Research Letter

The Effect of COVID-19 on Medication Adherence in a Rheumatoid Arthritis (BRAGGSS) and Psoriatic Arthritis (OUTPASS) UK Cohort

To the Editor:

Suboptimal treatment adherence has been reported in patients with arthritic diseases; is associated with psychological factors, including anxiety; and correlates with future treatment response.1,2 During the coronavirus disease 2019 (COVID-19) pandemic, patients who identified as clinically extremely vulnerable, including people prescribed ≥ 2 immunosuppressives, were advised to shield and continue treatment unless they developed COVID-19 symptoms. The aim of this multicenter study was to investigate the effect of the COVID-19 pandemic on adherence to disease-modifying antirheumatic drugs (DMARDs) in patients with established rheumatoid arthritis (RA) and psoriatic arthritis (PsA) in the United Kingdom.

Between August 2020 and June 2021, patients with RA and PsA from 2 multicenter observational studies (Biologics in Rheumatoid Arthritis Genetics and Genomics Study Syndicate [BRAGGSS] and Outcomes of Treatment in PsA Study Syndicate [OUTPASS]) who were within 12 months of commencing biological or targeted synthetic DMARDs, were sent a questionnaire on adherence and medication perceptions. Adherence during the COVID-19 pandemic was assessed using a 5-point Likert scale, as described previously2,3 and the reason for nonadherence recorded. Pandemic adherence was compared to paired prepandemic data (before 2020), where available, using similar questionnaires. Summary statistics for pandemic and prepandemic data and Pearson chi-square tests were used to investigate variables associated with self-reported nonadherence. Linear and logistic regression were used to investigate the association between returning questionnaires, Hospital Anxiety and Depression Scale (HADS), and drug response. This study complies with the Declaration of Helsinki. The locally appointed ethics committee has approved the research protocol, and written informed consent has been obtained from the subjects (or their legally authorized representative; BRAGGSS-MREC No: 04/Q1403/37, OUTPASS-REC ref: 13/NW/0068). The lists of OUTPASS and BRAGGSS collaborating sites and authors are available in Appendix 1 and Appendix 2.

One hundred fifty-nine questionnaires were returned (81.1% RA and 18.9% PsA). Seven patients reported COVID-19 symptoms, and 2 of 5 patients who tested positive were hospitalized. Methotrexate (53.5%) was the most frequently prescribed agent, followed by etanercept (25.2%), sulfasalazine (22.6%), adalimumab (22%), and hydroxychloroquine (21.4%), with 72.3% of patients being prescribed ≥ 2 immunosuppressives. In the PsA cohort, there was no significant association between questionnaire responders and nonresponders and 6-month drug response, demonstrating no evidence of responder bias. Information was not available from the RA cohort. Of patients with adherence information, 43.2% reported missing or delaying a treatment dose. Of those who missed or delayed therapy, 59.7% reported nonmedically advised nonadherence. Overall, this resulted in 25.8% of patients self-reporting nonadherence during COVID-19.

There was no significant difference in nonadherence rates between the different DMARDs. Further, there was no association between disease type (RA vs PsA) or perception of disease control (good vs bad) and adherence. Of nonadherent patients, 22.5% reported increased anxiety and fear of a greater risk of infection because of the COVID-19 pandemic as an influencing factor. Twenty-five percent listed non–COVID-19 intentional reasons for nonadherence, such as fear of treatment, side effects, and aversion to injections, whereas 55% reported nonintentional reasons, with forgetting and lack of treatment availability listed most frequently, similar to previous literature.4,5 A higher HADS total score was associated with increased self-reporting of missing or delaying a dose of treatment (odds ratio 1.11, 95% CI 1.01-1.14, P = 0.01); however, there was no significant association with nonmedically advised nonadherence during COVID-19.

Considering prepandemic data, 26.7% of the OUTPASS cohort had adherence information available, with 100% self-reporting complete adherence within the first 3 months of treatment. In the BRAGGSS cohort 21.7% had prepandemic adherence information available. Of these patients, 25% reported nonadherence within the first 3 months of treatment. Compared to prepandemic data, nonadherence was seen to increase during the pandemic for both patients with RA and PsA. In international cohorts, nonadherence of patients on immunosuppressive therapy was described at similar levels (Table).4,6-8

Throughout the pandemic, there was a vast amount of conflicting information, which may have contributed to increased anxiety and exacerbated symptoms in patients prescribed immunosuppressants.4,5 In contrast, patients with higher adherence had lower levels of relapse.7 In 1 cohort, only 1 patient who stopped therapy did not restart following reassurance, highlighting the benefits of good communication skills.7 This was supported by findings from the current study, with 1 patient describing stopping treatment because of fear of COVID-19 before restarting after discussion with their rheumatology team.

Strengths of the study include the multicenter recruitment, inclusion of patients with both RA and PsA, and the availability of prepandemic adherence data. Despite this, adherence information was available for only 3 months following treatment commencement, which could have led to overestimated treatment adherence. Limitations include the inability to explore the influence of telemedicine, which may support higher levels of adherence as a result of a continuation of disease management.8 In this multicenter UK study of patients with RA and PsA commencing antirheumatic therapy 12 months prior, nonadherence during COVID-19 was identified at a national level and...

increased in these patients compared to prepandemic available data. Increased anxiety and fear of infection were contributory factors to nonadherence. Lack of clear communication was cited as a reason for nonadherence both in the current UK study and in previous reports internationally. Clear, nonjudgmental, and transparent communication and further education about infection risk in immunosuppression are pivotal for improving adherence behaviors and potential drug response in immunosuppressed patients in the context of infectious diseases.

Table. International nonadherence to immunosuppressive therapy during COVID-19.

<table>
<thead>
<tr>
<th>Population</th>
<th>Period</th>
<th>Sample Size</th>
<th>Cohort</th>
<th>Study Type</th>
<th>Nonadherence Rate (%)</th>
<th>Adherence Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK</td>
<td>August 2020-May 2021</td>
<td>159</td>
<td>RA and PsA</td>
<td>Multicenter</td>
<td>25.8</td>
<td>Ever nonadherent</td>
</tr>
<tr>
<td>Greece</td>
<td>March 2020-April 2020</td>
<td>237</td>
<td>PsO and PsA</td>
<td>Single center</td>
<td>23.6</td>
<td>Not as prescribed</td>
</tr>
<tr>
<td>Ireland</td>
<td>April 2020-May 2020</td>
<td>1032</td>
<td>RMD</td>
<td>Multicenter</td>
<td>15.9</td>
<td>Health authority (HSE) guidelines</td>
</tr>
<tr>
<td>Korea</td>
<td>April 2020-May 2020</td>
<td>544</td>
<td>IBD</td>
<td>2 centers</td>
<td>27.8</td>
<td>Postponed or withheld</td>
</tr>
<tr>
<td>Turkey</td>
<td>June 2020</td>
<td>133</td>
<td>PsO and PsA</td>
<td>Single center</td>
<td>39</td>
<td>Short- or long-term suspension</td>
</tr>
</tbody>
</table>


increased in these patients compared to prepandemic available data. Increased anxiety and fear of infection were contributory factors to nonadherence. Lack of clear communication was cited as a reason for nonadherence both in the current UK study and in previous reports internationally. Clear, nonjudgmental, and transparent communication and further education about infection risk in immunosuppression are pivotal for improving adherence behaviors and potential drug response in immunosuppressed patients in the context of infectious diseases.

Philippa D.K. Curry1,3, PhD
Hector Chinoy1,3,4, PhD
Meghna Jani3,3, PhD
Darren Plant1,2, PhD
Kimmie L. Hyrich1,3, PhD
Ann W. Morgan3,4, PhD
A.G. Wilson4, MB PhD
John D. Isaacs7, PhD
Andrew P. Morris1,2, PhD
Anne Barton1,2, PhD
James Bluett1,2, PhD

1 Centre for Genetics and Genomics Versus Arthritis, Centre for Musculoskeletal Research, Faculty of Biology, Medicine and Health, The University of Manchester, Manchester, UK;
2 National Institute for Health Research Manchester Biomedical Research Centre, University NHS Foundation Trust, The University of Manchester, Manchester, UK;
3 Department of Rheumatology, Salford Royal Hospital, Northern Care Alliance NHS Foundation Trust, Manchester Academic Health Science Centre, Salford, UK;
4 Centre of Epidemiology Versus Arthritis, Centre for Musculoskeletal Research, Faculty of Biology, Medicine and Health, The University of Manchester, Manchester, UK;
5 School of Medicine, University of Leeds and NIHR Leeds Biomedical Research Centre, Leeds Teaching Hospitals NHS Trust, Leeds, UK;
6 School of Medicine & Medical Science, Conway Institute, University College Dublin, Dublin, Ireland;
7 Translational and Clinical Research Institute, Newcastle University, and Musculoskeletal Unit, The Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK.

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Address correspondence to Dr. J. Bluett, Centre for Musculoskeletal Research, Faculty of Biology, Medicine and Health, The University of Manchester, Oxford Rd, Manchester, M13 9PL, UK. Email: james.bluett@manchester.ac.uk.

DATA AVAILABILITY

The data that support the findings of this study are available on request from the corresponding author (JB). The data are not publicly available due to privacy/ethical restrictions.

REFERENCES


APPENDIX 1. List of study collaborators. Members of the Biologics in Rheumatoid Arthritis Genetics and Genomics Study (BRAGGS). Steering Committee members: Prof. Anne Barton, Prof. John Isaacs, Prof. Ann Morgan, Prof. Gerry Wilson; Chief Investigator: Prof. Anne Barton. The Newcastle upon Tyne Hospitals NHS Foundation Trust (Prof. J.D. Isaacs [Principal Investigator (PI)]); Prof. H. Foster, Dr. B. Griffiths, Dr. I. Griffiths, Dr. L. Kay, Dr. W.E. Ng, Dr. P.N. Platt, Dr. D.J. Walker, Dr. P. Peterson, Dr. A. Lorenzi, Dr. M. Friiswell, Dr. B. Thompson, Dr. M. Lee, Dr. A. Pratt; St Helens and Knowsley Hospitals NHS Trust (D. Graham [PI], Dr. R. Abernethy [former PI], Dr. A.R. Clewes, Dr. J.K. Dawson); Gateshead Health NHS Foundation Trust (S. Pugmure [PI], Dr. C.A. Kelly, Dr. J. Hamilton, Dr. C.R. Heycock, Dr. V. Saravanam); West Suffolk NHS Foundation Trust (Dr. S. Bhagat [PI], Dr. D.T. O’Reilly [former PI], Dr. V. Rajagopal); Sheffield Teaching Hospitals NHS Foundation Trust (Dr. M. Akil [PI], Prof. G. Wilson [former PI], Dr. S. Till, Dr. L. Dunkley, Dr. R. Tattersall, Dr. R. Kilding, Dr. T. Tait, Dr. J. Maxwell, Dr. K.P. Kuc); Leeds Teaching Hospitals NHS Trust (Prof. P. Emery [PI], Prof. M. Buch, Dr. S. Bingham, Prof. A. Morgan, Prof. H.A. Bird, Prof. P.G. Conaghan, Dr. C.T. Pease, Dr. R.J. Wakefield, Dr. S. Dass); Portsmouth Hospitals University NHS Trust (Dr. J. Ledingham [PI], Dr. R.G. Hull, Dr. F. McCrae, Dr. A. Cooper, Dr. S.A. Young Min, Dr. Wong, Dr. Shaban); Manchester Royal Infirmary (Manchester University NHS Foundation Trust; Prof. A. Barton [PI], Prof. I. Bruce [former PI], Dr. R. Gorodkin, Dr. P. Ho, Dr. K. Hyrich); Royal Lancaster Infirmary (University Hospitals of Morecambe Bay NHS Foundation Trust; Dr. M. Bukhari [PI], Dr. L. Otwell, Dr. Palkonaya); Hampshire Hospitals NHS Foundation Trust (Dr. E. Williams [PI], Dr. P. Prouse [former PI], Dr. R.K. Moitra, Dr. D.J. Shawe); The Dudley Group NHS Foundation Trust (Prof. G. Kitas [PI], Dr. K. Douglas [former PI], Dr. C. Koutsianas, Dr. N. Erb, Dr. R. Klocke, Dr. A.J. Whallrett, Dr. A. Pace, Dr. R. Sandhu, Dr. H. John); University Hospitals Birmingham NHS Foundation Trust (Dr. A. Filer [PI], Dr. Bowman, Dr. P. Jibanputra, Dr. E.C. Rankin); South Tees Hospitals NHS Foundation Trust (Dr. M. Plant [PI], Dr. F. Clarke, Dr. J.N. Fordham, Dr. S. Tuck, Dr. S.K. Pathare, Dr. A. Paul); Royal Derby Hospital (University Hospitals of Derby and Burton NHS Foundation Trust; Dr. S. Reilly [PI], Dr. T. Ding, Dr. I.J. Badcock, Dr. C.M. Deighton, Dr. N. Raj, Dr. M.R. Regan, Dr. G.D. Summers, Dr. R.A. Williams); Northumbria Health care NHS Foundation Trust (Dr. F. Birell [PI], Dr. P.R. Crook); University Hospitals Coventry and Warwickshire NHS Trust (Dr. S. Dubey [PI], Dr. M. Allen [former PI], Dr. K. Chaudhuri, Dr. A. Price-Forbes, Dr. J. Ravindran); North Manchester General Hospital (Manchester University NHS Foundation Trust; Dr. L. Das [PI], Dr. M. Ahmad [former PI], Dr. M. Pattrick, Dr. H.N. Snowden, Dr. A.P. Bowden, Dr. E.E. Smith, Dr. P. Klimiuk [PI], Dr. J. McHale [PI], Dr. I. Pande, Dr. I.C. Gaywood, Dr. C. Godsme, Dr. M. Rutter, Dr. A.C. Jones, Dr. P. Lanyon, Prof. M. Doherty, Dr. A. Gupta, Dr. P.A. Courtney, Dr. A. Srikanth, Dr. A. Abhishek); Salford Royal (Northern Care Alliance NHS Foundation Trust; Prof. H. Chiniy [PI], Prof. T. O’Neil, Prof. A. Herrick, Prof. A. Jones, Dr. R. Cooper, Dr. W. Dixon, Dr. B. Harrison); South Warwickshire University NHS Foundation Trust (Dr. C. Marguerie [PI], Dr. S.P. Rigby, Dr. N. Dunn); Northern Lincolnshire and Goole Hospitals NHS Foundation Trust (Dr. B. Szebenyi [PI], Dr. D. Bates, Dr. D. James, Dr. T. Gillott, Dr. A. Alvi, Dr. C. Grey, Dr. Browning); York Hospital (York and Scarborough Teaching Hospitals NHS Foundation Trust; Dr. M. Green [PI], Dr. M. Quinn, Dr. A. Isdale, Dr. A. Brown, Dr. B. Saleem); University Hospitals of Leicester NHS Trust (Dr. A. Moorthy [PI], Dr. A. Memon, Dr. P. Sheldon, Dr. W. Hassan, Dr. J. Francis, Dr. A. Kinder, Dr. R. Neame); New Cross Hospital (The Royal Wolverhampton NHS Trust; Dr. S. RaiAZa [PI], Dr. W. Al Allan [former PI], Dr. N. Barkham); Harrogate and District NHS Foundation Trust (Dr. M. Green [PI], Dr. A. Gough, Dr. C. Lawson); Chesterfield Royal Hospital NHS Foundation Trust (Dr. K. Fairburn [PI], Dr. M. Piper [former PI]); Royal United Hospitals Bath NHS Foundation Trust (Dr. J. Pauling [PI], Dr. E. Korendowych, Dr. T. Jenkinson, Dr. R. Sengupta, Dr. N. McHugh, Dr. W. Tillett, Dr. T. Ahmed); Liverpool University Hospitals NHS Foundation Trust (Dr. D. Mewar [PI], Dr. E.J. Tunnn, Dr. K. Nelson, Dr. T.D. Kennedy, Dr. C. Dubois); Countess Of Chester Hospital Foundation Trust (Dr. J. Nixon [PI], Dr. T. Barnes, Dr. M. Hut); Royal Cornwall Hospitals NHS Trust (Dr. D. Hutchinson [PI], Prof. A.D. Woolf [former PI], Dr. M. Davis, Dr. A. Endean); County Durham and Darlington NHS Foundation Trust (N. Rasy [PI], Dr. R. Reece [former PI], Dr. M. Bridges [former PI], Dr. D. Armstrong, Dr. A.J. Chuck, Dr. S. Hallwood, Dr. N. Kumar, Dr. D. Ashok); South Tyneside and Sunderland NHS Foundation Trust (Dr. D. Coady [PI], Dr. C. Morley, Dr. D. Wright, Dr. G. Raftery, Dr. C. Bracewell); Stockport NHS Foundation Trust (Dr. L. Mercer [PI], Dr. A. Ismail [former PI], Dr. C. Filer); Trafford General Hospital (Manchester University NHS Foundation Trust; Dr. P. McCabe [PI], Dr. F. McKenna [former PI]); Kettering General Hospital NHS Foundation Trust (Dr. A. Kuttikat [PI], Dr. G. Kallarackal [former PI], Dr. D. Das [former PI], Dr. D. Parthajit, Dr. E. Borbas, Dr. T. Wazz); Wrighington, Wigan and Leigh Teaching Hospitals NHS Foundation Trust (Dr. E.G. Chelliah [PI], Dr. C. Chattopadhyay); Queen’s Hospital Burton (University Hospitals of Derby and Burton NHS Foundation Trust; Dr. M. Nizar [former PI]); East Suffolk and North Essex NHS Foundation Trust (Dr. S. Lane [PI], Dr. L. Shand [former PI]); Fairfield General Hospital (Northern Care Alliance NHS Foundation Trust; Dr. S. Naz [PI], Dr. L. Das); Canknok Chase Hospital (The Royal Wolverhampton NHS Trust; Dr. D. Mulherin [PI], Dr. S. Chalam, Dr. T. Price, Dr. T. Sheeran, Dr. S. Venkatachalam, Dr. S. Baskar); Midlands Partnership NHS Foundation Trust (Dr. S. Hider [PI], Dr. A. Menon, Dr. C. Dowson, Dr. S. Dutta, Dr. S. Kamath, Dr. J. Packham, Dr. S. Price, Dr. E. Rody, Dr. Z. Paskins, Prof. A. Hassell); Scarborough Hospital (York and Scarborough Teaching Hospitals NHS Foundation Trust; Dr. Z. Al-Saffar [PI], Dr. J. Foo [former PI], Dr. G. Koduri); Furness General Hospital (University Hospitals of Morecambe Bay NHS Foundation Trust; Dr. M. Bukhari [PI], Dr. F. Wood); Barts Health NHS Trust (Prof. C. Pitzalis [PI]); Bolton NHS Foundation Trust (Dr. S. Ling [PI], Dr. S. Wig [former PI]); Tameside and Glossop Integrated Care NHS Foundation Trust (Dr. D. Roy [PI]); Lancashire and South Cumbria NHS Foundation Trust (Dr. S. Horton [PI], Dr. A. Madon); Northampton General Hospital NHS Trust (Dr. J. Taylor [PI]); University College London Hospitals NHS Foundation Trust (Dr. M. Castelino [PI]); Wythenshawe Hospital (Manchester University NHS Foundation Trust; Dr. S. Haque [PI]).
APPENDIX 2. List of study collaborators. Members of the Outcome of Treatment Response in Psoriatic Arthritis Studies Syndicate (OUTPASS).

Chief investigator: Dr. James Bluett. Wrightington, Wigan and Leigh Hospitals NHS Foundation Trust (Dr. E.G. Chelliah [Principal Investigator (PI)], Dr. C. Chattopadhyay [former PI]); Manchester Royal Infirmary (Manchester University NHS Foundation Trust; Dr. P. Ho [PI], Prof. A. Barton [former PI], Dr. M. Castelino, Prof. I. Bruce, Dr. R. Gorodkin, Dr. K. Hyrich, Dr. B. Parker); Salford Royal (Northern Care Alliance NHS Foundation Trust; Dr. H. Chinoy [PI], Prof. T. O’Neill, Prof. A. Herrick, Prof. A. Jones, Dr. R. Cooper, Prof. W. Dixon, Dr. B. Harrison); Royal United Hospitals Bath NHS Foundation Trust (Dr. E. Korendowycz [PI], Prof. N. McHugh, Dr. W. Tillett); Aintree University Hospital (Liverpool University Hospitals NHS Foundation Trust; Dr. N. Goodson [PI]); East Suffolk and North Essex NHS Foundation Trust (Dr. S. Lane [PI], Dr. L. Shand); Nottingham University Hospitals NHS Trust (Dr. I. Pande [PI], Dr. I. Gaywood [former PI], Dr. F. Rees, Dr. M. Rutter, Dr. S. Hayat, Dr. J.F. McHale, Dr. A.C. Jones, Dr. P. Lanyon, Dr. A. Gupta, Dr. P.A. Courtney, Dr. A. Srikanth, Dr. A. Abhishek); Royal Devon University Healthcare NHS Foundation Trust (Dr. S. Kyle [PI], Dr. R. Manhas); Mid and South Essex NHS Foundation Trust (Dr. A. Nandagudi [PI], Dr. S. Selen [former PI], Dr. A. Bharadwaj, Dr. N. Gendi, Dr. R. Alshakh); Fairfield Hospital (Northern Care Alliance NHS Foundation Trust; Dr. S. Naz [PI], Dr. M. Ahmad [former PI]); North Manchester General Hospital (Manchester University NHS Foundation Trust; Dr. L. Das, Dr. M. Patrick, Dr. A.P. Bowden, Dr. E.E. Smith, Dr. P. Klimiuk, Dr. D.J. Speden); University Hospitals of Morecambe Bay NHS Foundation Trust (Dr. M. Bukhari [PI], Dr. S. Kavaklieva, Dr. L. Ottewell, Dr. M. Massarotti); Midlands Partnership NHS Foundation Trust (Dr. J. Packham [PI]); Wye Hospital (Manchester University NHS Foundation Trust; Dr. P. Watson [PI], Dr. P. Sanders [former PI], Dr. S. Hague, Dr. B. Pal, Dr. E. Bruce); The Yorkshire Hospitals NHS Trust (Dr. Z. Karim [PI]); Torbay and South Devon NHS Foundation Trust (Dr. K. Mackay [PI], Dr. H. Shicks); Northampton General Hospital NHS Trust (Dr. J. Taylor [PI], Dr. R. Jeffery, Dr. P. Nandi); Stockport NHS Foundation Trust (Dr. C. Filer [PI], Dr. A. Ismail, Dr. L. Mercer); North Cumbria Integrated Care NHS Foundation Trust (Dr. A. Hassan [PI], Dr. A. Russell); University Hospitals of Leicester NHS Trust (Dr. M. Durrani [PI], Dr. W. Hassan [former PI], Dr. A. Samanta, Dr. P. Sheldon, Dr. J. Francis, Dr. A. Kinder, Dr. R. Neame, Dr. A. Moorthy); Barts Health NHS Trust (Prof. M. Bombardieri [PI], Dr. S. Kelly [former PI]); Sheffield Teaching Hospitals NHS Foundation Trust (Dr. J. Maxwell [PI], Dr. M. Akil, Dr. S. Till, Dr. L. Dunkley, Dr. R. Tattersall, Dr. R. Kilding, Dr. T. Tait, Dr. K.P. Kuet, Dr. B. Grant, Dr. M. Kazmi); St. Helens and Knowsley Teaching Hospitals NHS Trust (Dr. Graham [PI], Dr. V.E. Abernethy, Dr. A.R. Clewes, Dr. J.K. Dawson); NHS Greater Glasgow and Clyde (Dr. S. Siebert [PI], Dr. G. Fragoulis); Royal Liverpool and Broadgreen (Liverpool University Hospitals NHS Foundation Trust; Dr. D. Mewar [PI], Dr. E.J. Tunn, Dr. K. Nelson, Dr. T.D. Kennedy, Dr. C. Dubois); The Dudley Group NHS Foundation Trust (Dr. K. Douglas [PI], Dr. E. Ladoyanni, Dr. C. Koutsianas, Dr. N. Erb, Dr. R. Klocke, Dr. A.J. Whallott, Dr. A. Pacc, Dr. R. Sandhu, Dr. H. John); Portsmouth Hospitals University NHS Trust (Dr. S.A. Young Min [PI], Dr. A. Cooper, Dr. J.M. Ledingham, Dr. R.G. Hull, Dr. F. McCrac, Dr. W. Wong, Dr. Shaban); Mid Cheshire Hospitals NHS Foundation Trust (Dr. K. Purkayatsa [PI]); The Rotherham NHS Foundation Trust (Dr. R. Kumari [PI], Dr. G. Smith [former PI]); South Warwickshire NHS Foundation Trust (Dr. C. Marguerie [PI]); Homerton Healthcare NHS Foundation Trust (Dr. P. Reynolds [PI], Dr. C. Thornton [former PI], Dr. C. Gorman, Dr. C. Murphy); Tameside and Glossop Integrated Care NHS Foundation Trust (Dr. D. Roy [PI]); Lancashire and South Cumbria NHS Foundation Trust (Dr. S. Horton [PI]); University College London Hospitals NHS Foundation Trust (Dr. M. Castelino [PI]).