Monitoring clinical trials during the COVID-19 pandemic

A review of a paper submitted to *Trials* looking at innovative ways of setting up and monitoring trials during the pandemic

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UKCRC Registered Clinical Trials Units

Monitoring Advances Including Consent; Learning from COVID-19 Trials and Other Trials Running in UKCRC Registered Clinical Trials Units During the COVID-19 Pandemic

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Andrea Corkhill, Southampton Clinical Trials Unit

https://www.researchsquare.com/article/rs-43727/v1

UKCRC Registered Clinical Trials Units

Purpose of Monitoring

- Protect the rights and well-being of the participants
- To ensure the trial data are accurate, complete and verifiable
- To confirm the trial is being run in compliance with the currently approved protocol
- To confirm the trial is in compliance with good clinical practice and the relevant regulatory requirements

ICH E6 (R2) 5.18

"The sponsor should ensure that the trials are adequately monitored. The sponsor should determine the appropriate nature and extent of monitoring….In general there is a need for on-site monitoring, before, during and after the trial; however in exceptional circumstances the sponsor may determining that central monitoring in conjunction with procedures such as investigator's training and meetings, and extensive written guidance can assure appropriate conduct of the trial…The flexibility in the extent and nature of monitoring….is intended to permit varied approaches that improve the effectiveness and efficiency of monitoring".

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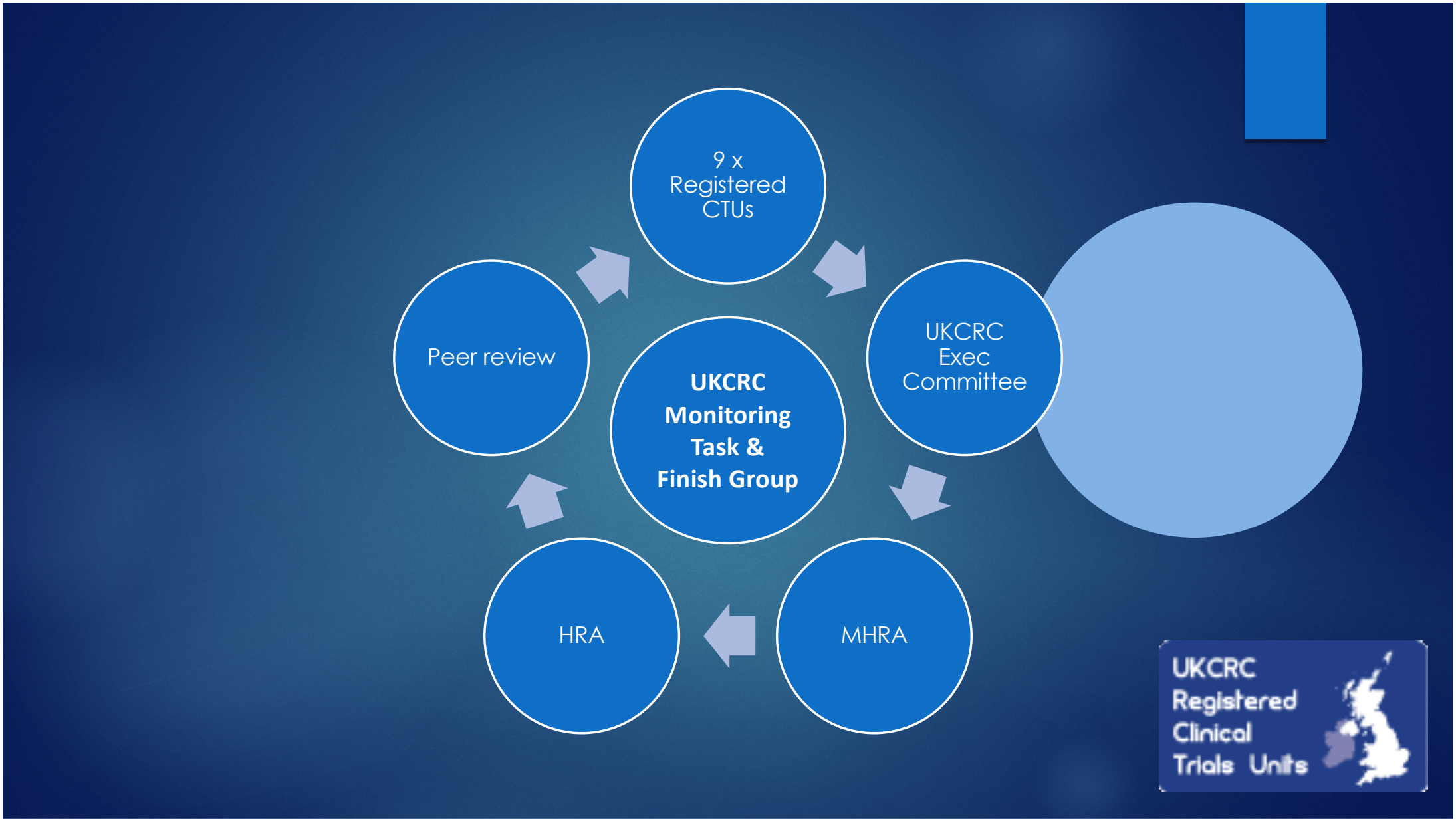
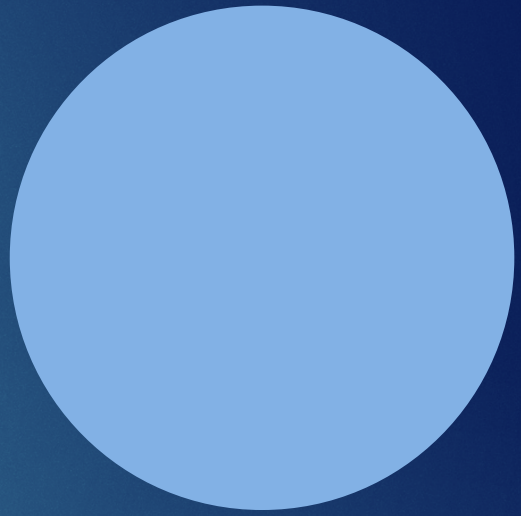

9 x Registered CTUs
UKCRC Exec Committee
MHRA
HRA
Peer review
UKCRC Monitoring Task & Finish Group
UKCRC Registered Clinical Trials Units

Topics for today

- Speed of trial development
- Data minimisation
- Site set-up
- Consent
- On-site; remote; central monitoring
- Impact on non-COVID portfolio



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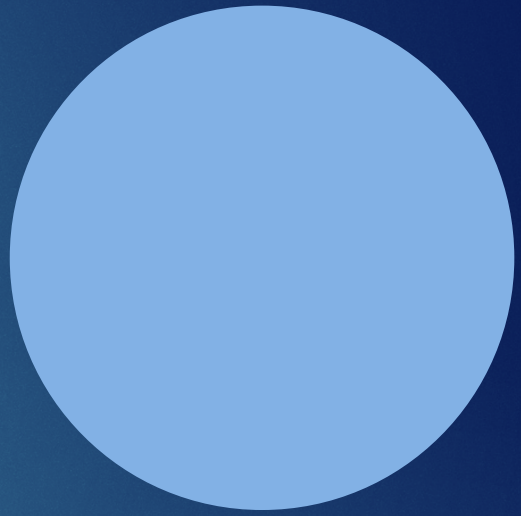

Data minimisation

- Non-essential data collection an established known risk
- COVID Trials set up knowing that on-site monitoring not an option
- Still require assurance that data collected are complete & accurate
- Focus on safety data, primary outcome data, other CDIs
- Mitigation to reduce paper burden
- Consistent with Data Protection Act 2018
- Sponsor oversight is critical

Reduced burden on sites
Reduced burden on trial team
Reduced data points to monitor
Faster database development
Efficient statistical analysis

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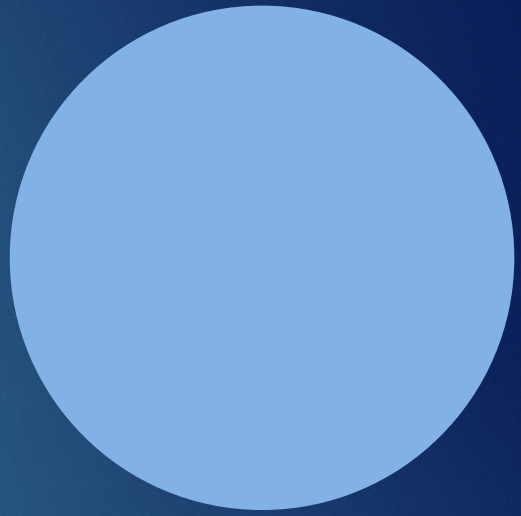

Site set-up

Site Initiation Visits

- Video conference
- Live presentation
- Clinical & Trial Management input
- Q&A
- Multiple sites in one session
- Clear housekeeping

Site Oversight

- Online training resources
- Self certification
- Central record on training
- Staff delegation
- PI oversight
- Central oversight
- Website

Contracts & Approvals

- Urgent Public Health trials
- Electronic transfer of documents
- Pre-signed mNCA

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Consent

Evidence	Strategies	Challenges	Set up
• Procedure • Documentation • Consistency • Audit trail	• eConsent • Video • Phone • Photos • Scripts	• Technology • Witness • Data protection • Devolved Nations • ICU-specific	• Approvals • Monitoring • Deviations

ongoing process

- Speed of trial development
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Risk & monitoring

What could go wrong?

What would the impact be if it did go wrong?

What can we do to stop it going wrong?

Is it worth the risk?

On-site Monitoring

- At investigator site
- Input and availability from investigator sites.

Remote Monitoring

- At CTU or sponsor office
- Input from investigator sites
- Recreate elements of an on-site visit

Central Monitoring

- At CTU
- In-built trial management activities
- No/limited input from investigator sites

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Central Monitoring

- At co-ordinating centre
- In-built trial management activities
- No/limited input from investigator sites

Central & remote monitoring

- What, who, where, when, how…and why
- Use information & technology available
- GDPR
- How much?
- How often?
- In what format?
- How is this recorded?
- Deviation, file note, amended monitoring plan

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On-[illegible]itoring

- At investiga[illegible]
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Rem[illegible]itoring

- At CTU
- Input fr[illegible]
- Recr[illegible]ments of an on-si[illegible]

Central Monitoring

- At co-ordinating centre
- In-built trial management activities
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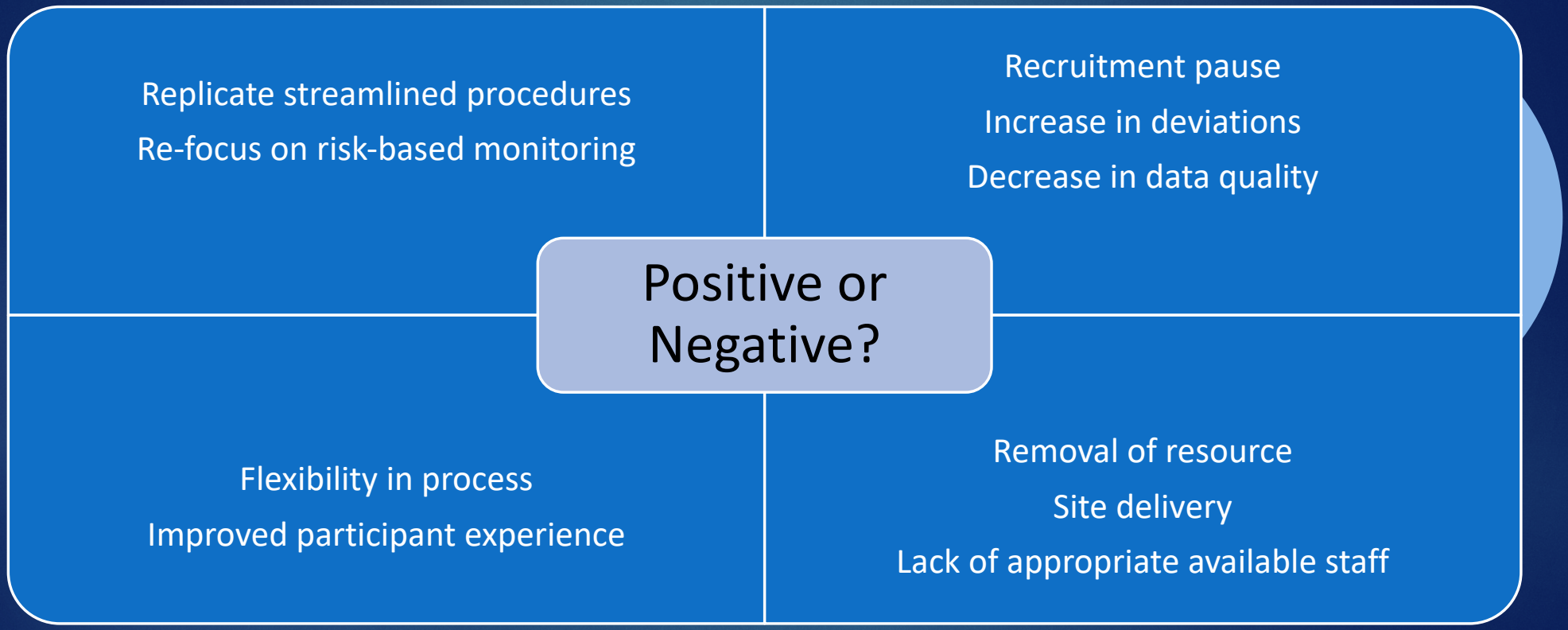
Non-COVID portfolio monitoring

Keep staff safe	Decrease site burden	Adapt RA & MP	Mixed methods	HRA support
• Non-clinical staff outside clinical setting	• Remove workload • Retain support	• Acceptance of risk • Triggers	• Can we do it differently? • Site involvement	• Amendments

COVID Trials: Minimise data requirements

Impact on non-COVID portfolio



Monitoring challenges

- Resource
- Direct access to site EHR
- Provision of pseudonymised source documents
- Use of a secure VC platform and enable viewing of EHRs
- Monitoring by phone
- Questionnaires, site QC checklists with CTU follow up
- Data protection considerations
- Support

What can we take forwards?

- Strategies for trial set up and management during future pandemics
- Permanent strategies
- Home working
- SIV options
- eConsent & eTMFs
- Improved participant experience
- Re-thinking the Risk Assessment & risk-based monitoring

Thank-you

This work was supported and endorsed by the
UK Clinical Research Collaboration Registered Clinical Trials Unit Network

Thank you to RECOVERY-RS and the many other unnamed trials, trial teams, site staff and their participants who helped to make this review possible

Discussion ideas

- Would anyone like to summarise their experience of remote monitoring using video call or direct access to records?
- Has anyone looked at the volume of data collected in 2020 trials and if so could you comment?
- "In the future, centralised monitoring with a small amount of remote monitoring will be sufficient for many trials" Do you agree? If not, could you explain the reasons?
- "In the future, econsent will be the norm" Do you agree? If not what do you think the obstacles are?
- Covid has initiated a big shift in monitoring. How much of this shift can we retain going forward? How much do we want to retain?