NOTTINGHAM CLINICAL TRIALS UNIT

PROTECT-CH

Prophylactic Therapy in Care Homes Trial

# Data Monitoring Committee (DMC) Charter

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| **EudraCT Number:** | 2021-000185-15 |
| **ISRCTN Number:** | N/A |
| **SPONSOR'S Name and Reference Number:** | University of Nottingham (21001) |
| **FUNDER'S Name and Reference Number:** | NIHR 133443 |
| **DMC Charter Version Number and Date:** | 1.0 09-Jun-2021 |

**Prepared by:**

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| Name: | Ed Juszczak | Role: | Investigator/Professor of Clinical Trials & Statistics in Medicine |
| Signature: |  | Date: | **09 June 2021** |

**Reviewed on behalf of NCTU by:**

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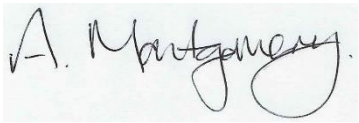
| Name: | Alan Montgomery | Role: | Investigator/Professor of Medical Statistics/CTU Director |
| Signature: |  | Date: | **09 June 2021** |

| 1. Introduction | |
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| Full name of the platform. | PROTECT-CH - PROphylactic ThErapy in Care homes Trial |
| Objectives of the platform. | To set in place an overarching platform for the efficient delivery of a suite of randomised comparisons to provide reliable evidence on the efficacy of candidate therapies for preventing SARS-CoV-2 infection and transmission in care homes. |
| Objectives of the platform, including interventions being investigated. | Primary objective:<br>To provide reliable estimates of the effect of study treatments for each pairwise comparison with the standard care arm on SARS-CoV-2 infection, morbidity and mortality at 60 days after randomisation.<br><br>Secondary objectives:<br>To assess the effects of study treatments on mortality (all-cause and cause specific), hospitalisation, healthcare referrals for COVID-19, infection (asymptomatic, symptomatic), time to symptomatic infection and serious adverse reactions.<br><br>Tertiary objectives:<br>To assess the cost-effectiveness of study treatments and evaluate processes/formative learning in the platform and contextual variation in outcomes. |
| Outline of scope of Charter. | The purpose of this document is to describe the roles and responsibilities of the independent Data Monitoring Committee (DMC) for this platform, including the timing of meetings, methods of providing information to and from the DMC, frequency and format of meetings, statistical issues and relationships with other committees. |
| Facilitation. | A member of the Platform Management Team at the coordinating centre (Nottingham Clinical Trials Unit (NCTU)) will facilitate the organisation of meetings and attend the open session for minute taking. |
| **2. Roles and responsibilities** | |
| Role of the DMC. | The role of the DMC is to safeguard the interests of potential or actual trial participants, their relatives, their carers, investigators, and the Sponsor. The DMC assesses the safety and efficacy of the intervention(s) being investigated, monitors the platform's overall conduct and aims to protect its validity and credibility.<br><br>The DMC is the only body involved in the platform that has access to unblinded data presented separately by randomised comparison. It will receive and review the progress and accruing data of the comparison(s) under investigation and provide advice on the conduct of the comparison(s) to the Platform Steering Committee (PSC).<br><br>The role of its members is to monitor these data and make recommendations to the PSC on whether there are any ethical or safety reasons why a particular comparison should not continue or requires modification. The safety, rights and well-being of the participants are paramount.<br><br>The DMC should inform the Chair of the PSC if, in its view, the results are likely to convince a broad range of clinicians, including those supporting the platform and the general clinical community, that one intervention is clearly indicated |

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| | or contraindicated, and there was a reasonable expectation that this new evidence would materially influence patient management and/or health policy.<br>Collaborators and anyone involved with the study (e.g. care home manager, GP, resident or relative) may write through the trial office to the DMC, to draw attention to any concern they may have about the possibility of harm arising from the treatment under study, or about any other matters that may be relevant. |
| Responsibilities of the DMC | The responsibilities of the DMC include an interim review of the platform's progress including updated figures on ongoing comparisons including recruitment, data quality, main outcomes and safety data. Responsibilities include;<br>• monitor balance in randomisation allocation<br>• assess data quality, including completeness (encouraging collection of high-quality data)<br>• monitor recruitment figures and losses to follow-up<br>• monitor compliance with the Protocol by residents/carers and investigators monitoring evidence for treatment differences in the main efficacy outcome measures<br>• monitor evidence for treatment harm (e.g. SARs, SUSARs, deaths)<br>• decide whether to recommend that a particular active treatment comparison continue to recruit participants or whether recruitment should be temporarily paused allowing further follow-up data to be received, or permanently terminated, either for everyone or for some treatment groups and/or some participant subgroups<br>• suggest additional data analyses if necessary<br>• monitor and advise on the appropriateness of the original parameters used in the sample size calculations<br>• review and make recommendations to PSC on sample size re-estimation<br>• maintain confidentiality of all study information that is not in the public domain<br>• monitor compliance with previous DMC recommendations<br>• considering the ethical implications of any recommendations made by the DMC<br>• consider the impact and relevance of data emerging from other related studies<br>• consider the need for any interim analysis advising the PSC regarding the release of data and/or information<br>If funding is required above the level originally requested, the DMC may be asked by the Chief Investigator (CI), PSC, Sponsor or Funder to provide advice and, where appropriate, information on the data gathered to date in a way that will not compromise the platform. For example, on occasion, the DMC Chair might be asked to provide advice based on a confidential interim or futility analysis, if serious concerns are raised about the viability of the study or if the research team are requesting significant extensions. |

| 3. Before or early in the platform | |
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| Whether the DMC will have input into the Protocol. | The Master Protocol has undergone review by the Funder and Sponsor, and the favourable opinion of a Research Ethics Committee will be in place prior to commencement of recruitment. DMC members are independent and should be constructively critical of the Protocol and on-going platform, but also supportive of its aims and methods. |
| Will the DMC meet before the start of the platform? | The DMC will meet before the platform starts or early in the course of the study to discuss the Master Protocol, the comparison(s), and future meetings. Where a meeting is not possible prior to the establishment of the platform, DMC members will be given an opportunity to review the Master Protocol prior to recruitment commencing. |
| Any specific regulatory issues. | The DMC is aware that this platform is established to evaluate Clinical Trials of Investigational Medicinal Products (CTIMPs) and requires a Clinical Trials Authorisation from the Medicines and Healthcare products Regulatory Agency and is governed by UK legislation. |
| Any other issues specific to the intervention under study. | None. |
| Whether members of the DMC will have a contract. | DMC members will be asked to sign a contract and formally confirm their agreement (1) to be a member of the platform DMC and (2) with the contents of this Charter. Any potential competing interests should be declared at the same time. Members should complete and return the form at the end of this charter to confirm their agreement (Annexe 3). Members of the DMC will be indemnified by the Sponsor through the trial's insurance.<br>Any observers (attendees who are not members) and any attendees who are shadowing a DMC member will sign a confidentiality agreement following agreement by the DMC Chair for their attendance (Annexe 4). |
| Format of initial meeting. | The first meeting of the DMC will usually be to introduce members to the platform and to review the Master Protocol. No data will be examined at this meeting; therefore, the initial meeting format will not follow that suggested in Section 6 for all subsequent meetings. Where the first meeting of the DMC is joint with the PSC, the attendees suggested in this charter may be expanded to include additional members of the PMG. |
| **4. Composition** | |
| Membership and size of the DMC. | The members of the DMC (detailed in Annexe 1) are independent of the platform. This DMC is possibly larger than usual to take into account the specific circumstances, urgency and frequency of meetings, due to the pandemic. Competing Interests are defined for both independent and non-independent members in Table 1 and 2.<br>Attendance at DMC meetings by non-members is at the discretion of the Chair and should be agreed in advance of the meeting. |
| The Chair (and Vice-Chair), how they are chosen and their role. | The Chair and members of the DMC were nominated by the Investigators. The funding body (NIHR) subsequently approved the membership. The Chair has previous experience of serving on Trial Committees and experience of chairing meetings and should be able to facilitate and summarise discussions. |

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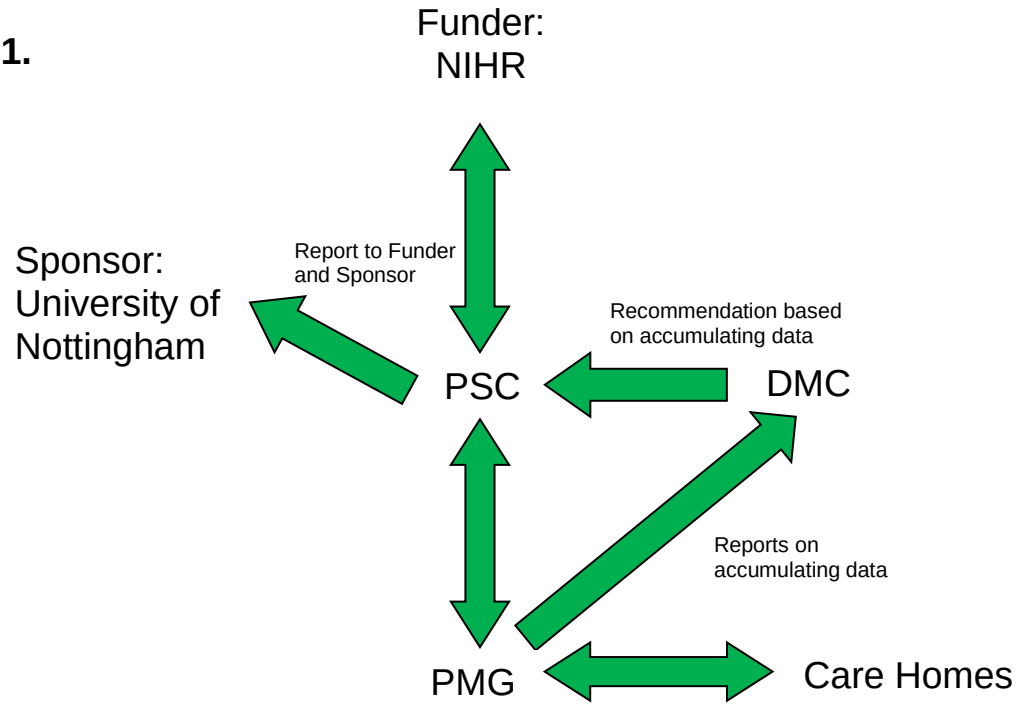
| | Prof Tim Peters was nominated by the independent members and appointed Vice-Chair at the first meeting. |
| The responsibilities of the DMC statistician. | The DMC membership includes independent statisticians to provide statistical expertise and to further guide the other DMC members through the DMC reports which will be prepared by the unblinded trial statisticians. |
| The responsibilities of the unblinded statisticians. | The unblinded statisticians will produce open report(s) for the DMC and will participate in the open session of the DMC meetings, guiding the DMC through the report. A template report/dummy tables will be agreed prior to the first presentation of data. The blinded statisticians will validate the open report(s).<br>The unblinded statisticians will also produce the confidential closed report(s) containing a breakdown by pairwise comparison, for review by the DMC during their closed session. They will ensure confidentiality. |
| The responsibilities of the CI and other members of the PMG. | Responsibility for convening and organising DMC meetings lies with the Facilitator, in association with the CI and Chair of the DMC. The Platform Management Group (PMG) should provide the DMC with a comprehensive update, the content of which should be agreed in advance with the DMC. The CI (or their deputy or a nominated representative if the CI is unable to attend) is expected to attend open sessions. The Senior Platform Statistician(s) will also attend the open session of the meeting in addition to the Platform Manager.<br>Other PMG members and observers will not routinely attend however may join the open session when invited and with permission of the Chair. |
| The responsibilities of the observers | Additional observers may be in attendance through (parts of) the DMC meetings in order to provide input on behalf of the NCTU or the Sponsor/Funder or to provide specific relevant expertise. These include but are not limited to the blinded statisticians (open session only). |
| **5. Relationships** | |
| Relationships with CI, other platform Committees (e.g. PMG and PSC), Sponsor/Funder, regulatory bodies. | The responsibilities of each Platform Committee are outlined in the Protocol and detailed in the respective Charters. The relationships between these groups are summarised in Figure 1. |

**Figure 1.**

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| Clarification of whether the DMC is advisory (makes recommendations) or executive (makes decisions). | In accordance with NIHR research governance guidelines, the DMC is advisory to the PSC. The PSC is the executive body for the platform and is delegated roles and responsibilities by the Sponsor. All substantial issues regarding the platform must go to the PSC for consideration. |
| Payments to DMC members. | Where applicable, standard travel and subsistence costs will be paid to members of the DMC. No other payments or rewards will be given to professional members. |
| The need for DMC members to disclose information about any real or potential competing interests. | Any competing interests, real or potential, should be disclosed. These are not restricted to financial matters – involvement in other platforms, trials or intellectual investment could be relevant.<br>Competing interests of DMC members should be recorded on their DMC Charter signature page (Annexe 3) and reviewed at the start of each DMC meeting (as a standing item on the agenda), where additional conflicts should be declared and documented. |
| **6. Organisation of DMC meetings** | |
| Expected frequency of DMC meetings. | The exact frequency of meetings will depend upon the stage and progress of the individual comparisons, a minimum of 3–4 times a year, more often as appropriate, and meetings should be timed so that recommendations can be presented to the PSC prior to their meetings. Combined meetings for multiple comparisons will take place, whenever possible.<br>Major study issues may need to be dealt with between meetings, by videoconference ideally, or by email. DMC members should be prepared for such instances. |

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| Will DMC meetings be face-to-face? | One of the Co-CIs is expected to attend all meetings. If, at short notice, any DMC members cannot attend then the DMC may still meet if quorate.<br>It is anticipated that most meetings will be virtual, at least for the foreseeable future. Every effort will be made to ensure that all members can attend. The Facilitator will arrange dates that enable this. |
| How will DMC meetings be organised, especially regarding open and closed sessions, including who will be present in each session? | DMC meetings will be organised by the Facilitator (a member of the Platform Trial Management Team), in conjunction with the Chair of the DMC.<br>The DMC meeting will comprise of an initial open session where the open report will be reviewed. This will be attended by the CI(s), plus the Senior Platform Statistician(s), Platform Manager and blinded statisticians as observers. This will be followed by a closed session attended only by the DMC and unblinded statistician(s) where they will discuss the closed report which presents data by treatment allocation.<br>Notes from the open session will be taken by a member of the NCTU for circulation to the DMC, PSC and PMG. Notes from the closed session will be taken by a member of the DMC to provide a recommendation to the PSC Chair. These will be retained by the DMC Chair. |
| Absence of Chair | Should the Chair be unexpectedly unavailable to attend a meeting, the Vice Chair (as appointed at the first meeting) should act as Chair. The meeting should only take place if the DMC remains quorate (defined in section 8). Should both the Chair and Vice Chair be unavailable, an alternative date should be sought. |
| **7. Platform documentation and procedures to ensure confidentiality and appropriate communication** | |
| Intended content of material to be considered during **open sessions**. | Data presented in the open sessions will include; accumulating information relating to recruitment and data quality (e.g. data return rates, treatment compliance); and based on pooled data per comparison - baseline characteristics; safety details; pre-specified outcome measures as required by the DMC. |
| Intended content of material to be considered during **closed sessions**. | The closed session material will include efficacy and safety data summarised and analysed by comparison (either coded or actual treatment allocation). |
| Will the DMC be blinded to the treatment allocation? | The DMC will receive the closed report with summary tables and analyses where appropriate presented by treatment code (e.g. A and B). Provision will be made if the code break is required at the DMC meeting. |
| Who will see the accumulating data and interim analysis? | DMC members do **not** have the right to share confidential information with anyone outside the DMC, including the CIs, unless the DMC deems this to be absolutely necessary. The unblinded statisticians will prepare the closed report for the DMC and send to members using appropriate security including encryption of files sent by email. |
| Who will be responsible for identifying and circulating external evidence (e.g. from other trial, platforms or systematic reviews)? | Identification and circulation of external evidence (e.g. from other trials, platforms and systematic reviews) is not the responsibility of the DMC members. This is the responsibility of the CIs. |
| To whom will the DMC communicate the decisions/ recommendations that are | The DMC Chair will report its recommendations in writing to the PSC Chair. If required, this may be copied to the Platform Manager in time for consideration at a PSC meeting. If the comparison is to continue largely unchanged then the report from the DMC may include a summary paragraph suitable for |

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| reached? | promotional purposes. See Annexe 5. |
| Will reports to the DMC be available before the meeting or only at/during the meeting? | The DMC will receive the report(s) at least 48 hours before the meeting. |
| What will happen to the papers after the meeting? | All documentation should be considered confidential. The DMC members will store their copies of the meeting papers securely after each meeting so they can check future reports against them. At the end of the study, DMC members will destroy all papers. A central record of all minutes, reports and correspondence by the DMC will be filed in the eTMF. Minutes from closed meetings should be made available to the NCTU for archiving after the platform has ended. |
| **8. Decision making** | |
| What recommendations will be open to the DMC? | • No action needed; platform and/or particular comparison continues as planned<br>• Early stopping due, for example, to clear benefit or harm of a treatment, futility, or external evidence<br>• Temporarily pausing recruitment allowing further follow-up data to be received<br>• Stopping recruitment within a subgroup (this should generally involve a recommendation to unblind the PSC to these data)<br>• Extending recruitment (based on actual control arm response rates being different to predicted rather than on emerging differences)<br>• Extending follow-up<br>• Stopping a single treatment arm of a multi-arm platform<br>• Approving the Statistical Analysis Plan |
| The role of formal statistical methods, specifically which methods will be used and whether they will be used as guidelines or rules. | There are no formal interim analyses planned during the platform.<br>Formal statistical methods are more generally used as "stopping guidelines" rather than absolute rules. This is because they generally only consider one dimension of the study. Reasons should be recorded for disregarding a stopping guideline.<br>In the light of interim data, and other evidence from relevant studies (including updated overviews of the relevant randomised controlled trials), the DMC will inform the PSC, if in their view there is proof beyond reasonable doubt that the data indicate that any part of the Protocol under investigation is either clearly indicated or contra-indicated, either for all or for a particular subgroup of study participants. A decision to inform the PSC will in part be based on statistical considerations. Appropriate criteria for proof beyond reasonable doubt cannot be specified precisely. A difference of at least 3 standard errors in the analysis of a major endpoint may be needed to justify halting, or modifying, a comparison prematurely.<br>If this criterion were to be adopted by the DMC, it would have the practical advantage that the exact number of analyses would be of little importance, and so no fixed schedule is proposed. Unless the DMC recommends modification or cessation of the Protocol, the PSC, collaborators and administrative staff (except those who supply the confidential information) will remain blind to the results of the analyses.<br>The Data Monitoring Committee (DMC) will also monitor futility of a treatment |

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| | continuously. If the conditional power at a given point is low, then stopping for futility should be considered. |
| How will decisions or recommendations be reached within the DMC? | The process of decision making will aim for consensus. The method of deliberation should not be revealed to the PSC as this may reveal information about the status of the platform's data.<br>The Chair will summarise discussions and encourage consensus and will give his own opinion last.<br>Every effort will be made by the DMC to reach a unanimous decision. If the DMC cannot achieve this, a vote will be taken, although details of the vote will not routinely be included in the report to the PSC as these may inappropriately convey information about the state of the platform data.<br>Implications (e.g. ethical, statistical, practical and financial) for the platform will be considered before any recommendation is made. |
| When is the DMC quorate for decision-making? | The Funder's guidelines for quoracy will always be adhered to which state the minimum quoracy for the DMC meeting to conduct business is at least two-thirds of the appointed independent membership.<br>Members of the DMC will make every effort to attend all meetings, and the Facilitator will try to ensure that a date is chosen to enable this. If, at short notice, any DMC member cannot attend at all, then the DMC may still meet if the Chair or Vice-Chair is present and two other independent members. If the Chair is unable to attend, they should confirm in writing their agreement with action as soon as possible after the meeting, or else call a further meeting. Members who cannot attend virtual meetings (or face-to-face when applicable) should provide comments to the Chair prior to the meeting if possible. If the DMC is considering recommending major action after such a meeting, the DMC Chair will speak with the absent member(s) as soon after the meeting as possible to assess whether they agree. If they do not, a further meeting will be arranged with the full DMC. |
| What happens to members who do not attend meetings? | If a member does not attend a meeting, every effort will be made to ensure that the member is available for the next meeting. If a member does not attend a second meeting, they will be asked if they wish to remain part of the DMC. If a member does not attend a third meeting, they will be replaced. |
| Will different weights be given to different endpoints (e.g. safety/efficacy)? | The primary outcome is assessed over 60 days post-randomisation and is ascertained from routinely collected health data. It comprises a four-level ordered categorical scale (modelled on the WHO recommendation):<br>1. No SARS-CoV-2 infection.<br>2. SARS-CoV-2 infection but resident remains in care home.<br>3. Admission to hospital (all-causes).<br>4. Death (all-causes).<br><br>Greatest importance will be afforded the primary outcome.<br><br>Secondary outcomes include important indications which may provide a safety signal. |
| Specific issues relating to the platform design that might influence the proceedings. | Given that the sample size parameters were estimated using data from the first COVID-19 wave, it is anticipated that the unblinded trial statisticians will conduct a review of the parameters during the trial, with a view to sample size re-estimation, for review by the DMC. |

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| | In addition, given the nature and urgency of the pandemic in care homes, it is anticipated that the Trial Committees (PSC, DMC and PMG) will meet regularly, the frequency dictated by the recruitment rate. |
| **9. Reporting** | |
| To whom will the DMC report their recommendations/decisions, and in what form? | The primary DMC reporting line is via the DMC Chair to the PSC Chair and copied to the CI. This will be via written communication of recommendations to the PSC, usually within 48 hours of the meeting and ahead of any scheduled PSC meeting. Minutes of the open session are shared with the PMG. Unless the DMC is recommending that the platform Protocol be changed in some way, the documentation of recommendations to the PSC should not reveal any closed session data. Additionally, the letter should be copied to the CI although this copy should have any closed session data removed and noted as such. See Annexe 5. |
| Will minutes of the meeting be made and, if so, by whom and where will they be kept? | Minutes of the open session will be taken by a member of the NCTU. Once agreed by the DMC, these should be sent to all members of DMC, the Sponsor, the Funder, the PSC and the PMG. Notes of the closed session(s), taken by the DMC Chair or another member, will remain confidential to the DMC. The recommendations for the PSC made by the DMC are sent to the PSC and CI as detailed above. The DMC Chair will approve all minutes. |
| What will be done if there is disagreement between the DMC and the body to which it reports? | If the DMC has serious problems or concerns with a PSC decision, a joint meeting of these groups will be held, if possible face-to-face. The information to be shown will depend upon the action proposed and the DMC's concerns. Depending on the reason for the disagreement, confidential data may have to be revealed to those attending such a meeting. The meeting should be chaired by a senior member of NCTU or an external expert who is not directly involved with the platform. If disagreement persists, the Sponsor and/or Funder should become involved as appropriate. |
| **10. After the platform** | |
| Publication of results. | The CI has the responsibility for ensuring that the results for each comparison will be published in a correct and timely manner. |
| What information about the DMC will be included in published platform reports? | DMC members will be named, and their affiliations listed in the main report unless they explicitly request otherwise. |
| Will the DMC have the opportunity to approve publications, especially with respect to reporting of any DMC recommendation regarding termination of a platform? | Members of the DMC may wish to be given the opportunity to read and comment upon any reports of the platform before these are submitted for publication. |
| Are there any constraints on DMC members divulging information about their deliberations after the platform has been published? | Unless permission has been agreed with the PSC, individual DMC members will not discuss confidential information to which they have become party as a result of their involvement in the platform until 12 months after the primary results have been published for each comparison. |

## Figures and Appendices

## Annexe 1 - Committee membership

| Data Monitoring Committee (DMC) member | Membership status |
|---|---|
| *Name, Title, Institute* | |
| Prof Kennedy Lees, Emeritus Professor of Cerebrovascular Disease, University of Glasgow | Chair, Independent member |
| Prof Tim Peters, Professor of Primary Care Health Services Research, University of Bristol | Independent member |
| Dr Ben Carter, Senior Lecturer in Biostatistics, King's College London | Independent member |
| Prof Finbarr Martin, Emeritus Professor of Medical Gerontology, King's College London | Independent member |
| Dr Eileen Burns, Consultant in Care of the Elderly, Leeds Teaching Hospitals NHS Trust | Independent member |
| Prof Philip Bath, Prof of Stroke Medicine, University of Nottingham | Non-independent member (open session only) |
| Prof Adam Gordon, Professor of the Care of Older People, University of Nottingham | Non-independent member (open session only) |
| Dr Reuben Ogollah, unblinded trial statistician, University of Nottingham | Observer |
| Mr Martin Law, unblinded trial statistician, University of Cambridge | Observer |
| Prof Alan Montgomery, Professor of Medical Statistics, University of Nottingham | Observer (open session only) |
| Prof Thomas Jaki, Professor of Statistics, University of Cambridge | Observer (open session only) |
| Dr Christopher Partlett, blinded trial statistician, University of Nottingham | Observer (open session only) |
| Ms Lucy Bradshaw, blinded trial statistician, University of Nottingham | Observer (open session only) |
| Dr Caroline Rick, Associate Professor of Clinical Trials, University of Nottingham | Observer (open session only) |

| Platform Steering Committee (PSC) member | Membership status |
|---|---|
| *Name, Title, Institute* | |
| Prof Alistair Burns, Prof of Old Age Psychiatry, University of Manchester | Chair, Independent member |
| Prof Shaun Treweek, Professor of Health Services Research, University of Aberdeen | Independent member |
| Prof James Wason, Professor of Biostatistics, Newcastle University | Independent member |
| Prof Anne Forster, Professor of Stroke Rehabilitation, University of Leeds | Independent member |
| Prof Azhar Farooqi, General Practitioner, East Leicester Medical Practice | Independent member |
| Prof Martin Vernon, Consultant Geriatrician, Manchester University NHS Foundation Trust | Independent member |
| Mr Peter Pratt, Pharmacist, NHS England/NHS Improvement | Independent member |
| Ms Linda Hamlin, Patient and Public Involvement representative | Independent member |
| Ms Vic Rayner, Executive Director, National Care Forum | Independent member |
| Prof Philip Bath, Prof of Stroke Medicine, University of Nottingham | Non-independent member |
| Prof Adam Gordon, Professor of the Care of Older People, University of Nottingham | Non-independent member |
| Prof Alan Montgomery, Professor of Medical Statistics, University of Nottingham | Observer |
| Prof Ed Juszczak, Professor of Clinical Trials & Statistics in Medicine, University of Nottingham | Observer |
| Dr Christopher Partlett, blinded trial statistician, University of Nottingham | Observer |
| Ms Lucy Bradshaw, blinded trial statistician, University of Nottingham | Observer |
| Dr Caroline Rick, Associate Professor of Clinical Trials, University of Nottingham | Observer |

## Annexe 2 - Abbreviations

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| CI | Chief Investigator |
| CTIMP | Clinical Platform of an Investigational Medicinal Product |
| DMC | Data Monitoring Committee |
| ISRCTN | International Standard Randomised Controlled Trial Number |
| NCTU | Nottingham Clinical Trials Unit |
| NIHR HTA | National Institute for Health Research Health Technology Assessment |
| PMG | Platform Management Group |
| PPI | Patient and Public Involvement |
| PSC | Platform Steering Committee |

## Table 1 - Potential competing interests for <u>independent</u> members

- Stock ownership in any commercial companies involved
- Stock transaction in any commercial company involved (if previously holding stock)
- Consulting arrangements with the Sponsor/Funder
- Ongoing advisory role to a company providing drugs to the platform
- Frequent speaking engagements on behalf of the intervention
- Career tied up in a product or technique assessed by platform
- Hands-on participation in the platform
- Involvement in the running of the platform
- Emotional involvement in the platform
- Intellectual conflict e.g. strong prior belief in the platform's experimental arm
- Involvement in regulatory issues relevant to the platform procedures
- Involvement in the writing up of the main platform results in the form of authorship

The definition of <u>independent</u> is as follows:

- Not part of the same institution as any of the applicants or members of the project team
- Not part of the same institution that is acting as a recruitment or investigative centre
- Not related to any of the applicants or members of the project team
- For the Chair only – not an applicant on a rival proposal

## Table 2 - Potential competing interests for <u>non-independent</u> members

- Stock ownership in any commercial companies involved
- Stock transaction in any commercial company involved (if previously holding stock)
- Consulting arrangements with the Sponsor/Funder
- Ongoing advisory role to a company providing drugs to the platform
- Frequent speaking engagements on behalf of the intervention
- Intellectual conflict e.g. strong prior belief in the platform's experimental arm
- Involvement in regulatory issues relevant to the platform procedures

## Annexe 3 - Agreement and competing interests form for DMC members

(please initial box)

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| I have read and understood the PROTECT DMC Charter Version 1.0 dated 09-Jun-2021 | |
| I agree to join the DMC for this platform | |
| I agree to treat all sensitive platform data and discussions confidentially | |

The avoidance of any perception that independent members of a DMC may be biased in some fashion is important for the credibility of the decisions made by the PSC and for the integrity of the platform.

Potential competing interests should be disclosed via the NCTU. In many cases simple disclosure up front should be sufficient. Otherwise, the (potential) independent DMC member should remove the conflict or stop participating in the DMC. **Table 1** lists potential competing interests for independent members. **Table 2** lists potential competing interests for non-independent members.

(please initial box)

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| **No,** I have no potential competing interests to declare | |
| **Yes,** I have potential competing interests to declare (please detail below) | |

Please provide details of any potential competing interests:

Name:_____

Signed:_____ Date:_____

## Annexe 4 - Agreement and confidentiality agreement for observers

(please initial box)

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| I have read and understood the PROTECT DMC Charter Version 1.0 dated 09-Jun-2021 | |
| I agree to attend the Data Monitoring Committee meeting as an observer | |
| I agree to treat as confidential any sensitive information gained during this meeting unless explicitly permitted | |

Name:_____

Signed:_____ Date:_____

## Annexe 5 - Suggested letter from DMC to PSC where recommendation is to continue

<Insert date>

**To:** Chair of Platform Steering Committee

Dear Professor Burns

The Data Monitoring Committee (DMC) for the PROTECT platform met on <meeting date> to review its progress and interim accumulating data. <List members> attended the meeting and reviewed the report.

We congratulate the platform organisers and collaborators on the progress and conduct of the platform and the presentation of the data. The research question(s) remains/remain important and, on the basis of the data reviewed at this stage, we recommend continuation of the <comparison name> according to the current version of the Master Protocol <specify protocol version number and date> with no changes.

We shall next review the progress and data <provide approximate timing>

Yours sincerely,

Prof Kennedy Lees

**Chair of Data Monitoring Committee**

On behalf of the DMC (all members listed below)

DMC members:
Prof Kennedy Lees, Emeritus Professor of Cerebrovascular Disease, University of Glasgow

Prof Tim Peters, Professor of Primary Care Health Services Research, University of Bristol

Dr Ben Carter, Senior Lecturer in Biostatistics, King's College London

Prof Finbarr Martin, Emeritus Professor of Medical Gerontology, King's College London

Dr Eileen Burns, Consultant in Care of the Elderly, Leeds Teaching Hospitals NHS Trust

## Annexe 6 - Summary of changes from previous version of DMC Charter

| Version Number | Details/reason for change | Authorised by (print name) | Role | Signature | Date |
|---|---|---|---|---|---|
| **1.0** | This is version 1.0 of the DMC charter for this platform. There are no changes to be reported. | | | | |
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