who hand in their diary are also presented with a gift certificate.

11.1.4 Usual care

The three schools that do not receive ASSIST, ASSIST+Frank or Frank friends will continue their usual activities. These may or may not involve education on smoking or drug use.

12 Adverse Events

Adverse Event (AE): Any untoward medical occurrence in a trial participant which does not necessarily have a causal relationship with the intervention. An AE can therefore be any unfavourable and unintended sign (including abnormal laboratory finding), symptom, or disease. Within this study, this may include a young person revealing incidences of self-harm, sexual abuse, and grooming by being provided drugs.

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

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

Related AE/SAE: *The AE/SAE resulted from administration of any of the research procedures (causal to the research process or intervention).*

There are no AE's/SAE's expected to be related specifically to the study interventions. All intervention materials will be based on ASSIST or the Talk to Frank website and as a result are in line with the current, widely publicised UK governmental guidelines.

12.1 Causality

The ASSIST+Frank Senior Trial Manager and the Chief Investigator will assess the nature of the SAE for causality and expectedness. Following the initial report, follow up data may be requested by the ASSIST+Frank Senior Trial Manager. Where the SAE and is both related and unexpected, the ASSIST+Frank Study Manager will notify the Chair of the TSC and the main REC within 15 days of receiving notification of the SAE. All SAEs will be recorded and reported annually to the main REC. A standard template will be used to record SAEs.

12.2 Reporting procedures

We do not intend to have a formal process to monitor SAEs as this would not be practical in this population. The risk of the intervention causing an adverse event is extremely unlikely. Where the adverse event meets one of the above categories for an SAE, an SAE form should be completed by Study Manager within 24 hours of becoming aware of the event.

13 Study procedures

13.1 Stage 1: Development of the ASSIST+Frank and Frank friends intervention

Semi structured interviews will be conducted with ASSIST trainers (n=8) to explore the feasibility of delivering ASSIST+Frank and Frank friends in a school setting. We will evaluate the existing ASSIST intervention manual, the resources required for delivery, and staff skills and training requirements. This will inform the aims, objectives and membership of an intervention development group to develop materials, protocols and a logic model for ASSIST, ASSIST+Frank and Frank friends (see appendix). Members of the intervention development group will include the CI, Study Manager, selected co-investigators, Decipher-Impact and PHW delivery staff. Young people's engagement in this process will be

facilitated via meetings with the ALPHA group. We will develop a training package and intervention manual for the PHW ASSIST delivery staff on the ASSIST+Frank and Frank friends interventions. Prior to the piloting of the intervention, PHW staff will be trained to deliver the intervention using existing ASSIST materials and methods by members of the intervention development group including the CI and Study Manager.

13.2 Stage 2: Piloting and refinement of the ASSIST+Frank and Frank friends interventions

PHW will recruit two schools for the piloting of ASSIST+Frank and Frank friends. The aim of these pilots will be to refine the intervention materials and delivery mechanisms. The following methods will be used to gather data to refine the intervention: semi structured interviews with the trainers (n=2), school SMT members (n=2), other staff (n=5) and peer-supporters (n=20); structured observation of training sessions; two focus groups with pupils and questionnaires on the frequency of conversations with peer supporters. Semi-structured interviews will explore the feasibility of delivering ASSIST+Frank and Frank friends in a school setting; staff skill mix and turnover, resources, role development and training needs. Peer supporters will be asked to bring their diaries logging conversations to interviews and focus groups to act as a prompt for discussion. The participant/parent interviews will explore acceptability of the intervention including: consent procedures, parental involvement in consent and/or intervention, the comprehensibility and burden of study measures and follow-up procedures; and the appropriateness of school-led health promotion. Interviews will be conducted face-to-face or by telephone. Pilot findings will be reviewed by the intervention development group and ALPHA. We will then develop refined intervention manuals and training for PHW delivery staff using the pilot findings to try to ensure that the intervention is delivered in a consistent way.

We will offer all peer supporters who return their diary a £20 gift voucher. Teachers, parents and school staff will be offered £10 high street voucher for participation.

13.3 Stage 3: Exploratory cluster randomised trial

Piloting

Questionnaires (baseline, 18 month follow-up) within the trial will be piloted to assess the adequacy of the assessments and presentation. Participant materials (letters, information sheets, posters, leaflets) will also be evaluated. The feasibility and acceptability to

participants of materials will be assessed. Piloting will involve lay people acting in an advisory capacity.

Process evaluation

Following the framework proposed by Steckler and Linnan (2002)(25) the process evaluation will address the following issues:

Fidelity: The process evaluation will assess whether training of peer supporters was delivered as intended, and how frequently conversations on drug use between peers occurred. Semi-structured interviews with ASSIST+Frank and Frank friends trainers (n=4), focus groups with peer-supporters (n=4) and structured observation (n=4) will be used to explore variation in training and the interaction between the schools' contexts and delivery by PHW staff. A documentary analysis of peer-supporters diaries will also be used to assess how frequently conversations are reported, and the topic of these conversations. Data will be compared and contrasted across respondents and schools to explore potential variation. Measures of fidelity will be used in secondary analysis of primary and secondary measures to explore programme pathways and refine the programme logic model.

Feasibility and acceptability: The feasibility and acceptability of delivering ASSIST+Frank and Frank friends will be examined via semi-structured interviews with trainers (n=4), peer supporters (n=24), school staff (n = 12) and a focus group with parents (n=6). Another important aspect of examining acceptability will be to assess the existing provision of drug-focused education or interventions in both intervention and control schools via focus groups with school SMT members (n=5). Approximately a third of the focus groups with staff and parents will take place in each trial arm to assess trial acceptability. Interviews with PHW staff (n=2) and members of the Area Planning Board for Substance Misuse in Cardiff, a multi-agency group tasked with implementing Welsh Government policy (n=2) will explore national and local implementation issues.

Programme reach and reception: A random sample of peer supporters (n=12) will be interviewed in schools which have the highest and lowest incidence of drug use. With information on FSM entitlement, parental social class and other demographic variables, we will explore evidence of and reasons for variation in the receipt of ASSIST+Frank.

Sustainability: The interviews with trainers and teachers in intervention schools and PHW staff will examine what structures and resources need to be in place for sustained implementation by schools and facilitate a definitive trial.

13.4 Data collection

Baseline and 18-month follow-up self-report questionnaires will be completed under 'exam conditions'. To minimise the burden on staff and students, two members of the research team and two fieldwork staff will attend baseline and follow-up surveys. All research staff involved in collecting data will be subject to a clean Disclosure and Barring Service check (DMB; previously a Criminal Records Bureau check). As far as possible they will be blinded to the allocation of the participants, although during interaction with them the group allocation may become apparent. Where this occurs it will be recorded. Data collection at each time point will take around 40 minutes. At the end of each data collection a list of absent students will be prepared and an additional data collection arranged with a school contact (typically the head of year).

Interviews and focus groups will be conducted with parents, peer supporters and trainers. Interviews may be conducted in-person or by telephone. All interviews and focus groups will be audio recorded and take around 30-50 minutes.

13.5 Follow-up

All outcomes will be assessed after randomisation and intervention delivery (baseline) and 18 months later.

14 Statistical considerations

14.1 Sample size

The total sample size of 12 schools for the exploratory trial is anticipated to equate to approximately 2040 students (assuming a 170 pupils in a year), which with a response rate of 90% (based on 1-year follow-up in the RCT of ASSIST (10), will achieve a sample of 1632 students (408; 408; 408; 408 per arm). If the average year group had 150 students, we would expect 1800 to be sampled; 1440 respond with an 80% response rate, equating to 360 per arm. The choice of 12 schools will provide some information on variability within and between schools at baseline and follow-up. This sample is not anticipated to provide adequate

power to detect a statistically significant difference across groups, as this is an exploratory trial. However, the sample will indicate the likely response rates, and permit estimates (with 95% confidence intervals) of likely effect sizes, and intra-cluster correlations (ICCs) of drug incidence in each group in anticipation of a larger trial.

15 Analysis

15.1 Main analysis

The statistical analyses will be primarily descriptive, providing a realistic estimate of eligibility, recruitment, intervention delivery and retention rates in the study population. We will analyse key secondary outcomes that are more immediate targets of the intervention (e.g. knowledge of the harms of drug use; mean peer level drug use) to consider the potential of the intervention. We will undertake mediator analysis to see if the identified pathways in the logic model are associated with the uptake of drug use. Individuals lost to follow-up will be compared to those who complete follow up to identify any potential biases.

An intention to treat (ITT) analysis will compare the prevalence of any drug use across the 4-arms using a two-level logistic regression model to account for clustering within schools. The main analysis will examine prevalence of any drug use at 18 months. The baseline prevalence of any drug use, as well as age, sex, free school meal entitlement, and family affluence will be included as covariates. As an exploratory trial the proposed analysis is not powered to provide a definitive comparison between the intervention and control groups and as such p-values will not be presented. An exploratory analysis will nevertheless be undertaken. We will model comparisons between: a) ASSIST and the usual care control (to examine any unintended effects of ASSIST on drug use), b) ASSIST+Frank and the usual care control, c) Frank friends and the usual care control, and d) ASSIST and ASSIST+Frank to estimate the added value of the Talk to Frank content. These key trial parameters will inform the power calculations for a future definitive trial.

Between-group comparisons for secondary outcomes will be modelled similarly using either linear (e.g. frequency of drug use) or logistic (e.g. cannabis dependence) regression models with the focus on 95% confidence intervals to estimate possible effect sizes.

Exploratory analysis will consider the impact of demographic factors as well as other theoretical moderators on the intervention effect using interaction terms included in the main

analysis models. We will model interactions between potential intermediary factors (e.g. changes in: the perceived prevalence of drug use within the year group, knowledge on the harms of drug use, methods of help seeking, frequency of drug use offers, and attitudes towards heavy drug use and drug dependency, adolescent mental health (Short mood and feelings questionnaire (22)); school engagement (using the Beyond Blue 'School climate' scale(23)), attitudes towards heavy drug use, average level of drug use amongst peers; and average level of drug use amongst peer-leaders) and allocation to: ASSIST+Frank vs. usual care; Frank friends vs. usual care; ASSIST vs. usual care; and ASSIST vs ASSIST+Frank. It is acknowledged that any interactions are unlikely to be adequately powered to provide precise estimates, but 95% confidence intervals will indicate the feasible effect sizes in a full trial.

Analysis will be conducted using Stata v.11 (26) and R statistical packages (27).

15.2 Sub-group analysis

Primary sub-group analysis will investigate the effect of ASSIST+Frank and Frank friends interventions on the frequency of any and specific drugs in a sub-group who report ever having used drugs at baseline. Exploratory sub-group analysis will investigate the association between the incidence of drug use and sex, family affluence, smoking status, and different peer social networks of tobacco and drug use.

15.3 Qualitative analysis

We will aim for a maximum variation sample to achieve a broad perspective on the issues. The sampling criteria will be: school, trial arm, participant type (teacher, peer-supporter, pupil, parent) and gender. Emergent issues from earlier interviews and focus groups will be explored in subsequent interviews. We anticipate that 55 interviews will be undertaken, although this will depend on the depth and detail of information provided. All interviews will be recorded and transcribed verbatim. Analysis will be conducted using a structured thematic approach to systematically code, classify and organise interview content into key themes. Broad themes will then be broken down to identify commonly expressed themes and unusual cases. 10% of the data will be coded by two team members to check that the coding scheme is identifying all of the themes and concepts, and that there is a shared understanding of what

they are. Analysis will be conducted using QSR NVivo 10 software to assist systematic coding to identify emerging patterns between teachers, peer-supporters, pupils, parents and schools.

15.4 Cost effectiveness analysis

To enable an economic evaluation to be conducted as part of a future definitive trial we will map in as much detail as possible the key cost and outcomes domains. This will include the costs of training the PHW trainers, the peer selection, recruitment and training, and follow-up sessions with peers. The provisional costs of running ASSIST+Frank and Frank friends have been calculated by PHW. We will identify any additional contributions by young people, parents, schools and other agencies to provide a more comprehensive estimate of cost. The extent to which these inputs can be translated into financial costs will be determined. The primary and secondary outcomes will be considered for their suitability as measures of output and outcomes for an economic evaluation. Cost effectiveness data may be used to inform the sample size calculation for a subsequent trial, if warranted.

15.5 Data storage & retention

All data will be kept for 15 years in line with Cardiff University's Research Governance Framework Regulations for clinical research. This data will be stored confidentially on password protected servers maintained on the Cardiff University Network. Files will only be accessible to researchers responsible for the running of the trial and the Chief Investigator (CI). All procedures for data storage, processing and management will comply with the Data Protection Act 1998. All paper records will be stored in a locked filing cabinet, with keys available only to researchers and the Chief Investigator. The Trial Statistician (JW) will carry out analysis. All essential documents generated by the trial will be kept in the Trial Master File. Archiving and access to archive will be managed in accordance with the Standard Operating Procedures of the South East Wales Trials Unit (SEWTU).

16 Study closure

The end of the study/ will be considered as the date on which the last participant has completed their follow-up assessment.

17 Regulatory issues

17.1 Ethical and research governance approval

The study will be conducted in accordance with the recommendations for physicians involved in research on human participants adopted by the 18th World Medical Assembly, Helsinki 1964 and later revisions. The study has be granted ethical approval by Cardiff University School of Social Sciences Research Ethics Committee (Reference: SREC/ 1103). After consulting the Wales NHS REC, feedback was that NHS Research Ethics Committee approval for this study was not necessary. NHS R&D approval will however be sought.

17.2 Consent

Schools

The head-teacher (or designated member of the school senior management team) will be asked to sign a formal commitment for their school to take part in the study. The commitment will describe the roles and responsibilities of the school and the research team during the research period at the school.

Teachers, parents and PHW staff

The ASSIST+Frank Study Manager will provide all adult participants with information on the study, explain the aims of the study and they will then be asked to give informed consent prior to participation in the research. They will be assured that if they decide not to participate, their decision will be handled confidentially. Written informed consent detailing the right to withdraw will be collected for all participants.

Student consent

Written consent will be sought from young people. Age-appropriate information sheets will be provided, together with verbal explanation by researchers. Parents who do not wish their child to participate will be able to 'opt-out'. Letters will be sent to parents/guardians to contact the school if they do not wish their child to participate in the trial. At the beginning of

data collections, it will be made clear that participation by students is optional. Note that this 'opt-out' consent is acknowledged standard practice for school-based studies in the UK, used by members of our investigator team in school-based interventions in England (e.g. Pupil-led sex education in England (RIPPLE study) (24)), and the original ASSIST RCT held in 59 schools (N students = 10,730) in South Wales and Bristol (10)).

17.3 Confidentiality

The Chief Investigator and the research team will preserve the confidentiality of participants in accordance with the Data Protection Act 1998.

Data will be entered and transcribed by the project staff using a secure data management system at SEWTU, a UKCRC-registered trials unit. Completed questionnaires will be transported to SEWTU by the CI or the Study Manager. 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. Individuals' names will be replaced with pseudonyms in interview/focus group transcripts. A list of participant names, pseudonyms and their unique identification number will be held in a separate location. Digital recordings of interviews/focus groups will be stored securely, and will be held separately from transcripts and information on participant identities. In reporting the results of the process evaluation, care will be taken to use quotations which do not reveal the identity of respondents and anonymised data will be used wherever possible.

The main circumstances under which the researchers would break confidentiality are where participants were at risk of serious harm. This would be most likely to occur as a result of a disclosure during a focus group, or if responses to questionnaires raised serious concerns regarding individuals' wellbeing. All participants will be informed that if they disclose information about neglect, abuse, serious suicidal thoughts or self-harm that we will pass this information on to an appropriate source; consent for this will be sought prior to the collection of any data. Procedures will be put in place to deal with instances of participants requesting help with issues related to substance misuse. Each school participating in the study will be asked to identify a named individual who can provide support to any pupils who become upset or distressed. All research staff involved in collecting data will be subject to a clean

Disclosure and Barring Service check (DMB; previously a Criminal Records Bureau check). All staff involved in collecting data will be provided with a fact sheet which lists contact numbers for local support agencies.

17.4 Indemnity

Cardiff University will provide indemnity and compensation in the event of a claim by, or on behalf of participants, for negligent harm as a result of the study design and/or in respect of the protocol authors/research team. Cardiff University does not provide compensation for non-negligent harm.

17.5 Study sponsorship

Cardiff University will act as sponsor for trial.

17.6 Funding

The trial is funded by the National Institute for Health Research Public Health Research Programme. The grant awarded is £606, 377.

To pay schools for staff cover during data collections, all schools will receive £300 when the final 18 month absentee sessions have been completed. Peer supporters who return their diaries logging conversations with peers will be offered £20 in high street vouchers. Teachers, parents, PHW delivery staff will be offered £10 in high street vouchers to compensate for the time taken to participate in any interviews or focus groups conducted as part of the process evaluation.

17.7 Audits & inspections

The study is participant to inspection by the NIHR-PHR as the funding organisation. The study may also be participant to inspection and audit by Cardiff University under their remit as sponsor.

18 Study management

Internal Project Group: This group will consist of the CI, ASSIST+Frank Study Manager and co-ordinating team within SEWTU who will meet weekly to discuss the day to day issues that arise from the study. All important discussions will be relayed to the TMG for final decision.

Trial Management Group (TMG): The TMG will consist of the Chief Investigator (chair), co-applicants including the ASSIST+Frank Study Manager, Trial Administrator and a representative from Public Health Wales. The role of the TMG will be to assist in the study set up by providing specialist advice, input to and comments on the study 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, every three months throughout the course of the study and if necessary, additional/more frequent meetings may occur particularly at crucial time points during the study.

19 Data monitoring & quality assurance

19.1 TSC (Trial Steering Committee)

A TSC will be established and will meet annually, consisting of an independent chair, and two other independent scientific members. These are: Linda Bauld (Chair; University of Stirling); Russell Viner (University College London) and Prof Glyn Lewis (University College London). Additional members will include Julie Bishop (Public Health Consultant in PHW), who has coordinated the roll out of ASSIST, Stewart Killala (a member of the Department of Health's alcohol and drugs policy team) responsible for drugs education policy including Talk to Frank and Stephen Thomas (PPI representative: father of a 14 year old). The first meeting will be to review the protocol and arrange the timelines for the subsequent meetings. If necessary, additional/more frequent meetings may occur. The Chief Investigator, Study Manager and Laurence Moore will attend as observers. The Trial Steering Committee (TSC) will provide overall supervision for the trial and provide advice through its independent chair. Members will be required to sign up to the remit and conditions as set out in the TSC Charter.

19.2 DMC (Data Monitoring Committee)

The nature of this study makes it unlikely that a Data Monitoring and Ethics Committee (DMEC) will be required; however, this will be discussed with the TSC at their first meeting and a DMEC will be set up if deemed necessary.

20 Publication policy

A publication policy will be drafted and approved by the Trial Management Group. 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 study to be appropriately acknowledged. Authorship of parallel studies initiated outside of the Trial Management Group will be according to the individuals involved in the project but must acknowledge the contribution of the Trial Management Group and the Study Coordination Centre.

21 Milestones

M-3-0	Recruitment of RA and schools;
M 1-3	Recruitment of schools; post information sheets and consent forms;
M 4	Exploratory trial: baseline data collection
M 5	Year 8: intervention delivery of ASSIST
M 6	Input/clean baseline questionnaire data
M 6-7	Develop intervention materials
M 7-9	Pilot intervention in two schools, interviews and focus groups
M10-13	Input, clean and analyse pilot data; revise interventions
M14-20	Year 9: intervention delivery, 10-week follow-up; conduct interviews and focus
M21-22	18 month follow-up; final interviews conducted
M21-25	Input/clean questionnaire data; transcription; qualitative and statistical analysis
M25-31	Report writing; dissemination; potential phase III trial application

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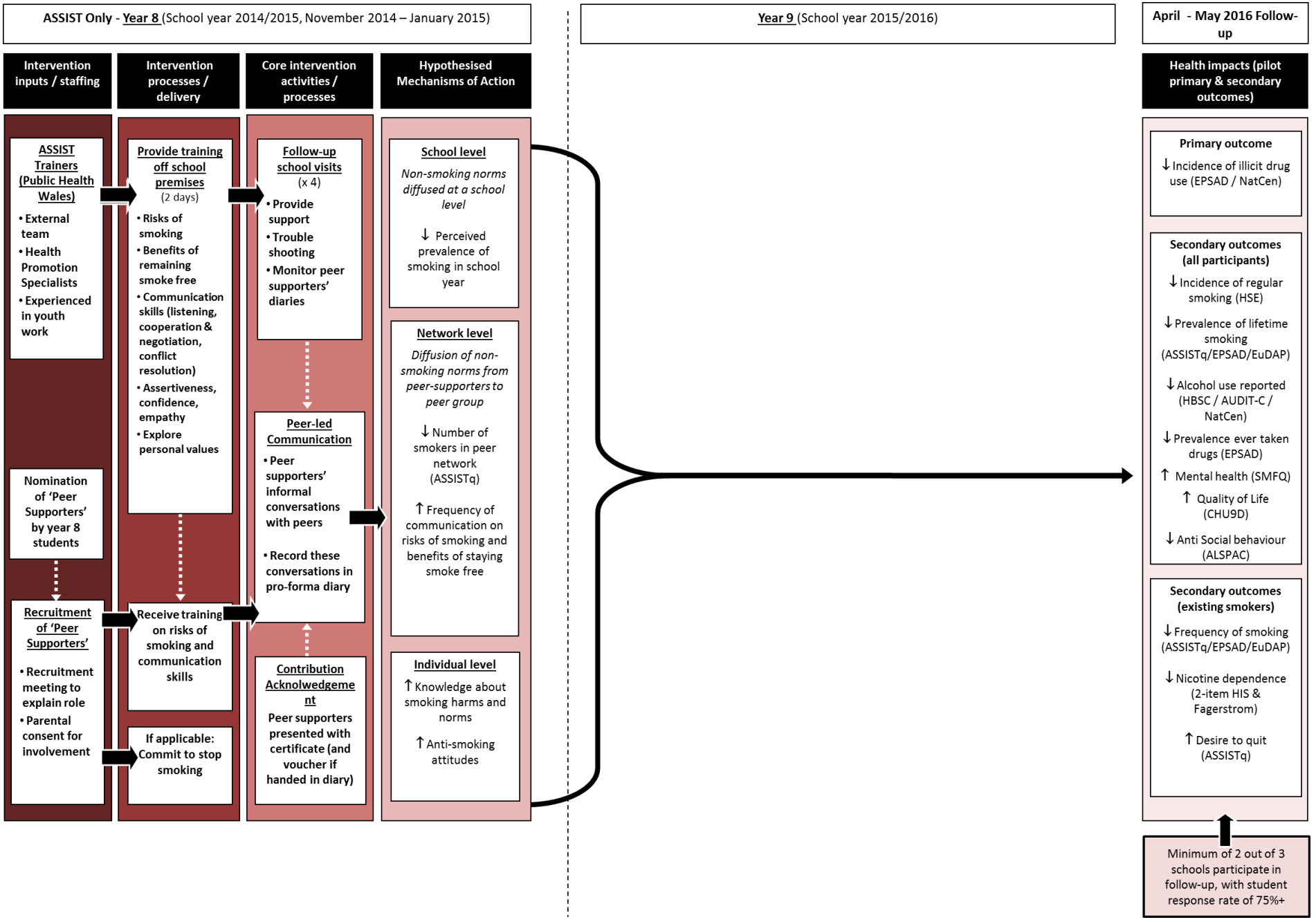
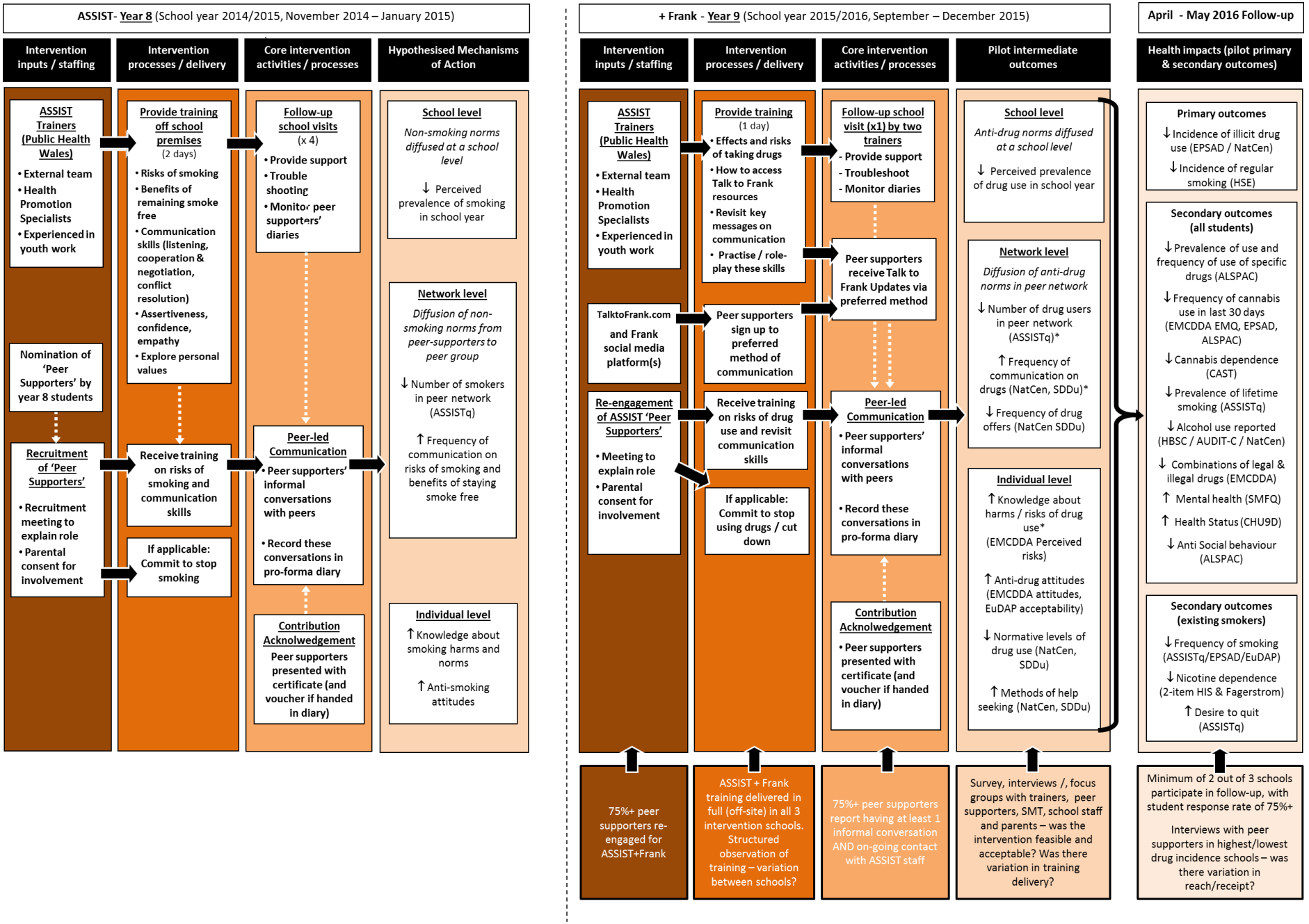

ASSIST Only - Year 8 (School year 2014/2015, November 2014 – January 2015)
Year 9 (School year 2015/2016)
April - May 2016 Follow-up
Intervention inputs / staffing
Intervention processes / delivery
Core intervention activities / processes
Hypothesised Mechanisms of Action
Health impacts (pilot primary & secondary outcomes)
ASSIST Trainers (Public Health Wales)
• External team
• Health Promotion Specialists
• Experienced in youth work
Provide training off school premises
(2 days)
• Risks of smoking
• Benefits of remaining smoke free
• Communication skills (listening, cooperation & negotiation, conflict resolution)
• Assertiveness, confidence, empathy
• Explore personal values
Follow-up school visits
(x 4)
• Provide support
• Trouble shooting
• Monitor peer supporters' diaries
School level
Non-smoking norms diffused at a school level
↓ Perceived prevalence of smoking in school year
Nomination of 'Peer Supporters' by year 8 students
Recruitment of 'Peer Supporters'
• Recruitment meeting to explain role
• Parental consent for involvement
Receive training on risks of smoking and communication skills
If applicable: Commit to stop smoking
Peer-led Communication
• Peer supporters' informal conversations with peers
• Record these conversations in pro-forma diary
Network level
Diffusion of non-smoking norms from peer-supporters to peer group
↓ Number of smokers in peer network (ASSISTq)
↑ Frequency of communication on risks of smoking and benefits of staying smoke free
Contribution Acknolwedgement
Peer supporters presented with certificate (and voucher if handed in diary)
Individual level
↑ Knowledge about smoking harms and norms
↑ Anti-smoking attitudes
Primary outcome
↓ Incidence of illicit drug use (EPSAD / NatCen)
Secondary outcomes (all participants)
↓ Incidence of regular smoking (HSE)
↓ Prevalence of lifetime smoking (ASSISTq/EPSAD/EuDAP)
↓ Alcohol use reported (HBSC / AUDIT-C / NatCen)
↓ Prevalence ever taken drugs (EPSAD)
↑ Mental health (SMFQ)
↑ Quality of Life (CHU9D)
↓ Anti Social behaviour (ALSPAC)
Secondary outcomes (existing smokers)
↓ Frequency of smoking (ASSISTq/EPSAD/EuDAP)
↓ Nicotine dependence (2-item HIS & Fagerstrom)
↑ Desire to quit (ASSISTq)
Minimum of 2 out of 3 schools participate in follow-up, with student response rate of 75%+

ASSIST+Frank logic model

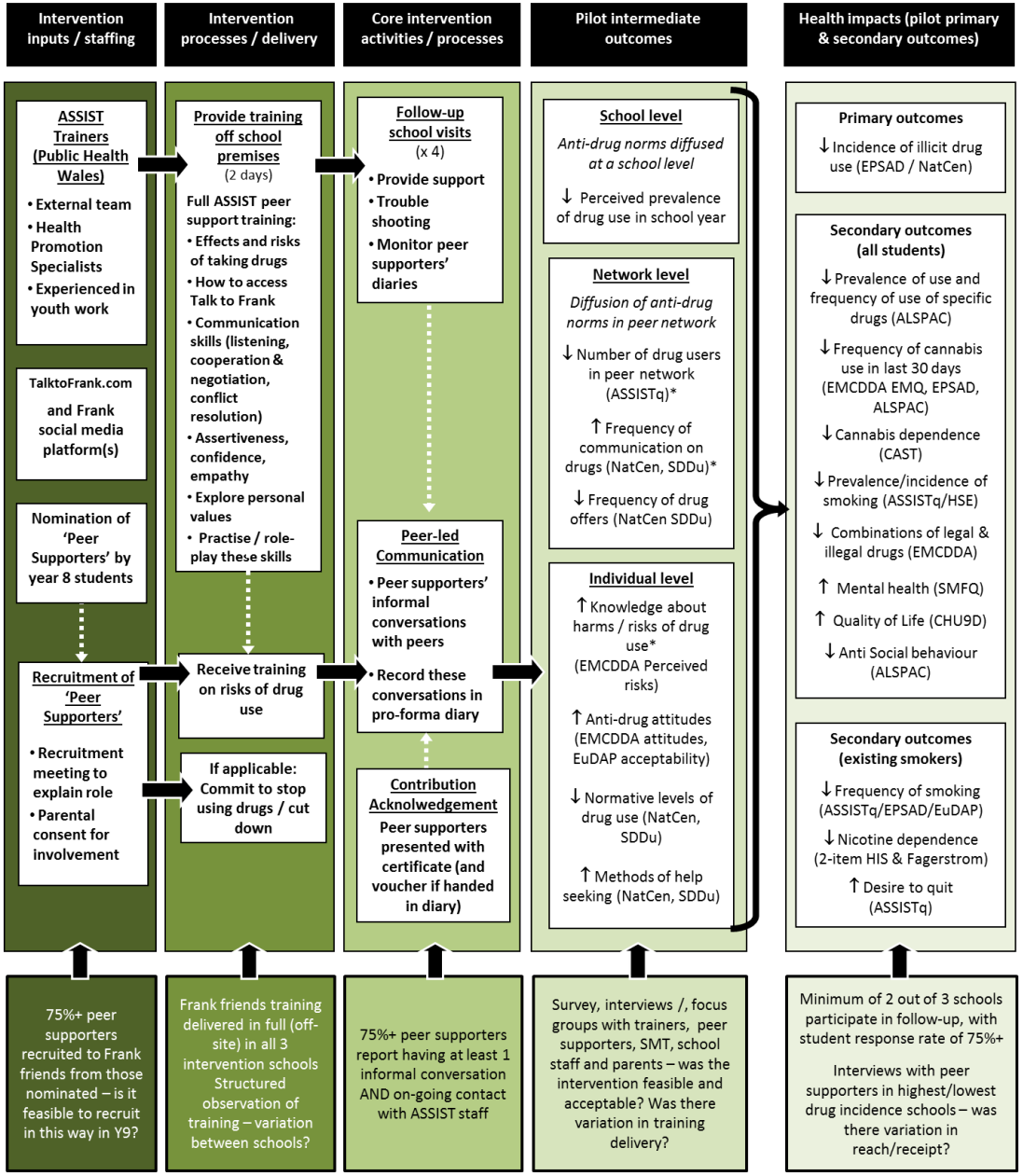


Frank friends logic model

Year 8 (School year 2014/2015, November 2014 – January 2015)

Frank Friends - Year 9 (School year 2015/2016, September – December 2015)

June/July 2015 Follow-up



KEY / Abbreviations

* = Bespoke questions

ALSPAC – 'Avon Longitudinal Study of Parents and Children' - Life of a 16+ survey
ASSISTq – 'A Stop Smoking in Schools Trial' - questionnaire from original trial
AUDIT-C – 'Alcohol Use Disorders Identification Test'
CAST – 'Cannabis Abuse Screen Test'
EMCDDA – 'European Monitoring Centre for Drugs and Drug Addiction' - example questions
EPSAD – 'European School Survey Project on Alcohol and other Drugs' 2003 questionnaire
EuDAP – 'European Drug Abuse Prevention Trial' questionnaire
HBSC – 'Health Behaviour in School-aged Children' survey
HSE – 'Health Survey for England'
NatCen SDDu – Smoking, Drinking and Drug use among young people in England 2012 survey
SMFQ – 'Short Mood and Feelings Questionnaire'