LESSONS LEARNED REPORT

Funder	National Institute for Health Research (NIHR) Public Health Research Programme (PHR)
PHR reference	17/97/02
Short title	The FRANK friends study
Title	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)
Sponsor	Cardiff University
Sponsor reference	SPON 1753-19
Host organisation CTU	Centre for Trials Research (Cardiff University)
Trial registration	ISRCTN : ISRCTN72047541
Chief investigator	Dr James White
Trial design	Parallel-group, multicentre, two-arm, cluster RCT, with process and economic evaluations.
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.
Intervention	FRANK friends is a peer-led drug prevention intervention to prevent drug use in UK year 9 secondary school children (aged 13-14). It aims to diffuse information from www.talktofrank.com via secondary school students' social networks.
Comparator	Usual practice which may or may not involve drug education.
Number of participants	6,672
Start date	01/03/2019
End date	30/11/2020
Study duration	12 months
PHR Programme Manager	Sue Pargeter
Closedown date	22/03/2022

The FRANK friends study was led by Dr James White. The co-investigators on the study were Dr Kim Smallman, Dr Rebecca Cannings-John and Dr Jemma Hawkins, Professor Laurence Moore, Professor Matthew Hickman, Professor Rona Campbell, Professor Simon Murphy, and Dr Steve Parrot. The trial project team was led by Dr Linda Adara. A copy of this report has been forwarded to the members of the trial steering committee.

Disclaimer

Background

Reducing youth drug use is a public health priority.

Illicit drug use in UK adolescents is still among the highest in Europe. The latest UK data, from 2018, indicate around 37% of 15-year-olds have used illicit drugs.[1] This is a 13-percentage point increase from the 2014 [2] and one percentage point increase from 2016.[3] In 2019/2020, 18,464 11-18 year olds received specialist drug treatment, 69% doing so for cannabis use; the median age at treatment was 15-years old.[4] The latest data on traffic to the Talk to FRANK website showed it received 180,000 more visitors in January 2019 than the previous year, suggesting demand for information on drugs had increased.[5]

The impact of the COVID-19 pandemic on adolescent drug use is unclear. The five pre-print or peer review publications examining drug use before to after pandemic restrictions were introduced have reported drug use increasing, [6] [7] decreasing [8], and remaining stable.[9] [10] One Canadian cohort found the use of cannabis among 16-year olds increased. [6] Of the two US cohorts, one with 17-18 year olds found no change in the prevalence of cannabis use, [9] and the other with 14 year olds found the misuse of prescription drugs increased but other illicit drugs remained stable.[10] A Spanish cohort of students aged 14–18 years found the percentage screening for cannabis dependency decreased from 5.6 to 4.6%,[8] and a Dutch cohort of adults who were daily cannabis users found cannabis use increased.[7] We could not find any published studies or pre-prints on the impact of the pandemic on UK adolescents' illicit drug use.

To our knowledge, there has not been a comprehensive systematic review of school-based drug prevention since the study was funded. The latest Cochrane review of school-based drug prevention showed, on average, no protective effect on illicit drug use after 12 months (only 2 out of 51 RCTs were in the UK).[11] This review and other studies highlight the methodological weaknesses in the existing evidence base. These include: small sample sizes, potential contamination, [12] inadequate reporting of randomisation, [11] a failure to account for clustering,[13] a lack of registered protocols and independent evaluation.[14]

Expressed need for drug prevention and evaluation of FRANK friends

FRANK friends was developed in a NIHR PHR funded pilot study.[15] This pilot was funded under a PHR commissioned call. The study met all progression criteria, leading to this full-scale evaluation. The acknowledged public health importance of new research into youth drug use by the NIHR has continued with a NIHR Policy Research Programme commissioned call to explain increases in youth drug use that closed in January 2021.

The UK Government's Advisory Council for the Misuse of Drugs has noted that the majority of drug prevention in the UK is not evaluated and recommended more economic analyses are funded.[16] The National Institute of Health and Care Excellence (NICE) guidance on drug prevention for vulnerable people noted the recommendations made were limited due to the lack of evidence.[17] In 2020, Dame Carol Black's independent review of drugs focused on prevention, treatment and recovery recommended that UK government policy focused on school-based drug prevention coupled with robust scientific evaluation.[18] The UK government response committed to school-based drug education with evaluative research.[19] The FRANK friends study directly addresses this expressed lack of robust evaluation and economic analysis of illicit drug prevention in the UK.

The UK Home Office included the ASSIST+FRANK study, which led to the development of FRANK friends, in their 2017 review of the drug strategy[20] and Scottish Government similarly also noted their interest.[21] A report in 2019 by the All Party Parliamentary Group into the Psychoactive Substances Act also highlighted the evaluation of FRANK friends.[22] These reports demonstrate a strong and sustained interest in an evaluation of the FRANK friends intervention among UK policy makers.

The NIHR PHR programme funded a multicentre cluster randomised controlled trial to evaluate the effectiveness and cost-effectiveness of FRANK friends in May 2018. The latest protocol is available here: https://fundingawards.nihr.ac.uk/award/17/97/02.

Progress

The study met all of its milestones up until the UK wide lockdown on the 9th of March 2020. Forty schools in England and Wales were recruited, randomised, and baseline data collected from 6,672 students (response rate = 94.3%). By March 2020 intervention delivery was complete in five schools and had begun in another eight. In the process evaluation case study schools, data collection was complete in one of the two case studies in the Welsh site and partially complete in the second. The UK wide lockdown resulted in the cancellation of all remaining intervention delivery sessions and case study process evaluation data collection. In June 2020, the FRANK friends Trial Management Group decided the impact of COVID-19 related delays on intervention delivery was likely to reduce the effectiveness of the intervention to such an extent that it was no longer scientifically sensible to continue with the cohort of recruited students and that the study should be restarted. The study was therefore placed on hold and all trial staff were made redundant or redeployed onto other studies. All schools were informed that the study would close on 30th November 2020.

In January 2022 the Trial Steering Committee (TSC) reviewed a proposal to restart the study in April 2023 and provided a letter supporting this plan. However in March 2022, after careful consideration, the NIHR decided not to fund the variation to contract required to restart the study.

Lessons learned

The study met all its milestones up until the UK wide lockdown. There are therefore limited lessons to be learned. The following are reflections on the trial methods processes used with suggestions that may increase the efficiency of recruitment and data collections. These may be useful to consider in the design of other studies.

Identifying the number of eligible sites at centres

FRANK friends was conducted in two geographical areas (South Wales and the West of England). All state secondary schools within a one and half hours travel time from the recruiting centres based in the Centre for Trials Research in Cardiff and the University of Bristol were eligible for inclusion in the sampling frame. Schools were then excluded if they were: fee paying, special schools (e.g. for those with learning disabilities), pupil referral units, 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.

In South Wales there were 138 schools in the sample frame and 13 (9.4%) did not meet the eligibility criteria. In the West of England, there were 173 schools in the sample frame and 54 (31.2%) that did not meet the criteria. Of the 54 ineligible in the West of England, 43 (79.7%) were excluded because they were fee paying. The larger number of ineligible schools in the West of England meant fewer were available to recruit.

Lesson learned: Removing the eligibility criteria that schools are not fee paying could have potentially expanded the sample frame. However, as many fee-paying schools have fewer than 60 students per year, removing this criterion may not have added many schools. Studies would ideally make assessments of the number of eligible sites before centres are chosen. As this requires significant staffing to determine this may not be realistic. If this study were restarted, removal of either the fee paying criterion or West of England centre would likely speed up recruitment.

Impact of stratified random sampling on recruitment

The study used stratified random sampling. The two strata were country (South Wales, West of England) and the school-level percentage of students eligible for free school meals (above

the country level median vs. below). A list of schools that were eligible were created in each of the study strata and then randomly ordered.

The sample size calculation indicated that we needed to recruit 40 schools (24 in South Wales; 16 West of England). In order to meet study milestones, we initially invited more than 40 schools. In South Wales 48 eligible schools were initially invited to participate. Of these, 24 were recruited and four also interested so held in reserve, resulting in a school recruitment rate of 28/48 = 58.3%. In the West of England, 48 schools were also initially invited. As recruitment was slower in the West of England, the rest of the schools in the sample frame were invited in blocks over a three-month period. Recruiting the required 16 schools required all schools in the West of England sample frame to be invited, resulting in a school recruitment rate of 16/119= 13.4%.

Lessons learned: An alternative approach to school recruitment would be to invite all schools in each stratum at the study outset. This would have likely reduced the staff time spent on recruitment and sped up school recruitment. Other studies that have taken this approach have found that schools recruited were comparable to those who were not on school and student-level characteristics available in routine data (e.g. % students eligible for free schools means, % with special educational needs).[23]

Impact of stratified randomisation on the time to intervention delivery

In the study, stratified block randomisation using the same stratifying variables as in the sample frame were used. Block sizes of varying block size (2, 4 or 6) were selected at random within each of the four strata (South Wales/ West of England and above vs below the median percentage of students eligible for FSM). To minimise ascertainment bias, allocations were only revealed after baseline data collections were completed. The impact of stratified randomisation was that we needed to wait until baseline data collection was completed (i.e. including collecting data from all absentee sessions) in a block before allocations were revealed and intervention delivery can start to be planned. For example, using the presents study as an example, a worst-case scenario would be a block size of six being selected. This would mean allocations would not be revealed, and intervention delivery not start to be planned, until the sixth schools data collections in that strata was complete.

If the median school-level FSM eligibility was prognostic of our primary end point, stratification on this factor should increase precision in the treatment effect. Table 1 below shows exploratory analysis of the baseline data. In this multilevel (students nested within schools) logistic regression model, school-level FSM eligibility is not cross-sectionally associated with lifetime illicit drug use. Individual-level FSM eligibility is positively associated

with illicit drug use. Whilst the primary end point was lifetime illicit drug use at 15 years of age, these analyses suggest there may be limited value in stratifying the study sample and randomisation by school-level FSM. A more efficient method of increasing the precision of the treatment effect would be to adjust for individual-level FSM eligibility.

Table 1. Association between school and individual free school meal eligibility and lifetime drug use

	Odds ratio (95% confidence interval)		
Exposure	**Model 1 (n = 5,787)**	**Model 2 (n = 6,390)**	**Model 3 (n = 5,787)**
Individual-level free school meal eligibility	1.67 (1.33, 2.10)		1.66 (1.32, 2.09)
School-level free school meal eligibility		1.25 (0.96, 1.62)	1.11 (0.83, 1.47)

Reference categories are: an individual not reporting being eligible for FSM; a school being below the median FSM eligibility percentage.

Lessons learned: The median percentage of students eligible for free school meals stratifying factor was not associated with illicit drug use in the baseline data. This suggests there will be minimal impact of stratification on this variable on precision in the estimated treatment effect. Stratifying randomisation delays intervention delivery as you have to wait until baseline data collections are completed in all schools in a block within each stratum. Removal of this stratifying factor would increase the number of schools to fill a block as a larger number would be available within each stratum (e.g. all schools in England regardless of free school meal entitlement could be used to complete a block). The removal of the school-level median percentage of FSM would mean randomisation could occur quicker and the intervention could be implemented earlier. It may be more efficient to account for the impact of FSM eligibility on the treatment effect by adjusting for student-level FSM eligibility in the analysis rather than stratifying randomisation by school-level FSM eligibility.

References

1. NHS Digital. Smoking, Drinking and Drug Use among Young People in England 2018 [Internet]. NHS Digital; Available from: https://digital.nhs.uk/data-and-information/publications/statistical/smoking-drinking-and-drug-use-among-young-people-in-england/2018

2. Health and Social Care Information Centre. Smoking, Drinking and Drug Use Among Young People in England - 2014 [Internet]. Health and Social Care Information Centre; 2015. Available from: http://content.digital.nhs.uk/catalogue/PUB17879

3. NHS Digital. Smoking, Drinking and Drug Use among Young People in England 2016 [Internet]. NHS Digital; 2017 Nov. Available from:

https://www.gov.uk/government/statistics/smoking-drinking-and-drug-use-among-young-people-in-england-2016

4. Substance misuse treatment for young people: statistics 2019 to 2020 [Internet]. GOV.UK. [cited 2021 Feb 12]. Available from: https://www.gov.uk/government/statistics/substance-misuse-treatment-for-young-people-statistics-2019-to-2020

5. Duncan Selbie's Friday message - 25 January 2019 - Public health matters [Internet]. [cited 2021 Feb 12]. Available from: https://publichealthmatters.blog.gov.uk/2019/01/25/duncan-selbies-friday-message-25-jan-2019/

6. Dumas TM, Ellis W, Litt DM. What Does Adolescent Substance Use Look Like During the COVID-19 Pandemic? Examining Changes in Frequency, Social Contexts, and Pandemic-Related Predictors. J Adolesc Health. 2020 Sep;67(3):354–61.

7. Cousijn J, Kuhns L, Larsen H, Kroon E. For better or for worse? A pre–post exploration of the impact of the COVID-19 lockdown on cannabis users. Addiction [Internet]. [cited 2021 Feb 12];n/a(n/a). Available from: https://onlinelibrary.wiley.com/doi/abs/10.1111/add.15387

8. Rogés J, Bosque-Prous M, Colom J, Folch C, Barón-Garcia T, González-Casals H, et al. Consumption of Alcohol, Cannabis, and Tobacco in a Cohort of Adolescents before and during COVID-19 Confinement. Int J Environ Res Public Health. 2021 Jan;18(15):7849.

9. Miech R, Patrick ME, Keyes K, O'Malley PM, Johnston L. Adolescent drug use before and during U.S. national COVID-19 social distancing policies. Drug Alcohol Depend. 2021 Sep 1;226:108822.

10. Pelham WE, Tapert SF, Gonzalez MR, McCabe CJ, Lisdahl KM, Alzueta E, et al. Early Adolescent Substance Use Before and During the COVID-19 Pandemic: A Longitudinal Survey in the ABCD Study Cohort. J Adolesc Health. 2021 Sep 1;69(3):390–7.

11. Faggiano F, Vigna-Taglianti FD, Versino E, Zambon A, Borraccino A, Lemma P. School-based prevention for illicit drugs' use. Cochrane Database Syst Rev [Internet]. 2005 [cited 2012 Dec 3];2. Available from: http://www.cochrane.org/CD003020/ADDICTN_school-based-prevention-illicit-drug-use

12. Valente TW, Ritt-Olson A, Stacy A, Unger JB, Okamoto J, Sussman S. Peer acceleration: effects of a social network tailored substance abuse prevention program among high-risk adolescents. Addict Abingdon Engl. 2007 Nov;102(11):1804–15.

13. MacArthur GJ, Sean H, Caldwell D, Hickman M, Campbell R. Peer-led interventions to prevent tobacco, alcohol and/or drug use among young people aged 11–21 years: a systematic review and meta-analysis. Addiction. 2016 Mar 1;111(3):391–407.

14. Flynn AB, Falco M, Hocini S. Independent Evaluation of Middle School–Based Drug Prevention Curricula: A Systematic Review. JAMA Pediatr. 2015 Nov 1;169(11):1046–52.

15. White J, Hawkins J, Madden K, Grant A, Er V, Angel L, et al. Adapting the ASSIST model of informal peer-led intervention delivery to the Talk to FRANK drug prevention

programme in UK secondary schools (ASSIST+ FRANK): intervention development, refinement and a pilot cluster randomised controlled trial. Public Health Res. 2017;5(7).

16. Advisory Council on the Misuse of Drugs. Prevention of drug and alcohol dependence – summary [Internet]. UK Home Office; Available from: https://www.gov.uk/government/publications/prevention-of-drug-and-alcohol-dependence

17. Overview | Drug misuse prevention: targeted interventions | Guidance | NICE [Internet]. NICE; [cited 2021 Feb 12]. Available from: https://www.nice.org.uk/guidance/ng64

18. Review of drugs part two: prevention, treatment, and recovery [Internet]. GOV.UK. [cited 2022 Jan 4]. Available from: https://www.gov.uk/government/publications/review-of-drugs-phase-two-report/review-of-drugs-part-two-prevention-treatment-and-recovery

19. From harm to hope: A 10-year drugs plan to cut crime and save lives [Internet]. GOV.UK. [cited 2022 Jan 4]. Available from: https://www.gov.uk/government/publications/from-harm-to-hope-a-10-year-drugs-plan-to-cut-crime-and-save-lives/from-harm-to-hope-a-10-year-drugs-plan-to-cut-crime-and-save-lives

20. United Kingdom Home Office. An evaluation of the Government's Drug Strategy 2010 [Internet]. UK Home Office; 2017. Report No.: ISBN 978-1-78655-397-3. Available from: https://www.gov.uk/government/publications/drug-strategy-2017

21. Warren F. "What Works" in Drug Education and Prevention? [Internet]. Health and Social Care Analysis, Scottish Government; 2016 Dec. Available from: http://www.gov.scot/Publications/2016/12/4388/0

22. Broughton N. Report for the All Party Parliamentary Group on Novel Psychoactive Substances Act and Volatile Substances Act. :38.

23. Bonell C, Allen E, Warren E, McGowan J, Bevilacqua L, Jamal F, et al. Effects of the Learning Together intervention on bullying and aggression in English secondary schools (INCLUSIVE): a cluster randomised controlled trial. The Lancet. 2018 Dec 8;392(10163):2452–64.