Table 2: Efficiency of the adaptations, challenges and benefits, and considerations					
	Adaptation	**Potentially efficient adaptation, and reason if not**	**Studies/populations in which adaptation may be efficient**	**Challenges and benefits**	**Guidance or considerations** [guidance from existing literature is in *italics*]
Recruitment	Two-stage remote-first eligibility assessment	Yes – NHS sites and trial participants	• Smaller studies • Studies not involving sensitive topics/questions • Studies requiring the participant to make a decision regarding their involvement in the trial prior to a fixed event (e.g., surgery). • Studies where eligibility assessments can be undertaken remotely by CTU staff. • Low risk studies. • Studies where a high proportion of participants can be screened out prior to an in-person visit (e.g., studies involving recruitment via social media).	**Challenges** • Discussion of sensitive topics or questions over telephone may be challenging. • Reading participant's expressions and body language is important and may be missed if undertaken remotely. • May be more challenging to describe recruitment procedure due to increased complexity. • Eligibility and baseline data no longer collected directly prior to randomisation. • If undertaken by CTU staff, clinical staff may have less ownership over the consent process. • May be problematic for CTUs to receive identifiable data if the participant is not self-referring. • Certain measures may not be validated for use outside the in-person clinic setting. **Benefits**	• Some investigations may need to be undertaken in person after the remote eligibility assessment (e.g., pregnancy test). • The eligibility process may be able to be undertaken quicker by a CTU, but overall, the process may take longer due to multiple steps. • May be unsuitable for studies that require a qualified medical professional to confirm eligibility. • Unlikely to be resource saving unless participants are screened out prior to an in-person eligibility assessment.

Table 2: Efficiency of the adaptations, challenges and benefits, and considerations					
	Adaptation	**Potentially efficient adaptation, and reason if not**	**Studies/populations in which adaptation may be efficient**	**Challenges and benefits**	**Guidance or considerations** [guidance from existing literature is in *italics*]
				• Ability to screen out participants early may save time. • Centralisation of eligibility process may allow faster completion. • May allow participant more time to consider participation in trial. • If undertaken by a CTU, may allow clinical staff more time to discuss the trial at a later appointment.	
	Recruitment outside the NHS via a charity	Yes – NHS sites and trial participants	• May be best used as an adjunct to recruitment within the NHS, rather than by itself, due to a potential impact on the sampling frame. • Low risk studies not requiring medical input into participant recruitment. • Studies for which there is a relevant condition specific charity which is suitability large.	**Challenges** • Issues with participant sampling – either the charity not sampling correctly, self-selection bias, or inability to access population of interest. • Relationship between the participant and researcher/clinician is important – remotely conducting recruitment via a charity may impede this. • Low response rate (20% in one study) if emails are used.	• A range of recruitment techniques (involving both NHS and non-NHS routes) may be preferable. • Reminders required to prompt participants to complete recruitment steps. • *In-person approaches may result in a better recruitment rate* [1]. • Recruitment could be undertaken by CTU, unless study is high risk of a CTIMP, in which case a clinically qualified

Table 2: Efficiency of the adaptations, challenges and benefits, and considerations					
	Adaptation	**Potentially efficient adaptation, and reason if not**	**Studies/populations in which adaptation may be efficient**	**Challenges and benefits**	**Guidance or considerations** [guidance from existing literature is in *italics*]
			• Studies where potential sampling biases have a limited effect on the external validity of the trial.	• The charity may not have the expertise or resources to conduct research processes. **Benefits** • Many participants can be contacted at once, potentially quicker than can be achieved by individually contacting participants within NHS Trusts.	person may be required to confirm eligibility. • Charities may require training in recruitment processes, requiring time and input from CTUs and the charities. • Charities may not have the necessary information to be unable to identify those individuals who are too vulnerable to participate in the trial.
	Remote consent	Yes – NHS sites and trial participants	• Studies where a close relationship between the researcher and participant is not critical. • Has the potential to increase efficiency by improving recruitment rates.	**Challenges** • May impact on the participant-researcher relationship, if consent is undertaken remotely and/or by a member of CTU staff. • Risk of a shift in the sampling frame of the study if consent is obtained using a technology/platform that some potential participants are unlikely to have access to.	• Do not assume that the REC will not support a method of consent that may not be the 'safest' or most secure. • Remote consent (i.e., consent via telephone or video calls) may be easier to implement compared to electronic consent, for both participants and CTU, due to limited access to this technology.

Table 2: Efficiency of the adaptations, challenges and benefits, and considerations					
	Adaptation	**Potentially efficient adaptation, and reason if not**	**Studies/populations in which adaptation may be efficient**	**Challenges and benefits**	**Guidance or considerations** [guidance from existing literature is in *italics*]
				• Digital literacy is a concern. • Consent may be more challenging to undertake remotely. • Not always possible to know if participants have been pressured by family or others when consent is not in person. • Sensitive conversations may be difficult to have remotely. **Benefits** • May enable participants more time to consider the trial. • Trial sites do not have to use limited clinic space to facilitate in-person consent. • Allows the participant flexibility. • May allow family members/friends to be present during conversation.	• Clear guidance to sites is important. • Sites with more motivated investigators may be more successful at gaining remote consent – more support may be required for other sites. • Reminders may be required to obtain responses from participants. • It may take significant resources for CTUs to develop remote consent procedures. • Multiple options or mediums of gaining informed consent may be required if there is a risk that using only one technique may bias the sample. • Some participants may benefit from in person informed consent – flexibility is key.

Table 2: Efficiency of the adaptations, challenges and benefits, and considerations					
	Adaptation	**Potentially efficient adaptation, and reason if not**	**Studies/populations in which adaptation may be efficient**	**Challenges and benefits**	**Guidance or considerations** [guidance from existing literature is in *italics*]
					• *Participants may prefer paper consent methods due to concerns around trust and data security* [2,3]. • *Using interactive features may aid comprehension* [2]. • It may be necessary to maintain an audit trail of the consent conversations that are had if the participant isn't able to physically sign the consent form. • If possible, avoid the need for participants to type a URL into a browser – this may result in participants making data errors and becoming disengaged from the recruitment process.

Table 2: Efficiency of the adaptations, challenges and benefits, and considerations					
	Adaptation	**Potentially efficient adaptation, and reason if not**	**Studies/populations in which adaptation may be efficient**	**Challenges and benefits**	**Guidance or considerations** [guidance from existing literature is in *italics*]
Intervention delivery	Remote delivery of the intervention by CTU staff	No. Pandemic specific. Does not allow trial to be tested in 'real world' setting		**Challenges** • The scientific integrity of the trial may be impacted by the fact that the intervention is not being tested in the 'real world'. • Range of facilitators reduced, meaning each facilitator may have an increase influence over delivery of the intervention. **Benefits** • A smaller, centralised team allows more controlled facilitation of the intervention • Direct feedback between participants and CTU staff	
	Delivery of the trial intervention by any interventionists	Unknown	• Studies with a HEI sponsor • Studies involving interventions that can be carried out remotely, where there are	**Challenges** • Seeking excess treatment costs, transfer of data between Trusts, and agreement of whom takes responsibilities for the	• Avoid including PIs who are not engaged in trial as receivers of external referrals. • Allows therapist absence at one site to be covered by therapists from other sites.

Table 2: Efficiency of the adaptations, challenges and benefits, and considerations					
	Adaptation	**Potentially efficient adaptation, and reason if not**	**Studies/populations in which adaptation may be efficient**	**Challenges and benefits**	**Guidance or considerations** [guidance from existing literature is in *italics*]
	at any NHS Trust		numerous trained individuals across the UK	participant's clinical care may be challenging. **Benefits** • May increase the pool of potential participants, therefore increasing recruitment throughput.	
	Couriering the IMP to the participant's home	Yes – benefits participants	• IMPs not requiring strict temperature regulation • Studies that can incorporate costs for IMP couriering into their grant.	**Challenges** • Significant resources required at site or the CTU to track and organise the courier, including outside of normal office hours. • Significant resources may also be required to review SOPs and formulate courier processes. • Expensive. • Logistical issues, including the requirement for wet ink signatures, and pharmacies closing before the courier attends. • May result in poor external validity, if, in the 'real-world', the drug would not be couriered to the participant.	• Return of the IMP important to consider. • Confirmation that the participant has received the IMP may be required – either by directly contacting the participant or receiving notifications from the courier. • Ensure packaging is correct and the site pharmacy approve it. • Adherence data may be difficult to collect and be reliant on trusting the participant to provide reliable data. • Sites may automatically defer to using a courier and may need reminding that the participant can attend in-person.

Table 2: Efficiency of the adaptations, challenges and benefits, and considerations						
		Adaptation	**Potentially efficient adaptation, and reason if not**	**Studies/populations in which adaptation may be efficient**	**Challenges and benefits**	**Guidance or considerations** [guidance from existing literature is in *italics*]
					Benefits • Couriering the IMP may make the trial more desirable and increase participant recruitment and retention.	• Sites may need time to update their SOPs if they have not couriered medications in the past, which the CTU may need to review. • Between arm differences in how the drug is couriered may result in bias.
Follow-up	Remote collection of PROMs	Telephone & postal	Yes – benefits participants	• Studies may consider using this adaptation as a back-up for remote patients or those that cannot attend the study site	**Challenges** • Risk of missing side effects when participant cannot be seen in person. • Data may be missing if limited guidance or input is provided to the participant when completing measures. • May be difficult to ask sensitive conversations remotely. **Benefits** • Allows trial participants increased flexibility in how trial procedures are undertaken, and therefore may improve recruitment rates	• Training may be required if CTU staff are to deliver PROMs. • *There were differences in responses to the questionnaires when comparing telephone vs mail, or paper to electronic versions* [4,5]. • Certain instruments may not be validated for use outside the in-person clinical setting. • Maintaining blinding was challenging in one trial. In order resolve this, each site has a blinded and non-blinded research assistant.

Table 2: Efficiency of the adaptations, challenges and benefits, and considerations						
		Adaptation	**Potentially efficient adaptation, and reason if not**	**Studies/populations in which adaptation may be efficient**	**Challenges and benefits**	**Guidance or considerations** [guidance from existing literature is in *italics*]
					through making the trial more appealing. • Telephone data collection may lead to particularly good compliance and low missing data but may be onerous for long questionnaires. • Postal data collection may require high levels of CTU input – including dealing with missing data and administering reminders to participants.	• Participants may not pick up the telephone for outcome collection if being called from an unknown number. • As the clinical team may not be directly involved in the follow up, criteria may be required for stopping the IMP, e.g., in the case of high depression levels. • Telephone follow-ups may need to be split into multiple sessions if many measures are being collected and may require out of hours working at the CTU. • Postal data collection may require follow-up windows to be extended. • Repetitive question formats should be avoided over the telephone. Questions should be kept as simple as possible via all mediums.

Table 2: Efficiency of the adaptations, challenges and benefits, and considerations						
		Adaptation	**Potentially efficient adaptation, and reason if not**	**Studies/populations in which adaptation may be efficient**	**Challenges and benefits**	**Guidance or considerations** [guidance from existing literature is in *italics*]
						• Inform participant prior to the call the nature of the conversations to assist them in dealing with sensitive questions. • Trial sites can be involved in prompting participant for missing data or checking potentially erroneous or clinically concerning data. • There may be generational differences in the acceptability of different data collection techniques – the younger generation may not want to use the telephone, and may prefer text messages; older generations may prefer telephone.
		Video	Unknown			• Used in a study involving populations with chronic conditions that reduce ability to communicate via other methods.

Table 2: Efficiency of the adaptations, challenges and benefits, and considerations						
		Adaptation	**Potentially efficient adaptation, and reason if not**	**Studies/populations in which adaptation may be efficient**	**Challenges and benefits**	**Guidance or considerations** [guidance from existing literature is in *italics*]
	Remote collection of biological measures	Blood pressures collected remotely	Yes – benefits participants	• Studies where taking blood pressures remotely would avoid the need for participants to attend an appointment. • Studies where participants can measure their own blood pressure.	See also "remote delivery of PROMs" **Challenges** • Participants may provide erroneous values – e.g., supply their lowest blood pressure readings. • Potential for loss of data if readings are not automatically uploaded. • Concerns around calibration and quality of devices – good quality devices may be very expensive. • May work against inclusivity – e.g., those with chaotic lifestyles	• Unlikely to be more efficient, but more flexible for participants. • Compliance may depend on patient group or individual patient's motivations, e.g., patients who are less engaged in their therapy may be less likely to provide accurate data. • Participants may want to see a clinician. • Participant's readings may better reflect their 'actual' blood pressure levels when measured in the home environment.
		Spirometry & cough data collected remotely	Unknown	• Studies collecting biological measures, where technology assists to collect the outcome remotely and automatically (e.g., spirometry data)	**Challenges** • Cost implications **Benefits** • Remote collection of spirometry data, and automated upload to the trial database, allowed for	• Unknown acceptability from participant's point of view.

Table 2: Efficiency of the adaptations, challenges and benefits, and considerations						
		Adaptation	**Potentially efficient adaptation, and reason if not**	**Studies/populations in which adaptation may be efficient**	**Challenges and benefits**	**Guidance or considerations** [guidance from existing literature is in *italics*]
				• Studies that have the budget to invest in such technologies	additional secondary outcomes to be collected.	
		Remotely collected blood glucose measure (Hb1Ac)	Yes – benefits participants	• Studies where taking Hb1Ac remotely would avoid the need for participants to attend an appointment. • Studies where participants can measure their own blood glucose levels.	**Challenges** • Extensive resources required at CTU to administer and send packs. • Potential poor response rate. • Participants accessing a post box to return the kit may be the most challenging part for more ill or vulnerable participants. **Benefits** See "remote delivery of PROMs"	• Unknown acceptability from participant's point of view. • Need to ensure process isn't too burdensome for participants.
	Other	Collection of outcomes from a routine source	Unknown			• Cheaper and involves less travel for participants.

Table 2: Efficiency of the adaptations, challenges and benefits, and considerations						
		Adaptation	**Potentially efficient adaptation, and reason if not**	**Studies/populations in which adaptation may be efficient**	**Challenges and benefits**	**Guidance or considerations** [guidance from existing literature is in *italics*]
		Prioritisation of trial outcomes or in-person visits	No. Pandemic specific			

CTIMP – Clinical Trial of an Investigational Medicinal Product; CTU – Clinical Trials Unit; HEI – Higher Education Institution; NHS – National Health Service; PI – Principal Investigator; PROM - Patient Reported Outcome Measure; REC – Research Ethics Committee; SOP – Standard Operating Procedure; URL – Uniform Resource Locator.

References

1 Brøgger-Mikkelsen M, Ali Z, Zibert JR, *et al.* Online patient recruitment in clinical trials: systematic review and meta-analysis. J. Med. Internet Res. 2020;**22**:e22179. doi:10.2196/22179

2 Skelton E, Drey N, Rutherford M, *et al.* Electronic consenting for conducting research remotely: A review of current practice and key recommendations for using e-consenting. Int. J. Med. Inform. 2020;**143**:104271. doi:10.1016/j.ijmedinf.2020.104271

3 Chen C, Lee P-I, Pain KJ, *et al.* Replacing Paper Informed Consent with Electronic Informed Consent for Research in Academic Medical Centers: A Scoping Review. *AMIA Jt Summits Transl Sci proceedings AMIA Jt Summits Transl Sci* 2020;**2020**:80–8.http://www.ncbi.nlm.nih.gov/pubmed/32477626 (accessed 16 Mar 2021).

4 Erhart M, Wetzel RM, Krügel A, *et al.* Effects of phone versus mail survey methods on the measurement of health-related quality of life and emotional and behavioural problems in adolescents. *BMC Public Health* 2009;**9**:491. doi:10.1186/1471-2458-9-491

5 Nishimura K, Kusunose M, Sanda R, *et al.* Comparison between electronic and paper versions of patient-reported outcome measures in subjects with chronic obstructive pulmonary disease: an observational study with a cross-over administration. *BMJ Open* 2019;**9**:e032767. doi:10.1136/bmjopen-2019-032767