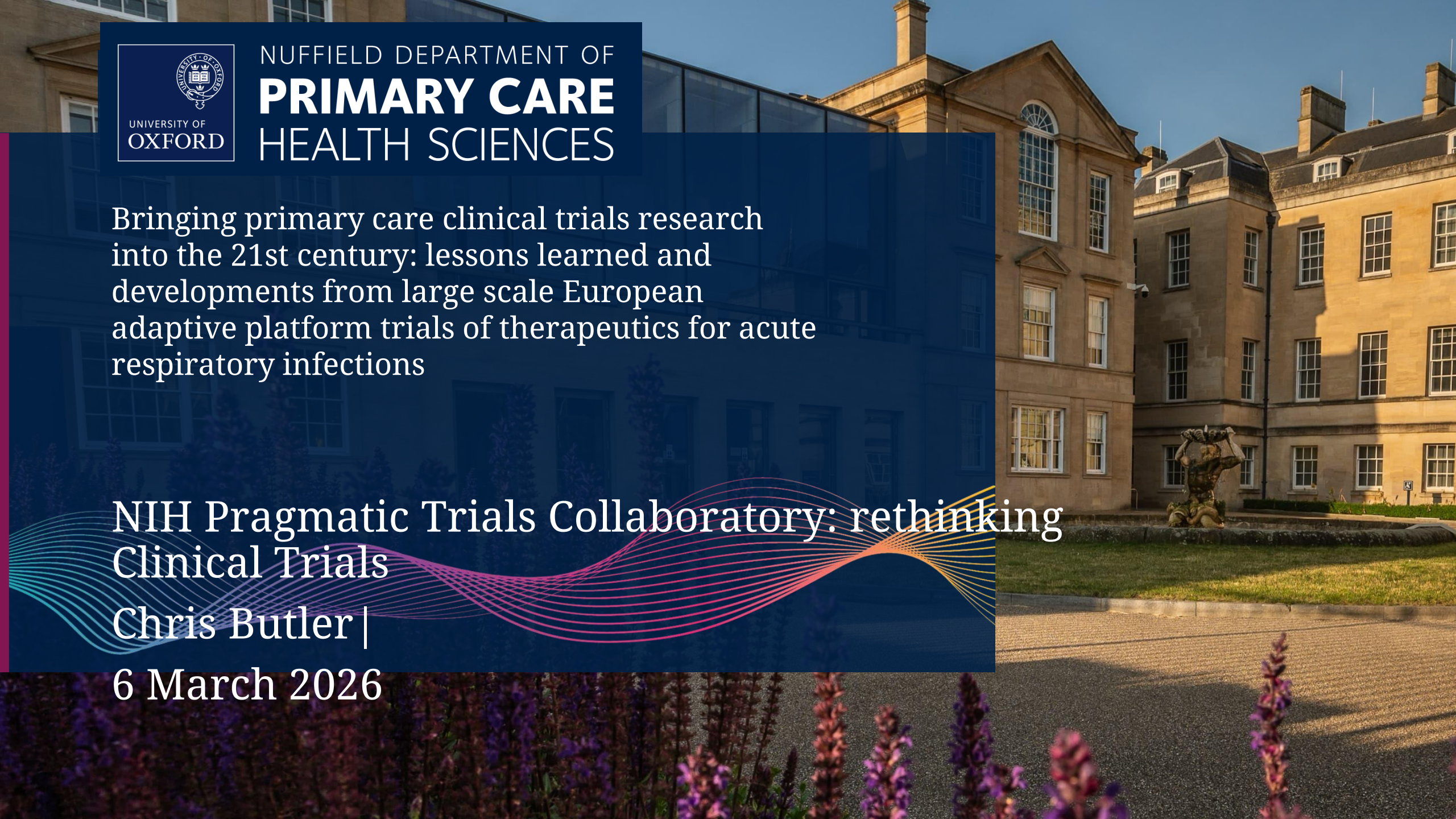


UNIVERSITY OF OXFORD

NUFFIELD DEPARTMENT OF PRIMARY CARE HEALTH SCIENCES

Bringing primary care clinical trials research into the 21st century: lessons learned and developments from large scale European adaptive platform trials of therapeutics for acute respiratory infections

NIH Pragmatic Trials Collaboratory: rethinking Clinical Trials

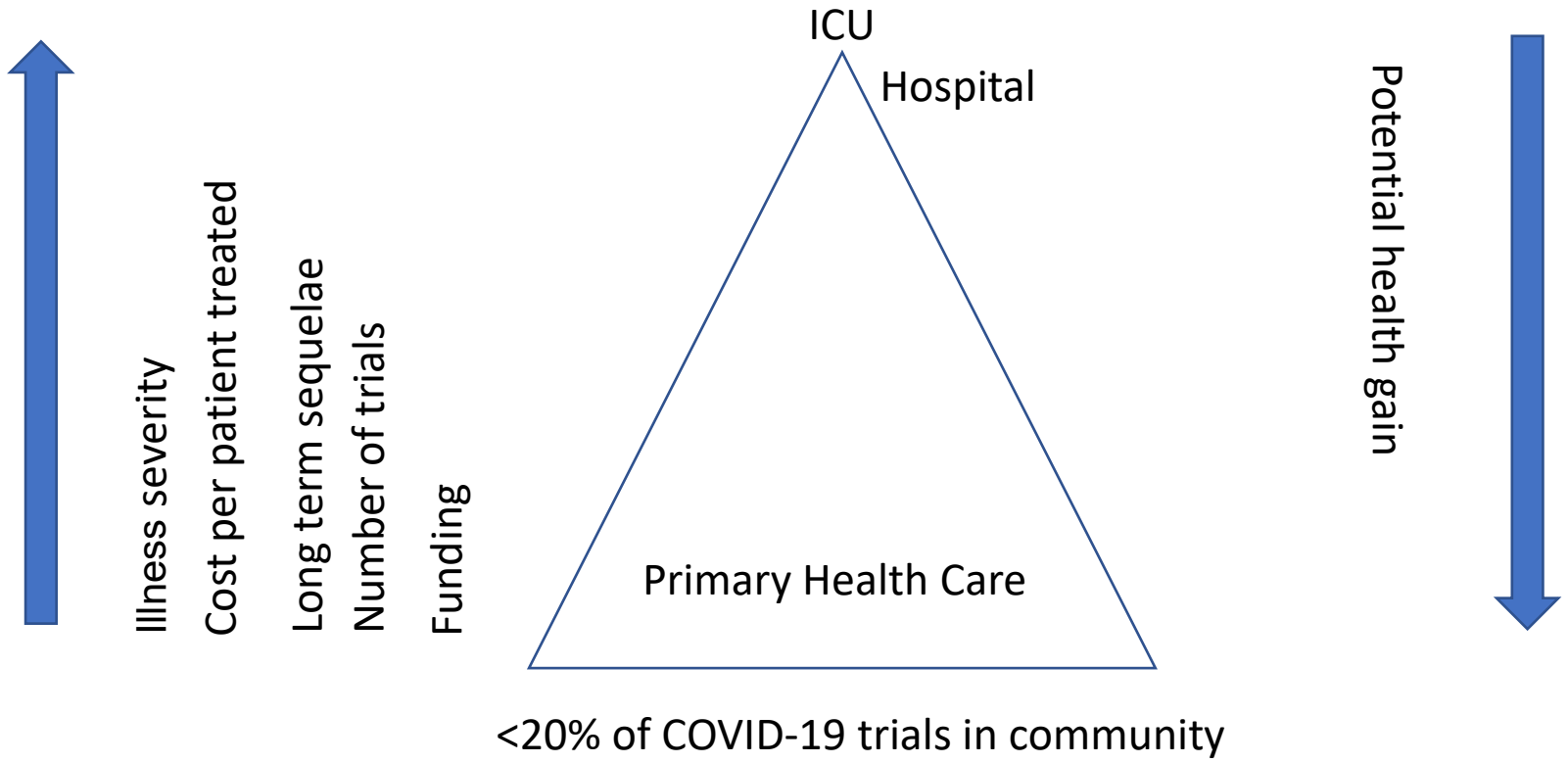
Chris Butler |

6 March 2026

Why primary care? (They are not proper doctors, they don't have labs or rats, and they don't have machines that go 'ping')

- Effective interventions will have greatest reach and impact in the community
- Early interventions, especially is they can be self initiated, limit illness and enhance the sustainability of health care
- NHS 10-year plan: Hospital to community care, and we can add, "to self care"
- World Health Assembly Resolution 75.8 "Bigger and better, more pragmatic, diverse study populations, greater applicability: i.e. do research with those who have the most to contribute and gain ("intended use population")

Inverse funding and potential health gain law



<20% of COVID-19 trials in community

World Health Assembly Resolution 75.8 on strengthening clinical trials..

- "…that clinical trials on new health interventions are likely to produce the clearest result when carried out in diverse settings, including all major population groups the intervention is intended to benefit, with a particular focus on under-represented populations"

World Health Organization

SEVENTY-FIFTH WORLD HEALTH ASSEMBLY
Agenda item 16.2

WHA75.8
27 May 2022

Strengthening clinical trials[1] to provide high-quality evidence on health interventions and to improve research quality and coordination

The Seventy-fifth World Health Assembly,

Recalling resolutions WHA58.34 (2005) acknowledging that high-quality, ethical research and the generation and application of knowledge are critical in achieving internationally agreed health-related development goals, WHA63.21 (2010) outlining WHO's role and responsibilities in health research, WHA66.22 (2013) and WHA69.23 (2016) on the follow-up of the report of the Consultative Expert Working Group on Research and Development: Financing and Coordination, WHA67.20 (2014) on regulatory system strengthening for medical products, WHA67.23 (2014) on health intervention and technology assessment in support of universal health coverage, WHA74.6 (2021) on strengthening local production of medicines and other health technologies to improve access, and WHA74.7 (2021) on strengthening WHO preparedness for and response to health emergencies, which notes the importance of basic and clinical research and recognizes the critical role of international collaboration in research and development, including in multicountry clinical and vaccine trials, as well as rapid diagnostics test and assay development, while acknowledging the need for further rigorous scientific evidence;

Challenges of Traditional Clinical Trials in Primary Care (PC)

- GP's excessive clinic-level workflow & workload crisis
- Lack of time, funding, resources & research experience
- Failure to recruit sufficient participants – opportunistic recruitment
- Geographical constraints – smaller scope of recruitment
- Delays in getting clinical records from practices UK wide: e.g. faxes, consent forms lying in GP trays for hours before action
- The need for patients to travel to a site
- GPs had to repackage, label and issue study meds
- No research enabled pharmacy or research diagnostics in the community

No treatment, no research opportunity

Inverse research participation law

Access to research is often inversely proportional to a participants' potential contribution and to where the research findings should be most applicable

Transformation ‘by implementation’: digital enablement and inclusion and follow up

Site-based & site-dependent process

Recruitment
conducted opportunistically through GPs and requires proximity to trial sites

Screening
Requires in-person visits for physical assessment & interviews

Informed consent
Obtained in-person with site staff to explain study procedures

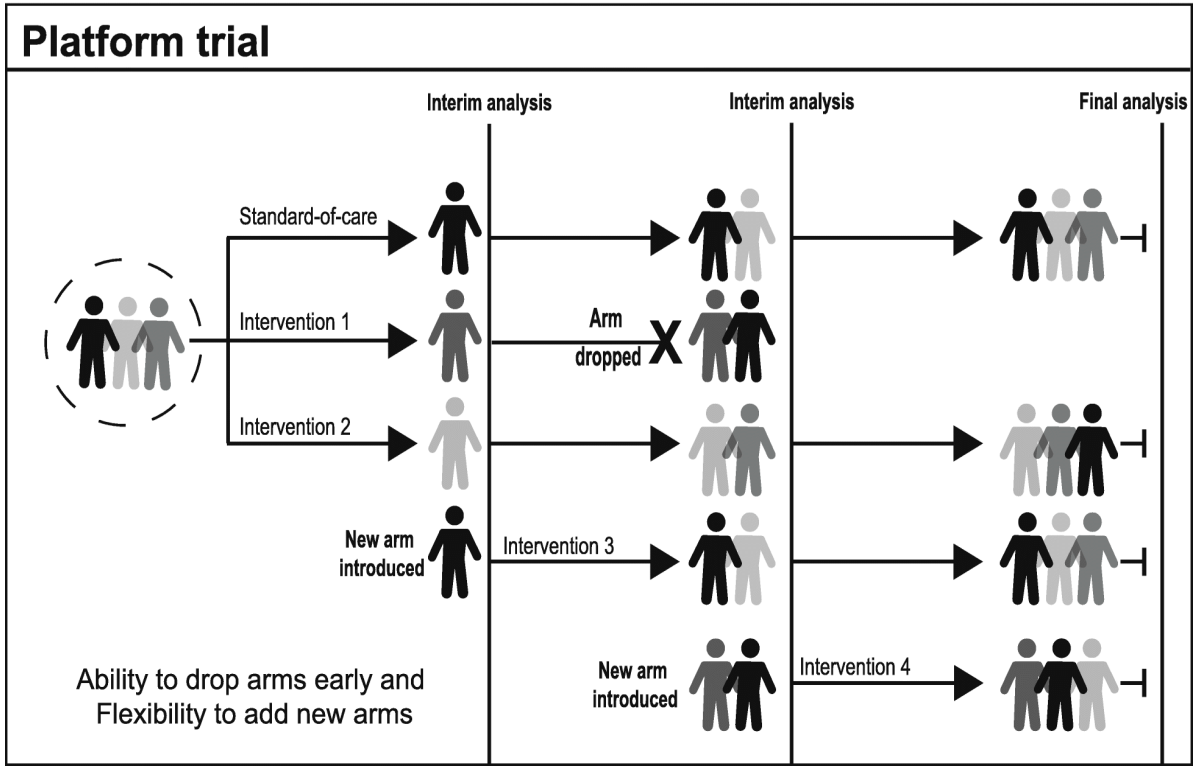
Randomisation
Managed by trial staff during in-person visit using computerised system or manual methods

Intervention
Participants receive interventions or controls during site visits

Monitoring & Follow up
Scheduled visits for assessments & data collection

Transformation ‘by design’: the now famous APT

- Setting up a new trial for each intervention is inefficient and can result in successive underpowered studies (e.g. HCQ!!)
- Arose from ALIC4E (PREPARE), PRINCIPLE and PANORAMIC: Rapid, large-scale evaluation of new treatments for ‘flu, COVID-19 and for future epidemic/pandemics
- REACH and IMPACT: Low cost, safe, effective (broad-spectrum) treatment of respiratory viruses prescribed in PC, or self-initiated (OTC) allow for early treatment at scale without the need for testing



It all started with GRAC4E

GRACE

enomics to combat Resistance against
otics in Community-acquired LRTI in Europe

GRACE news

Spreading Excellence in Respiratory Tract Infections

April - July 2010, Volume 5 (2-3)

able of content

1 Editorial
News Flash
2 News
WP9-10 Update:

Editorial

Dear GRACE Fans!

We did it! Yes we could!

Thanks to a tremendous effort of our 16 participating primary care networks we reached our most important and ambitious milestone: on April 12th 2010 we reached the target of 6000 inclusions for our observational and intervention study. Thousands and thousands of blood samples, nose & throat swabs, and urine samples are waiting in our freezers in European research sites for microbial and human phenotypic and genotypic studies. That will make this by a long way the largest trial and observational cohort for acute LRTI in typical primary care settings - and with good clinical characterisation and unprecedented microbiological and genetic information. The trial data set alone will be significantly larger than the existing systematic review - and that means that the data from this study will dominate the evidence for clinical management of LRTI for some time to come. This study shows better than any other we can think of, what great clinically relevant research is possible when we work together. What a great excitement to finally start analysing all these patient data and laboratory results.

Oseltamivir plus usual care versus usual care for influenza-like illness in primary care: an open-label, pragmatic, randomised controlled trial

Christopher C Butler, Alike W van der Velden, Emily Bongard, Benjamin R Saville, Jane Holmes, Samuel Coenen, Johanna Cook, Nick A Francis, Roger J Lewis, Maciek Godycki-Cwirko, Carl Llor, Sławomir Chlabicz, Christos Lionis, Bohumil Seifert, Pär-Daniel Sundvall, Annelies Colliers, Rune Aabenhus, Lars Bjerrum, Nicolay Jonassen Harbin, Morten Lindbæk, Dominik Glinz, Heiner C Bucher, Bernadett Kovács, Ruta Radzeviciene Jurgute, Pia Touboul Lundgren, Paul Little, Andrew W Murphy, An De Sutter, Peter Openshaw, Menno D de Jong, Jason T Connor, Veerle Matheeussen, Margareta Ieven, Herman Goossens, Theo J Verheij

Age	Severity	Comorbid	Symptom duration, h	n	Mean days benefit	95% Bayesian credible interval	Pr (days>0)
<12 years							
	Low	No	≤48	79	0·70	0·30 to 1·20	0·999
			>48	44	1·10	0·50 to 1·60	1·000
		Yes	≤48	10	1·30	0·50 to 2·10	0·999
			>48	9	1·80	0·90 to 2·80	1·000
	Medium	No	≤48	139	0·70	0·20 to 1·30	0·998
			>48	71	1·10	0·50 to 1·80	1·000
		Yes	≤48	17	1·40	0·50 to 2·30	1·000
			>48	8	2·00	0·90 to 3·10	1·000
	High	No	≤48	38	1·20	0·50 to 2·00	0·999
			>48	10	1·70	0·80 to 2·60	1·000
		Yes	≤48	0	2·00	0·90 to 3·20	1·000
			>48	1	2·70	1·40 to 4·20	1·000
12–64 years							
	Low	No	≤48	258	0·70	0·20 to 1·10	0·998
			>48	128	1·10	0·50 to 1·70	1·000
		Yes	≤48	34	1·30	0·50 to 2·10	0·999
			>48	22	1·90	0·80 to 2·90	1·000
	Medium	No	≤48	871	0·70	0·30 to 1·10	0·999
			>48	429	1·10	0·60 to 1·70	1·000
		Yes	≤48	139	1·40	0·60 to 2·20	0·999
			>48	69	2·00	1·00 to 3·10	1·000
	High	No	≤48	270	1·20	0·50 to 1·90	1·000
			>48	135	1·80	0·90 to 2·70	1·000
		Yes	≤48	48	2·10	1·00 to 3·30	1·000
			>48	22	2·80	1·50 to 4·30	1·000
≥65 years							
	Low	No	≤48	20	0·70	−0·40 to 1·90	0·894
			>48	19	1·30	−0·00 to 2·60	0·972
		Yes	≤48	9	1·60	0·00 to 3·20	0·976
			>48	9	2·30	0·50 to 4·10	0·994
	Medium	No	≤48	40	0·70	−0·60 to 2·00	0·850
			>48	25	1·30	−0·20 to 2·80	0·954
		Yes	≤48	28	1·60	−0·10 to 3·30	0·964
			>48	22	2·30	0·40 to 4·20	0·992
	High	No	≤48	13	1·40	−0·30 to 3·10	0·951
			>48	7	2·10	0·30 to 4·00	0·987
		Yes	≤48	11	2·40	0·40 to 4·50	0·989
			>48	5	3·20	1·00 to 5·50	0·998

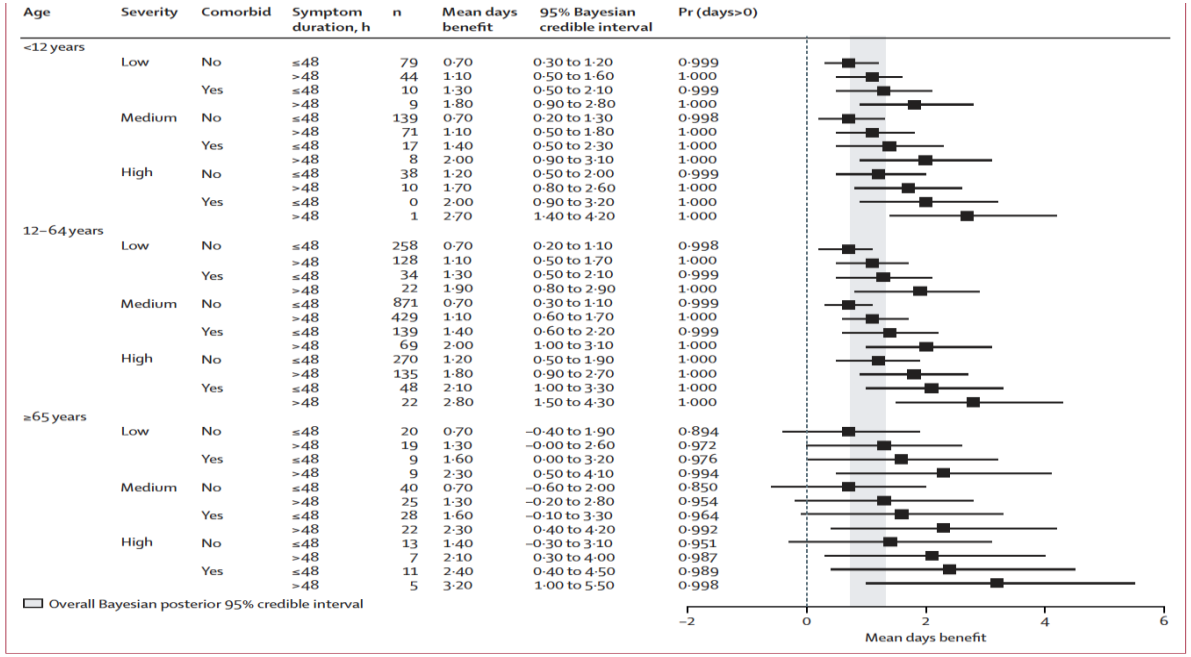


Figure 3: **Estimated mean days of oseltamivir benefit for all subgroups in the intention-to-treat population**
Pr (days>0)=Bayesian posterior probability mean days benefit is greater than 0.

27 March 2020

Cardiff Road Medical Centre,
Mountain Ash
Cynon Valley
South Wales

Managing uncertainty… ???

Only just

UNIVERSITY OF OXFORD

PRINCIPLE

Platform Randomised Trial of Treatments in the Community for Epidemic and Pandemic Illnesses

3 years on

March 2020
PRINCIPLE Trial begins

April 2020
First participant joins the trial

April 2020
Chief Medical Officers from all four UK nations endorse the PRINCIPLE Trial

PRINCIPLE selected to be a national priority clinical trial on COVID-19

May 2020
Hydroxychloroquine shown in other trials not to be effective against COVID-19 in hospitalised patients. Trial arm closed

October 2020
1000th participant recruited to the trial

January 2021
Azithromycin and Doxycycline are shown not to be effective against COVID-19 in patients treated at home

April 2021
Asthma drug inhaled Budesonide found to be effective in reducing recovery time by a median of three days

April 2021
Favipiravir added to the trial

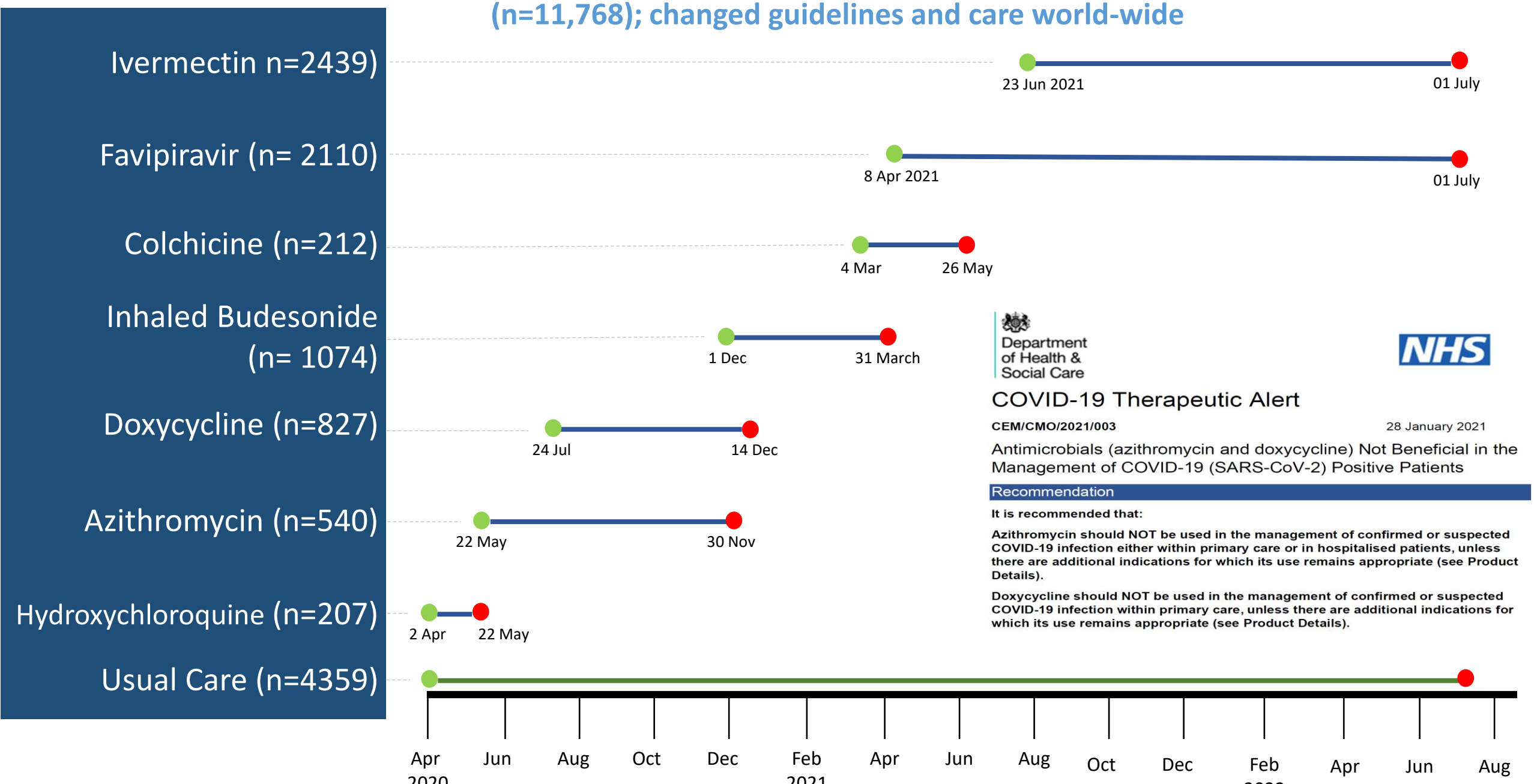
May 2021
Colchicine shown not to improve time to recovery in patients at higher risk of complications with COVID-19 in the community

June 2021
Ivermectin added to the trial

July 2021
The PRINCIPLE Trial 'highly commended' for innovative use of health data

April 2022
PRINCIPLE celebrates the 10,000th recruit joining the Trial

PRINCIPLE Recruitment and intervention timeline in (n=11,768); changed guidelines and care world-wide



Department of Health & Social Care

NHS

COVID-19 Therapeutic Alert

CEM/CMO/2021/003 28 January 2021

Antimicrobials (azithromycin and doxycycline) Not Beneficial in the Management of COVID-19 (SARS-CoV-2) Positive Patients

Recommendation

It is recommended that:

Azithromycin should NOT be used in the management of confirmed or suspected COVID-19 infection either within primary care or in hospitalised patients, unless there are additional indications for which its use remains appropriate (see Product Details).

Doxycycline should NOT be used in the management of confirmed or suspected COVID-19 infection within primary care, unless there are additional indications for which its use remains appropriate (see Product Details).

Home run for antimicrobial stewardship

Doxycycline for community treatment of suspected COVID-19 in people at high risk of adverse outcomes in the UK (PRINCIPLE): a randomised, controlled, open-label, adaptive platform trial

Christopher C Butler, Ly-Mee Yu, Jienchi Dorward, Oghenekome Gbinigie, Gail Ha
Michelle A Detry, Christina Saunders, Mark Fitzgerald, Victoria Harris, Ratko Djuk
Emma Ogburn, Philip H Evans, Nicholas P B Thomas, Mahendra G Patel, F D Rich

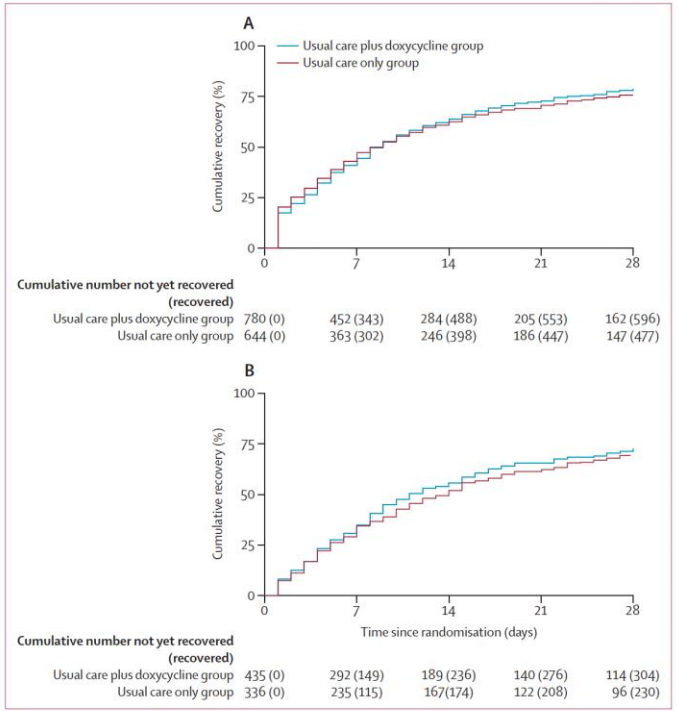


Figure 2: **Time to first self-reported recovery**
(A) Concurrent randomisation analysis population. (B) SARS-CoV-2 PCR-positive participants in the concurrent randomisation analysis population. The concurrent randomisation analysis population was defined as all participants who were randomly assigned to usual care plus doxycycline or usual care only during the time period

Azithromycin for community treatment of suspected COVID-19 in people at increased risk of an adverse clinical course in the UK (PRINCIPLE): a randomised, controlled, open-label, adaptive platform trial

*PRINCIPLE Trial Collaborative Group**

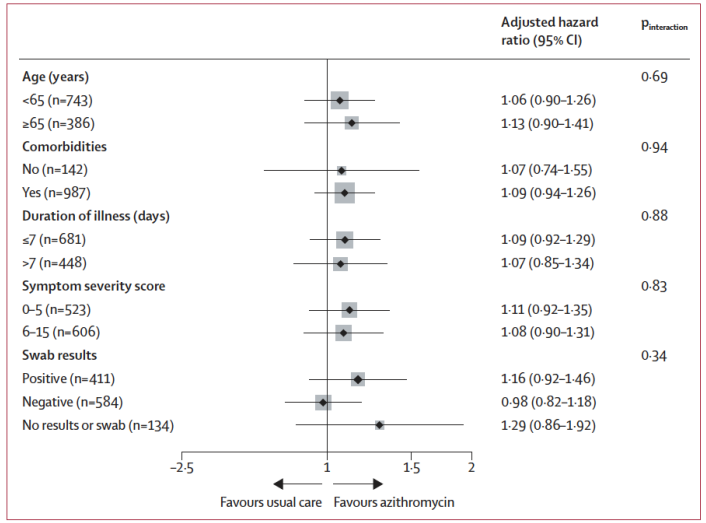


Figure 3: **Subgroup analysis of time to recovery outcome (concurrent randomisation analysis population)**

Impact

Department of Health & Social Care

NHS

COVID-19 Therapeutic Alert

CEM/CMO/2021/003 28 January 2021

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Doxycycline should NOT be used in the management of confirmed or suspected COVID-19 infection within primary care, unless there are additional indications for which its use remains appropriate (see Product Details).

PRINCIPLE's interim analysis also concluded that doxycycline (administered as 200mg on the first day, followed by 100mg a day for 6 days) offered no meaningful beneficial effect compared to standard of care in patient aged over 50 who are treated at home in the early stages of COVID-19. The estimated clinical benefit in terms of both time to recovery and hospital admission were small.

Chief Medical Officer Directorate
Pharmacy and Medicines Division

Scottish Government
Riaghaltas na h-Alba
gov.scot

Dear Healthcare Professional,

COVID-19 THERAPEUTIC ALERT – ANTIMICROBIALS (AZITHROMYCIN AND DOXYCYCLINE) NOT BENEFICIAL IN THE MANAGEMENT OF COVID-19 (SARS-CoV-2) POSITIVE PATIENTS

Please see attached CMO letter about the results from the RECOVERY trial, and interim analysis from the PRINCIPLE trial which demonstrated that azithromycin should **NOT** be used in the management of confirmed or suspected COVID-19 infection either within primary care or in hospitalised patients. Doxycycline should **NOT** be used in the management of confirmed or suspected COVID-19 infection within primary care. I would be grateful if you could cascade this information to relevant colleagues.

NICE National Institute for Health and Care Excellence

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COVID-19 rapid guideline: managing COVID-19

NICE guideline [NG191] Published: 23 March 2021 Last updated: 08 May 2024

Guidance | Tools and resources | Evidence | History

World Health Organization

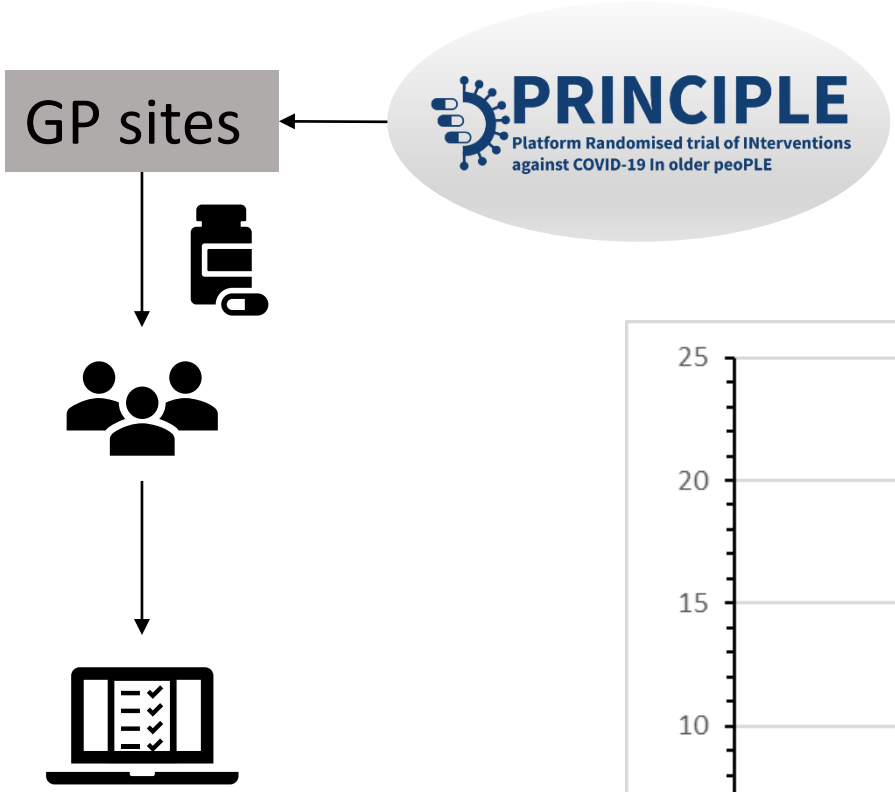
Health Topics | Countries | Newsroom | Emergencies | Data | About WHO

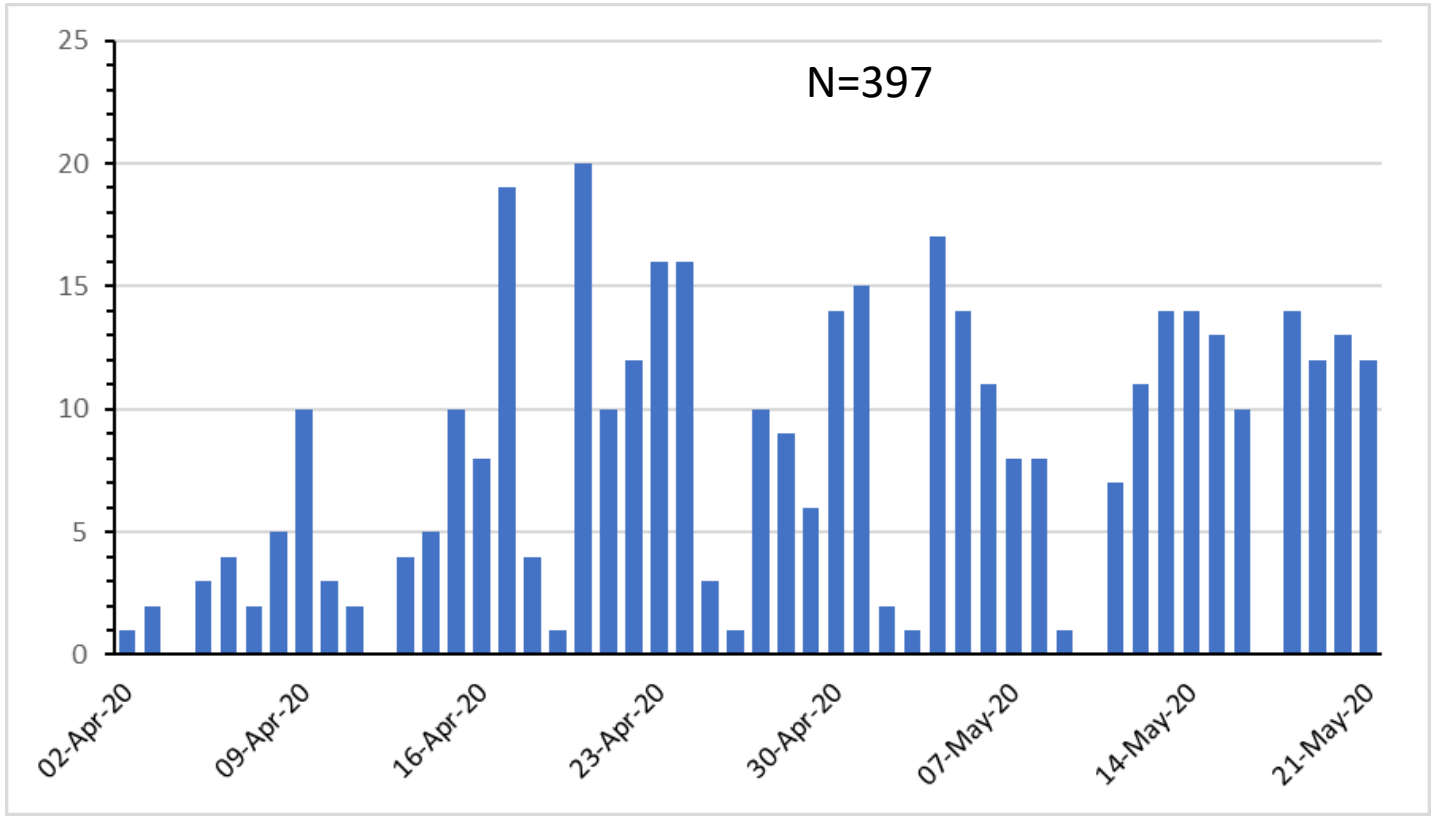
Home / Publications / Overview / Living guidance for clinical management of COVID-19

Living guidance for clinical management of COVID-19

23 November 2021 | COVID-19: Clinical care

PRINCIPLE
Platform Randomised trial of INterventions against COVID-19 In older peoPLE





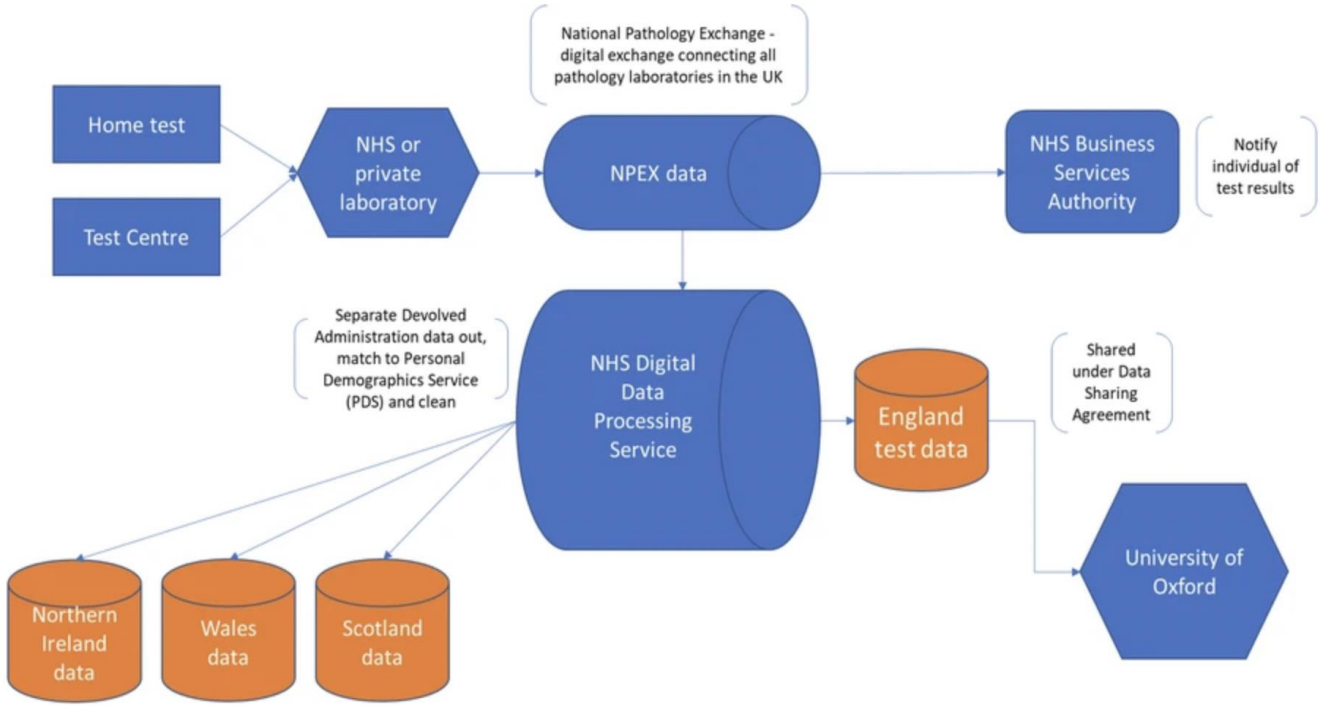
Methodology | Open Access | Published: 20 January 2022

Development and evaluation of rapid data-enabled access to routine clinical information to enhance early recruitment to the national clinical platform trial of COVID-19 community treatments

Caroline Cake, Emma Ogburn, Heather Pinches, Garry Coleman, David Seymour, Fran Woodard, Sinduja Manohar, Marjia Monsur, Martin Landray, Gaynor Dalton, Andrew D. Morris, Patrick F. Chinnery, UK COVID-19 National Core Studies Consortium, F. D. Richard Hobbs & Christopher Butler

Trials **23**, Article number: 62 (2022) | Cite this article

From: Development and evaluation of rapid data-enabled access to routine clinical information to enhance early recruitment to the national clinical platform trial of COVID-19 community treatments



Overview process diagram for test data route to the clinical trial

Major win 1: remote eligibility check

From: Christopher Butler <christopher.butler@phc.ox.ac.uk>
Sent: 30 November 2020 15:05
To: PINCHES, Heather (NHS DIGITAL) <h.pinches@nhs.net>
Cc: Emma Ogburn <emma.ogburn@phc.ox.ac.uk>; BOWKER, Philip (NHS DIGITAL) <phil.bowker@nhs.net>
Subject: Re: SCR access IG Review

Hi Heather,

This is my view:

The SCR is designed to maximise safe prescribing. The patients in our trial has consented for the trial to access their medical records for the purposes of their care during the trial, amongst other tings, and specifically give permission for SCR access for the purpose of their care in the trial. I am part of an NHS Organisation providing health care, and have a contract with Oxford Health. My name is on the medication being given to patients. I am therefore the prescriber. I need to prescribe as safely as possible. For that, I need access to the SCR. Being denied this access means that a safety check on prescribing is being denied to those providing consent for their SCR to be viewed for this purpose .

In addition,

a. The Trust does have a contract with the University for implementing the trial.
b. The University sponsors the Trial and is responsible for proper design, delivery and interpretation.
c. The Trust has a responsibility for delivering the trial to people in accordance with the h approved procedures outline in the study protocol and governance procedures as approved by Ethics, the MHRA and in their contract with the sponsor.
d. The Trial does indeed wish to have access to the SCR in order for the prescribing process to be as safe as possible.
e. Access to the SCR will only be for properly registered and accredited heath professionals.
f. These health professionals are acting in their capacity as clinicians holding contracts with the Trust.

Interestingly, a clinician in a hospital is free to access a participants SCR to ensure safe prescribing and care within a trial. Why should this be different because our participants are in the community? I am a fully registered GP. Why should patients in a community trial be denied the safety precaution of a SCR check before they are prescribed a medicine, when this safety check is open to those in a hospital study?

Best wishes

Chris

Summary care record access

care system involved in the patient's direct care.

With this in mind, the following settings and use cases are not in scope for SCR viewing and will not be approved for rollout for:

- research purposes, including clinical trials
- police and other government departments
- non-clinical cosmetics

The PRINCIPLE and PANORAMIC trials

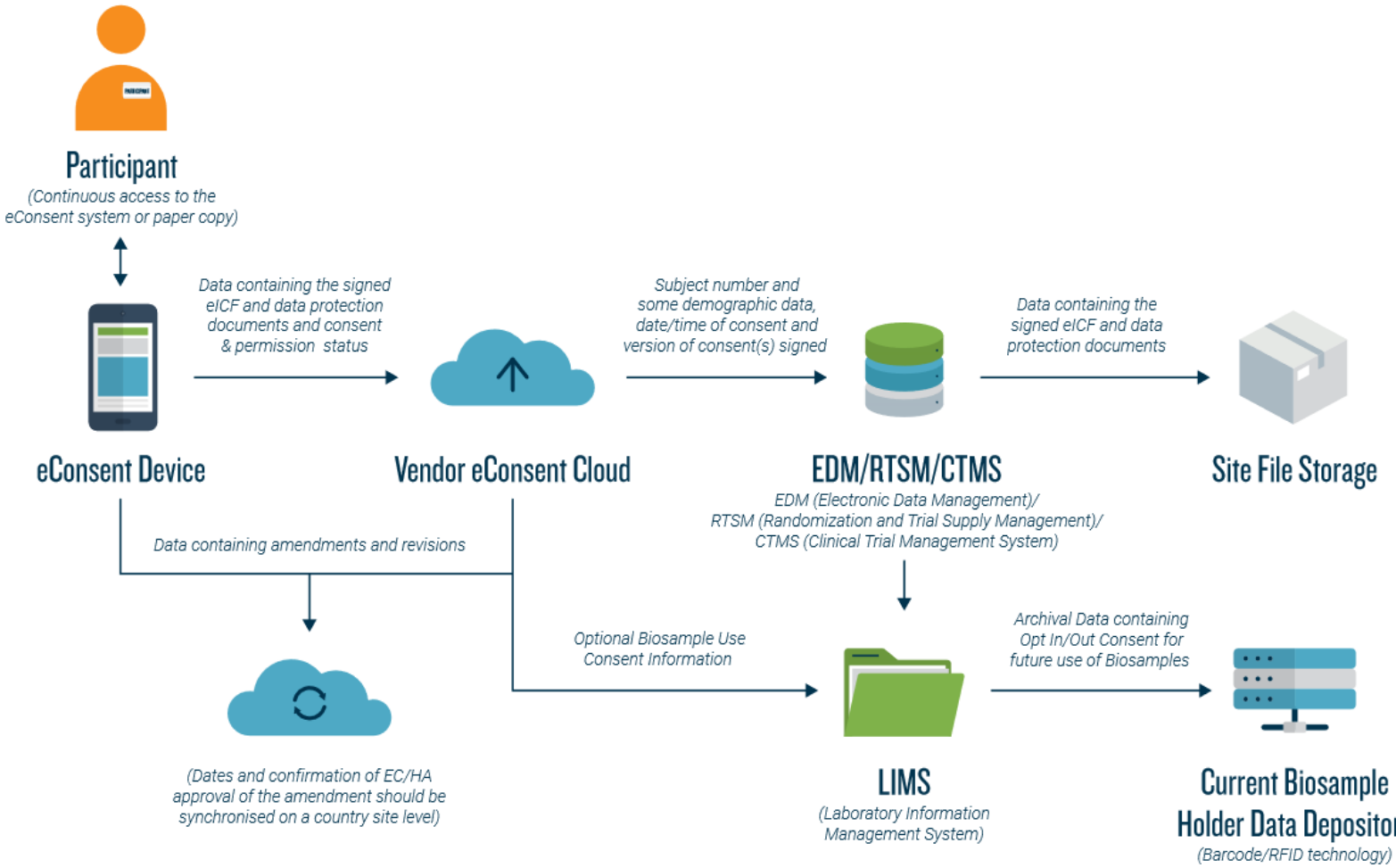
Two exceptions have been agreed for accessing the SCR to ensure timely prescribing and safe patient care by clinical staff working within the PRINCIPLE and PANORAMIC. These are both urgent public health COVID-19 clinical trials.

The PRINCIPLE and PANORAMIC trials seek to identify treatments that, if used early in the course of a coronavirus (COVID-19) infection, will reduce the duration of symptoms, prevent the need to admit people to hospital and reduce deaths.

SCR access has been assessed as essential to ensure individuals are safely brought onto the trial within the very restrictive timeframe of five days since symptom onset. This access enables vital safety checks to be undertaken with the permission of the participants.

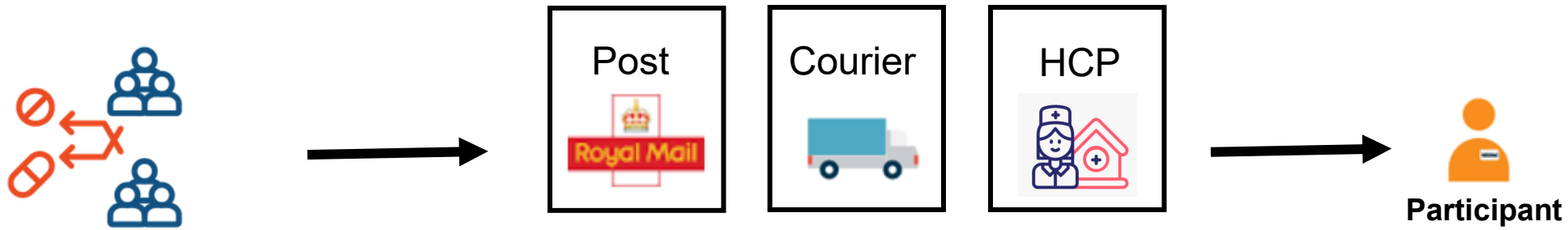
Access is sought only for those people who have been screened as eligible to be part of the trial, and who have already signed informed consent for participation.

eConsent



Source: Association of Clinical Research Organizations (ACRO)

Direct-to-Participant Supply of IP & Testing Kits



Randomisation & intervention allocation

Direct delivery of IP & testing kits to participant's home

Follow-ups


Daily diary
(online and/or phone)
Nurse home visit
Participant
Questionnaires
(online or phone)
Source System
(EHR/eSource)
Electronic medical
notes review
Safety phone calls

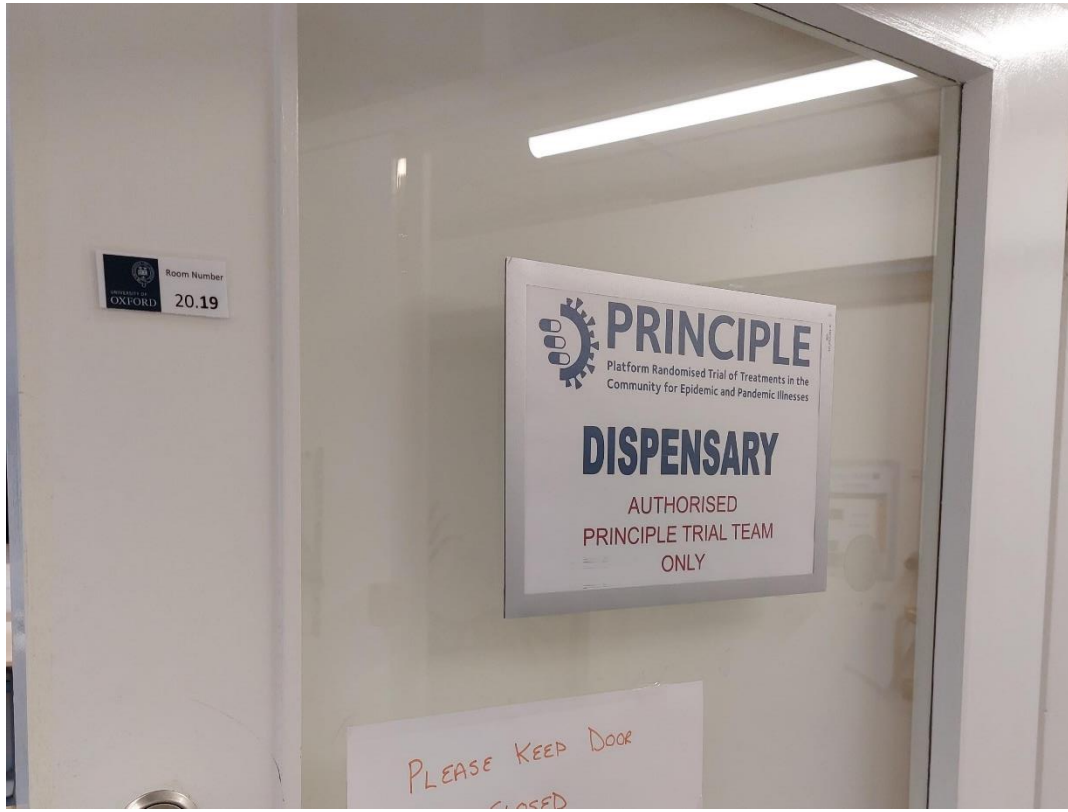
PRINCIPLE: Time from registration to eligibility/randomisation

	Median	IQR
Before SCR access		
Randomised	2 days	1 to 4 days
Not randomised	8 days	5 to 12 days
After SCR after		
Randomised	1 day	0 to 2 days
Not randomised	4 days	2 to 8 days

PRINCIPLE
Platform Randomised trial of INterventions against COVID-19 In older peoPLE

Participate without leaving your sick bed

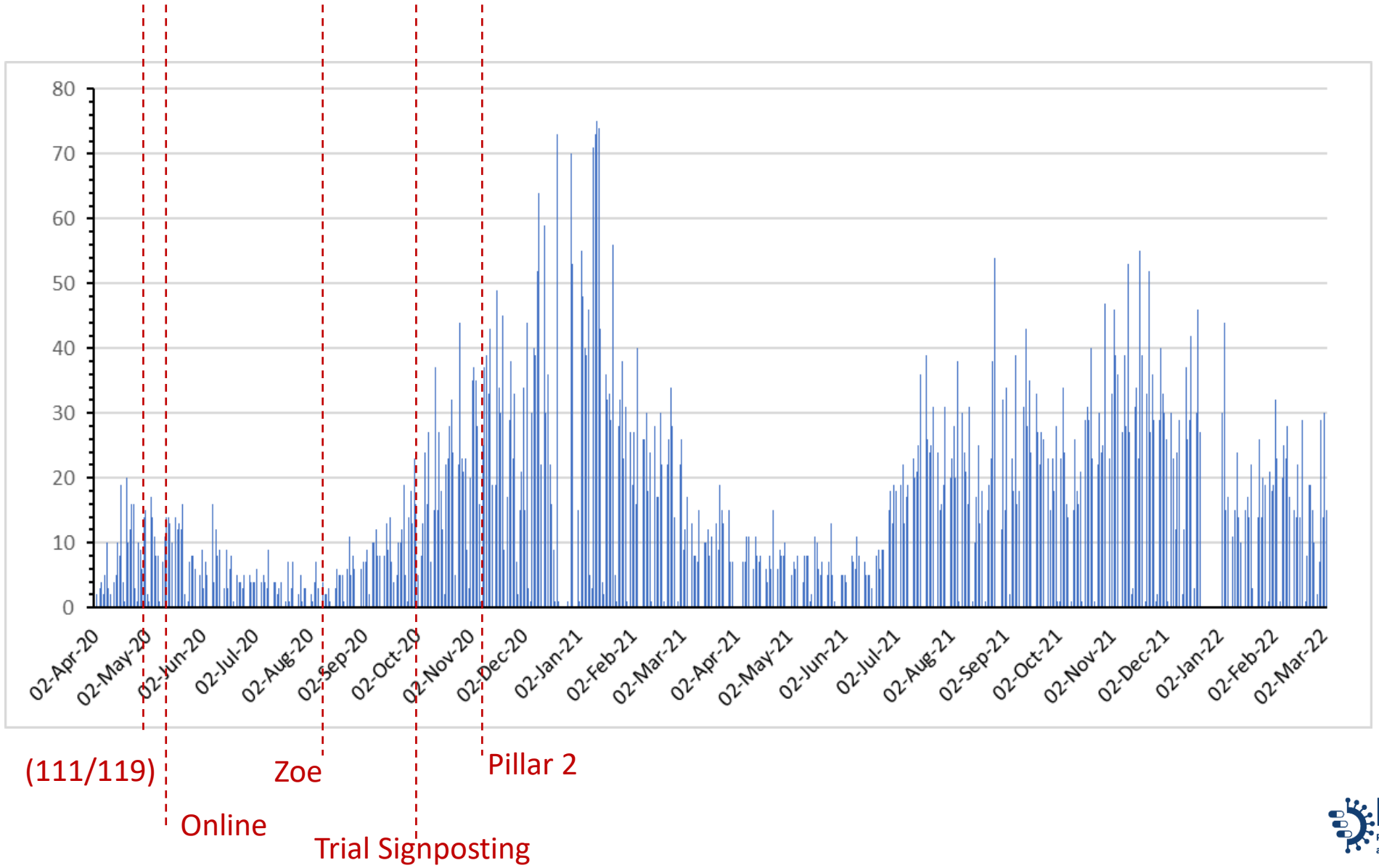
A meeting room was converted to be functional space for carrying out over-labelling, storage and trial dispensing for use in PRINCIPLE trial



Major win2 : in-house drug labelling and delivery

- Over-labelling IMPs by clinicians
- Assembly and packaging
- Storage and handling (including distribution)
- Temperature controlled
- Need for exemption for each IMP within same trial
- MHRA exemption in place for over-labelling
- Couriered to patient’s home UK-wide by next morning

Daily randomisation (n=9,371)



PRINCIPLE
Platform Randomised trial of INterventions against COVID-19 In older peoPLE

4,582 GP practices contributed at least one participants to PRINCIPLE

PANORAMIC
Platform Adaptive trial of NOvel antiviRals for eArly treatMent of COVID-19 In the Community

Platform Adaptive trial of Novel antiviRals for eArly treatment of COVID-19 in the Community (PANORAMIC)

Network and Support	
Sponsor	University of Oxford
Funder(s)	NIHR Evaluation, Trials and Studies Co-…
Lead Admin	England
Lead LCRN	Thames Valley and South Midlands
Managing Specialty	Primary Care
All Specialties	Infection, Primary Care
Primary Sub-Specialty	Infection
All Sub-specialties	Infection, Respiratory infections, Virolog…

UCL
University of Southampton
University of Glasgow
Cardiff University
Prifysgol Caerdydd
University of Liverpool

The NEW ENGLAND JOURNAL of MEDICINE

CURRENT ISSUE SPECIALTIES TOPICS

ORIGINAL ARTICLE

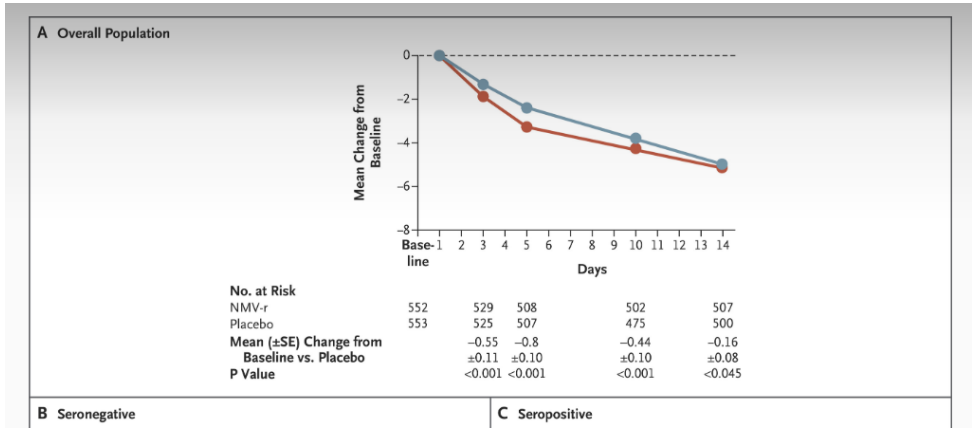
Oral Nirmatrelvir for High-Risk, Nonhospitalized Adults with Covid-19

Authors: Jennifer Hammond, Ph.D., Heidi Leister-Tebbe, B.S.N., Annie Gardner, M.P.H., M.S.P.T., Paula Abreu, Ph.D., Weihang Bao, Ph.D., Wayne Wisemandle, M.A., MaryLynn Baniecki, Ph.D., +5 , for the EPIC-HR Investigators* Author Info & Affiliations

Published February 16, 2022 | N Engl J Med 2022;386:1397-1408 | DOI: 10.1056/NEJMoa2118542

VOL. 386 NO. 15 | Copyright © 2022

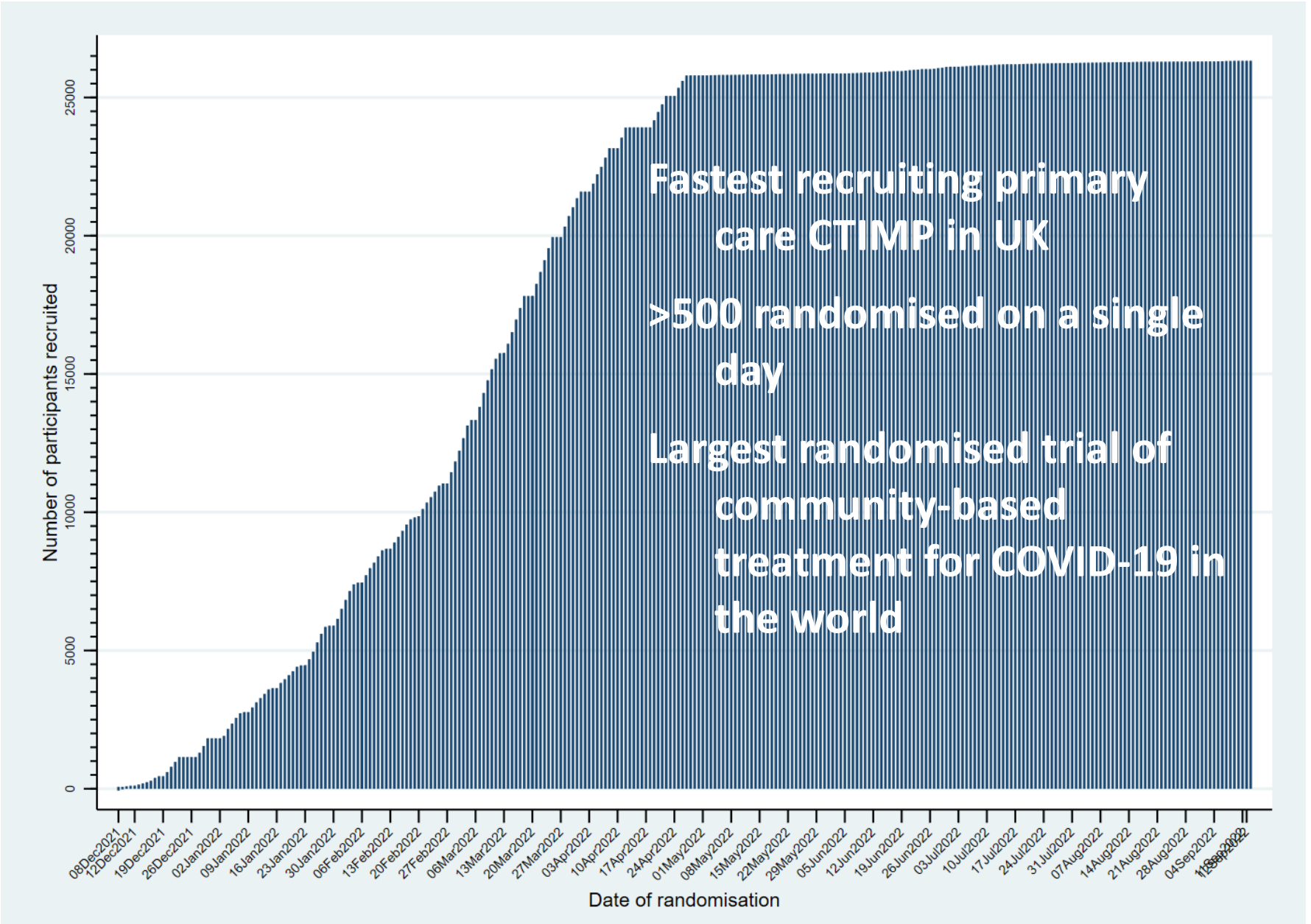
- 2246 Unvaccinated HR participants (1120 on nirmatrelvir)
- 5.81% (RR 88.9%) Reduction in hospital admission/death



Do these findings apply in the vaccinated population in the UK under omicron?

JVT: Let's do a trial in the intended use population to find out!

Daily Cumulative Recruitment, 13 Sept 2022 (n=26,326)



NUFFIELD DEPARTMENT OF
PRIMARY CARE
HEALTH SCIENCES

PRINCIPLE
Platform Randomised Trial of Treatments in the Community for Epidemic and Pandemic Illnesses

UNIVERSITY OF OXFORD

COMMUNITY OUTREACH: UK-WIDE COLLABORATION AND SUPPORT

University communities

Primary Care and NHS organisations

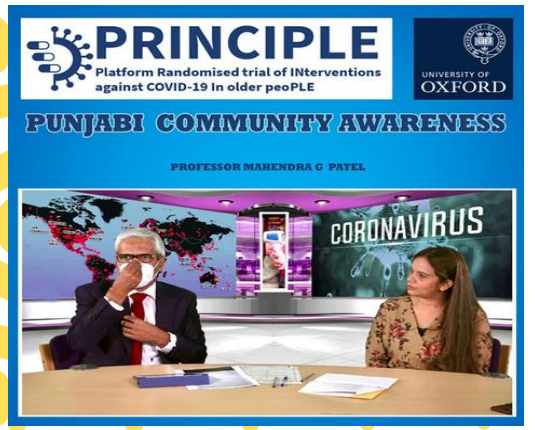
Medical, nursing, pharmacy, AHP, public health HCP and community organisations

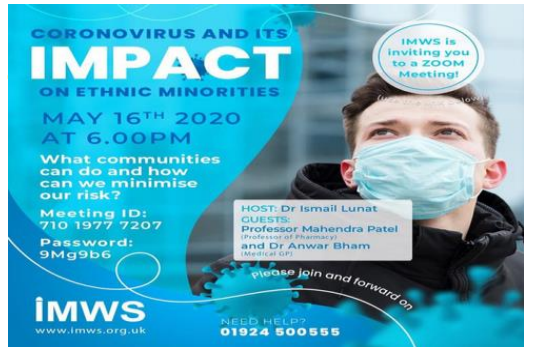
Research networks

NIHR CRNs

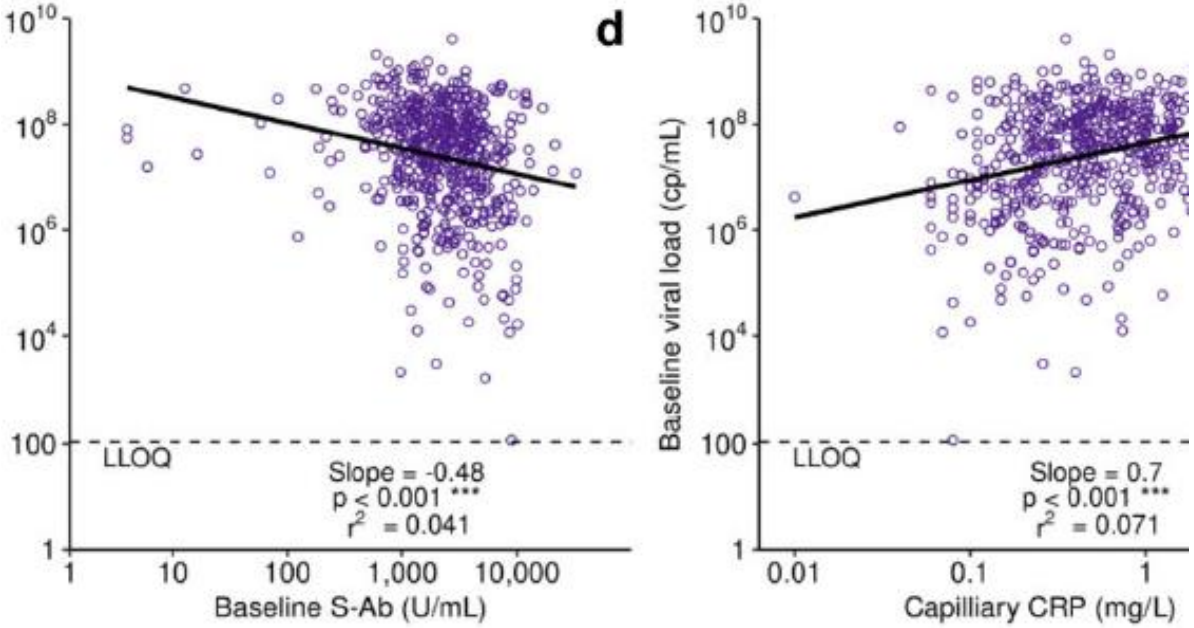
Charity organisations, faith groups, places of worship, local communities

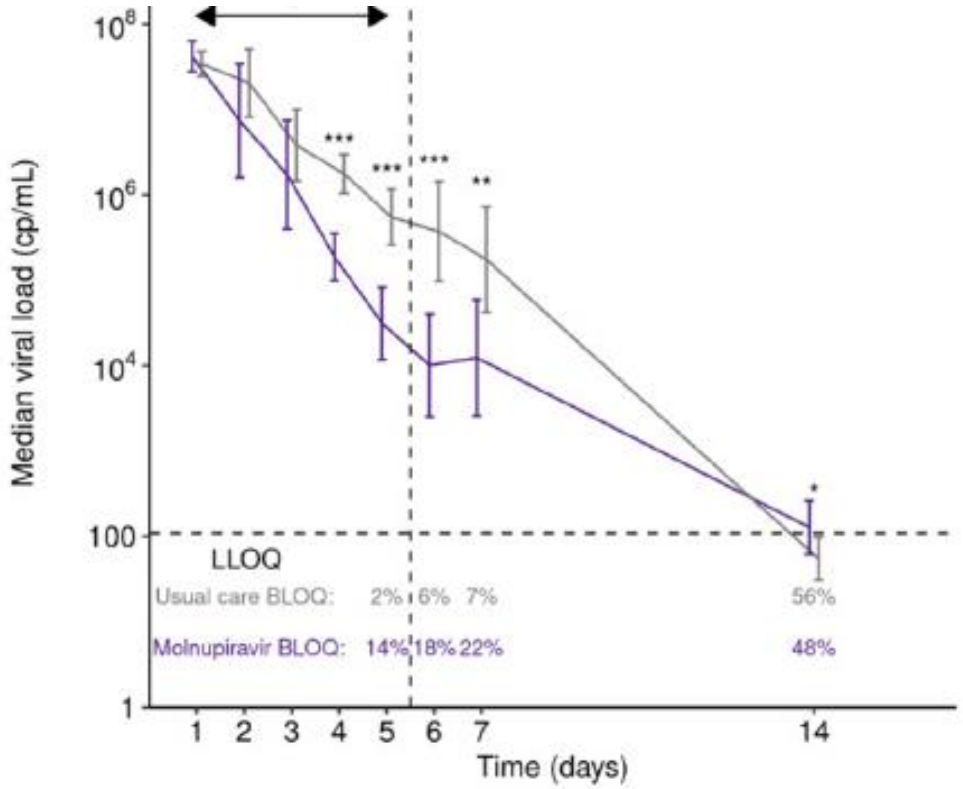
Media





Self sampling

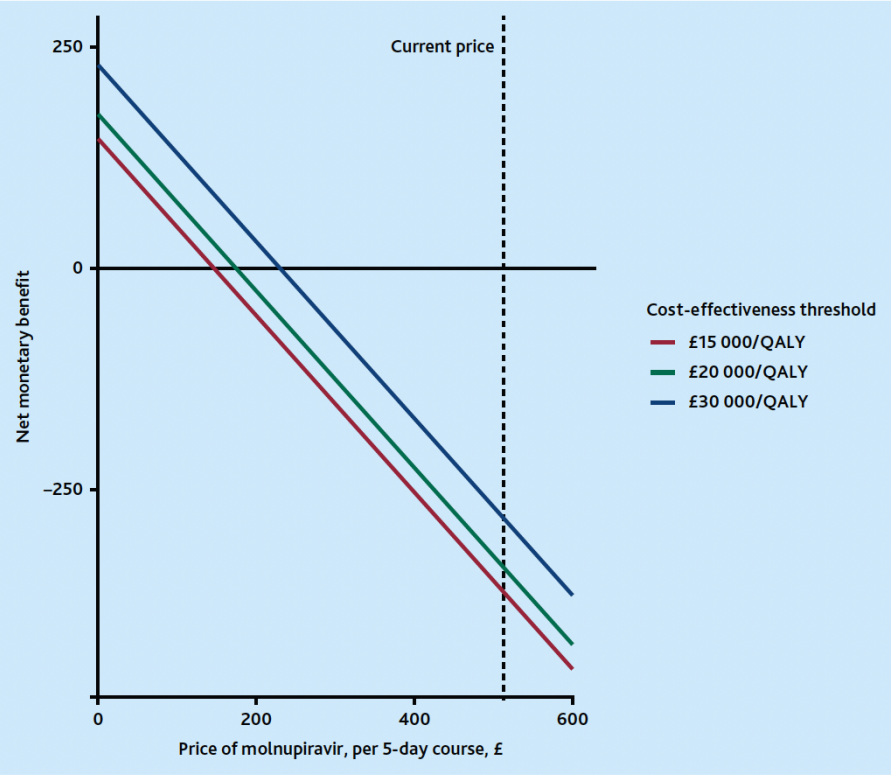


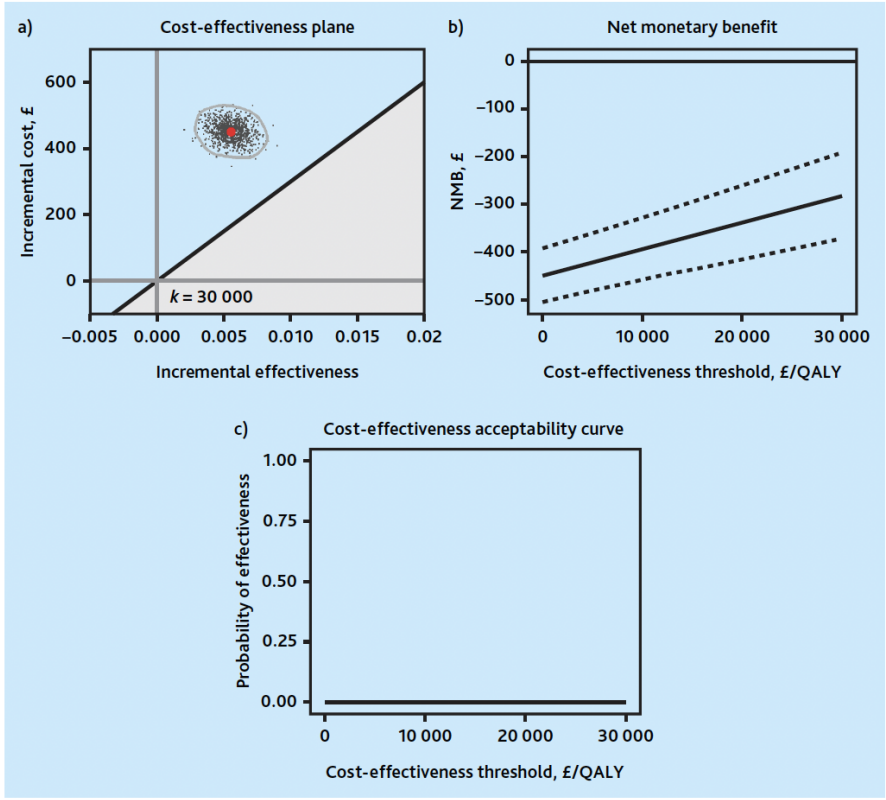


Cost-utility analysis of molnupiravir for high-risk, community-based adults with COVID-19:

the PANORAMIC trial

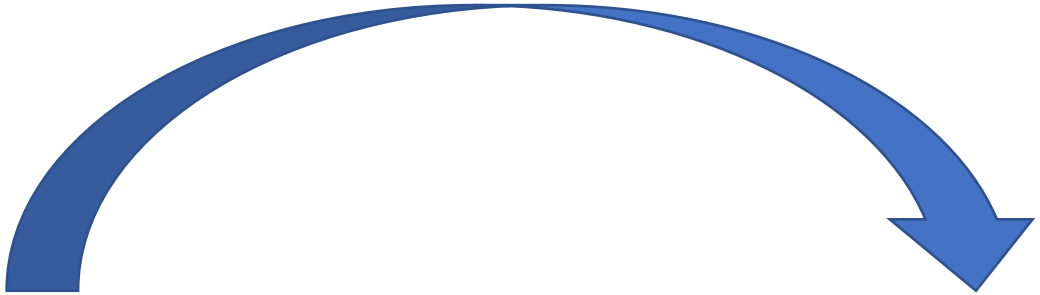
May Ee Png, Victoria Harris, Jenna Grabey, Nigel D Hart, Bhautesh D Jani, Daniel Butler, Andrew Carson-Stevens, Maria Coates, Lucy Cureton, Melissa Dobson, Jienchi Dorward, Philip Evans, Nick Francis, Oghenekome A Gbinigie, Gail Hayward, Jane Holmes, Kerenza Hood, Saye Khoo, Haroon Ahmed, Mark Lown, Micheal McKenna, Sam Mort, Jonathan S Nguyen-Van-Tam, Najib M Rahman, Duncan B Richards, Nicholas PB Thomas, Oliver van Hecke, Richard Hobbs, Paul Little, Ly-Mee Yu, Christopher C Butler and Stavros Petrou on behalf of the PANORAMIC Trial Collaborators





From PANORAMIC to ECRAID Trials - Combined Trial Design

How do we run ECRAID trials in PC?



PANORAMIC
Platform Adaptive trial of NOvel antiviRals for eArly treatMent of COVID-19 In the Community

ecraid
Prime

ECRAID-Prime: At last, an international community based APT that is recruiting and adapting!

- To efficiently and rigorously evaluate candidate therapeutic agents for community treatment of *COVID-19 and COVID-like-illness* in an early phase study with a platform trial architecture

- *Phase 3 evaluation allowed, if phase 2 evaluation is performed in ECRAID-Prime*

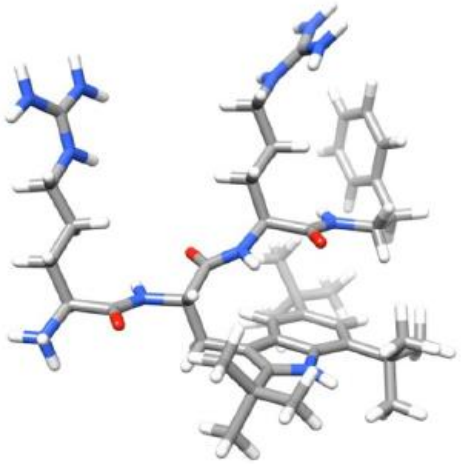
- ECRAID-Prime: key component of pandemic preparedness as a sustainable trial infrastructure

1. Low cost, effective (broad-acting) treatment of respiratory viruses can be highly impactful in community/primary care
   - speed up recovery
   - decrease viral transmission
   - reduce complications
   - reduce long-term consequences
2. Prescribed in PC, or upon self-initiation (OTC) allow for early treatment without the need for testing

Third selected compound: LTX-109

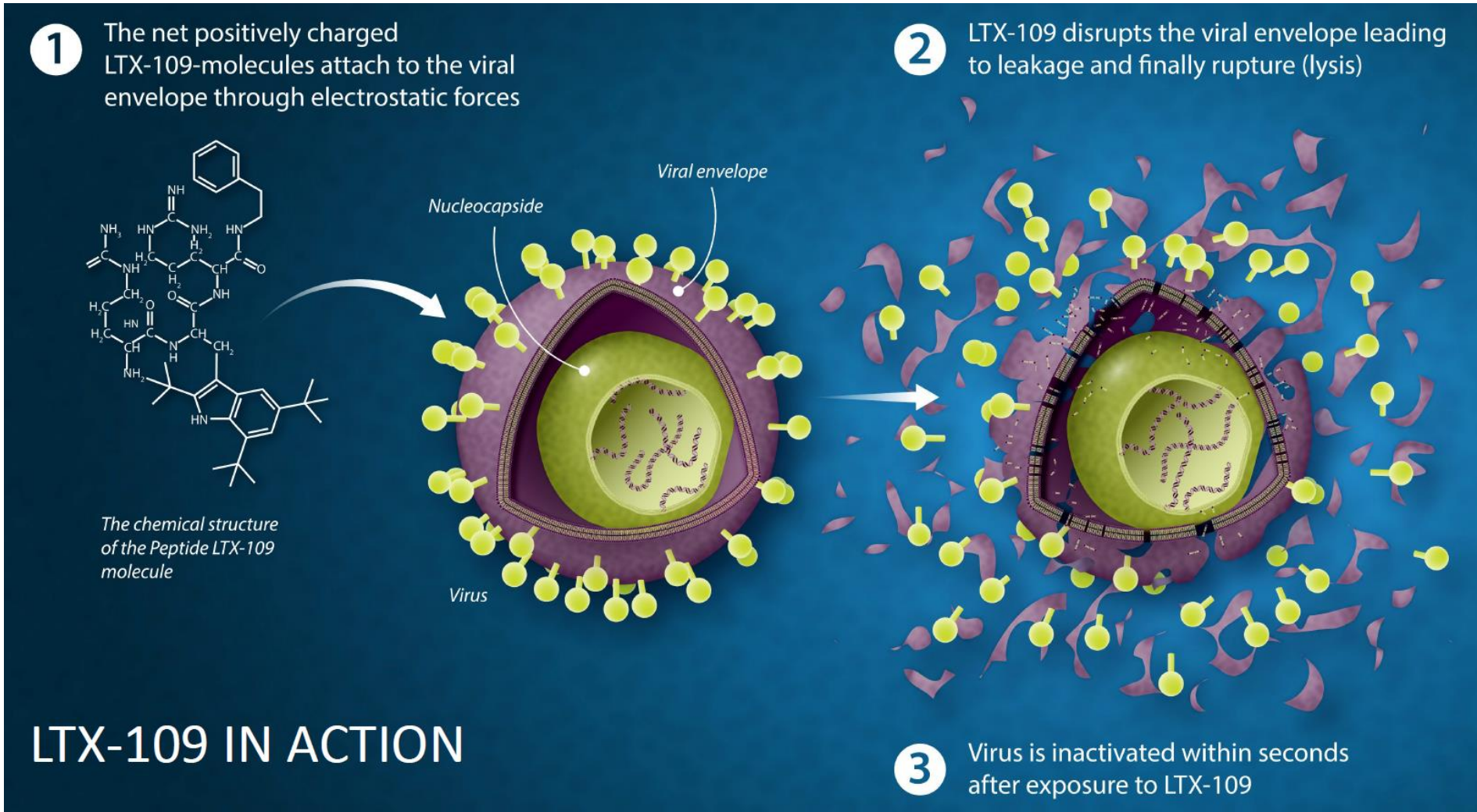
PharmaHoldings

Norway



LTX-109

A patented cationic synthetic peptide based on lactoferrin, a protein found in cow and human milk, targeting both bacterial and viral diseases



First selected compounds: NONS and Saline

- Nitric Oxide Nasal Spray: NO formed during spraying
- Direct virucidal and virus trapping activity
- Topical action, no systemic absorption
- 7 days, 6 times/day, 2 sprays per nostril
- Started ECRAID-Prime with 3 arms:
  - Usual Care
  - Usual Care + NONS
  - Usual Care + Saline

Primary comparisons:

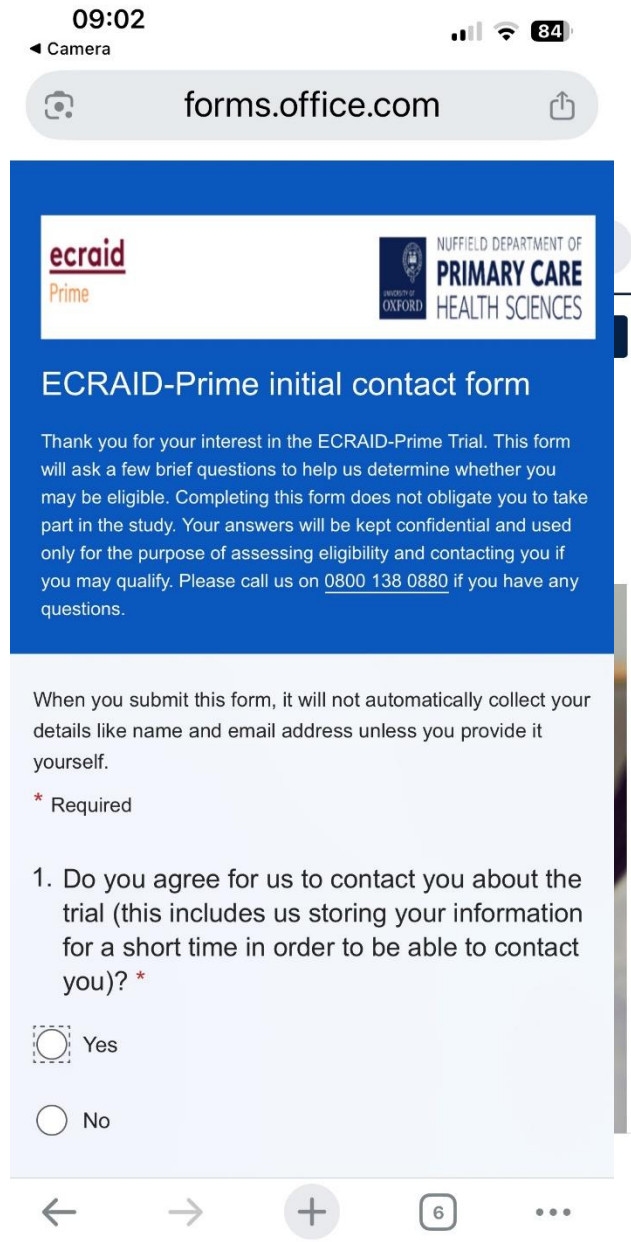
- NONS versus Saline
- Saline versus Usual Care

PRIME takes trials research to the people

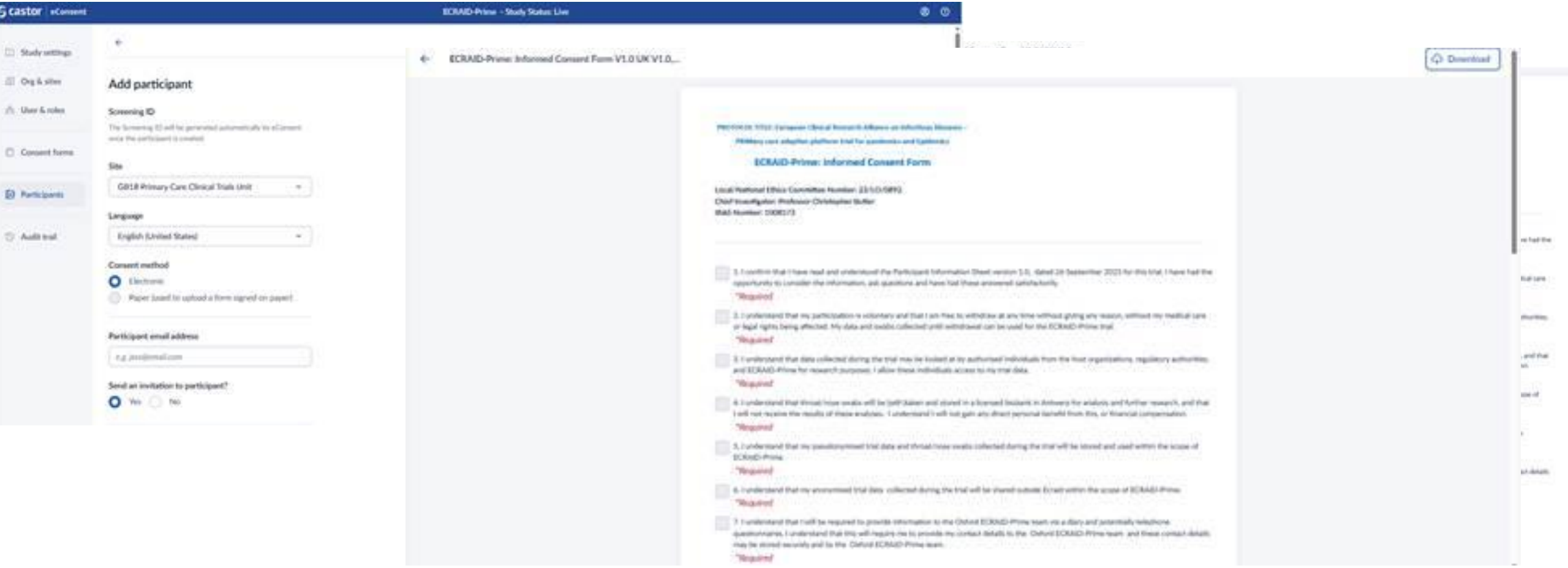
- People find out about us is via the NIHR ‘Be Part of Research’ initiative – they have 600,000 (!) people signed up; WE email mail-out to a random number of those people 1-2 times per week – they get sent the link to our website in the email.
- Also social media posts, physical posters, via word-of-mouth
- Link on our website to an online form: basic screening questions
- Team checks eligibility response, then email the person:
- if non-eligible: thank them and let them know they are not eligible
- If eligible: send them the PIS and link to eConsent form
- Clinician later phones them to complete Consent, check eligibility, randomise, and do baseline data collection
- if they were randomised to IMP, the admin team at CTU dispenses the drug (in pairs), supervised by a pharmacist
- Post the pack to them the same day (swabs, IMP if applicable, return instructions)
- eDiary is triggered for the following 28 days

Easy peezy


Do you have cold or flu-like symptoms?
Join our clinical trial!
We are assessing nasal spray treatments aimed at helping you recover faster and reduce complications
Be part of this important research - sign up today!
Who can participate?
Adults (18+) experiencing symptoms suggestive of a cold, flu or COVID-19 (such as cough, sore throat, runny/blocked nose, fever or headaches)
that started in the last 2-3 days
What is involved?


09:02
Camera
84
forms.office.com
ecraid
Prime
NUFFIELD DEPARTMENT OF
PRIMARY CARE
HEALTH SCIENCES
OXFORD
ECRAID-Prime initial contact form
Thank you for your interest in the ECRAID-Prime Trial. This form will ask a few brief questions to help us determine whether you may be eligible. Completing this form does not obligate you to take part in the study. Your answers will be kept confidential and used only for the purpose of assessing eligibility and contacting you if you may qualify. Please call us on 0800 138 0880 if you have any questions.
When you submit this form, it will not automatically collect your details like name and email address unless you provide it yourself.
* Required
1. Do you agree for us to contact you about the trial (this includes us storing your information for a short time in order to be able to contact you)? *
Yes
No
6

Lemon squeezy…



ECRAID-Prime recruitment numbers

Clear all filters

Country

United Kingdom

Number of patients enrolled cumulative in ECRAID-Prime

69

Patients enrolled

Country	# Participants
United Kingdom	69
Total	**69**

Global action plan for clinical trial ecosystem strengthening

Strengthen local leadership and national support for sustained infrastructure and funding

Enhance involvement and engagement with patients, communities and the public in clinical trial lifecycle

Address barriers to clinical trials in under-represented populations

Enable effective trials through adoption of innovative designs and digital technologies

Accelerate access to fit-for-purpose training packages for clinical trials

Improve coordination and streamlining regulatory and ethics review

Engage clinical practitioners to integrate clinical trials into health systems and practices

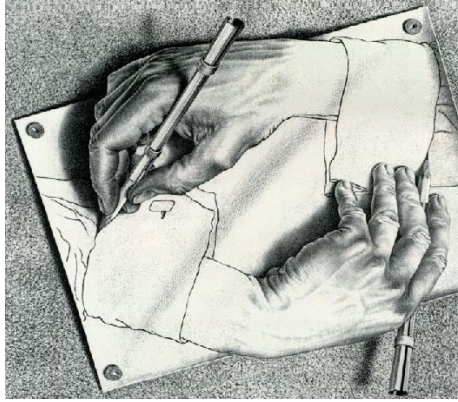
Step up the use of trial registries to improve research transparency

Expand international health research and clinical trial collaboration

Outcome measures to monitor how reforms can accelerate generation of quality evidence

World Health Organization

The funders are happy



GENERAL PROJECT REVIEW CONSOLIDATED REPORT (HE)

COVER PAGE

PROJECT	
Project number:	101046109
Project acronym:	ECRAID-Prime
Project name:	European Clinical Research Alliance on Infectious Diseases - PRIMary care adaptive platform trial for pandemics and Epidemics
Call:	HORIZON-HLTH-2021-CORONA-01
Topic:	HORIZON-HLTH-2021-CORONA-01-02
Type of action:	HORIZON-RIA
Service:	HADEA/A/03
Project starting date:	1/12/2021

"This project contributes to be better prepare for and respond to future epidemics and to secure the supply of medical products. It is an action aiming to ensure better health for all in the EU and to provide a united response to infectious diseases menaces within the EU. The project will also contribute to the European Health Data Space, helping to create a common base for improving health knowledge. Early access to international network of ambulatory clinical sites to perform clinical trials of new medical compounds makes Europe a leading region in clinical development.

Facilitators

- Experience of **EU funded ALIC4E trial** (PREPARE Consortium)
- **Nimble peer-review and funding** from NIHR-UKRI
- Early **dialogue with regulators** (now completely lost for MHRA)
- **National prioritization**: Urgent Public Health status badging
- **Standing infrastructure:** NIHR **Clinical Research Network: GPs and practices in all four UK nations**
- **Independent appraisals of candidate drugs** (Covid Therapeutics Advisory Panel)
- **Digitally enabled awareness** of trial opportunity
- **Access to Summary Care Record** for central eligibility check (eventually)
- **Online eligibility consent**
- **Online/telephone follow up**
- **Trial partner**
- Trial **materials direct to homes**
- **NHS capable of rapid implementation**

Ongoing challenges

- **Skills shortages**; Design, delivery , dissemination intensive and simultaneous
- **DATA protection defeats patient autonomy**: checking eligibility, access to clinical data, even for consenting participants
- **Differing and disproportionate regulations** in UK Devolved Administrations, and other countries (tried to open PRINCIPLE in NL, RoI, Canada, Oz)
- **Primary care under pressure**; sickness, too many patients, shift in care
- **Peer and regulatory review** struggles with
    - PROs vs surrogate measures
    - Open studies
    - Use of non-contemporary controls
    - Bayesian approach e.g. Probability vs statistical significance, Y vs N
- **NHS 111 failure**

Coming soon to a trial near you…

Single application for:

- Identification
- eligibility check
- Consent (if needed)
- Randomisation
- follow up (including data linkage) implementation

Diolch yn fawr

ECRAID-Prime is funded by the European Union's HORIZON 2021 – 2027 Research and Innovation Programme, under Grant Agreement number 101046109.

The PRINCIPLE trial was funded by the UK National Institute for Health and Care Research/United Kingdom Research Innovation (MC_PC_19079)

PANORAMIC was funded by the UK National Institute for Health and Care Research

ALIC4E was part of the PREPARE consortium, funded by the EU FP 7