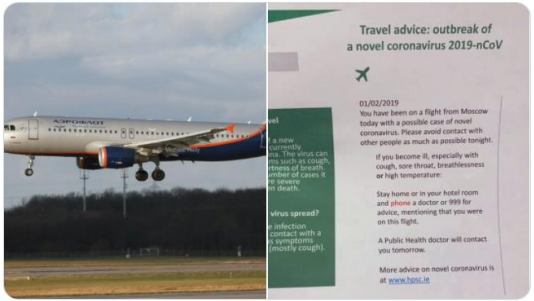
COVID-19 & Clinical Research

Eoghan de Barra
Consultant in Infectious Diseases
Senior Lecturer RCSI

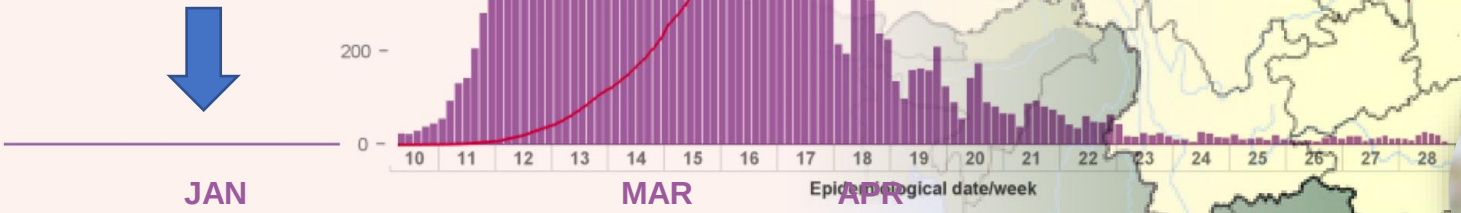
Michael Kelly
@Michaelkelly707

Tonights Aeroflot flight #AFL2590 / #SU2590 from Moscow to Dublin, parked remote on arrival and met by ambulance crews. Pax removed by guys wearing hazmat suits. #Coronovirus suspicions in play



12:14 AM · Feb 2, 2020

hpsc



RCSI
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OF MEDICINE
AND HEALTH
SCIENCES

Remdesivir in adults with severe COVID-19: a randomised, double-blind, placebo-controlled, multicentre trial

CrossMark

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Observational Study of Hydroxychlo
in Hospitalized Patients with Cov

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

A Trial of Lopinavir–Ritor
with Seve

World Health Organization

Health Topics | Countries | Newsroom | Emergencie

D Director-General / Speeches / Detail / WHO Director-General's opening remarks

WHO Director-General's opening remarks at the media briefing on COVID-19 - 25 May 2020

RECOVERY

lomised Evaluation of COVID-19 Therapy

JAMA | Original Investigation

Association of Treatment With Hydroxychlor
With In-Hospital Mortality in Patien

Eli S. Rosenberg, PhD; Elizabeth M. Dufort, MD
Jessica Kumar, DO; James Tesoriero
Jack DeHovitz, MD; Debra

PEN ACCESS

ck for updates

Clinical efficacy of hydroxychloroqu
pneumonia who require oxygen: c
study using routine care data

design:

CONDUCT

ANALYSE

ADAPT

CONDU

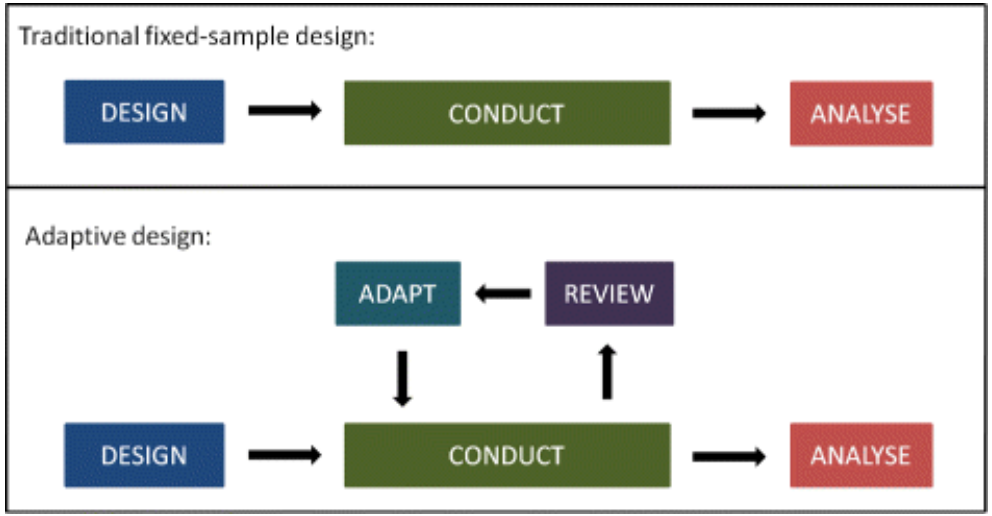
ANALYSE

RECOVERY

Randomised Evaluation of COVID-19 Therapy

UNIVERSITY OF OXFORD

- Protocol draft 10th March 2020
- Dexamethasone result in 98 days
- 11,000 patients enrolled



AIID cohort

UCD School of Medicine

RCSI University of Medicine and Health Sciences

The Mater Hospital

CUH Ospidéal na hOllscoile Corcaigh Cork University Hospital

St. Vincent's University Hospital Elm Park

Beaumont Hospital

Wexford General Hospital

NICB

PRECISE study

St James's Hospital

University Hospital Galway Ospidéal na h-Ollscoile, Gaillimh Galway University Hospitals

Trinity College Dublin Coláiste na Tríonóide, Baile Átha Cliath The University of Dublin

UCC University College Cork, Ireland Coláiste na hOllscoile Corcaigh

REMAP-CAP

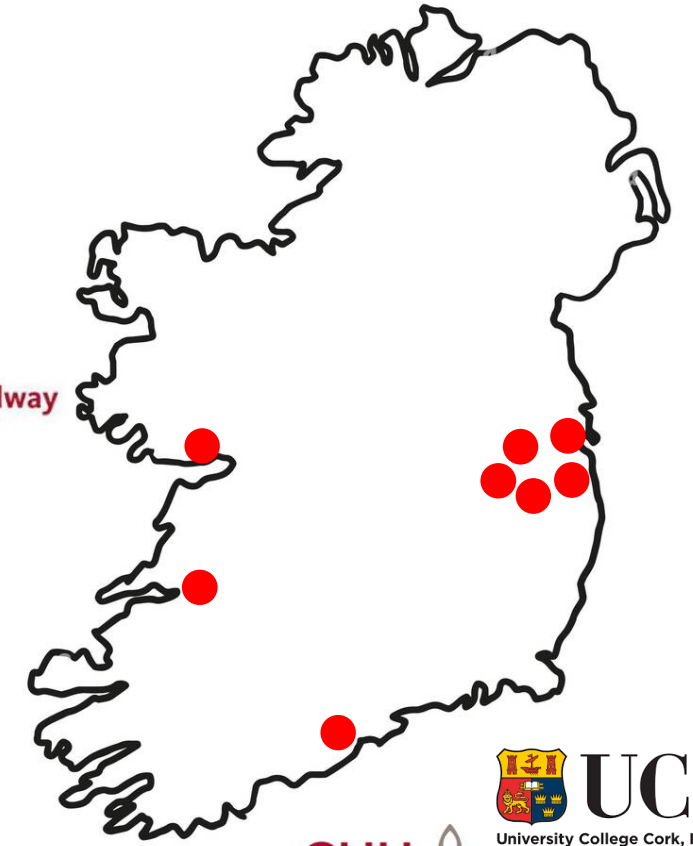
SPRINT SARI

WHO COVID-19 Solidarity Therapeutics Trial

World Health Organization

An Roinn Sláinte
Department of Health

Health Research Board
NCTO
National Clinical Trials Office



BEAUMONT HOSPITAL

THE MATER HOSPITAL

ST JAMES'S HOSPITAL

University Hospital Galway
Ospidéal na h-Ollscoile, Gaillimh
GALWAY UNIVERSITY HOSPITALS

Tallaght University Hospital
Ospidéal Ollscoile Thamhlachta
An Academic Partner of Trinity College Dublin

Ospidéil OL
UL Hospitals

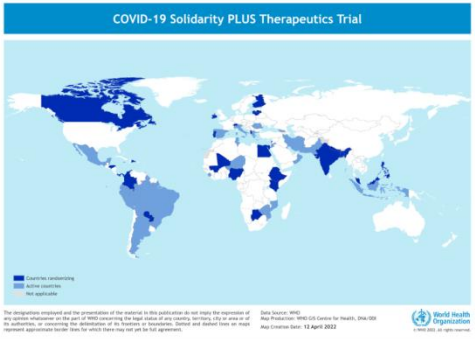
ST. VINCENT'S UNIVERSITY HOSPITAL
Elm Park

UCC
University College Cork, Ireland
Coláiste na hOllscoile Corcaigh

CUH
Ospidéal na hOllscoile Corcaigh
Cork University Hospital


CLINICAL AREA
NO WALK THROUGH
OUTBREAK
NO
VISITING
DO NOT
ENTER
NO ENTRY
CLINICAL AREA
NO WALK THROUGH
DO NOT
ENTER
DO NOT
ENTER
ALERT
FOR INFECTION
CONTROL REASONS
THERE IS CURRENTLY
NO
Face Shield


zoom



Ethics Approvals

Argentina 4 May 2021
Lebanon 4 May 2021
Honduras 5 May 2021
Lithuania 7 May 2021
Bangladesh 11 May 2021
Trinidad and Tobago 12 May 2021
Mali 17 May 2021
Colombia 20 May 2021
Latvia 27 May 2021

Egypt 21 April 2021
Finland 27 April 2021
Brazil 2 June 2021
India 8 June 2021
Ethiopia 14 June 2021

Portugal 5 July 2021
Philippines 7 July 2021
Sierra Leone 14 July 2021
Dominican Republic 20 July 2021

Panama 5 August 2021
Paraguay 5 August 2021
Switzerland 9 August 2021
Canada 11 August 2021
Nigeria 23 August 2021
Botswana 25 August 2021
Albania 26 August 2021

Malaysia 14 September 2021
Nepal 24 September 2021
Pakistan 28 September 2021

Ireland 4 October 2021
Niger 7 October 2021

Iran 28 November 2021

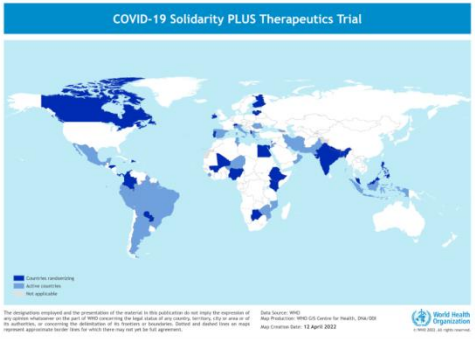
Mozambique 3 December 2021
Kenya 22 December 2021

Georgia 8 January 2022
Tunisia 19 January 2022

2021 2022

April July October

World Health Organization



Regulatory Approvals

Finland 22 April 2021

Lebanon 4 May 2021
Lithuania 7 May 2021

Bangladesh 1 June 2021
Brazil 2 June 2021

Ethiopia 1 July 2021
Latvia 2 July 2021
India 6 July 2021
Honduras 9 July 2021
Portugal 20 July 2021
Dominican Republic 20 July 2021
Mali 26 July 2021
Philippines 28 July 2021
Sierra Leone 28 July 2021

Panama 5 August 2021
Canada 6 August 2021
Argentina 12 August 2021
Trinidad and Tobago 18 August 2021
Egypt 29 August 2021

Botswana 6 September 2021
Paraguay 13 September 2021
Switzerland 17 September 2021
Ireland 23 September 2021
Malaysia 24 September 2021
Albania 28 September 2021

Nepal 11 October 2021
Nigeria 26 October 2021

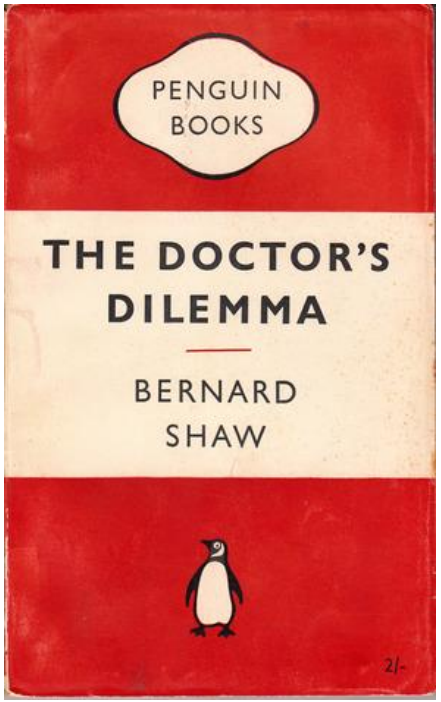
Colombia 14 January 2022
Kenya 13 January 2022
Mozambique 19 January 2022
Niger 27 January 2022

Tunisia 18 March 2022

April | July | Oct | Ja | 2021 | 2022

World Health Organization

Non-Pharmacological



Solidarity

Solidarity Plus

vaccine

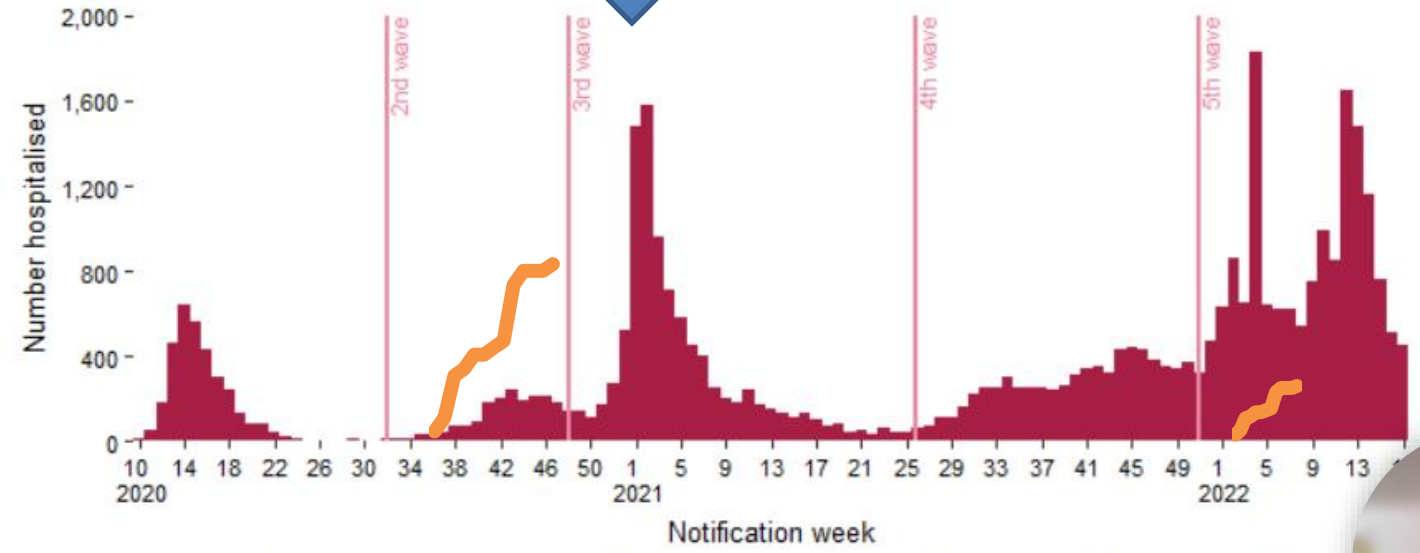
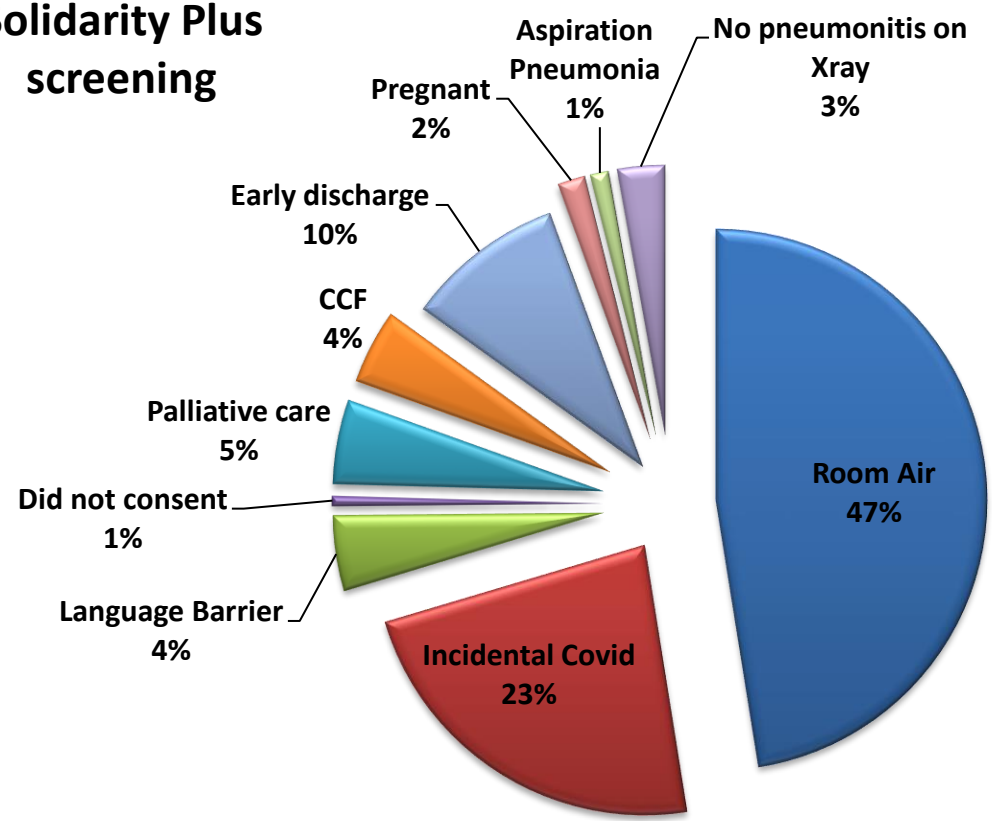


Figure 5: Hospitalisations among confirmed COVID-19 cases notified on CIDR in Ireland between week 10, 202 week 17, 2022

Beaumont recruitment

Solidarity Plus screening



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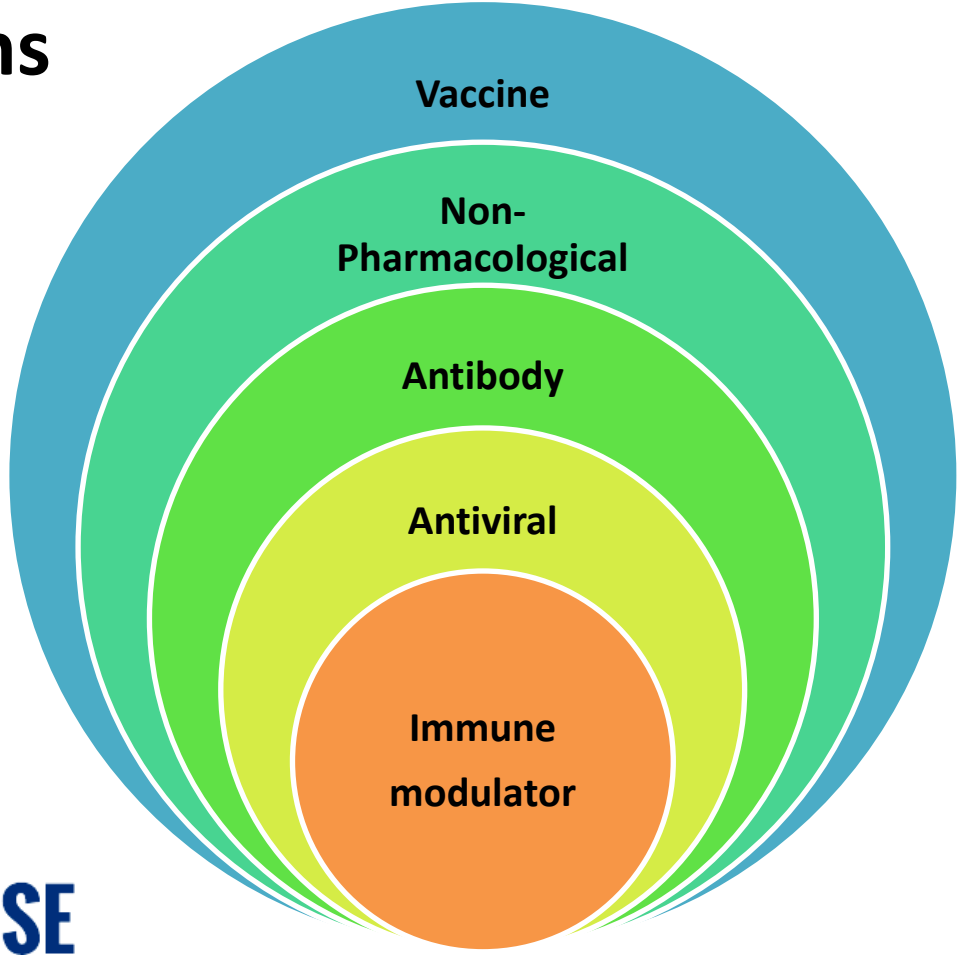
RCSI UNIVERSITY OF MEDICINE AND HEALTH SCIENCES

n=180

Interventions



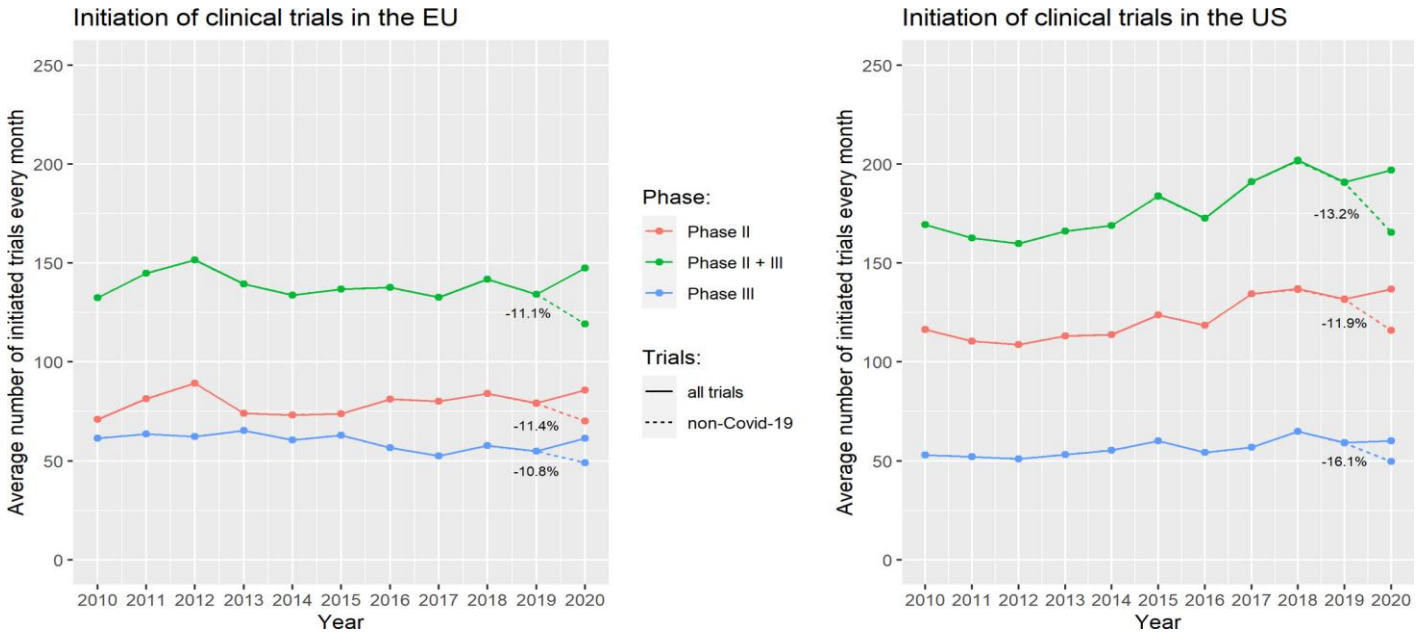
Exposure

Incubation

Disease

Death

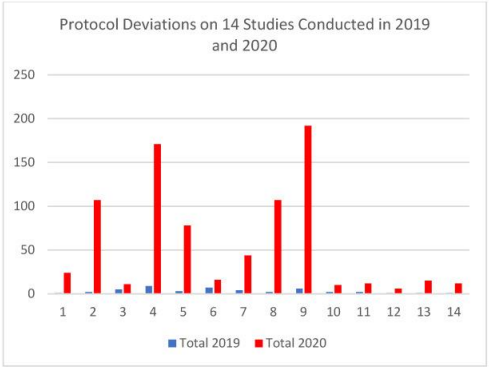
The Impact of COVID-19 on the Initiation of Clinical Trials in Europe and the United States



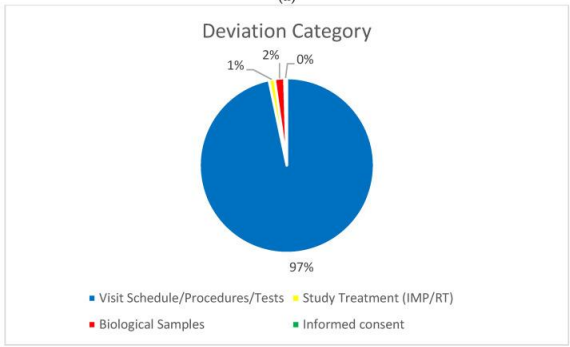
Clin Pharma and Therapeutics, Volume: 111, Issue: 5, Pages: 1093-1102,
First published: 28 January 2022, DOI: (10.1002/cpt.2534)

The SARS-CoV-2 Pandemic and Cancer Trials Ireland: Impact, Resolution and Legacy

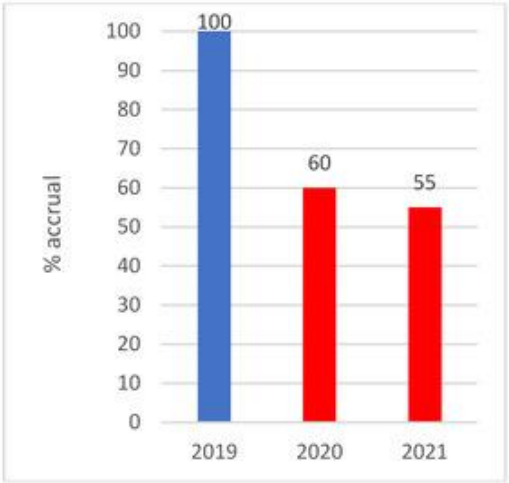
Cancers **2022**, *14*(9), 2247;



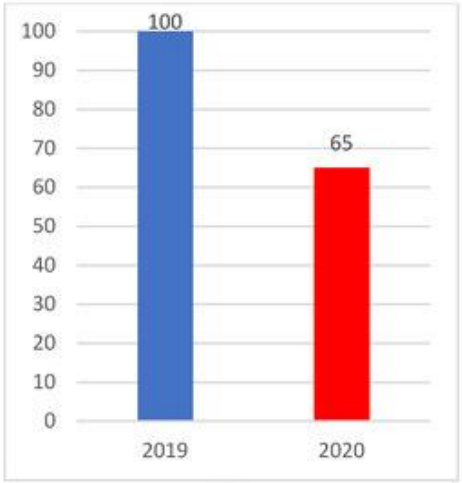
(a)



(b)



(A)



(B)

Makeshift intensive-care units were set up to deal with the influx of people with COVID-19.

THE COVID PANDEMIC'S LINGERING IMPACT ON CLINICAL TRIALS

The pandemic could continue to affect studies focused on other diseases.

By Heidi Ledford

"It's like time stopped," says Emilia Bagiella, a clinical-trial statistician at the Icahn School of Medicine at Mount Sinai in New York City.

When Bagiella left work one day in early March 2020, she hadn't fully grasped how at the US National Cancer Institute (NCI) in Bethesda, Maryland. "But when you lose time, you lose time. It's going to delay results."

Enrolment paused

For many regions in the United States, the biggest blows to clinical research came between March and May 2020. Trial enrolment plum-

often focus on establishing the safety of a new medicine — were more likely to pause enrolment than were larger trials designed to demonstrate how well a therapy works against disease, Mooney found when analysing data from two large NCI study networks.

The pandemic also took a bite out of new study launches: one analysis, which examined more than 62,000 trials that started before and during the pandemic, found that the number of studies initiated in the United States from February to May last year was only 57% of what would have been expected had the pandemic not occurred (J. M. Unger and H. Xiao *Trials* **22**, 260; 2021). The impact outside the United States was smaller, with 77% of the expected number of new studies launching.

Flexible arrangements

Funders and the US Food and Drug Administration responded with a series of guidelines on how clinical trials could be altered to allow them to continue during the public-health emergency. Investigators were allowed to deliver some experimental medicines to participants' homes, and participants could use online platforms to consent to taking part in a clinical trial. Investigators lengthened the time between doctors' visits for some study participants and performed more of those visits remotely. And participants were sometimes allowed to visit their local doctor for basic procedures and assessments, rather than travelling to a central study site.

Charles Blanke, an oncologist at Oregon Health & Science University in Portland, credits those policies with getting SWOG's enrolment back up to near-normal levels, and keeping it there even during the country's biggest COVID-19 surge, in early 2021. "We truly believe this made a gigantic difference," says Blanke. "And we and our patients are desperate to keep it in place."

But that added flexibility could have come at

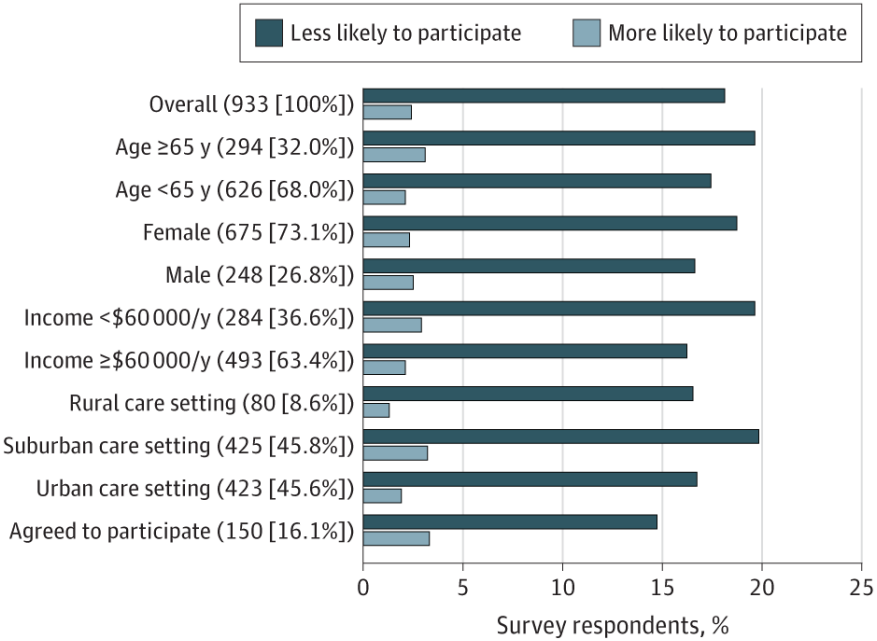
Nature | Vol 595 | 15 July 2021 | 341

- **Funding pattern**
- **Screening and enrolment**
- **Local procedures**
- **Biobanks**
- **Patient willingness**

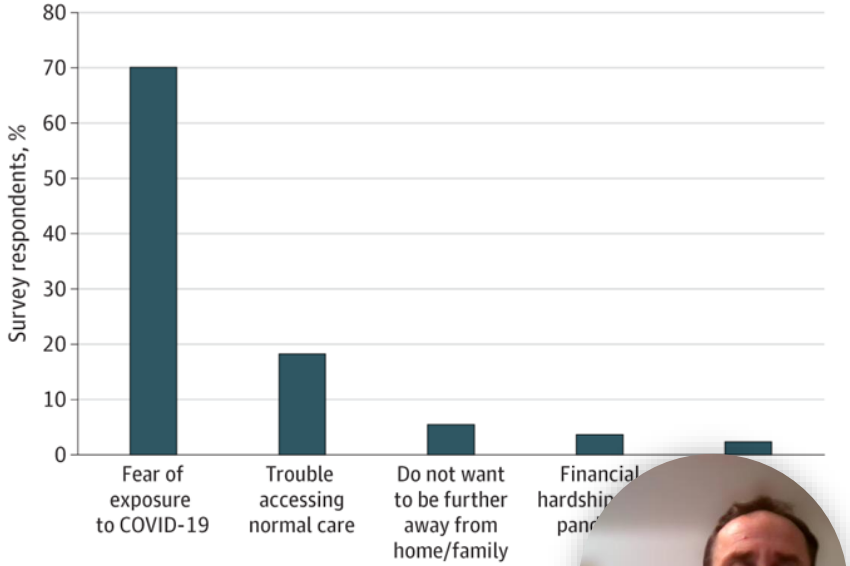
JAMA Network

From: **Association of the COVID-19 Outbreak With Patient Willingness to Enroll in Cancer Clinical Trials**

JAMA Oncol. 2021;7(1):131-132. doi:10.1001/jamaoncol.2020.5748



Reasons for Reduced Likelihood of Participating in Clinical Trials



Beyond the lessons learned from the COVID-19 pandemic: opportunities to optimize clinical trial implementation in oncology

Table 1. Obstacles in clinical research and their changes during the pandemic

Obstacles in clinical trial research before the SARS-CoV-2 pandemic	Deterioration during the SARS-CoV-2 pandemic
Excessive burden of administrative tasks	More difficult to accommodate with restrictions in clinical and research activities
Organizational, resource, and staff limitations to accommodate a growing number of novel-design clinical trials	Pandemic and quarantine policies significantly affected research staff availability and their burnout levels; significant reduction in clinical trial performance; inability to rapidly adapt to new research and clinical conditions
Excessive time in research meetings (local visits, audits, and data monitoring events)	Extremely difficult to accommodate with lockdown policies and reduced staff available
Length and complexity of informed consent	Patient empowerment reduced due to the distancing between investigators, patients, and caregivers; more reconsents needed
Patient difficulties to access research centers (living far, elderly, comorbidities, economic conditions)	Aggravated following lockdown measures and quarantine policies
Disproportionate/unnecessary number of time-demanding clinical trial appointments for patients	More difficult to maintain following lockdown measures and changes in hospital-care and research pathways
Restrictive eligibility criteria and under-representation of real-world population	Increased difficulty to keep enrollment goals with many patients reducing their hospital visits; low representativeness of patients at a higher risk of death from COVID-19 (e.g. elderly; patients with cancer or heart dysfunction) in vaccine pivotal trials.
Weak correlation between some surrogate endpoints and clinical meaningful outcomes	Unprecedent short landmarks in time for (COVID-19) vaccines efficacy considering the global urgency.
Significant dropout rates from clinical trials due to excessive administrative load, visits, or uncertainties with treatment efficacy and toxicity	Patients refraining from visiting cancer centers for treatments or follow-ups

COVID-19, coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

European Society Medical Oncology Open, Vol. 6, Issue 5, 2021

Table 2. Pathways for optimizing oncology clinical trial implementation based on the coronavirus disease 2019 (COVID-19) pandemic experience as a catalyst

Pathways
Reduce administrative load, optimize performance of clinical trials
• Reduce redundant documentation or procedures in strict compliance with good research practices
• Revisit burdensome internal procedures of research sponsors
• Reduce on-site and increase remote visits for research staff meetings, audits, and monitoring
• Increase the use of validated artificial intelligence tools and text-mining technologies for data collection and monitoring
• Develop organizational flexibility for novel research methodologies and technologies
• Optimize research cooperation with national and international networks expanding clinical trial access to more centers and patients
• Develop shared databases of resources and operational information related to investigators and logistics of trial implementation
Improve informed consent
• Simplify informed consent (IC) and reconsent documents using readability methodologies
• Promote use of remote electronic consent (eConsent), by either videoconference (oral) or procedures for e-signatures. Facilitate face-to-face meetings when easy to schedule or requested by patients
• Develop specific eConsent guidelines to ensure patient empowerment
• Engage patient representatives in the development of IC and eConsent documents
• Increase patient literacy in clinical trial research, improving sources of e-information and web-based networking
Promote telemedicine and decentralize point of care
• Expand use of telemedicine in oncology clinical trials
• Provide research, training, and validate guidelines for telemedicine and remote procedures in clinical trials
• Develop and use validated electronic patient reported outcomes and tools (quality of life scales; wearable devices; phone apps; online reports) with continuous data collection from patients, particularly in the adjuvant and curative trial settings
• Involve regional centers close to patient residency as co-research institutions, allocating proper training and incentives
• Allow examinations (clinical; laboratory; radiology) to be performed close to patient home with easy assessment by the main research institution
• Deliver oral medicines to patient homes, with accountability, monitoring, compliance and follow-up procedures in place
Optimize clinical trial impact: trial population, endpoints, and validation
• Use broader inclusion criteria in trials in select clinical circumstances, simulating real-world settings
• Further develop novel trial designs, based on molecular enrichment, master protocols, and pragmatic control arms
• Promote generation of real-world evidence from well-designed, high-quality complementary RWD studies
• When surrogate endpoints are used in trials in areas of unmet need, validate any benefit from new drugs with the impact on clinically meaningful patient-centered endpoints in trials supplemented by RWD, preferably on overall survival and/or quality of life
• Build consensus on significant methodology and quality requirements of RWD, along with development and validation of artificial intelligence tools linked to clinical evaluation of therapeutics and biomarkers

RWD, real-world data.

European Society Medical Oncology Open, Vol. 6, Issue 5, 2021

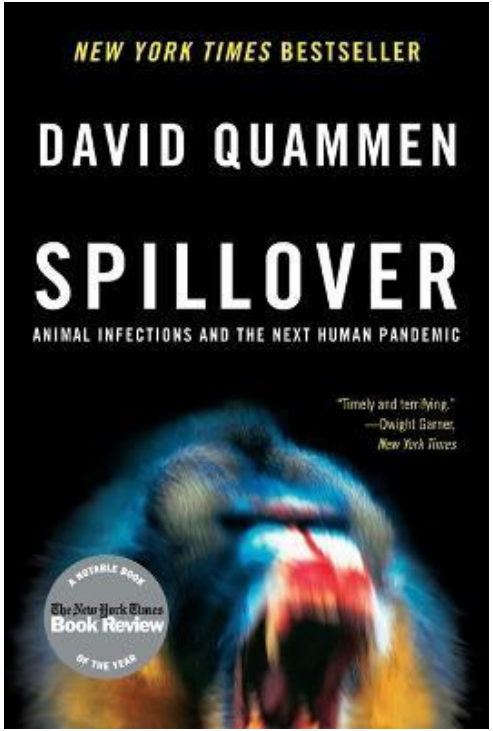
Coronavirus COVID-19 Public Health Advice

The impact of the COVID-19 pandemic and the societal restrictions on the health and wellbeing of the population, on our staff and on health service capacity and delivery:

A plan for healthcare and population health recovery

Champion
Partner
Enable
Demonstrate

V 2: May 2021



World Health Organization

The Lancet Commission on lessons for the future from the COVID-19 pandemic

The Lancet Comissions| Vol 400, Issue 10359, October 08, 2022

IRNM
Irish Research Nurses & Midwives

RCSI UNIVERSITY OF MEDICINE AND HEALTH SCIENCES

BEAUMONT HOSPITAL

- Speed & flexibility
- Infrastructure
- Networks
- Patient and public engagement