CRUK Clinical Research Committee Clinical Trials – Pandemic Recovery Update Oct 2021

Executive Summary (figures representative from September 2021)

- 46% of CRUK funded or endorsed trials open to recruitment in March 2020 were halted at some point during the COVID-19 pandemic (largely in March-April 2020). Median time to re-start was 105 days (ranging from 45-518 days) with 77% of paused trials reopening between May - July 2020. 5 out of 40 trials halted are yet to re-start.
- For trials that have restarted the majority have 80-90% of sites re-opened. Relative to projections before March 2020 - roughly half of the trials report a significant reduction (i.e. >20% less) to recruitment rates. Recruitment rates are at approximately 68.5% of pre-pandemic levels.
- 69% of trials have set-up less than 40% of their planned sites since the start of the pandemic.
- Limited resource at sites and reduced patient availability are the most reported reasons that have impacted trial progress over the last 12 months and are anticipated to be the key challenges that will impede progress over the next 12 months.
- Estimating the financial impact of the COVID-19 pandemic on CRUK's clinical research budget is difficult but is currently forecast to be £1-4M between 2022-2027.

Background

Following on from the comprehensive CRUK Clinical Trial Portfolio Review in July 2020, in 2021 we have continued to monitor (via a lighter touch data collection) the impact of the Covid-19 pandemic on our Clinical Research Committee portfolio.

Data Collection

Analysis included all active grants funded or endorsed by CRUK's Clinical Research Committee that were in set up, recruiting and follow-up on 15th September 2021. 141 awards were included in the analysis, this includes 102 funded Clinical Trial Awards, 30 endorsed Clinical Trial Awards, 2 Biomarker Project Awards, 6 Experimental Awards, 4 Sample Collection Awards and 1 Science Committee Programme Award. Data was collected from 3rd August 2021 – 15th September 2021 and was generally provided by the Clinical Trials Unit responsible for managing the trial.

It is proposed this exercise is undertaken again in Spring 2022.

Data Analysis - figures representative from September 2021

Impact on Trials in set-up in March 2020

17 trials included in the analysis were in set-up in March 2020 - activity was not paused or halted for any of these trials. Whilst it is assumed that set-up was delayed, full impact on trials in set-up is currently unclear, this will be reviewed as part of CRUKs Annual Trials Set-Up analysis next year. Some trials in set up detailed challenges around sites having limited resource to set up of new studies with priority being given to re-start trials that were already open or to COVID-19 research.

Impact Trials open to recruitment in March 2020

88 trials included in the analysis were open to recruitment in March 2020. 40 trials halted recruitment due to the pandemic and 40 trials did not halt recruitment due to the pandemic. 8 trials that were open to recruitment in March 2020 closed for reasons not attributable to the pandemic.

Trials that were halted (n=40)

46% of CRUK funded or endorsed trials open to recruitment in March 2020 were halted at some point during the COVID-19 pandemic (largely in March-April 2020). Median time to re-start was 105 days (ranging from 45-518 days), with 77% of paused trials reopening between May - July 2020. 5 trials are yet to re-start.

For sites that were set up pre-pandemic we see a heavy weighting towards the majority of trials having 80-100% of site's re-opened (Figure 8) – however since re-opening, two thirds of the trials have set up less than 40% of their planned sites (Figure 7).

In terms of number of re-opened sites that are actively recruiting we see a mixed picture - 28% of trials have less than 50% of sites actively recruiting, 44% of trials have between 50-89% of sites actively recruiting, and 28% of trials have 100% of sites actively recruiting (Figure 9). Relative to projections before March 2020 - roughly half of the trials report a significant reduction (i.e. >20% less) to the recruitment rate seen since re-starting recruitment (Figure 10) and just over half of the trials are recruiting at 75-100% of pre-pandemic recruitment rates since reopening (Figure 11). For the trials that were halted, recruitment rates are at approximately 70% of pre-pandemic levels.

Trials that were not halted (n=40)

70% of the trials have set up less than 40% of their planned sites since the start of the pandemic (Figure 13). For sites that are open to recruitment, 16% of trials have less than 50% of sites actively recruiting, 42% of trials have between 50-89% of sites actively recruiting, and 42% of trials have between 90-100% of sites actively recruiting (the majority of these are at 100%) (Figure 14).

Relative to projections pre-pandemic, just over half of the trials report a significant reduction (i.e. >20% less) to the recruitment rate between March 2020 – March 2021 (Figure 15), with approximately two thirds of trials recruiting at 75-100% of pre-pandemic recruitment rates since March 2021 (Figure 16). For the trials that were not halted, recruitment rates are at approximately 66% of pre-pandemic levels.

Impact Trials in follow-up/analysis in March 2020

35 trials included in the analysis were in follow up/analysis in March 2020. Activity was not paused or halted for any of these trials, however issues were highlighted around delays to in person assessments and reduced capacity at sites to provide case report forms/respond to data queries. The full impact to trial follow-up is unclear.

Financial Impact

Current projected submissions for costed extensions to CRUK 2022-2027 total £4,262,348. However, this includes extensions to trials for between 36 -111 months which is therefore unlikely to be fully attributable to delays caused by the pandemic. A number of trials anticipate submitting a costed extension of 24 month or less between now and 2027, totalling £991,400. Realistically, estimating the exact cost of the pandemic to CRUK's clinical trials portfolio will be a challenge and is likely to be somewhere between these two figures, and may be subject to further change as the recovery of clinical research is very much on-going.

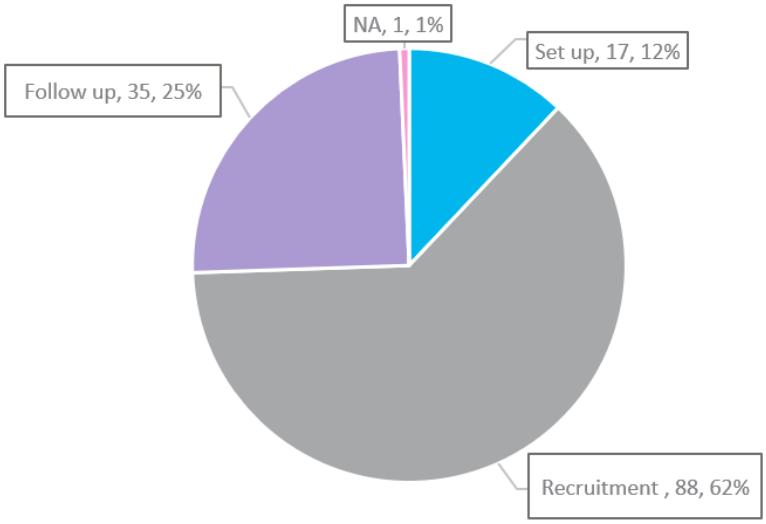
Next Steps for Recovery

The report shows that limited resource at site and reduced patient availability are the most commonly reported barriers to progress over the last 12 months (Figure 17). Limited resource at site and reduced patient availability is also anticipated to be the key challenge that will impede improvement over the next 12 months (Figure 18). Tackling these two main barriers will be key to ensuring we continue to see an upward trajectory in the recovery of site set up and recruitment to ensure timely delivery of our CRUK trial portfolio and to reduce the duration of future trial extensions.

Appendix 1 – Supplementary Graphs

A. Trials in set up, recruitment, follow-up/analysis in March 2020 (n=141)

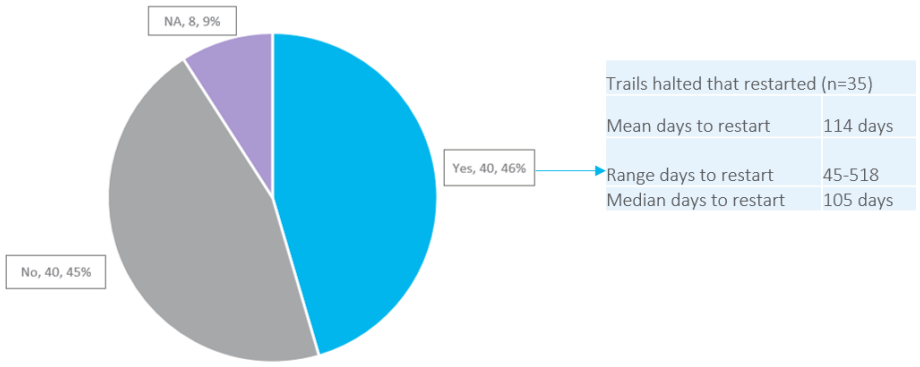
Figure 1: Percentage of trials in set up, recruitment and analysis/follow up on March 2020 (n=141)



Notes: Set up: n=17, Recruitment: n=88, Closed to recruitment/follow up: n=3, N/A: n=1 (endorsement that funding was not identified for)

B. Trials open to recruitment in March 2020 (n=88)

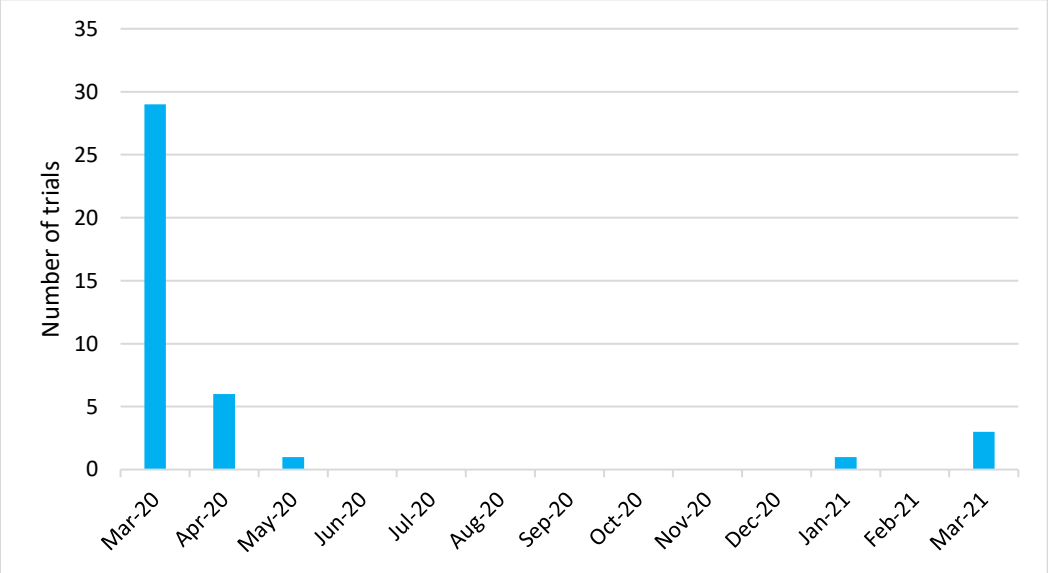
Figure 2: Was recruitment halted due to the pandemic? (n=88)



Notes: Yes; n=40 (31 open to recruitment, 9 closed to recruitment now but were open in March 2020). No; n=40 (38 open to recruitment, 2 closed to recruitment now but were open in March 2020). N/A; n=8 (open to recruitment in March 2020 but closed for non-pandemic related reason)

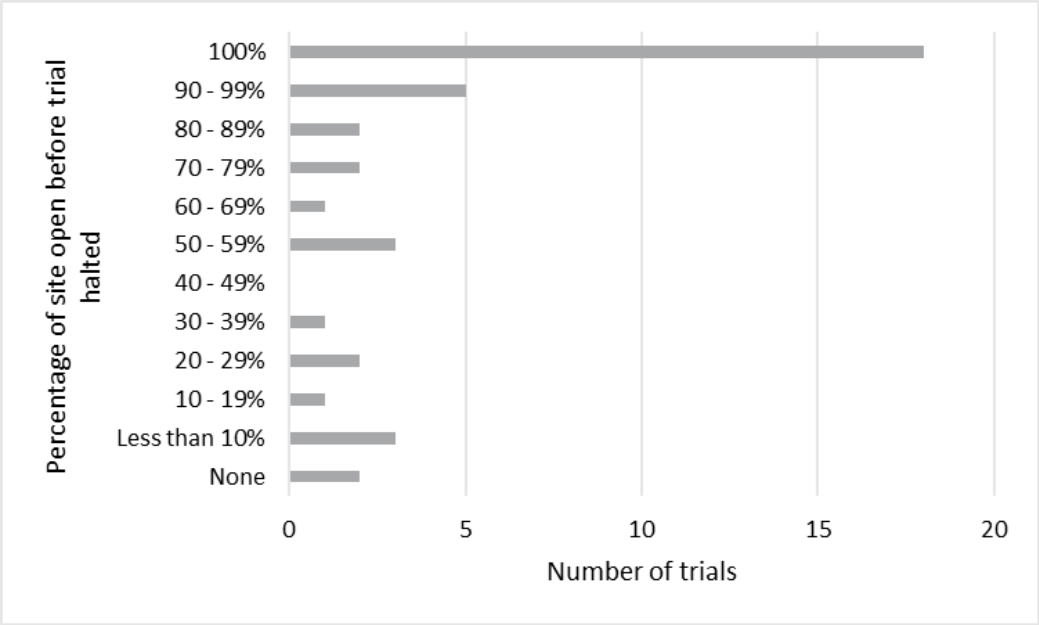
1. Trials Open to Recruitment in March 2020 that Halted (n = 40)

Figure 3: When did recruitment stop? (n=40)



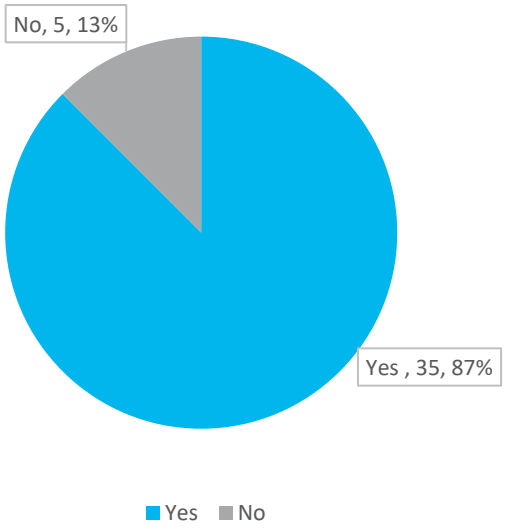
Notes: Trials halted due to pandemic, n=40 (31 open to recruitment, 9 closed to recruitment now but were open).

Figure 4: What percentage of planned sites were set up before halting? (n=40)



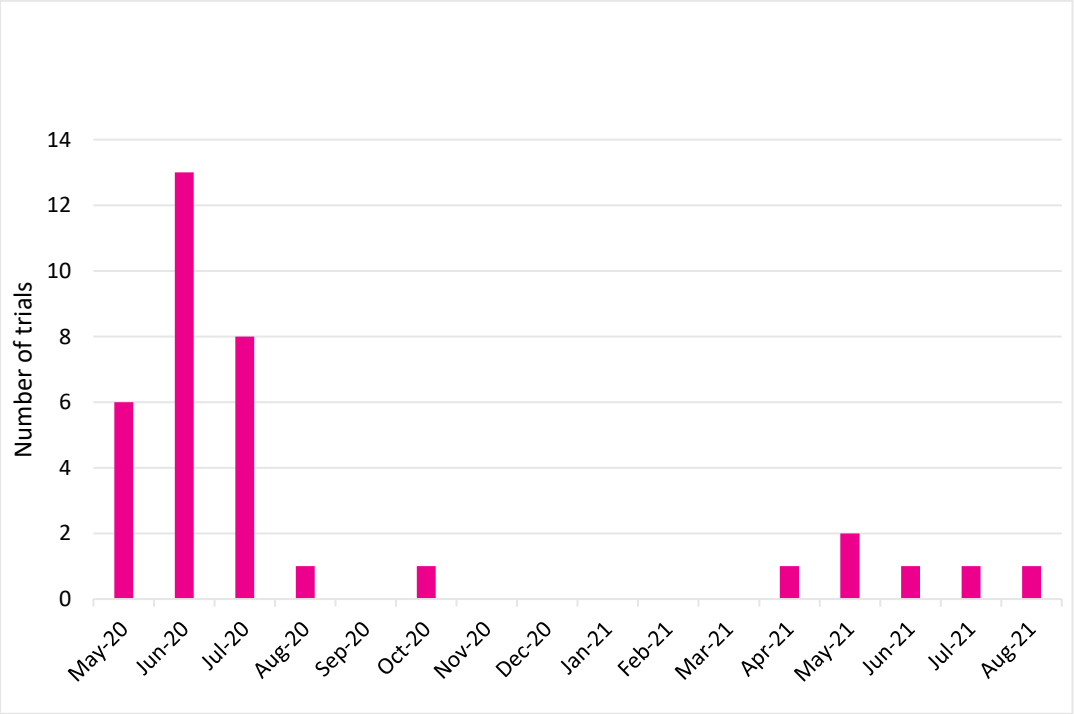
Notes: Trials halted due to pandemic, n=40 (31 open to recruitment, 9 closed to recruitment now but were open).

Figure 5: Did recruitment at sites restart? (n=40)



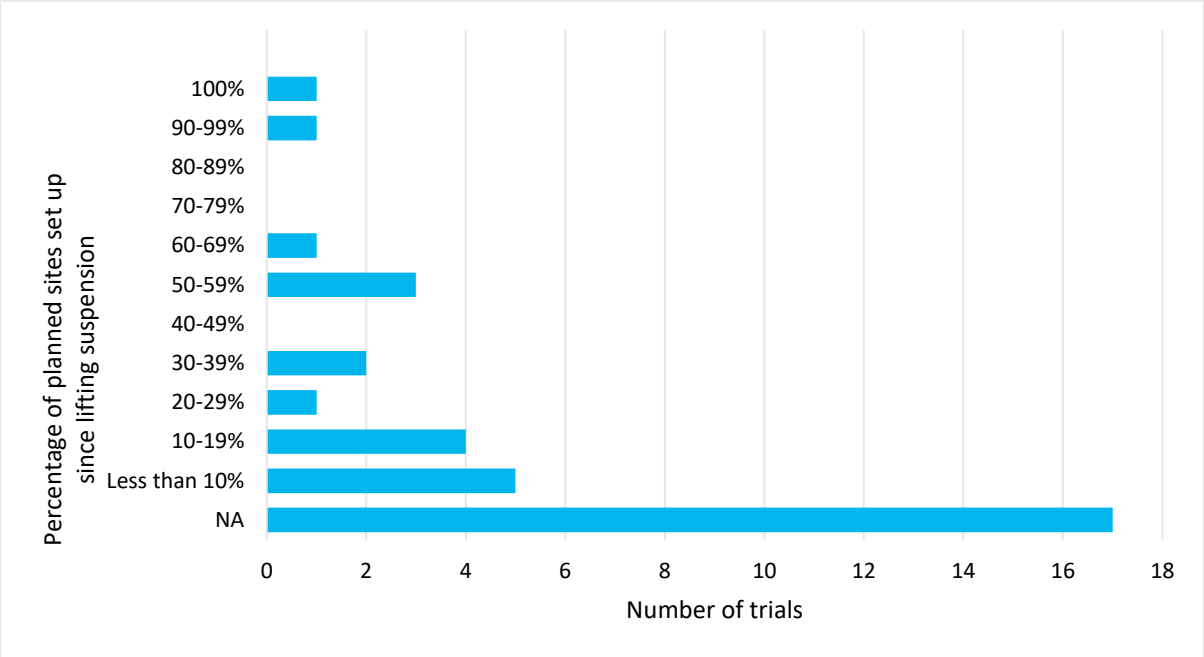
Notes: Trials halted due to pandemic, n=40 (31 open to recruitment, 9 closed to recruitment now but were open).

Figure 6: For trials that have restarted, when did recruitment restart? (n=35)



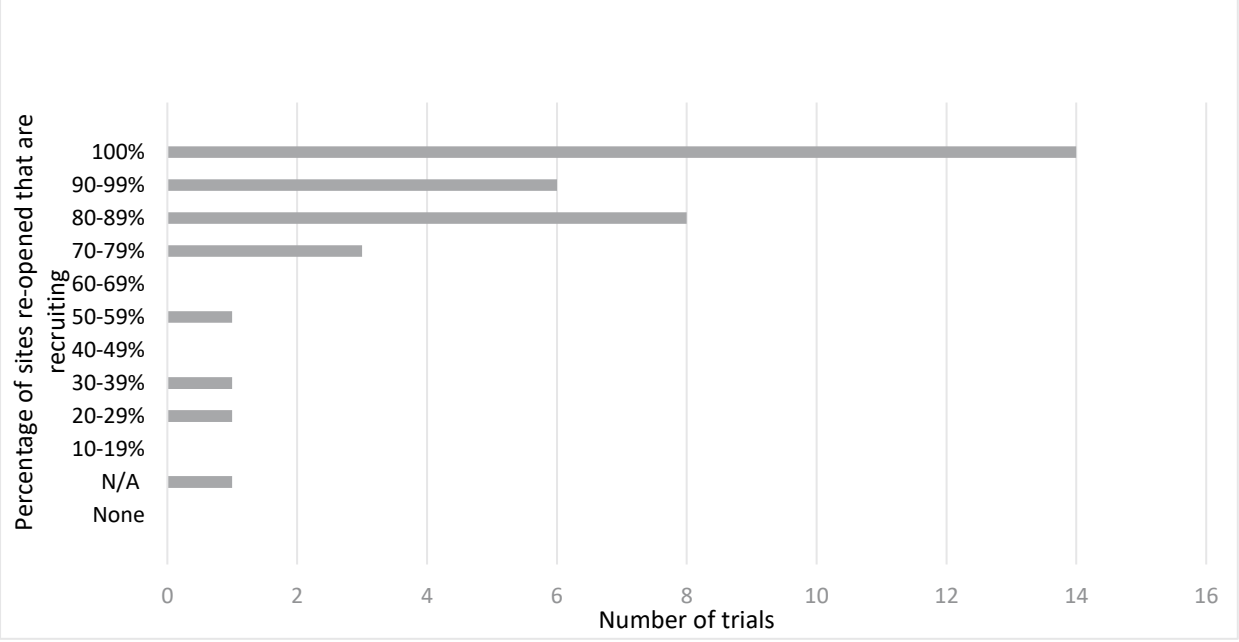
Notes: Trials that were halted that restarted, n=35.

Figure 7: For trials that have restarted, what percentage of planned sites have been set up since lifting the suspension? (n=35)



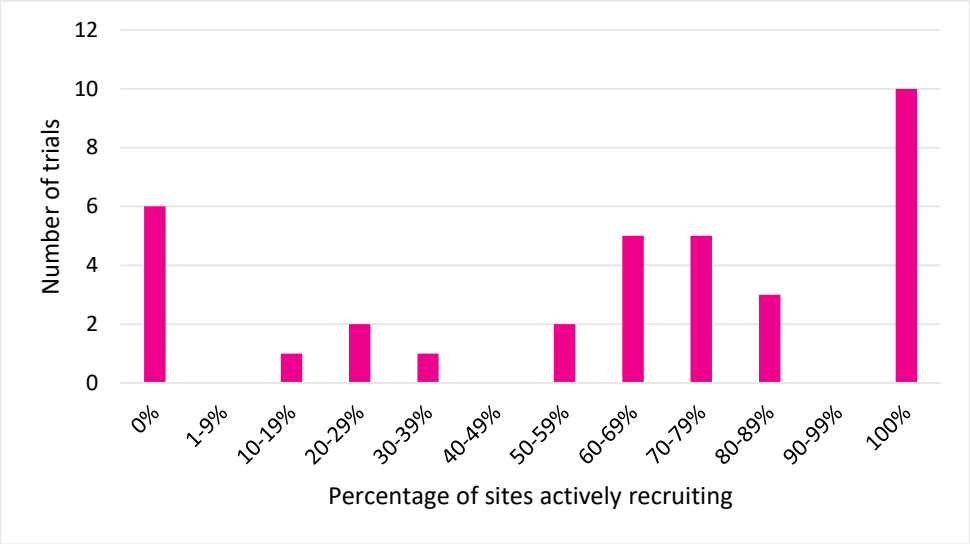
Notes: Trials that were halted that restarted, n=35. 17 N/A as all sites set up pre-pandemic.

Figure 8: For trials that have restarted, what percentage of the sites have re-opened to recruitment? (n=35)



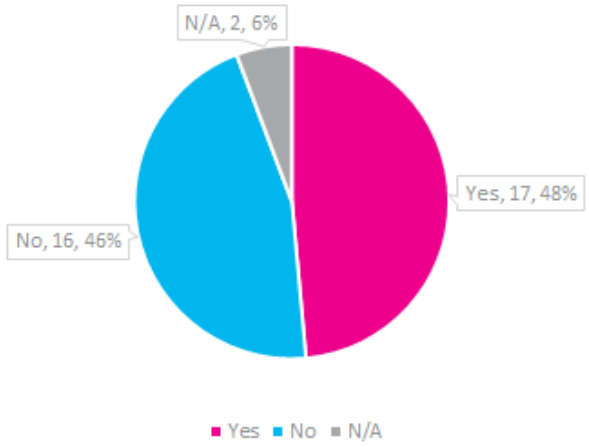
Notes: Trials that were halted that restarted, n=35.

Figure 9: For trials that have restarted, what percentage of the sites open are actively recruiting? (n=35)



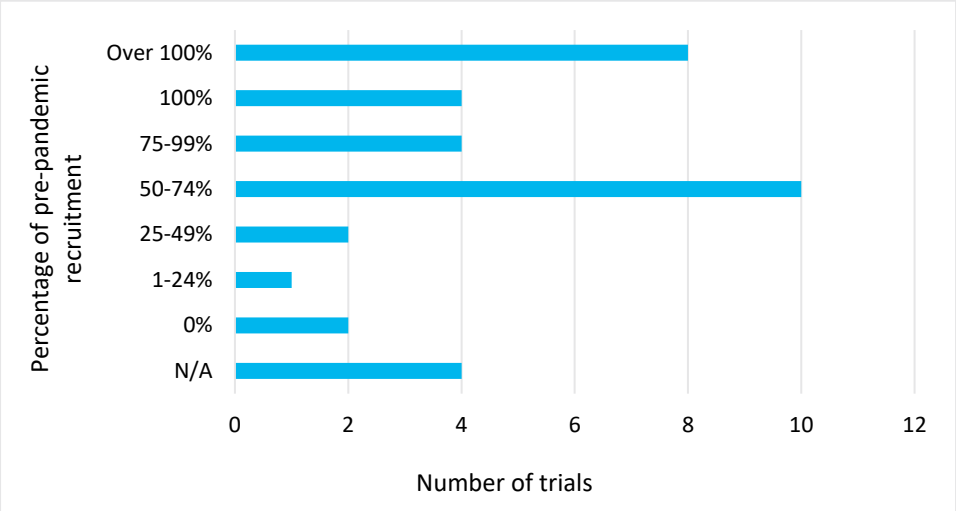
Notes: Trials that were halted that restarted, n=35.

Figure 10: For trials that have restarted, relative to projections before March 2020, has there been a significant reduction (i.e. >20% less) to the recruitment rate seen since re-starting recruitment? (n=35)



Notes: Trials that were halted that restarted, n=35.

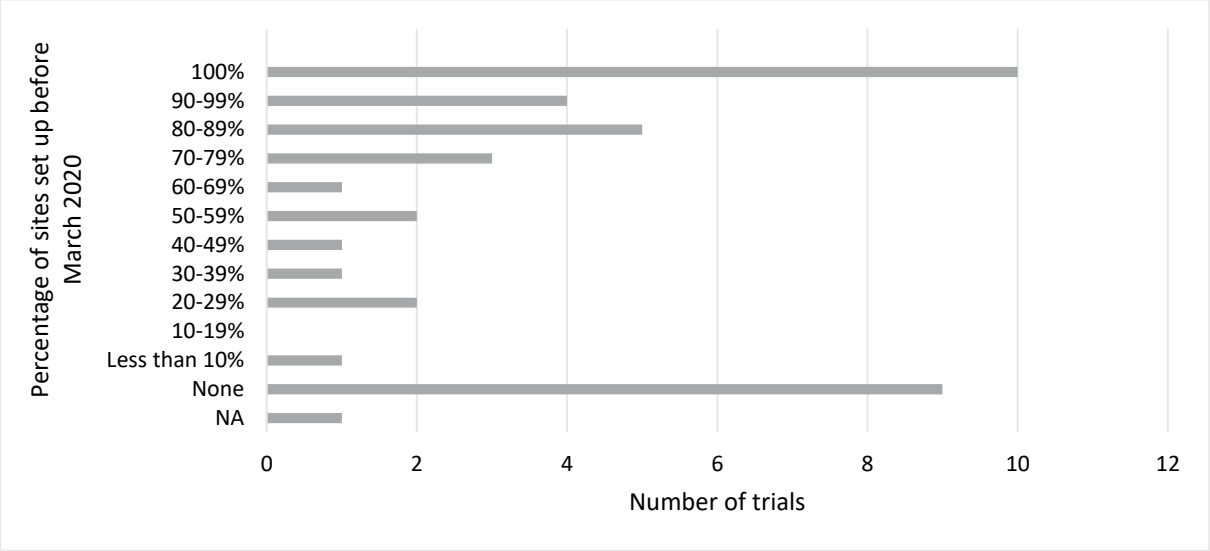
Figure 11: What is the average percentage of pre-pandemic recruitment reached since restarting? (n=35)



Notes: Trials that were halted that restarted, n=35. 4 were N/A – reason unclear but perhaps as site have not started recruiting yet. Compares average monthly recruitment rate before March 2020 to average monthly recruitment rate since re-starting recruitment. Graph shows that just over half of the trials are recruiting at 75-100% of pre-pandemic recruitment rates since reopening.

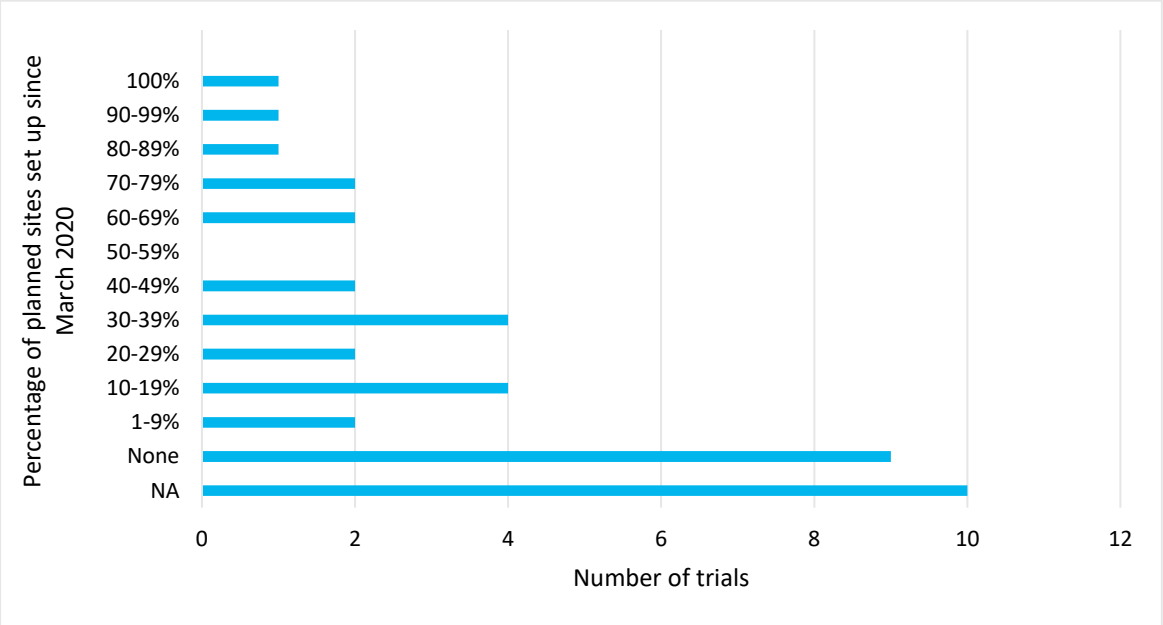
2. Trials Open to Recruitment in March 2020 Not Halted (n = 40)

Figure 12: What percentage of planned sites were set up before March 2020? (n=40)



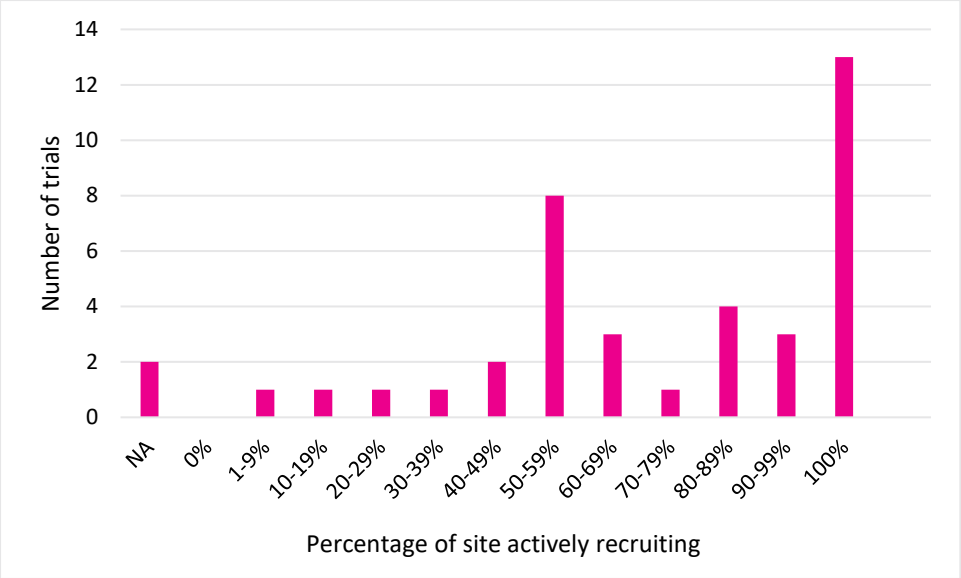
Notes: Trials not halted due to pandemic; n=40 (38 open to recruitment, 2 closed to recruitment now but were open). 1 is N/A as it was not open before March 2020.

Figure 13: What percentage of planned sites have been set up since March 2020? (n=40)



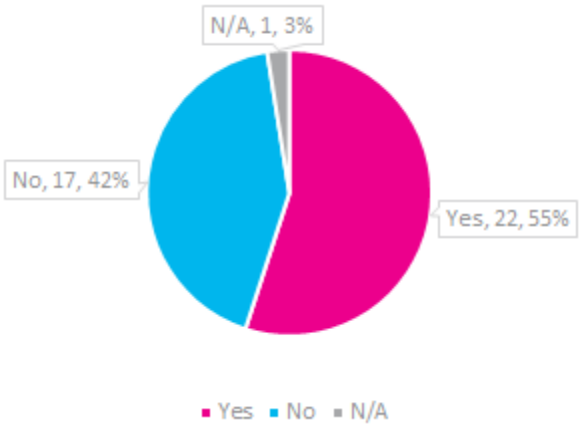
Notes: Trials not halted due to pandemic; n=40 (38 open to recruitment, 2 closed to recruitment now but were open).

Figure 14: What percentage of the sites that are open are actively recruiting? (n=40)



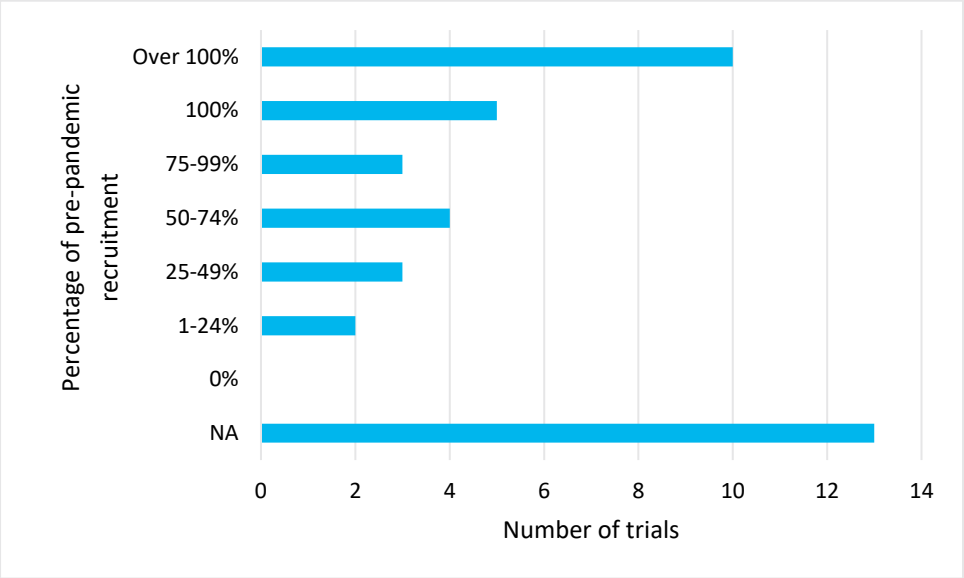
Notes: Trials not halted due to pandemic; n=40 (38 open to recruitment, 2 closed to recruitment now but were open). 2 are N/A as recruitment have finished.

Figure 15: Relative to projections pre-pandemic, has there been a significant reduction (i.e. >20% less) to the recruitment rate between March 2020 – March 2021? (n=40)



Notes: Trials not halted due to pandemic; n=40 (38 open to recruitment, 2 closed to recruitment now but were open). 1 is N/A as recruitment only started during the pandemic.

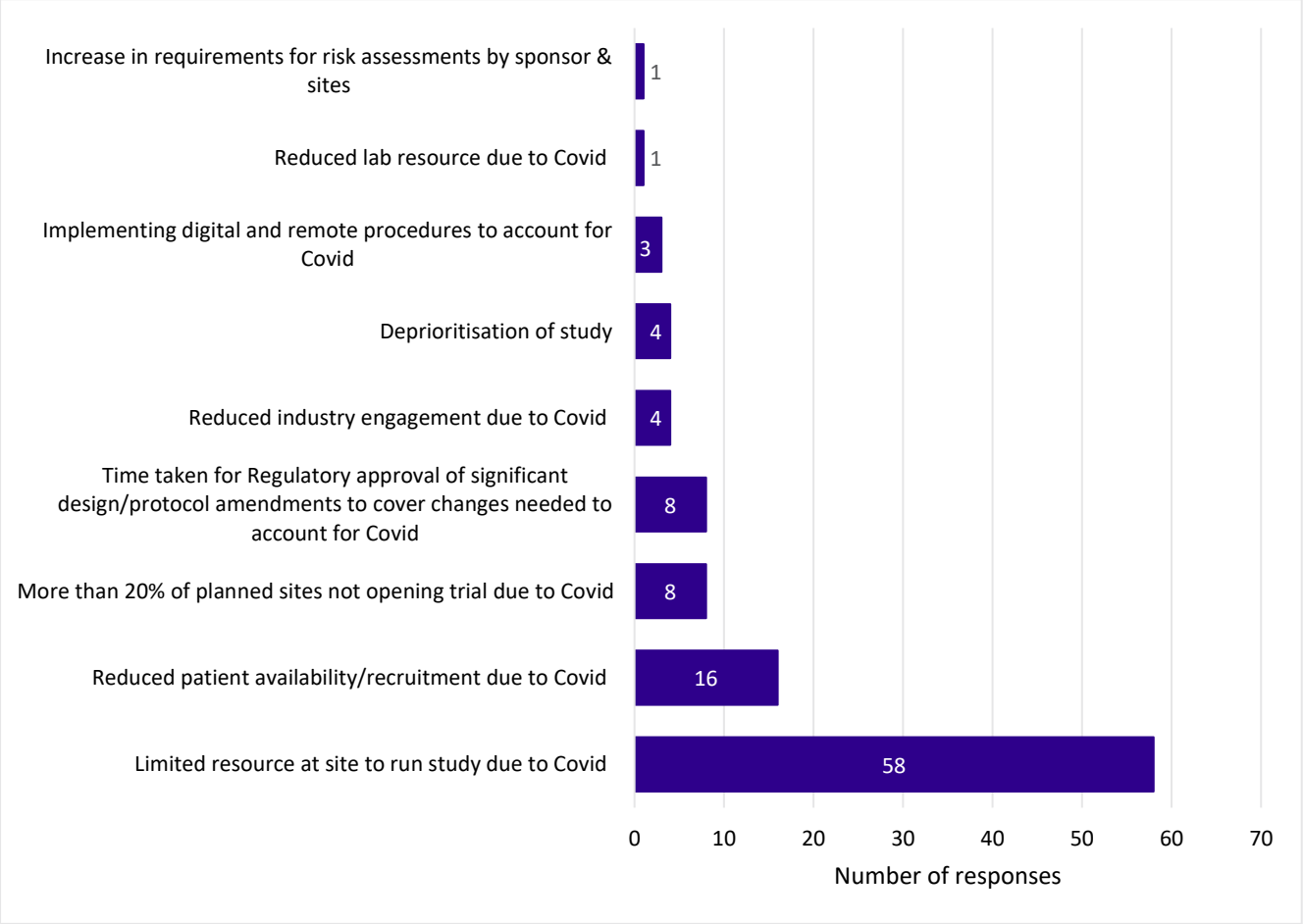
Figure 16: What is the average percentage of pre-pandemic recruitment reached since March 2021? (n=40)



Notes: Trials not halted due to pandemic; n=40 (38 open to recruitment, 2 closed to recruitment now but were open). 13 are N/A as recruitment either did not started before March 2020 or did not continued after March 2021.

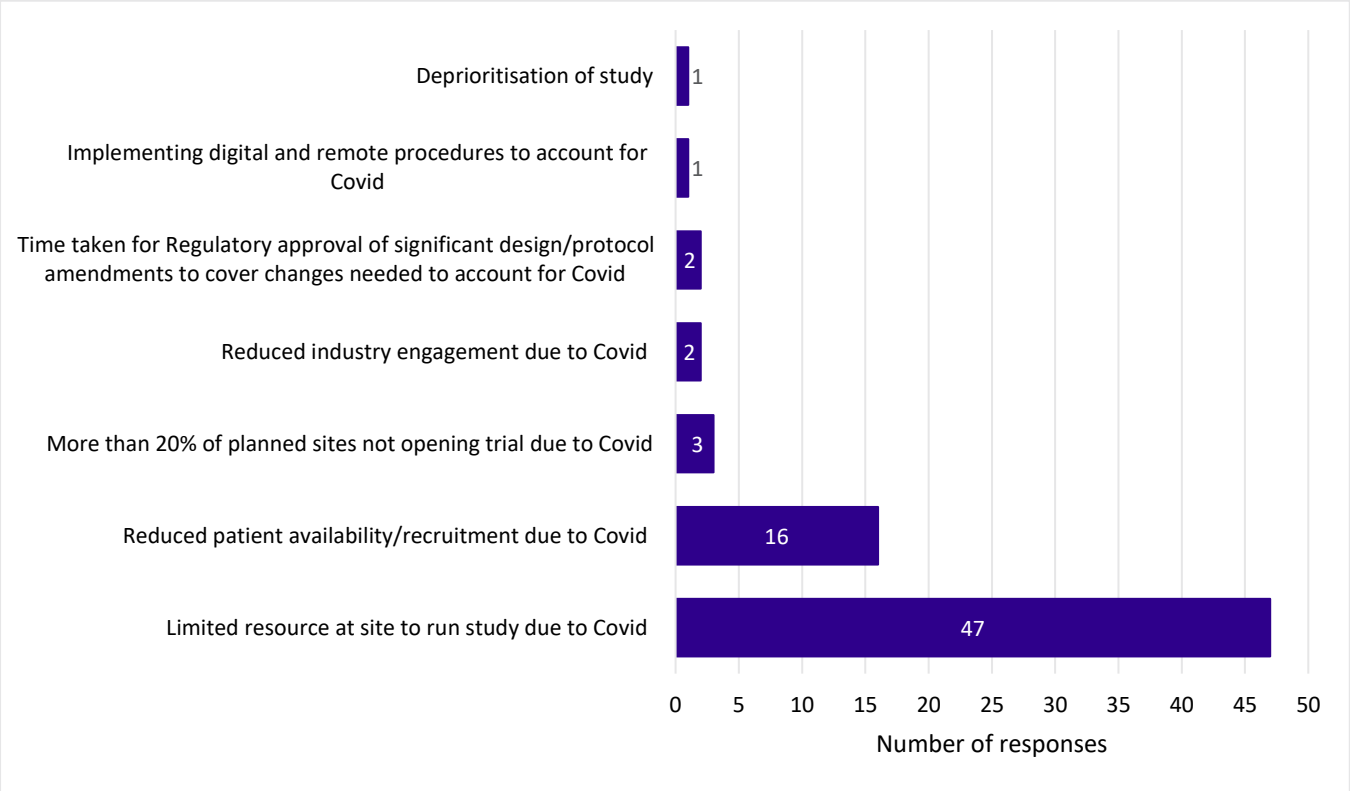
C. Key issues

Figure 17: What has been the key issues impacting trial progress over the last 12 months?



Notes: Answers based on input from N=141 trials but due to multiple choice nature of answer the response numbers do not total N number.

Figure 18: What key issues do you anticipate will have an impact on trial progress over the next 12 months?



Notes: Answers based on input from N=141 trials but due to multiple choice nature of answer the response numbers do not total N number.