Minutes of the NERVTAG Subgroup on Clinical Risk Stratification: First meeting

Date & Location: 14:30 – 16:00, 20 May 2020 - Via telecon only

In attendance:

Julia Hippisley-Cox (JHC) (Chair), Fran Parry-Ford (Secretariat/Minutes), Elaine Stanford (admin support).

NERVTAG Members: Peter Horby (PH), Andrew Hayward (AH)

Sub-group members: Elizabeth Williamson (EW), Ruth Keogh (RK), Karla Diaz-Ordaz (KDO), Harry Hemingway (HH), Ewen Harrison (EH), Jonathan Benger (JB), David Spiegelhalter (DS), Carol Coupland (CC) , [redacted]

DHSC Observers: [redacted], [redacted], [redacted], [redacted], [redacted]

1.0 Protocol and approach

1.1 The Chair provided some background to the project. DHSC/NHS are looking for one clinical risk stratification tool that can be used to develop policy. This group has been tasked to arrive at a best consensus view. This needs to be developed via a transparent process, with a clear methodology, and all papers and code will be made public and available for scrutiny and for other groups to validate the work. The main output of the work needs to be clear risk stratification with a clear methodology, that is defensible. JB confirmed that NHS Digital have a digital architectural technician who is starting to look at the final, public facing outputs for this.

1.2 The Chair noted that she has started work to develop a protocol that all of the group can feed into. This protocol will be hosted in the public domain and updated. The Chair noted that the group will need to agree on a place to host the protocol, where it can be accessed easily. NHS digital offered to host it on their website along with similar documents. The Chair commented that this could be a decision for later, but that wherever it was hosted, a mechanism to record outside comments and enquiries, and to feed these back into the group was required.

Action: All to review and send any comments on the current version of the protocol by 5pm Thursday 21 May.

Action: All to confirm by e-mail to JHC that they have reviewed the protocol, and are happy for their name to be associated with it by 5pm Thursday 21 May.

1.3 The Chair asked NM to provide some more detail on the ask from CMO. NM noted that the aim was to develop a way of risk stratifying the population at a population level, so

that policy decisions can be made, and also to develop a tool that clinicians can use to discuss individual risk. NM noted that they receive regular enquiries from patient groups around why specific conditions do not fall under the shielding group. The model is likely to be heavily age modulated, and may result in some people being taken out of shielding. It was noted there might be issues related to the granularity of data in the model.

1.4 The Subgroup commented on the need to involve patient groups at an early stage to test the presentation and communication of the data. The Chair asked if DS could support this work. DS replied that they were happy to be involved with testing of the final product via patient groups, but public facing communications around the protocol would be better done by someone else. The Chair suggested DHSC should take on this task.

Action: DHSC to start draf ting lay explanations of the work/proposals for the tool, which could be tested with the working group, and then with patient groups.

2.0 Development of the model

2.1 The group discussed the type of risk that the stratification should be based on. The group agreed it was key to get people into risk bands/strata – and not to apply numerical and individual risk scores. The group agreed to use relative risks (relative to another person's risk), rather than absolute risks.

2.2 The group agreed on the need to be clear that this risk stratification shouldn't be used to inform clinical decision making – such as decisions over who would or not get treatment, or qualify for ICU.

2.3 The group discussed possible outcome measures. Most members agreed that risk of death if positive for COVID-19 should be the primary outcome measures, noting that a definition of a COVID-19 positive death was required.

Action: All to contribute towards developing a precise definition of COVID-19 mortality - ideally to match the figures which the govt has been publishing.

2.4 The group discussed other possible outcomes, and whether a composite measure could be used. The group noted that including composite outcomes such as death and admission to hospital would provide greater clinical gr anularity, however composite outcomes would be harder to interpret. The group agreed that the public are likely to be more interested in the risk of death than other outcome measures.

2.5 The group agreed to use the following outcomes:

i. Primary outcome: COVID-19 positive death

ii. Secondary outcome: Hospital admission

2.6 The group discussed the study population and whether children should be included. NM noted the paediatric view that the shielding list for children is too large – and that the risk to children of being kept off school outweighs the risk of a child in a cli nically vulnerable group.

2.7 EW suggested it would be necessary to look at a separate risk model for children with difference outcomes, as their inclusion would skew the results. The group agreed that children should be excluded from the main analysis, and that a separate work stream should be established

2.8 The Chair raised the issue of which conditions to include in the analysis, and how these are coded. It was agreed to include all conditions on the current shielded list. NHSD has already published the coding for all the patients who are on the shielding list. The Chair asked other groups to share their coding lists.

Action: All who agreed to share code lists to aim to send these before 21 May

2.9 The group discussed the data quality and missing data, and whether there is any need to adjust for co-variates that are regularly missing. It was noted that co-variates which are non-significant will affect the model, but the level of available data means the power within the study should compensate for this.

2.10 The group discussed if there was value in having a dual tool - a detailed version with higher granularity that works within GP lists, and a public facing model that is usable for the public. However, it was noted that this could result in people being identified by their GP but not via the website.

2.11 The group agreed that as death is the primary outcome, and these are short term risks, a more complex competing risk model was unnecessary.

2.12 EW shared experience from the OPENSafely work, noting that some co variates on the list they don't have codes for, or would be difficult to code via primary care, such as chemo/radiotherapy, and pregnancy.

2.13 The group noted the need to consider pregnancy – increasingly facing questions around pregnancy and there is emerging evidence around vertical transmission. The group agreed not to put pregnancy into a Phase I model, but instead look at the epidemiology on this.

2.14 The group noted the Phase II development of the model could include linkage to the CO-CIN data.

3.0 Timelines and further actions

3.1 The group noted the very tight timelines for the work, which will be considered by SAGE w/c 25 May. The following actions were also noted:

Action: JHC to aim to produce a working model by the end of the week.

Action: NERVTAG Secretariat to schedule next meeting for **Monday 25 May** to discuss emerging findings.

Action: Anyone requiring access to the data to contact JHC to join the NHSD Data Sharing Agreement

Action: Anyone who wishes not to or does not have the time to comment on the paper for publication to let JHC know.

Minutes of the NERVTAG Subgroup on Clinical Risk Stratification: Second meeting

Date & Location: 9:00 – 11:30, 26 May 2020 - Via telecon only

In attendance:

Julia Hippisley-Cox (JHC) (Chair), [redacted], Elaine Stanford (admin support).

NERVTAG Members: Peter Horby (PH), Andrew Hayward (AH)

Sub-group members: Elizabeth Williamson (EW), Ruth Keogh (RK), Karla Diaz-Ordaz (KDO), Harry Hemingway (HH), Ewen Harrison (EH), Jonathan Benger (JB), David Spiegelhalter (DS), Carol Coupland (CC), Julian Thomas (JT), Kamlesh Khunti (KK), Ashley Clift (AC), [redacted]

DHSC Observers: [redacted], [redacted], [redacted] [redacted]

1.0 Discussion of protocol

1.1 The Chair requested that all members submit the ICJME forms on competing interests to complete the relevant section in the protocol (under Item 9 Other interests).

Action: All to complete ICJME forms and submit to JHC

Use of the tool

1.2 The sub group addressed the question of whether the tool is a risk calculator for people who have the virus, or a tool for providing people with their risk of getting the virus, and suffering severe complications. Members discussed the difficulty of teasing the two variables apart as the data currently available is a compilation of the two risks. It was noted that the perspective of public communication, combining the risk of contracting , and dying from COVID-19 could be confusing.

1.3 NM confirmed that the steer from cross-government is clear, the public want the risk of what happens if you get the virus, and the associated risk of dying. KK raised the point that there is little that can be done once the disease has been contracted and suggested that the public, and especially key workers, healthcare workers, and teachers are concerned about their risk of contracting COVID **and** their subsequent risk of dying.

1.4 PH expressed a view that the policy purpose of the risk stratification tool is to give advice on who should be more stringent about avoiding infection because their risk of dying is higher. The group agreed that the purpose of the current task is to develop a tool to identify the risk of severe outcome if infected.

1.5 The Chair suggested a potential second piece of work looking at a different outcome e.g. following hospitalisation with COVID, what are the determinants of whether you end up in ICU or not, and mortality.

1.6 The group discussed several aspects of the second piece of work such as geographical incidence, behaviour and occupation. JB suggested that analysis should be done on both a population level, as well as those who tested positive to determine the outcomes, noting that it is likely that the relative risks will be the same across both analyses, and that if the outcomes are different across the two groups, this will provide information about catching the disease.

1.7 JB made the point that the protocol that has been written does not answer the question that has been asked of the group, which is 'what is the r isk of dying if you are infected with coronavirus?'. DS stated the need to be explicitly clear in the protocol that the data currently available is unable to produce the risk of dying if infected. A strong element of judgment is required to interpret the results.

1.8 Chair stated a preference for going ahead with answering the question 'what is the risk of contracting and having severe outcomes', and once further data becomes available, asking the question 'what is the risk of dying if infected', and there was general agreement to this within the subgroup, noting the need to be extremely clear in the write up about what exactly it can be used for.

1.9 The Chair summarised that the project will be executed as it is currently written in the protocol, being extremely clear about the tool's abilities and limitations. A separate protocol will be written looking at the risk of dying once infected, Chair asks that if any member is interested in taking this piece of work forward, that they contact her.

Action: Any interested member to contact the Chair if they are interested in developing a secondary, more detailed protocol to further explore the findings of the current protocol.

Finalisation of outcome

1.10 The Chair proposed a definition; the fact of death as somebody who has had a positive test, or the fact of death in somebody who has an ICD10 code of suspected or confirmed COVID. These definitions include out of hospital deaths, and are the most inclusive.

1.11 The Chair suggested not using ICU data as an outcome for the current study, however potentially using as a process measure for a secondary, more detailed protocol. The Chair noted these definitions include only people who tested positive while in hospital, or before they went to hospital and not those who tested pos itive after returning home. The proposed admission criteria could be ICD10 code of hospital admission due to COVID, or hospital admission of any sort in a COVID positive case.

1.12 All members agreed with these definitions.

1.13 EH raised the issue of the definition of hospital admission, and that due to criteria changes on 10 March, those admitted to hospital before and after this date are two different cohorts. Those admitted prior to 10 March have a lower risk than those admitted following. As hospital admission is being used as a surrogate for severity of

disease, EH believes it necessary to exclude those patients who were admitted before 10 March, and would not require a positive test, it was agreed that excluding this cohort will make little difference, due to the small numbers.

1.14 The Chair lead a discussion around using hospital admissions, deaths, or a composite measure. Composite measure was favoured in the previous meeting due to power and competing risk. RK stated that competing risks are not difficult to deal with, and they didn't think the issue of having competing risk of death is a valid reason to have a composite outcome.

1.15 The Chair suggested a compromise of primary outcome being hospital admission, secondary being death, and tertiary being a composite measure. This allows comparison between the three. This was agreed by the group.

Finalisation of predictor variables

1.16 The group discussed where the definitions for specific variables have come from; and agreed on using standard definitions where they exist, existing GP definitions for Q risk etc., where there is a new variable, they started with NHS digital lists and colleagues have provided further definitions.

1.17 The group discussed how to classify severity of asthma, COPD etc. A suggestion made to use medications prescribed, however current definitions rely on good access to healthcare. The Chair suggested using the definitions that have been provided by NHSX, these could be updated in the future if required. It was noted that smoking appears to have a negative relationship with outcomes of COVID and caution is required when producing the risk score.

1.18 The Chair suggested that the current predictor variable list will be used unless people have strong views otherwise, the chair has noted comments regarding the difficulty of coding asthma and COPD.

Handling of obesity/BMI – categorical vs. continuous

1.19 There was general agreement to treat the variable as continuous and include non-linear terms, and the Chair suggested presenting results per unit increase in body mass index in a table. The group agreed to look at the interaction between ethnicity and BMI.

Analysis – Cox model vs competing risk

1.20 The sub-group discussed the pros and cons of competing risks. A competing risks model has some interpretation risks, and may produce some unintuitive results for example an older, more frail person may produce a lower risk than a younger healthier person, because they are more likely to die of other cause s.

1.21 The group suggested completing both a standard cox model, as well as a competing risk model, and then evaluating the ten-year risk of both models to see how closely they aligned. EH raised the point that the purpose of the study is not to identify causality, models are not set up to tease apart the actual causal path to death. Competing risks analysis will give the most accurate probability of death for individuals entering their data. CC agreed with completing both models and combine them to give a comp eting risk estimate, but there is a need to look at the individual cause specific effects to help with interpretation.

1.22 The group discussed how to deal with variables that have counter -intuitive results e.g. smoking. There was some disagreement within the group around whether to exclude them from the analysis.

1.23 The group agreed that if variables are to be removed, there should be a scientific basis or consistent rule for this. KDO offered to help via the use of a Lasso method to screen the variables, and then running the Cox model.

1.24 The Chair suggested reporting analysis that includes smoking in the paper, but taking it out for any public facing tool, ensuring that reasons are thoroughly explained, acknowledge that there is being work carried out attempting to understand the relationship with smoking.

1.25 The group agreed that regarding competing risks, both cause specific hazard ratios and causes of deaths, and the sub-distribution version would be completed and compared.

2.0 Implementation plan

2.1. The Chair agreed to work on version 1.3 of the protocol. The Chair asked CC, RK and KDO n the next 24 hours, to come up with some text that can be included in the protocol that describes both approaches that have been agreed upon, that can be used as methods for the analysis. This can then be implemented.

2.2. The group had a discussion regarding the imputational model, noting that all that is being imputed is BMI. Chair asks if people are happy with just one imputational model? There was general agreement from RK and CC that this would be ok.

2.3. The group agreed that there is nothing currently further to decide.

2.4. Chair will initially send version 1.3. of the protocol to AC, CC, RK and KDO to get the analysis section completed.

Action: CC, RK and KDO to send text to Chair, that will be included in the protocol describing both analysis approaches that have been agreed upon.

Action: Secretariat to schedule meeting for Chair, CC, RK, KDO and AC to be scheduled for 28/29 May 2020, to discuss analysis following implementation

Action: Chair to produce version 1.3. of the protocol and share with group.

Action: Secretariat to schedule a full group meeting for Monday 1 June 2020.

Minutes of the NERVTAG Subgroup on Clinical Risk Stratification: Third meeting

Date & Location: 10:00 – 11:00, 1 June 2020 - Via telecon only

In attendance:

Julia Hippisley-Cox (JHC) (Chair), Fran Parry-Ford (Secretariat)

NERVTAG Members: Peter Horby (PH), Andrew Hayward (AH)

Sub-group members: Elizabeth Williamson (EW), Ruth Keogh (RK), Karla Diaz-Ordaz (KDO), Harry Hemingway (HH), Ewen Harrison (EH), Jonathan Benger (JB), David Spiegelhalter (DS), Carol Coupland (CC), Julian Thomas (JT), Kamlesh Khunti (KK), Ashley Clift (AC), [redacted]

DHSC Observers: [redacted], [redacted]

1.0 Update on Validation of data sets

1.1 The group discussed whether to add further predictors at this stage, and agreed not to and to consider adding these to stage 2 of the project.

1.2 The Chair updated on the validation via the Open Safely platform – they are happy to proceed on the basis discussed over e-mail. The Chair noted possible time delays in creating the new variable – noting they are committed to creating those as quickly as possible. EW will lead on the validation of this work in the openSafely Platform.

1.3 The Chair noted discussions around the EAVES11 platform and whether a validation can be completed using the Scottish data set. NM noted that CMOs in DAs are aware of the work, and there is desire for alignment across the four nations as far as possible.

1.4 KDO is meeting Chris tomorrow to discuss SAIL and will raise it and provide an update.

2.0 Discussion of emerging results

2.1 The subgroup discussed variation in death rates from various sources, particularly compared to the death rate data in the model, compared to the ONS data. The Chair noted that she would like to include the data up to the end of April and then re-run e models.

2.2 CC presented the plots of f ractional polynomial terms for age, and body mass index – noting that the curves go up steeply with age, and that BMI is a U-shaped curve. The group suggested that it would be interesting to plot the data on a log scale.

2.3 The Chair noted that she has tried to categorise for overlapping variables. 70% of the records have complete BMI, alcohol, ethnicity and alcohol use.

2.4 The Chair gave a summary of some of the key variables that showed associations

- Pakistani men had 2x the risk compared to white men.
- There was an apparent negative association with smoking.
- Asthma not significant – but this may be due to the effect of shielding
- COPD patients on triple therapy did not show a significant risk, people not on triple therapy did have an increased risk. This could be due to the protective effect of the medications or an issue of power.
- Renal therapy/CKD – JHC noted she has used a graduated approach here. The risk for those on dialysis is high, this could reflect outbreaks on dialysis wards.
- JHC noted that she has combined rare neurological conditions into once group including: motor neuron, MS, myasthenia gravis, etc.
- Downs syndrome showed an association with increased risk, this was independent when adjusting for age, care home residence and learning disabilities. JHC noted the need to come up with recommendations for this group.
- Blood cancers still have an increased risk despite shielding.
- Lung and oral cancers are associated with an increased risk
- Care homes are associated with increased risk, despite there being some data missing.

2.5 The sub-group discussed the use of automatic back-wise selection –this needs careful consideration of the implications of using this so that the protocol has good face validity. The Chair expressed a preference not to use that route, until we have better data, and the group agreed.

2.6 The group discussed how to present the associations. HH made an observatio n around the difficulty of achieving face validity in a disease that hasn't been seen before – noting that it would be important to show the univariate or age adjusted hazard ratios for every variable we have included so that these are in the public domain .

2.7 The group agreed there would be a need for the presentation of the results to be clinically driven and supported by the data, but not constrained by p -values. Statistical significance may not be the best as a primary measure. NM agree it's important to use the best balance clinically and statistically, and test these with patient groups. And then go back with other predicted variables.

2.8 The group discussed whether it was possible to use the shielded patients list to undertake a further analysis. The Chair noted she now had the NHS numbers of all the shielded individuals and there were no deaths in that group – this is because the list only includes people who are shielded on the day that data is released, so those who may have died have been removed.

2.9 The group suggested running the original algorithm so that we have an approximate list of the original shielding list.

3.0 Implementation Plan

3.1 JB updated on the implementation plan within NHS Digital – they are working with DS and the Winton centre to collaborate around presenting the outputs. There will be a public facing tool, a clinical tool and tools to support work places, triage systems to put in place enhanced monitoring, and to inform policy around shielding. JB noted the need to make sure outputs support this effectively

3.2 This work has included discussions around how risk is communicated and the number of bands of risk – looking at international work to inform this.

3.3 The combination issue i.e. that the tool represents a combination risk of susceptibility to infection and risk of severe outcomes once infected is challenging. There are ongoing discussions around how best to disentangle those two issues so that those using the tool understand the risk. There will be a challenge in presenting this, and need some clinical/policy interpretation, and some senior clinical input to inform the outputs of the tool.

3.4 The Chair noted the need to be able to relate the end product back to the reference implementation of model – the modellers need to be involved with the loop at the end.

3.5 The Chair noted the need to work out how many people might be in these bands once we have developed them – this group might be able to help this. The Chair now has the shielded list, would be able to confirm how many would be on the new shielded list and the old shielded list.

3.6 The group noted that there were some outstanding intellectual property issues that need to be confirmed and the Chair asked all members to reply to the email from Oxford research services so that the contract with NIHR can be finalised.

3.7 JB raised the issue that GP suppliers will need to be able to include this tool in clinical systems – patients will want to discuss with the GP what their risk is, and GPs will need an evidence-based way of describing this. JH and JB are involved in this part of the work within NHSD. The group noted the priority is to get the risk stratification right to inform policy and produce a GP facing tool, a public facing tool may follow in a later phase.

4.0 Timelines

4.1 The group agreed the need to f inalise the protocol, particularly the issue around how the variables are selected. The Chair to circulate the final version to use a locked version.

4.2 Some edits to the protocol were discussed, including:

- Declaring within that age-adjusted univariate analysis will be provided

- DS to make some edits to the protocol specifying the limitations of the model, and consider changing the title.
- Including wording within the protocol about exploring anomalous findings.

4.3 On timelines NM noted that the timelines for this had been relaxed as the government is not planning to announce the work until there is a wider plan for engaging stakeholder therefore asked if the group could hold off from publishing at the moment. NM will provide an update later in the week on this.

4.4 The Chair highlights the next steps:

- Obtain the updated mortality data to run in the model
- Record that we have locked down the protocol
- Run the models considered to be the best and validate this against the validation set
- Begin to write up the paper and in parallel develop the communications around the publication of the protocol
- Include the univariate analysis alongside as this is important to patient groups

5.0 Summary of actions

The Chair summarised the actions as below:

- JB to aim to send the updated mortality and HES data to JHC by the end of the day (1 June)
- JB to share the project implementation plans/documents with the group.
- JHC to update the protocol based on comments from the meeting
  - DS to add in comments around what the model can be used for, and consider tweaking the title
  - Include note that we will look at age adjusted univariate analysis for a range of variables
  - Include note that we may do further analysis on anomalous results and revise the model based on that
- NM to summarise the next steps in terms of the policy work
- JHC to send Zoom link for next meeting on Monday 8 June

Minutes of the NERVTAG Subgroup on Clinical Risk Stratification: Fourth meeting

Date & Location: 10:00 – 11:30, 8 June 2020 - Via telecon only

In attendance:

Julia Hippisley-Cox (JHC) (Chair), Emma Petty (Secretariat), Elaine Stanford (Secretariat support)

NERVTAG Members: Peter Horby (PH), Andrew Hayward (AH), Calum Semple (CSm)

Sub-group members: Elizabeth Williamson (EW), Ruth Keogh (RK), Karla Diaz-Ordaz (KDO), Harry Hemingway (HH), Jonathan Benger (JB), Carol Coupland (CC), Kamlesh Khunti (KK), Ashley Clift (AC), Aziz Sheikh (AS), Ronan Lyons (RL), John Robson (JR), Jonathan Valabhji (JV), [redacted]

DHSC Observers: [redacted], Jenny Harries (JH)

Apologies:

Ewen Harrison (EH), David Spiegelhalter (DS)

1.0 Welcome and new members

1.1 The four new members (AS, RL, JR & JV) were welcomed to the subgroup.

2.0 Apologies

2.1 Apologies were noted from EW.
Post meeting – DS provided apologies for the meeting.

3.0 Competing interests

3.1 The Chair asked subgroup members to complete the competing interest forms, if they had not already done so.

*Action: **Members** to complete the competing interest forms*

4.0 Collaboration agreement

4.1 The Chair advised members that a collaboration agreement had been prepared by Oxford University. Members were asked to advise the Chair if their name should be included on the agreement as an investigator.

*Action: **Members** to indicate inclusion on the collaboration agreement to JHC by COP 8th June*

4.2 The Chair noted the grants available to cover aspects of the collaboration work and asked to be advised of potential funding requests to cover the development of the risk model using the Q research database. The resources available for the validation of the model would be covered separately.

Action: ***Members*** *to indicate potential funding requests for collaboration work to JHC*

4.3 The Chair advised members that there was an agreement in principle with Northern Ireland for facilitating the project, with data available from 200 GP practices for use in the validation of the model. It was noted that all of the UK CMOs were aware of the project and were looking for a collaborative approach across the UK, while recognising there may be challenges in implementation.

5.0 Minutes and matters arising

5.1 The minutes of the last meeting were reviewed. It was requested that clarification was made to state that the first priority for the risk stratification tool was for use in clinical practice. The minutes were agreed with no further amendments.

Action: ***Secretariat*** *to amend minutes to note the priority requirement for the risk stratification tool*

6.0 Policy update and publication of protocol and comms

6.1 NM noted that there is provisional agreement for the protocol to be published the week commencing 15th June 2020, in conjunction with the announcement of the changes in shielding measures. The site of publication will be confirmed, with consideration given to the lead-in times required by different sites. A document on the project is being produced for sharing with stakeholders across government and the importance of involving the DAs was recognised. Members were reminded that the work will remain confidential until the publication of the protocol.

7.0 Model development update

a. Update on data
b. Final list of predictors
c. Paper writing

7.1 The Chair updated members on the selection of predictors using the Lasso technique and not the numbers associated with each predictor, to produce a list. This approach can produce a tool for implementation into the GP system, but may generate problems for a web-based risk calculator. The results from the models will be circulated to the sub group and the selection of the model will be discussed at the next meeting.

7.2 Members discussed the datasets being used in the development and internal validation of models, and the data coverage across the UK. It was noted that complete data is available on outcomes to 30th April 2020. The current shielded patient list has also been provided. AH confirmed the discrepancy in the ONS data was due t o rates being annualised.

8.0 Model validation update including data access and governance approvals

a. OpenSafely
b. EAVES 11
c. SAIL
d. Northern Ireland

8.1 The access for OpenSafely was discussed. There is an agreement that new variables required for this work will be developed by OpenSafely.

8.2 The Chair asked for any resources required for the validation work to be flagged. It was proposed that a validation pack could be produced, wh ich would include definitions. The coding used in the various systems was discussed, with consideration of whether translation of codes was required. It was suggested that Snomed could be used. The Chair agreed to clarify the coding requirements required f or the validation.

*Action: **Members** to advise JHC on resources required to undertaken validations*

*Action: **JHC** to check on the coding requirements for a standardised format to use with the model validation*

8.3 Members were provided with details of the EAVES dataset, covering 5.3 million people in Scotland. It was noted that funding was in place to cover the validation work, but additional resource would be needed for the front -end work. Details on the SAIL dataset for Wales were provided to members, with agreement in place for the validation work to be undertaken. Members considered the minimum validation required for this project, and how many validation sets were required from each of the four UK countries. Members discussed region variables and nation variables, with consideration of differences between areas.

8.4 The issue of validation of specific disease states, such as diabetes, were discussed. It was suggested that type I diabetes could be used as a validation sample, with the protocol updated accordingly. The Chair noted that separate estimates would be produced for type I and type II diabetes, but these will not be further defined on medication. Duration of disease could be considered for future iterations of the model.

*Action: **JHC** to update the protocol to include a specific disease group (e.g. type I diabetes) as a validation sample*

8.5 Members discussed how to account for geographical areas, noting that there was limited ability to discriminate transmission in local areas. The Chair added that the model will produce some form of absolute risk with recognition of the limitations.

9.0 Patient engagement

9.1 AC informed members that a network of 30-40 PPI volunteers had been established, which is very responsive. It is suggested that between 5 -10 volunteers could provide feedback on the lay summary through answering a specific set of questions. It was agreed that this would not proceed until the protocol had be en published (w/c 15th June). Members were reminded that the protocol inclu des engagement with the public and it was agreed that the protocol should be updated to note that engagement would proceed immediately following publication.

*Action: **JHC** to update the protocol to state that patient involvement will commence in conjunction with publication of the protocol*

10.0 Professional engagement and piloting in GP practices

10.1 This item was covered in earlier discussions.

11.0 Implementation

11.1 Members discussed the utility of the model, not just its accuracy of prediction. It was noted that models developed in low risk populations may underestimate risk in high risk populations. The question of how the model would be operationalised was raised. The use of a risk threshold to produce a shielded population list was considered. The requirement is the production of a tool to either identify the numbers of patients at highest risk or to determine those at risk according to a set threshold. The approach will depend on the results from the model and the numbers involved. Member s discussed the possibility of a version that does not reference GP records, for use in areas of low GP registration and for certain highly vulnerable groups, and also the need for a public facing version. It was noted that the model does consider HIV, drug abuse and hepatitis, which will capture some vulnerabilities. Care needs to be taken to avoid different messages being made on risk from different versions. Consideration of different forms of the tool would be made sequentially, following the release of the GP version. It was noted that, in time, a simplified public version may be published, although this would need careful consideration to ensure that it was consistent with the under-pinning research and the reference implementation of algorithms which will be produced. The implementation of the tool will impact on several areas of government and will require co-ordinated engagement. It was proposed that there should be an agreed implementation plan, with the focus on producing a tool for use with the GP system to determine those at high risk. Cabinet Office should consider the implementation requirements and associated issues, including the use of the tool with regards to shielding, to contact tracing and to immunisation .

*Action: **NM** to confirm the requirement for the use of the tool – whether a threshold will be required or identification of a specific percentage*

12.0 General discussion

12.1 No points were raised for this item.

13.0 Summary of actions and next steps

13.1 The Chair requested that the secretariat circulate the lists of actions.

14.0 AOB

14.1 The Chair raised two issues. The first concerned the engagement of GPs in using the tool. The issue of remuneration for GPs was discussed similar to other risk stratification tools which have been associated with a Designated Enhance Service. It was noted that a number of approaches were available through NHS Digital; however, the complexity of the model and the parameters it encompasses will need to be understood

to determine the most appropriate approach to use. Further discussions will be needed with NHS Digital on taking this forward.

14.2 The second issue involved anonymously identifying roles of health care workers within data sets, which could be used in a separate project to determine health care worker risk. It was agreed that this work should be put on hold for review later.

15.0 Date of next meeting

15.1 The Chair confirmed that the next meeting would be held on Monday 15 th June 2020. The meeting was closed at 11.39am.

*Action: **JHC** to send Zoom link for next meeting on Monday 15th June*

Minutes of the NERVTAG Subgroup on Clinical Risk Stratification: Fifth meeting

Date & Location: 11:00 – 12:30, 15th June 2020 - Via telecon only

In attendance:

Julia Hippisley-Cox (JHC) (Chair), Emma Petty (Secretariat)

NERVTAG Members: Peter Horby (PH), Andrew Hayward (AH), Calum Semple (CSm)

Sub-group members: Elizabeth Williamson (EW), Ruth Keogh (RK), Karla Diaz-Ordaz (KDO), Harry Hemingway (HH), Jonathan Benger (JB), Carol Coupland (CC), Ashley Clift (AC), Aziz Sheikh (AS), Ronan Lyons (RL), John Robson (JR), Jonathan Valabhji (JV), [redacted], Ewen Harrison (EH), David Spiegelhalter (DS), Frank Kee (FK), Joanna Cottam (JC)

DHSC Observer: [redacted]

JCVI Observer: Ruth Parry (RP)

1.0 Welcome

1.1 The Chair welcomed everyone to the meeting. No apologies were recorded. Two new members (FK & JC) were welcomed to the subgroup. The Chair noted that both the link to the latest protocol and the draft press release had been circulated to members.

3.0 Minutes and matters arising

3.1 The minutes of the last meeting were reviewed and were agreed with no amendments. The majority of the actions from the last meeting were completed. The Chair noted that competing interest forms had been submitted by members and that comments had been received on the collaboration agreement.

3.2 The Chair referred to the coding requirements for the model validation and agreed to take this forward with NHS Digital and the devolved authorities to co-ordinate the list of codes for this work. It was noted that the priority was to finalise the model and to star t validation in the next couple of weeks. It was suggested that a subgroup could be established to determine how best to share the work operationally, including discussion of a validation pack.

- *Action: **JHC** to work with NHS digital and the devolved authorities to co-ordinate the list of codes required to validate the model*
- *Action: Establish a subgroup to consider the operational system requirements for the model, including discussion of a validation pack (HH + others)*

4.0 Policy update and publication of protocol and comms

4.1 NM noted preparations were underway for an announcement on shielding , hopefully on Thursday. The protocol will be published at the same time as an academic piece of work on the Oxford University website and there could be an announcement published via NIHR, which would signpost to the protocol. Publication of the protocol will be followed by clinician and academic engagement. NM noted that publication of the protocol would be flagged to relevant stakeholders. Members were requested to submit comments on the protocol to JHC for the production of the publication version for Thursday.

- *Action: **NM** to flag the publication of the protocol to relevant stakeholders, such as NHS England*
- *Action: **Members** to provide comments to JHC on the protocol for the production of the publication version*

4.2 The Chair advised members of the feedback from the cancer community, noting their anxieties and the desire to be involved in the work. It was recognised that it would not be possible to address all concerns submitted by stakeholders; however, these could be recorded for later review.

5.0 Model development update

a. Update on models
b. Final list of predictors
c. Paper writing

5.1 Members questioned whether an analysis could be run using pre -lockdown data and the numbers determined. Consideration has been given to running analyses with data to the middle of April. Another analysis would consider characteristics of shielded individuals vs non-shielded individuals. The Chair noted that the tool has to be registered with MHRA as a medical device and the uses of the tool will be included in the registration.

5.2 Members discussed factoring occupation into the model. It was agreed that the first iteration of the tool will be applied to the general population and will take into accounts factors such as ethnicity and obesity. Linkage with occupation could be considered for a later ite ration. Members were informed that following the publication of the protocol, there will be thorough discussion of the potential uses for the tool, recognising that the use in clinical practice will be the primary focus. Members discussed the output of the tool and the use of an absolute risk estimate. The potential for underestimation of mortality was considered since not all deaths associated with COVID might be identified and recorded . It was noted that results from analyses can be ordered in increasing level of risk and the risk groups for the top 4% of the population could be compared with the risk groups on the shielded list.

5.3 The Chair presented the academic version of the model and highlighted that asthma was not subcategorized in 3 levels. Instead, asthma treatments (use of inhalers and use of steroids) could be selected resulting in a more flexible approach which would also be easier to implement (noting that steroids can be used for multiple conditions) . There would be a need to link in with HES data to recognise those individuals on active cancer treatment. The provision of data regarding systemic anti-cancer therapy in the last 12 months was discussed and JB agreed to consider possible changes in data flow or alternative sources of data.

- *Action: **JB** to consider possible changes in data flow, or alternative sources of data for GPs to have information of patient who have undergone cancer therapy in the last 12 months*

5.4 Members suggested the inclusion of urban/rural factors in the model. The issue of considering region was discussed and the value it has for absolute risk. The Chair proposed that the hazard ratios for the different regions was included in the paper but not in the model. It was suggested that a comparison could be made from an analysis using the 1st temporal half of the data against the second temporal half. It was agreed that region should be considered as work in progress, noting that it should be removed for validation in Wales, Scotland and Northern Ireland. Members discussed whether localisation should be included inside or outside of the tool. The Chair agreed to add a paragraph to the protocol to cover localisation. The Stats group were actioned to consider inclusion of region and provide an update at the next meeting.

- *Action: **JHC** to consider inclusion of rural/urban factor in model.*
  (post meeting note: this variable is no longer collected on QResearch)
- *Action: **JHC** to consider adding a paragraph in the protocol on how the tool could be localised in the event of another upsurge*
- *Action: **Stats group** to consider whether regions should be included and to update at next week's meeting with how this issue might be operationalised*

5.5 In addition to a breakdown of different criteria, it was suggested there should be an indicator on the level of data underlying different categories. The Chair presented a comparison of those on the shielded list vs those not on the list and highlighted the differences in ethnicity factors. Members discussed the impact of age. It was suggested that using the risk stratification tool may identify different groups of at risk individuals not currently on the shielded list. Members proposed that it may be possible to set a threshold to ensure everyone currently on the shielded list is included.

6.0 Model validation update including data access and governance approvals

6.1 The Chair checked on the application process for the different systems . Data owners/representatives each confirmed that agreement to access datasets had been obtained and that no specific funding or forms were required. It was noted that the coding list would be required.

7.0 Patient engagement and press release

7.1 AC acknowledged comments provided by members on the press release. The document will be released from Oxford University Central Press Office, in conjunction with the publication of the protocol and the government announcement. It was requested that any additional quotes were submitted by COP today. The final version of the press release would be provided to JH.

7.2 The Chair noted the press release would include comments on from the national directors on diabetes and cancer as these groups had been particularly concerned. JC agreed to review the quotes for diabetes and cancer for the document. Members suggested that a comment on BAME should also be included.

- *Action: **Members** to provide comments to AC on the press release by COP on 15th June. Final version of press release to be copied to JH*
- *Action: **AC** to include comment on BAME in press release*
- *Action: **JC** to revise quote in press release to cover both cancer and diabetes*

7.3 It was noted that the tool could be used to identify areas of unmet need and those at risk. It may be used to add individuals to the shielded list, but should not be used to remove anyone from the list. This is because the current shielding policies are likely to result in a lower risk estimate. Members noted that the tool may also have a role in reassuring those at low risk. It was questioned what the recommendations will be for each of the risk levels. Members were advised that work is in progress on these policy issues, noting that the tool has been commissioned by government and the output of the work will inform the next steps for the vulnerable groups.

8.0 Professional engagement and piloting in GP practices

8.1 Members discussed the use of the tool by specialist clinicians in secondary care. It was suggested that a round table discussion could be held with the National Clinical Directors. NM agreed to consider the proposal.

- *Action: **NM** to consider a round table discussion with National Clinical Directors regarding the specialised use of the tool*

8.2 JR discussed the potentials for early piloting to discuss the utility of the tool and agreed to take the lead regarding professional engagement.

- *Action: **JR** to lead on professional engagement and to update the subgroup on the best way of taking engagement forward*

9.0 Implementation

9.1 This was covered under item 5.

10.0 General discussion

10.1 The Chair noted that the project unusually combined the development, validation and implementation of a tool altogether given the urgency of the research question and thanked members for their collaboration and generous input into this work.

11.0 Summary of actions and next steps

11.1 It was confirmed that the list of actions and draft minutes would be circulated to members.

12.0 AOB

12.1 With regards to consulting on the tool, NM requested that members feedback ideas for engagement to link in with the comms plans for this work.

- *Action: **Members** to feedback ideas on engagement to NM to link in with comms plans.*

13.0 Date of next meeting

13.1 The Chair confirmed that the next meeting would be held on Monday 22nd June 2020. The meeting was closed at 12.38pm.

Minutes of the NERVTAG Subgroup on Clinical Risk Stratification: Sixth meeting

Date & Location: 10:00 – 11:30, 22nd June 2020 - Via telecon only

In attendance:

Julia Hippisley-Cox (JHC) (Chair), Emma Petty (Secretariat)

NERVTAG Members: Peter Horby (PH), Andrew Hayward (AH), Calum Semple (CSm)

Sub-group members: Elizabeth Williamson (EW), Ruth Keogh (RK), Karla Diaz-Ordaz (KDO), Harry Hemingway (HH), Jonathan Benger (JB), Carol Coupland (CC), Ashley Clift (AC), Aziz Sheikh (AS), Ronan Lyons (RL), John Robson (JR), Jonathan Valabhji (JV), [redacted], Ewen Harrison (EH), David Spiegelhalter (DS), Frank Kee (FK), Tony Williams (TW), David Coggon (DC), Susan Jebb (SJ)

DHSC Observer: [redacted]

JCVI Observer: Ruth Parry (RP)

1.0 Welcome

1.1 The Chair welcomed everyone to the meeting and introductions of members were made. No apologies were recorded. Three new members (TW, DC & SJ) were welcomed to the subgroup. The Chair noted that AC was collecting the competing interest forms and any outstanding forms should be submitted .

2.0 Minutes and matters arising

2.1 The minutes of the last meeting were reviewed and were agreed with no amendments .

2.2 The actions were reviewed. The Chair informed members that the work with NHS digital on the coding lists was ongoing. The Chair thanked members for providing comments on the protocol and press release. The protocol (v1.12) should be published today (22nd June). NM advised that NHS England is aware of this proje ct and that the work will be included in the implementation plan for clinical stakeholder consultation. The Chair informed members that data from PHE provided better definition of who is undergoing specific cancer treatments, together with radiotherapy data and this ha s been incorporated into the model. JB added that to flow new data into GP systems will not be a simple or quick task, but the long-term options could be considered. JHC proposed a practical solution whereby the tool is configured to give a prompt to GPs t o check if a patient has received treatment for cancer in the last 12 months. The available data flows were discussed.

- *Action 6.1:* ***JHC*** *to work with NHS digital and the devolved authorities to co - ordinate the list of codes required to validate the model*

- *Action 6.2: **JHC** to configure model to produce a prompt to GPs to check if patient has received treatment for cancer in the last 12 months*
- *Action 6.3: **JB** to consider long term options of possible changes in data flow to provide information of patients who have undergone cancer therapy in the last 12 months or whether GP systems will need a prompt to check if a patient has received cancer therapy*

2.3 The actions regarding updates of the protocol and consideration of region would be discussed under agenda item 4. The actions on the press release had been completed. NM noted that consideration will be made for the discussion with the National Clinical Directors as part of the stakeholder consultation.

3.0 Policy update and publication of protocol and comms

3.1 NM advised members that an announcement on shielding was expected for 5 pm today (22nd June). The publication of the protocol will be handled separately from the announcement. The priority will now be to map out the engagement of potential stakeholders. A risk stratification implementation board has been established, who meet on a weekly basis to consider policy development and includes input from various stakeholder groups and government departments. NM confirmed that the UK CMOs and senior clinical advisors had been advised of the final policy position for today's announcement. It was noted that the press release refers only to the clinical tool, which is the priority of the project.

3.2 TW raised an issue with in appropriate coding in relation to shielding. NM responded that the tool should be more individualised and take risk factors into account in a cumulative way. The issue with current inappropriate coding would be considered separately from the sub group.

4.0 Model development update

a. Update on models and initial results
b. Update from Stats group on region

4.1 The Chair informed members that the model was being finalised and would take into account comments following the publication of the protocol, with the potential inclusion of additional risk factors. The predictors have been determined. The model currently considers three outcomes: mortality, hospital admission and a composite outcome ; however, the value of the composite indicator is less than anticipated. Members agreed that the model should focus on the other two outcomes. Suspected COVID-19 could be considered as an outcome in future iterations.

- *Action 6.4: **JHC** to focus analysis on two main outcomes for the model (hospital admission & mortality) and not include the composite outcome.*

4.2 CC described the analyses to consider shielding outcomes, using different options for shielded conditions to review the ranking and noted that there were only slight differences. Shielding is not currently included as a factor in the model; however, a question could be included to ask if an individual is on the shielded list. Members

discussed whether the differences in analyses may change as more data becomes available. The impact of timings of the interventions on the available data was also discussed, noting that it can be difficult to disentangle the effect of shielding . It was agreed that the Stats group would reconvene to consider the inclusion of shielding and update the sub group at the next meeting.

- *Action 6.5:* ***Stats group*** *to consider whether the shielding list should be used with the protocol and the analyses and update at the next meeting (meeting invite sent for 8.30 am 29th Jan 2020)*

4.3 CC advised members that the issue of region had been considered. The production of a transportable risk, not tied to region, would allow validation of the model outside of England. Analyses stratified by region showed little difference. Evaluation analyses will be run within regions to compare discrimination and calibration across regions. I n analyses stratified by region, the effects of ethnicity persisted. For operationalising the model, region will not be included in the final version . The Chair suggested that the various evaluation analyses could be included in a supplement to the final p aper.

4.4 Members discussed the use of region as a surrogate for exposure and how underlying local incidence rates could be considered. There may be a possibility to link test and trace data with local incidence data and combine this with personal risk. It was noted that there is no historical data for COVID-19 and the initial data is from hospital cases, which makes calibration against community incidence difficult.

4.5 The Chair demonstrated the academic calculator and members discussed the presentation of the results. It was suggested that the interface should be user tested.

4.6 Members queried the inclusion of an urban/rural factor. It was noted that this data is no longer collected; however, it may be possible to include it at a later date if required. Members questioned whether it was possibly to retrospectively fit in level of exposure, using serology data and considered the accuracy and value of such data. The tool could be developed to determine risk during the epidemic of an average person, which could later be tweaked to be adaptive to local circumstances. The level to which exposure should be taken into account was discussed. It was suggested that these issues, together with the limitations of the approach with the current available data could be discussed the final paper.

4.7 Members considered whether the rankings might change depending on the baseline exposure levels and the importance of geographical factors. The concept of determining the risk of vulnerability for possible outcomes once someone bec omes infected was discussed. This could be subsequently combined with the prevalence of infection at that time and in that locality to obtain an estimate of overall risk. It was noted that region was an important factor, but this level of importance may ch ange in the future. An estimate score of relative risk for vulnerability could be produced which wouldn't vary. The prevalence of infection in the local area could then be used to dictate behaviour for those over a certain score.

4.8 It was suggested that the model should also take into account COVID-19 treatments , such as dexamethasone.

4.9 The Chair noted that part of the work was to identify risk factors, initially based on no data and to review these as more data becomes available. The next stage will consi der

further factors, such as the introduction of a vaccine and possible mutations to the virus. The Chair advised members that some conditions not currently on the shielded list are showing as high risk in the models, such as Down's syndrome, and questioned how these conditions should be handled. It was noted that Down's syndrome has also been associated with increased risk from other infections. The current shielded list will be maintained until the stratification tool is available. There is a panel proces s for the addition or removal of groups to the list, with recommendations made to the UK CMOs. The Chair proposed to write a research letter presenting the evidence for the increased risk for adults with Down's syndrome. Members discussed whether Down's syndrome should be separated from learning disability for the model.

- *Action 6.6:* **JHC** to write a short paper on the number of cases and evidence of increased risk with Down's Syndrome for DCMO and publication as a research letter, with input from AC, AH & others. **Members** to volunteer to help with paper

5.0 Model validation update including data access and governance approvals

5.1 The Chair advised members that the model is not ready for external validation currently. A validation pack will be produced for use with external data sets. The Chair asked for contacts within NHS Digital who could assist with the coding lists needed for validation.

- *Action 6.7:* **JHC** to request NHS digital contact from JB to assist with coding lists

6.0 Patient engagement

6.1 SJ noted that the press release didn't include anything from patient or public representatives. It was noted that the public will be very invested in this work and that there could be some inclusion in the press release.

6.2 AC informed members that 5-10 patient representative opinions had been obtained on the lay summary, which will be collated into a report. No requests had been made for comments on the press release but including a public acknowledgement could be investigated.

- *Action 6.8:* ***JHC & AC*** *to consider inclusion of patient/public view in press release*

7.0 Professional engagement and piloting in GP practices

7.1 The Chair noted that, with the publication of the protocol, there will be opportunities to engage with stakeholders.

8.0 Implementation

8.1 DS confirmed that tests could be rapidly run on formats for the tool with the general population to consider comprehension and behaviour intention . There is a challenge with how to communicate small numbers which vary over orders of magnitude with individuals and ensuring that a false sense of security is not given. There was a suggestion of using comparators with other risks and the use of ranking by risk since

this may be stable despite variations in absolute incidence of a virus over time . Members considered formats of other risk tools, such as covid age and heart age, and what might be applicable for the risk stratification tool. However, DS noted that there was no single correct way to communicate risk and there may be concerns with fixing on age especially if the comparison was always with a white male. The Chair noted that this is complex since the UK BAME population generally has a younger age distribution. CC noted it is easier to see how an age-based concept might apply to chronic disease affecting an organ with increases steadily with age (such as the hear t disease), but less easy to see how it might work with an infectious disease in a pandemic which varies over time. It was suggested that using age may be a difficult concept to use for this context. This issue may need to be explored further.

9.0 General discussion

9.1 No matters were raised for this item.

10.0 Summary of actions and next steps

10.1 It was confirmed that the list of actions and the draft minutes would be circulated to members. It was hoped that a draft of the final paper would be available in the next two weeks and that the draft validation statistics could be reviewed at the next meeting.

11.0 AOB

11.1 No matters were raised for this item.

12.0 Date of next meeting

12.1 The Chair proposed that the next meeting would be held on Tuesday 30th June 2020 at 2.45pm. The meeting was closed at 11.44 am.

Minutes of the NERVTAG Sub-group on Clinical Risk Stratification: Seventh meeting

Date & Location: 14:45 – 16:00, 30th June 2020 - Via telecon only

In attendance:

Julia Hippisley-Cox (JHC) (Chair), Emma Petty (Secretariat)

NERVTAG Members: Calum Semple (CSm)

Sub-group members: Ruth Keogh (RK), Karla Diaz-Ordaz (KDO), Jonathan Benger (JB), Carol Coupland (CC), Ashley Clift (AC), Aziz Sheikh (AS), Ronan Lyons (RL), Jonathan Valabhji (JV), [redacted], Ewen Harrison (EH), David Spiegelhalter (DS), Frank Kee (FK), Tony Williams (TW), David Coggon (DC)

DHSC Observer: [redacted]

JCVI Observer: Ruth Parry (RP)

1.0 Welcome

1.1 The Chair welcomed everyone to the meeting. Apologies were noted from Susan Jebb.

2.0 Minutes and matters arising

2.1 The minutes of the last meeting were reviewed and were agreed with no amendments.

2.2 The actions from the last meeting were reviewed.

Minutes and matters arising

6.1 : JHC to work with NHS digital and the devolved authorities to co-ordinate the list of codes required to validate the model
There are ongoing discussions on this item.

6.2 : JHC to configure model to produce a prompt to GPs to check if patient has received treatment for cancer in the last 12 months
Completed

6.3 : JB to consider long term options of possible changes in data flow to provide information of patients who have undergone cancer therapy in the last 12 months or whether GP systems will need a prompt to check if a patient has received cancer therapy
This is not likely to be possible via NHS Digital. Peter Johnson highlighted three national electronic prescribing systems used in hospitals, which could potentially feed information on chemotherapy into GP records. This action will be carried forward.

Model development update

6.4 : JHC to focus analysis on two main outcomes for the model (hospital admission & mortality) and not include the composite outcome.
Completed

6.5 : Stats group to consider whether the shielding list should be used with the protocol and the analyses and update at the next meeting (meeting invite sent for 9.30 am 29th Jan 2020)
Covered under agenda item 5.b

6.6: JHC to write a short paper on the number of cases and evidence of increased risk with Down's Syndrome for DCMO and publication as a research letter, with input from AC, AH & others. **Members** to volunteer to help with paper *Covered under agenda item 4*
Model validation update **6.7: JHC** to request NHS digital contact from JB to assist with coding lists *On going*
Patient engagement **6.8: JHC & AC** to consider inclusion of patient/public view in press release *Completed*

- *Action 7.1: **JHC** to continue discussions on the flow of chemotherapy information into GP data systems (carry forward of action 6.3). **AS** to assist with entry points to electronic systems.*

2.3 Members discussed the date range of available data for outcomes and queried whether later data was available. The current model uses data up to the end of April.

- *Action 7.2: **JHC** to investigate the latest data available from ONS.*

  Post meeting note: Complete data is available up to 30th April 2020.

2.4 Members considered the levels of interest following the publication of the protocol. The BBC wanted to consider the final results and will review the work in August/September. There have been some contacts from the public and professionals over the press release. NM added that the protocol was mentioned in the shielding announcement last week. There have been no queries through CMO's office. The protocol has been shared with various charities, which generated interest. Further sharing with stakeholders is planned in the coming weeks.

3.0 Collaboration agreements and costs

3.1 The Chair advised members that the NIHR are forming a collaboration agreement with the University of Oxford for this work. Everyone named on the protocol is invited to be part of the agreement. Submissions have been requested for costs for this work and any outstanding submissions should be made by COP 30th June 2020.

- *Action 7.3: **Members** to provide any outstanding cost submissions to JHC by COP 30th June 2020.*

4.0 Policy update

4.1 NM advised members that the launch of the protocol was successful. A review of changes required for children on the shielded list is being undertaken. There is also focus on the situation in Leicester and consideration of shielding advice for local lockdowns. The Chair added there had been discussion with Kamlesh Khunti, the director of the Centre for BME Health in Leicester, on how to communicate findings to the BAME community.

4.2 Members discussed the circulated paper reporting the possible risk association between Down's syndrome mortality and COVID-19. The paper is under review by Nature Medicine. NM informed members that NHS England are drafting a paper, using this information, for review and for a recommendation to be made to the UK CMOs as to whether this grouping should be included on the shielded list. The Chair noted that for

some groups, who may be at increased risk, there are insufficient numbers to model. However, it may be possible to align these groups to others based on pathology or drug classifications in order to estimate risk. It was noted that if there were no deaths in the group, it would not be possible to run the model.

5.0 Model development update

a. Update on models and initial results
b. Update from Stats group on shielding

5.1 The Chair informed members that there had been work with Peter Johnson to categorise cancer treatments more finely in the model. Chemotherapy treatments have now been divided into three groups. There are still concerns with implementation in the GP systems, but it is hoped that using the electronic prescription data will help automate this process.

5.2 The Chair presented information on the hazards ratios for the revised groupings for both women and men and for each of the outcomes (mortality and hospital admission). JV suggested that the hazard ratios for both types of diabetes appeared different to those determined for the whole population of England and would review this with the Chair separately.

- *Action 7.4:* ***JHC*** *and JV to review the hazard ratios for both types of diabetes.*

5.3 The Chair advised members that only 20% of those currently on the shielded list were in the top 4% at risk according to the model and vice versa. The current shielded list accounts for 21% of the deaths, whereas the top 4% from the model accounts for ~69%.

5.4 CC described the approaches considered for including shielding as a variable for the model. Overall the study was not designed to test the effect of shielding. It was proposed that a question could be added as to whether an individual is on the shielded list and this would produce a cautionary message to note that the calculated risk level will be a minimum not a maximum level.

5.5 Members discussed the differences in policy approach to shielding between the devolved authorities.

5.6 The possibility of applying the model to the working age population, e.g. under 65s or 70s, was considered. It was noted that the function of the group was to create the tool; the application of the tool would be determined by policy. The tool was discussed at a meeting of the Moral and Ethical Advisory Group, who had suggested a cut off age of 70 could be used for stratifying risk for the working age population. The Chair suggested it was possible to produce one model that could then be applied to different subgroups.

- *Action 7.5:* ***JHC*** *to consider the application of the tool for people of working age.*

5.7 Members discussed the possibility of incorporating changing incidence of disease and changes in baseline over time and in different regions. Different approaches would be investigated. The importance of separating the risk of infection from the vulnerabilities for individuals if infected was considered. It was noted that there may be the possibility to adjust the absolute risk based on the baseline incidence, depending on available data. The model does not currently include region, but it may be feasible to consider stratifying by region and validating the model using data sets from different regions.

5.8 DS presented a potential mock-up created by the Winton Centre for the presentation of risk. There are issues with using a log-scale as no-one understood this and alternatives are being considered. A visual scale and colour coding was deemed to be helpful. Comparisons against people of other ages were preferred to comparisons with other risks, e.g. car crashes. Members discussed the types of comparisons with other people, using age, sex and ethnicity. These issues would need to be explored through testing and trials of the model. It was noted that a patient access app can provide access to an individual's medical records and it may be feasible to include the risk via the GP record. It was suggested that there may be concerns from employers on what to do with this information, but this would be considered through policy for the different stratification levels. The current stratification system would cover the return to work from 1st August and would be used until the tool is available.

- *Action 7.6:* ***Secretariat*** *to include the presentation of risk and the employment of stratification levels on future agendas.*

5.9 Members questioned whether there was a need for an at-risk list covering the working age group, who might need special consideration in the workplace. NM agreed to take the question away for consideration.

- *Action 7.7:* ***NM*** *to review the need for an at-risk list for the working age group with dCMO.*

6.0 Model validation update

6.1 There were no updates provided on this item.

7.0 MHRA medical device registration

7.1 The Chair advised members that a meeting had been held with MHRA regarding medical device registration and regulation. A public-facing calculator would be classified as a type 1 medical device and depending on the intent of use may be type 2 or type 2a. These types of devices need to be licenced for a particular purpose, with the appropriate documentation. Class 2a devices also require clinical investigation. It was proposed that two pilot studies could be carried out for the tool, one in east London and one with the occupational health group. The Chair informed members that Oxford University Innovations are working with MHRA on processing the registration of this tool.

8.0 Patient engagement

8.1 AC presented the results of a PPI engagement from 8 participants. Two of these were on the shielded list and one had been treated in an ICU. Responses were positive, and the idea of individualised information was welcomed.

9.0 Professional engagement and piloting in GP practices

9.1 This work had been discussed in a large meeting with the National Clinical Directors and further suggestions for the tool had been submitted for consideration. The Chair added that there was a meeting planned with the Royal Colleges as well as additional

professional consultations being arranged. There is consideration of how notifications of new groups at possible risk should be handled.

10.0 Implementation

10.1 NM noted that the third meeting of the implementation board is scheduled this week and will consider options for implementation of the tool.

11.0 General discussion

11.1 No matters were raised for this item.

12.0 Summary of actions and next steps

12.1 The Chair advised members that the aim is to submit a paper on the working model, identifying the limitations of the model. Now that the predictors have been categorised, it is hoped that a first draft may be available for next week for comment.

13.0 AOB

13.1 No matters were raised for this item.

14.0 Date of next meeting

14.1 The next meeting would be held on Tuesday 7th July 2020 at 2.45pm. The Chair thanked members for their attendance and their input. The meeting closed at 16.15 pm.

Post meeting note: the next meeting was arranged for Tuesday 14th July at 1.45pm.

Minutes of the NERVTAG Sub-group on Clinical Risk Stratification: Eighth meeting

Date & Location: 13:45 – 14:45, 14th July 2020 - Via telecon only

In attendance:

Julia Hippisley-Cox (JHC) (Chair), Emma Petty (Secretariat)

NERVTAG Members: Peter Horby (PH), Calum Semple (CSm), Andrew Hayward (AH)

Sub-group members: Elizabeth Williamson (EW), Ruth Keogh (RK), Karla Diaz-Ordaz (KDO), Carol Coupland (CC), Ashley Clift (AC), Aziz Sheikh (AS), Ronan Lyons (RL), Jonathan Valabhji (JV), [redacted], Ewen Harrison (EH), David Spiegelhalter (DS), Frank Kee (FK), Tony Williams (TW), David Coggon (DC), Susan Jebb (SJ), Kamlesh Khunti (KK), Harry Hemingway (HH)

JCVI Observer: Ruth Parry (RP)

1.0 Welcome

1.1 The Chair welcomed everyone to the meeting. Apologies were noted from Jonathan Benger. No competing interests were raised.

2.0 Minutes and matters arising

2.1 The minutes of the last meeting were reviewed and were agreed with no amendments.

2.2 The actions from the last meeting were reviewed.

Item	Action	
2 - Minutes and matters arising	Action 7.1: **JHC** to continue discussions on the flow of chemotherapy information into GP data systems (carry forward of action 6.3). **AS** to assist with entry points to electronic systems.	*Ongoing discussions.*
	Action 7.2: **JHC** to investigate the latest data available from ONS.	*Completed. Latest complete data is to 30/4/20.*
3 - Collaboration agreements and costs	Action 7.3: **Members** to provide any outstanding cost submissions to JHC by COP 30th June 2020.	*Completed.*
5 - Model development update	Action 7.4: **JHC** and **JV** to review the hazard ratios for both types of diabetes.	*Completed.*
	Action 7.5: **JHC** to consider the application of the tool for people of working age.	*Completed.*

	Action 7.6: **Secretariat** to include the presentation of risk and the employment of stratification levels on future agendas.	*Completed.*
	Action 7.7: **NM** to review the need for an at-risk list for the working age group with dCMO.	*Ongoing*

2.3 For action 7.1, the Chair noted that discussions were ongoing with GP systems suppliers and PHE to enable the flow of systemic anti-cancer treatment data into GP systems. This work is not essential for the project, but the aim is to undertake this in parallel in phases. For action 7.3, the contract is close to being signed. Once this is completed, a collaboration agreement will be sent to all participants for signing, within three weeks of the contract signing. For action 7.5, the Chair advised members that a prototype had been produced for people under the age of 70. For action 7.7, NM informed members that discussions were considering occupational health issues and the potential return to work for the current shielded group, but no decisions had been made yet. The principal use of the tool is for primary care and secondary uses, such as for a new shielded list or for use with vaccination, would be considered subsequently.

3.0 Collaboration agreements and costs

3.1 The Chair advised members that this aspect of the work had been completed.

4.0 MHRA medical device registration

4.1 The Chair noted that Oxford University Innovations are working on the registration of the tool as a medical device. It is likely to be a Class 1 device. A documentation pack will be produced by OUI to cover the requirements for implementation, e.g. for use by GP Systems Supplies.

5.0 Engagement

5.1 AC informed members that there had been discussions with clinicians about building a public strategy for certain high risk patients who have been shielding. It was noted that blood cancer patients have received mixed messages. A short paper on a strategy for having representation from patients with specific illnesses would be provided for the next meeting.

- *Action 8.1: **AC** to provide a paper on representation from specific high risk patients.*

5.2 The Chair advised members that discussions had taken place with the Royal College of Physicians and some of the sub-specialities regarding patients on immunosuppressive drugs. The potential risks for these patients could be investigated in a future iteration if the data is made available. There were also discussions regarding dermatology patients and the effect of immunosuppressants with the COVID risk.

5.3 Members discussed the need to include representation from groups living with obesity, who would not be included on medical lists. It was agreed that AC would liaise with **NR** for access to the groups who should be involved.

- *Action 8.2: **AC** to liaise with SJ on the representation of groups living with obesity.*

5.4 NM noted that this work was being discussed at the Senior Clinicians Group and included the work on public presentation and perception of risk. DS advised members of the work that had been undertaken on the presentation of the tool, which involved interviews and surveys. People wanted both something for use by GPs, but also a tool that the public could access to determine their risks. It was recognised that the numbers could be difficult to communicate, and the use of comparators was being explored. This work is not considering the operational use of the tool, only how best to present the information. Members discussed the uses for the tool and the difference between absolute risk and relative risk when considering different age groups.

5.5 The Chair noted that there had been a discussion with JCVI on public messaging and prioritising groups for when a vaccine is available.

6.0 Policy update

6.1 NM advised members that discussions were ongoing with stakeholders to support the public health management and include consideration of occupational risk and BAME issues. There is also a need to engage with charities regarding risk groups. The Risk Stratification Implementation Board is considering the options of a centralised risk engine with NHS digital or implementation via GP systems, with ongoing discussions with NHS Digital. The project is very complex and needs clear governance, as well as ensuring that it is consistent across the four national health departments. Members provided contact details for the devolved authorities for digital solutions. The Chair confirmed that a validation pack would be supplied to Northern Ireland to run against their IT platform. The results of the validation trails would be in a separate paper.

6.2 Members queried how the tool might be used with high-risk occupations. There are some occupations that appear high risk, where it is not necessarily the actual work that increases the risk, but the behaviours of workers in the workplace that increases risk. Other occupations are recognised as high risk, but the level of control and mitigation can be high, so the actual risk is lower. There will be some occupations that remain higher risk, where it is difficult to implement controls, such as control and restraint tasks, or performers in theatre or film. NM acknowledged that there is an occupational subgroup considering clinical principles. Members discussed the tools currently available. It was suggested that there could be a separate meeting to consider occupation issues.

- *Action 8.3:* ***Members*** *to register interest in a meeting on occupation issues with JHC.*

7.0 Model development update

a. Update on initial results
b. Draft paper

7.1 The Chair congratulated EW on the Nature paper on OpenSAFELY[1].

7.2 The Chair referred to the circulated draft paper and thanked members for their comments. There were specific questions to be reviewed on this work and consideration of where to send the paper.

[1] https://www.nature.com/articles/s41586-020-2521-4

7.3 First – whether or not to undertake validation of additional risk groups, such as diabetes and if these validations should be in a separate paper? Members suggested that the initial paper should consider only what was published in the protocol (age group, ethnicity, region and deprivation) and that additional subgroup validations could be a distraction from this paper. It was agreed that validation of diabetes and other risk groups would be covered in a separate paper.

7.4 Second – should more analyses be included on how the vaccine strategy might work? Members agreed that linking the tool to the vaccination strategy should be a separate exercise, although there should be mention of the potential role in vaccine strategy. Members discussed table 3 in the paper and agreed that it should be included for the sensitivity values. The specificity values were queried, and the inclusion of positive predictive value was suggested, as it was referred to in the text. The information provided in the table would be reviewed and the labels improved. The text relating to the table would also be reviewed.

- *Action 8.4:* ***CC*** *to review table 3 of the paper and improve the labelling.*

7.5 Members discussed including risks for lower levels, e.g. the lowest 20%. It was thought that with the majority of focus in those most at risk, including lower levels would be interesting but could add confusion. It was noted that the paper should clearly define two different risks at the beginning – that of being infected and that regarding the outcomes once infected. The current risks are adjusted for age, BMI and deprivation but it was not clear what the effects of each of these are.

- *Action 8.5:* ***JHC*** *to review the presentation of the effects of deprivation, age etc. in the determination of risk.*

7.6 Members discussed tables 4 and 5. Table 4 investigated those on the current shielded list with the highest risk group of the same size from the model and categorised the relevant risk level. There was concern that shielding is an intervention and risks may be underestimated in the shielded group, which doesn't lend to a fair comparison. Members felt that the current presentation of the table was confusing, and a 2 x 2 format would be preferable. Table 5 also illustrated the comparison with the current shielded group. It was noted that this work would be internationally important, but that the current shielded list is particular to the UK and including a comparison with the shielded list could reduce the international impact of the paper. It was felt that including comparison with the current shielded list would indicate that this tool could be used to generate a new list; however, there were other considerations for this work and that policy discussions are still ongoing on its use. It was agreed that the shielded comparison would be removed from table 5, together with the subsequent bar charts. Based on the updates to table 5, consideration would be given to revising table 4 or removing it completely.

- *Action 8.6:* ***JHC*** *to remove shielded comparison from table 5 and consider revising table 4 into a 2 x 2 format or remove completely.*

7.7 Members commented that hypertension was not included in Table 5 and were informed that it had not emerged as high risk when the Lasso model was used. It was noted that some of the variables didn't converge and were combined into other groups. The selection of variables and the convergence of models was discussed.

7.8 Members discussed the additional papers suggested for the validations of the datasets and the potential uses for the tool, such as with the vaccine strategy. It was suggested that potential uses for the tool could be define as a thought process, as no policy decisions on the tool had been made.

7.9 Members were informed that the aim was to submit the paper for publication this week. Consideration was given as to which journal to approach, noting the different manuscript requirements and recognising that the work demonstrated a substantial advance and will have a substantial change in policy and practice in at least one country. The selection of journal will determine how the argument is presented. The possibility of fast tracking the publication with specific journals was discussed. It was agreed that a pre-print would not be placed on medRxiv. Members were advised that there did not appear to be any work similar to this internationally and therefore it would have interest from the international public health community. NM agreed to discuss publication options with DHSC and CMO's office. Advice would also be sought from Oxford University Innovations, MHRA and CMO on the publication of the model as open source software. Members were requested to provide comments on the draft paper by Thursday 16th July.

- *Action 8.7:* ***NM*** *to discuss publication options with DHSC and CMO's office.*
- *Action 8.8:* ***Members*** *to submit comments on the paper by Thursday 16th July.*

8.0 Model validation update

8.1 This item was not considered due to available time.

9.0 Implementation

9.1 Discussion for this item was covered under item 5 regarding the presentation of the tool.

10.0 General discussion

10.1 This item was not considered due to available time.

11.0 Summary of actions and next steps

11.1 The Chair noted that the next meeting was on Tuesday 21st July but may be postponed to the following week to give time to consider additional papers.

12.0 AOB

12.1 No items were raised. The Chair thanked members for their attendance and their input. The meeting closed at 15.32.

Minutes of the NERVTAG Sub-group on Clinical Risk Stratification: Ninth meeting

Date & Location: 13:45 – 14:45, 8th September 2020 - Via telecon only
In attendance: Julia Hippisley-Cox (JHC) (Chair), Emma Petty (Secretariat) *NERVTAG Members:* Calum Semple (CSm) *Sub-group members:* Elizabeth Williamson (EW), Ruth Keogh (RK), Karla Diaz-Ordaz (KDO), Ashley Clift (AC), Aziz Sheikh (AS), Ronan Lyons (RL), Jonathan Valabhji (JV), Ewen Harrison (EH), David Spiegelhalter (DS), Frank Kee (FKe), Tony Williams (TW), Kamlesh Khunti (KK), Fred Kemp (FKp), B Manaley (BM), Harry Hemingway (HH)

1.0 Welcome

1.1 The Chair welcomed everyone to the meeting. Apologies were noted from [redacted], Carol Coupland (CC) and Jonathan Benger (JB). No competing interests were raised.

2.0 Minutes and matters arising

2.1 The minutes of the last meeting were had been reviewed and were agreed with no amendments.

2.2 The actions from the last meeting were reviewed.

Item	Action
5	*Engagement* Action 8.1: **AC** to provide a paper on representation from specific high risk patients. Action 8.2: **AC** to liaise with SJ on the representation of groups living with obesity.
6	*Policy update* Action 8.3: **Members** to register interest in a meeting on occupation issues with JHC.
7	*Model development update* Action 8.4: **CC** to review table 3 of the paper and improve the labelling. Action 8.5: **JHC** to review the presentation of the effects of deprivation, age etc. in the determination of risk. Action 8.6: **JHC** to remove shielded comparison from table 5 and consider revising table 4 into a 2 x 2 format or remove completely.

Action 8.7: **NM** to discuss publication options with DHSC and CMO's office.

Action 8.8: **Members** to submit comments on the paper by Thursday 16th July.

2.3 For action 8.1 and 8.2 would be covered under item 9. AC would provide the paper (action 8.1) to JHC for consideration.

- *Action 8.1 (carried over): **AC** to provide a paper on representation from specific high risk patients to share with JHC for consideration.*

2.4 Members had registered agreements for action 8.3. The Chair advised the subgroup of changes to the membership, noting that David Coggon would be acknowledged in the collaboration agreement and would withdraw from the subgroup, but may be involved in a later stage of the project. NHS Digital will be involved in the implementation of the tool and will not be included in the collaboration agreement.

3.0 Collaboration agreements and costs

3.1 The Chair advised members that work was ongoing on the research, but that the collaboration agreement was still to be signed and put in place to provide funding. A draft was sent to subgroup members in August and some comments were received. A query on the use of the algorithm in a clinical setting was answered. Members raised queries regarding the open source aspect of the tool. The original draft protocol stated that the project would be published under the GPL open source licence. Following advice from Oxford University Innovation, it has been agreed that an academic licence will be used, to allow the tool to be used for academic research purposes and there would be a separate licence for the clinical software, which will have gone the medical device regulations. DHSC are keen for there not to be multiple proliferations of the tool. The protocol has been updated accordingly. It was clarified that the use of the tool under the academic licence would still be free of charge.

3.2 It was acknowledged that there was no dissent from members to the collaboration agreement.

3.3 There was a query regarding access to OpenSafely and it was decided that reference to this would be removed from the collaboration agreement. The Chair agreed to discuss possible access to OpenSafey for separate validation with data controllers.

- *Action 9.1: all agreed that JHC can progress with the NIHR collaboration agreement as planned, with removal of reference to OpenSafely*
- *Action 9.2: JHC to identify data controllers for OpenSafely to discuss access to OpenSafely for validation independently of the NIHR collaboration agreement.*

3.4 FKp advised members on the details of the academic licencing of the technology, which ensure transparency and will allow access for research purposes. Requests for non-academic use would be reviewed on a case by case basis. No decisions have been made on charging for non-academic use.

4.0 Policy update

4.1 The Chair noted that NM had sent her apologies for the meeting and would not be able to provide a policy update. The Chair informed members that there had been numerous

engagement events organised by the CMO's office. Any suggestions made at these events for changes to the algorithm would be fed back into the subgroup.

5.0 Agreement of final version of protocol

5.1 Members approved the circulated version of the protocol. The Chair agreed that reference to OpenSafely would be removed from the protocol, in line with collaboration agreement.

- *Action 9.3:* ***JHC*** *to remove reference to OpenSafely from the protocol.*

6.0 Model development update

6.1 The Chair advised members that the paper had been submitted to BMJ and was fast tracked. Comments were received on the manuscript and these have been responded to. The BMJ is looking to publish the paper together with similar papers and is also working with the CMO's office on co-ordinating publication with the release of the policy. It is hoped that this will be achieved in the next few weeks.

6.2 Members were informed that the papers on the validation of the tool would most likely be submitted to another journal. The Chair added that it had been possible to undertake a temporal validation as an extra 60 days of data was available for calibration, to compare against the original data set for the first 90 days of the pandemic. A recalibration had also been carried out successfully demonstrating that the model was transportable.

7.0 Model validation update

7.1 FKp noted that the input parameters and Read 2 codes had been shared with the devolved authorities (DAs) for the validation process. It was assumed that the DAs would liaise with the academics to make sure that the data sets were available for validation; however, it is now recognised that a direct relationship with the academics is required.

- *Action 9.4:* ***JHC*** *&* ***FKp*** *to review access to coding lists and algorithm for DAs and prepare individual CDAs between Oxford and academic teams in Wales (Ronan Lyons), Northern Ireland (Frank Kee) and Scotland (Aziz Sheikh) and NHS England (Jonathan V).*

7.2 Members discussed the model validation for type 1 and 2 diabetes, using datasets within NHS England. The National Diabetes audit has been linked with the Master Patient Index to provide an extensive data set, although this does not have good representation of diagnosis acquired by GPs. Additional data sets could be considered subsequently as the model is updated. Validation of other conditions was also discussed.

7.3 The Chair described the issues with trying to get consistency in coding sets across the UK, with Snomed codes being used by NHS Digital in England but not used in Scotland, Wales or Northern Ireland. A list of Snomed codes will be produced for the tool and provided to NHS Digital, and this list, when ready, would be published. The inclusion or exclusion of particular codes could result mis-scoring, so consistency of coding sets is important. It was proposed that a project plan and road map should be drafted to outline the steps for validation, for use within the UK to ensure harmonisation between the four nations.

- *Action 9.5: JHC to produce project plan for validation, for use across the UK.*

7.4 It was suggested that in addition to a paper on the validation results of the tool, an additional paper could be drafted on the methodological challenges encountered in this project, particularly with regard to coding sets.

7.5 It was agreed that the focus of the next meeting would be on setting out the steps for validation, using a phased approach. The datasets from the DAs and the English data set for diabetes would be used in the initial validation. The OpenSafely data could also be used if access is enabled. Additional data could be considered for validation as the model is updated.

7.6 CSm informed members of a forthcoming publication on risk prediction for hospitalised patients with COVID using two different methods (a traditional clinical approach and an AI approach). It was determined that both approaches produced results within 1% of each other. It is hoped that the score tool (which is not an algorithm) will be used as a reassurance tool in hospitals. Credit was given to the team working with Ewen Harrison on this independent academic project, which involved manual collection of data from 80,000 patients. The details of the tool would be provided to the CMO's office.

8.0 Presentation of risk

8.1 DS discussed the information on presentation of risk, which had been circulated to members. Examples were used for individuals with no risk, with some risk and with multiple risks. Age was determined to be very important in the risk assessment and may dominate over other risks. It is possible that the absolute risk and the relative risk will give different messages, so a dog-leg criterion could be considered to provide a blended approach. Work is still ongoing on presenting risk in different ways and in terms of frequency.

8.2 Members discussed the breakdown of a risk value into the relevant components, e.g. what percentage is due to age, to weight or to other co-morbidities. Whilst it was thought this might be helpful, DS commented that similar approaches with other tools had not been useful for patients. RK raised concerns that it could be misleading since it might imply an element of causality. If an individual is presented with a breakdown, they may think that changing something (e.g. weight) would impact on the risk level. Caution is therefore needed if a breakdown is presented. It will not be considered until there is evidence-based research supporting its utility and an approach which addresses the concerns raised about its interpretation. Hence the group recommended this should not be used for the phase 1 release of the tool.

8.3 Members questioned if the coefficients should be displayed on the website. It was suggested that this would not for use with the public facing tool, but that there could be a link for these.

9.0 Engagement and implementation

9.1 AC updated members on the public engagement work. The panel at Oxford had provided feedback, as had the engagement with the CMO's office and clinical stakeholders. With the forthcoming publication of the paper, the consideration now is on how to get across the news of what QCovid is, separate from communicating risk. It has been suggested that the Centre for BAME Health and the OXFORD panel will be used in taking this forward and how the messaging will be done.

9.2 Members queried whether there were ethnic differences in how people interpret risk. The importance of ethnicity needs to be communicated carefully. DS agreed to investigate if there is any research into ethnic interpretation. Consideration may need to be given on producing culturally appropriate material, and whether different languages will be required for the public facing tool.

- *Action 9.6: **DS** to investigate ethnic differences in how people perceive risk.*

10.0 General discussion

10.1 This item was not considered due to available time.

11.0 Summary of actions and next steps

11.1 The Chair summarised the actions, noting that the protocol had been finalised and work will move forward on the collaboration agreement.

12.0 AOB & date of next meeting

12.1 No items were raised. The next meeting will be held in 2-3 weeks' time and would focus on validation and ethnic presentation of risk. A meeting appointment would be forwarded in due course. The Chair thanked members for their attendance and their input and closed the meeting at 15:17.

Minutes of the NERVTAG Subgroup on Clinical Risk Stratification: Tenth meeting

Date & Location: 16:00 - 16:45, 21st October 2020 - Via telecon only

In attendance:

Julia Hippisley-Cox (JHC) (Chair), Emma Petty (Secretariat)

NERVTAG Members: Calum Semple (CSm), Andrew Hayward (AH)

Sub-group members: [redacted], Elizabeth Williamson (EW), Ruth Keogh (RK), Karla Diaz-Ordaz (KDO), Ashley Clift (AC), Aziz Sheikh (AS), Jonathan Valabhji (JV), Tony Williams (TW), Carol Coupland (CC), Chris Robertson (CR), Tony Crockford (TC), Harry Hemingway (HH), Ben Humberstone (BH), Luke Collet-Fenson (LCF), Peter Johnson (PJ)

1.0 Welcome

1.1 The Chair welcomed everyone to the meeting. Apologies were noted from Frank Kee (FK), Kamlesh Khunti (KK) and Ruth Parry (RP). No competing interests were raised. Welcomes were given to new members of the subgroup – Ben Humberstone and Chris Robertson.

2.0 Minutes and matters arising

2.1 The minutes of the last meeting had been reviewed and were agreed with no amendments.

3.0 Collaboration agreements

3.1 The Chair advised members that the main agreement with NIHR had been signed. The agreements with partner institutions now need to be completed and signed. The Chair agreed to check with research services on any outstanding issues to ensure completion of the agreements. Once signed, the funds can be released to the participating departments.

3.2 The Chair advised members that Cambridge had pulled out of the agreement due to the terms and conditions, which could not be changed. It was noted that the Winton Centre at Cambridge has provided helpful input into this work on risk communication prior to this. The plans for investigating how ethnic groups perceive risk will be taken forward by Kamlesh Khunti.

- *Action 10.1:* ***JHC*** *to check on progress of the signing of the institution collaboration agreements.*
- *Action 10.2:* ***KK*** *to take forward investigation of how ethnic groups perceive risk.*

4.0 Policy update

4.1 The Chair informed members that the BMJ paper was published this week.

4.2 NM emphasised with the group that they should adhere to confidentiality principles agreed at the outset of the work. The discussions and results from this subgroup should not be shared externally until the work is published and available in the public domain. It is recognised that complex issues are being addressed in this risk stratification work which fed into sensitive policy discussions. Any unapproved discussion or reference of this work may result in confusion as to the focus of the stratification too l. NM had discussed with CMO prior to the meeting, who wanted to thank everyone for their valuable contribution, and he hoped that the collaboration of researchers in this group would lead to support for a single tool which would have the benefit of minimi sing confusion for the public and the profession and helping us move towards a more robust approach to risk stratification.

4.3 HH referred to his separate work being undertaken externally investigating mortality and other underlying conditions. It was agreed it would be helpful for the subgroup to be awar e of ongoing work from other groups. There should not be discouragement of research by colleagues; however, the subgroup collaboration was established to ensure a focused approach to produce a stratification tool. NM asked that the group does not make external reference to the subgroup's work which has not yet been published. Members were advised to check with the Chair or NM if specific material relating to the QCOVID model was in the public domain.

4.4 CSm requested if the subgroup and ISARIC could be appraised on how the risk scores will be taken forward in the NHS. NM confirmed that discussions, which included the Chair, were underway. With the publication of the BMJ paper, the priority was now to get the QCOVID model to the clinicians. NM agreed to discuss the involvement of ISARIC with CSm offline.

4.5 Members discussed the implementation of the QCOVID model and how to prepare GPs for enquiries regarding its use. NM noted that the National Clinical Directors were being updated on the project. It was acknowledged that DHSC were aware of the potential interest by the public following the BMJ publication and the possible impact for GPs, once the QCOVID model is available for use.

4.6 EW noted that OpenSAFELY had a number of complementary activities and that the OpenSAFELY risk prediction work had been put on hold, while the subgroup developed the QCOVID model. Work combining risk prediction with the outputs from dynamic transmission modelling is planned to be undertaken OpenSAFELY. A protocol detailing these plans has been published recently and is currently being reviewed.

4.7 The use of OpenSafely data for validation of the QCOVID model as originally planned was discussed, including the requirements to give permission to access the data. EW agreed to investigate approaches as to how this might be achieved.

- *Action 10.3:* ***EW*** *to check on approaches for using OpenSafely data for validation and to update the group*

4.8 TW reported that COVID-age had been running since May 2020 and is being promoted in Scotland and Northern Ireland. The tool continues to be developed. TW suggested that

a comparison between COVID-age and QCOVID might be useful and that clinicians may have a preference on which tool they wish to use. NM noted that DHSC had clearly prioritised the QCOVID model, which would be NHS branded. The production of a single tool that supported policy requirements was the reason for the establishment of the collaboration. It was noted that COVID-age had been produced to fill the gap as it was not known when the QCOVID model would be released. TW agreed to discuss the role of COVID-age with NM offline.

5.0 QCOVID publication

5.1 This item was covered in the discussions for item 4.

6.0 Model validation studies

6.1 Members discussed the progress with the validation of the QCOVID model. CR noted that there was an issue with obtaining chemotherapy data and questioned whether this needed to be included for the 1st validation. The issue with chemotherapy data had been recognised as a limitation for validation. Members discussed the provision of coding information and the algorithm and also issues with access to specific data. The Chair informed members that a pack was being produced to address the information available and dealing with limitations. The Chair agreed to check with Oxford University Innovations on the status of the information being provided for validation.

- *Action 10.4:* ***FKp*** *to update on progress with information being provided for validation .*

6.2 Members noted that reporting on the issues encountered with validation across the four nations was important to complete. HH volunteered to help with taking this work forward.

- *Action 10.5:* ***HH*** *to assist with the report on the issues encountered with cross nation validation.*

7.0 Risk model updates

7.1 JHC highlighted that several groups had been in touch regarding potential modifications to the algorithm to better characterise risks for clinical sub -groups such as those on chemotherapy, those with cirrhosis and those with transplants. JHC anticipated that some exploratory work will be undertaken to determine whether this would improve the model and provide more granular risks for patients.

8.0 New data linkages

8.1 The Chair advised members that potential new data linkages had been proposed which could enhance the development of the QCOVID model. One example was to create links with the blood and renal transplant service. It was suggested that a small subgroup could be established to undertake bespoke work on linkages and the resulting analyses which could then be undertaken. Members were asked to volunteer for this work. Expressions of interest were given by JV, TC, CC, NM and BH.

- *Action 10.6:* ***Members*** *to inform JHC of interest in bespoke work on linkages.*
- *Action 10.7:* ***JHC*** *to arrange a meeting of interested members to discuss data linkages.*

8.2 BH informed members of the ONS data linkages. The public health data asset links several datasets, including test and trace data. There has been work investigating socio - economic factors against risk of COVID, which has been published. There is the possibility that ONS demographics could be used to help inform QCOVID. NM added that a shared data asset with ONS was supported by DHSC.

9.0 Engagement and implementation

9.1 Due to time constraints AC agreed to provide an update on engagement at the next meeting.

10.0 General discussion

10.1 Members discussed the work on time varying incidence rates with OpenSafely and how this work differs from the subgroup's work. Members also suggested that calibrating the risk of infection and the risk of mortality following infection against community infection levels could be considered. The Chair confirmed that in the QCOVID model which has just been published, the model had been successfully recalibrated to a different time period with a different infection rates and so an approach to this was already developed.

10.2 The Chair noted that more COVID-19 positive and negative testing data was available now, which could be utilised. The Chair agreed to hold discussions with RK and CC and others offline to consider potential approaches.

11.0 Summary of actions and next steps

11.1 This item was not considered due to available time.

12.0 AOB & date of next meeting

12.1 No items were raised. The meetings will be scheduled monthly, going forward. A meeting appointment for the next meeting will be circulated in due course. Members were reminded that they could email the Chair with any issues between meetings.

12.2 The Chair thanked members for their attendance and closed the meeting at 17:13.

Minutes of the NERVTAG Subgroup on Clinical Risk Stratification: Eleventh meeting

Date & Location: 12:00 – 13:00, 3rd December 2020 - Via telecon only

In attendance:

Julia Hippisley-Cox (JHC) (Chair), [redacted], Emma Petty (Secretariat)

Aziz Sheikh (AS), Carol Coupland (CC), Tony Crockford (TC), Ben Humberstone (BH), Vahe Najilyan (VN), Jane Lyons (JL), Frank Kee (FK)

1.0 Welcome and introduction

1.1 The Chair welcomed everyone to the meeting, noting that this was a smaller subgroup of the Clinical Risk Stratification Subgroup. Introductions were given for all members. The Chair noted that [redacted] will be co-chairing the meeting on behalf of the CMO, covering the policy issues.

2.0 Outline

2.1 The Co-chair thanked members for their work to date. It was noted that the BMJ publication of the model was a significant milestone and policy work on version 1 of the model is being undertaken at pace. Consideration is being given to future work and how to adjust the model to best fit policy needs, including further validations, so that it is available across the UK. The development of the shared public data asset by ONS will be important for future work in validating the model.

2.2 It is requested that the work of the subgroup is held by members only and is not shared with colleagues. Any conflicts of interest should to be declared by members as they arise. The aim of the subgroup was to establish a collaboration to produce a tool to meet the policy needs and while there is no wish to stop other work being carried out, the priority lies with QCOVID.

2.3 The current model has been converted into a tool for NHS Digital and has been provided to a limited number of clinicians to give feedback on both the tool and accompanying clinical guidance. The aim is for the tool to be launched to the entire NHS in December. Consideration is also being given as to whether this model can be used to inform the national stratification work and the vaccine phase of the COVID response. The Co-chair noted that ministers are very pleased with the work from the subgroup and the progress that has been made.

3.0 Discussion of ONS validation results

3.1 The Chair presented a protocol produced with ONS on the process for validation of the QCOVID model, which could be applied (with modifications as required) to the validation work by the devolved administrations (DAs). The protocol covers the statistical validation

of the performance of the model, considering whether the algorithm predict hospitalisation and deaths accurately, whether it discriminates well, and whether it calibrates well. As the model was developed using English data, there is the opportunity to test it using data from Scotland, Wales and Northern Ireland and other sources, such as the ONS dataset. The document defines the validation steps and the tables required. The demographics of each dataset population will be used to compare the datasets.

3.2 The Chair noted that the model was developed using data to the end of April. A subsequent dataset to the end of June was used for temporal validation and allowed recalibration of the model.

3.3 The Chair advised members that the paper on the model was originally submitted to the Lancet, but eventually published by the BMJ. The Lancet noted an interest in publishing the validation of the model.

3.4 Members discussed the details of the protocol document. Practical issues had been raised with defining the temporal intervals for the records of some of the risk factors. The Chair responded to say that the intervals had been agreed and members should have received a spreadsheet from Oxford Computing Consulting containing the parameters and the associated criteria, with an accompanying database.

- *Action 11.1:* ***Members*** *to alert JHC if the download link for the Oxford Computing Consulting spreadsheet has not been received.*

3.5 VN presented the validation results available from ONS. The data is based on the 2011 census for individuals in England aged 19-100 and alive in January 2020, which was then linked to GPES data using NHS numbers. Approximately 1/8 of the people in the census data could not be linked. Members discussed the use of additional data, such as PDS data from NHS digital to compare against the ONS dataset. A note will need to be included in the publication to explain those people not linked. The ONS validation has included comorbidity derivation; however, a few issues have been identified. Prevalence is currently being checked against the QCOVID paper to highlight any discrepancies. Members discussed age banding in the model metrics. It was agreed that the concordance index provides good results, indicating that the tool ranks people effectively even with imperfect data.

- *Action 11.2:* ***VN*** *to contact NHS Digital to validate the ONS data against PDS*

3.6 The Chair added that there was further work to be carried out with other metrics. The Chair agreed to supply members with a file of Stata commands to produce the D statistic and R^2 statistic, with the use of CCReport to produce consistent tables from each dataset.

- *Action 11.3:* ***JHC*** *to circulate a file of Stata commands.*

3.7 Members discussed the time period of the ONS data. It was agreed it would be helpful to have a breakdown of the ONS validation into three periods – 1) to the end of April; 2) to the end of June and 3) to the end of July.

5.0 Update on validation in Scotland, Wales & Northern Ireland

5.1 FK advised members of the Northern Ireland Longitudinal Study, which has linked with one third of the census population (~500,000) to medical records and has governance

approval. It was suggested that validation could be run on this NILS dataset, noting there may be some limitations with certain links in the dataset, such as for chemotherapy.

5.2 Members referred to previous discussions regarding EMIS data access from Northern Ireland. The discussions had been paused but could be restarted if required.

5.3 JL informed members that work was progressing with the Welsh data. A baseline cohort had been established and continues to be updated. Data from GPs and SACTs will be included when available. Members discussed the handling of OPCS codes with SACTS data.

5.4 AS reported that Scottish Government has agreed to release the data to PHS in the next few days. An initial analysis will be run without the cancer data. It is hoped the data will be moved into the national safe haven, along with census data, which will help populate the ethnicity field. An analyst has been appointed for this work and will be invited to join the subgroup.

- *Action 11.4:* ***Secretariat*** *to invite SK to join the next subgroup meeting.*

4.0 Preparation of report/paper for publication and journal for submission

4.1 Members discussed the mode of release for the validations and whether to release the ONS results ahead of the DAs' results. NM thanked members for all of the work being done on this project and noted that it was critical to have the ONS validation to be able to use the tool at a national level. It was agreed there should be a peer-reviewed publication of the validation as soon as possible. The release of the DAs results could be determined in due course. Ministers will be advised that the results using the tool are valid and the Chair, BH and VN would assist with drafting the statement.

- *Action 11.5:* ***JHC, BH & VN*** *to assist in drafting a statement on the ONS validation.*

4.2 It was noted that there would be a COVID-O meeting next week to update the DAs on the tool and the feasibility for a bulk stratification of the population.

6.0 Timelines

6.1 The Chair stated that great progress had been made with the model and thanked everyone for their collaboration. It was noted that the model would continue to be updated over time as the data or parameters change; however, it was recognised that there would not be a need to carry out validations on all the data sets. The Chair requested that once a validation had been completed on a dataset, that the dataset continued to be maintained and updated for future analyses. This may require extensions to existing data agreements.

7.0 Next steps

7.1 It was agreed that the next meeting would be held in two weeks, with the date and time to be confirmed.

8.0 AOB

8.1 No items were raised. The Chair thanked members for their attendance and closed the meeting at 13.04.

Minutes of the NERVTAG Subgroup on Clinical Risk Stratification: Twelfth meeting

Date & Location: 14:00 – 15:00, 16th December 2020 - Via telecon only

In attendance:

Julia Hippisley-Cox (JHC) (Chair), Emma Petty (Secretariat)

Aziz Sheikh (AS), Carol Coupland (CC), Tony Crockford (TC), Vahe Najilyan (VN), Jane Lyons (JL), Ronan Lyons (RL), Frank Kee (FK), Tony Crockford (TC), Chris Robertson (CR), Steven Kerr (SK)

1.0 Welcome, introductions and apologies

1.1 The Chair welcomed everyone to the meeting. Introductions were given for new members and apologies were noted from [redacted].

2.0 Minutes and actions from the last meeting

2.1 The Chair asked for corrections to the minutes of the last meeting. The minutes were agreed without amendment.

2.2 The actions from the last meeting were reviewed:

- Action 11.1: Members to alert JHC if the download link for the Oxford Computing Consulting spreadsheet has not been received.
- Action 11.2: VN to contact NHS Digital to validate the ONS data against PDS
- Action 11.3: JHC to circulate a file of Stata commands
- Action 11.4: Secretariat to invite SK to join the next subgroup meeting
- Action 11.5: JHC, BH & VN to assist in drafting a statement on the ONS validation

Actions 11.1, 11.2, 11.4 and 11.5 had been completed. The file for action 11.3 was still to be circulated.

2.3 It was proposed that the link for the results of the ONS validation could be circulated to members, to ensure consistency between the analyses for the four countries.

- *Action 12.1: **JHC** to circulate ONS validation results link to members.*

3.0 Update on validation in Scotland, Wales and Northern Ireland

3.1 VN presented the validation results from ONS, noting areas with limitations to the data for certain groups. The metrics for the validation have been completed. Members discussed the best method to use for calculating R^2. It was suggested that the results presented in the paper would lead with the C statistic. Calibration of the tool has been completed for the first time period and is consistent with the BMJ paper. The validation results showed that the model performs well. The Chair agreed to send the commands round for the calculations. JL noted that the Welsh data preparation had been completed

and the ONS R codes would be used for the metrics. It was agreed that VN would circulate the R codes to members for use in the validations.

- *Action 12.2: **JHC** to circulate calculation commands.*
- *Action 12.3: **VN** to circulate R codes to subgroup members for validations.*

3.2 Members discussed the confidence intervals generated with the lower age groups and considered combining age groups under 50 years.

3.3 Members commented that the ONS validation only uses mortality data and that the hospitalisation data is not included. The priority was to produce a validation on the mortality data, but it was noted that hospitalisation data is available to the end of July and could be included. Members discussed the type of mortality data used. It was agreed that data with COVID listed on the death certificate should form the primary data set, and analyses using data where death occurred within 28 days of a positive test could be included in an appendix.

3.4 VN reported that the sensitivity assessment from the ONS validation was very similar to that given in the BMJ paper. Members discussed whether it was possible to produce relative risk results, in addition to the absolute risk. VN agreed to investigate this with the ONS validation.

- *Action 12.4: **VN** to investigate additional analyses; including mortality within 28 days; hospitalisations; and relative risk.*

3.5 The Chair noted that an international group had undertaken a critique of the BMJ paper and had come back with several questions requiring clarification. The critique stated that the paper was high quality, it used a strong data set and had a low risk of bias. Calibration against GP practice was queried, although it may be possible to carry this out with the ONS data. Members discussed and agreed presenting additional results restricting the validation to TPP practices.

3.6 JL reported that the validation work was progressing with the Welsh data and it should be possible to have the mortality results by early January. TC noted that the Northern Ireland data is still being compiled as alternative data sets are being considered where there are limitations. There are also legal framework issues with access to data sets. AS added that progress was being made with the Scottish validation. CR confirmed that the GP data cohort included deaths and hospitalisations up to 30th June; however, data is limited for chemotherapy treatments. Members agreed that it was not possible to have a perfect data set, but the work to date shows that the tool works well even when the data is not perfect.

3.7 Members discussed the potential of a publication on the preparation and methodology needed across the DAs for validation. SK agreed to put together a plan for a paper to discuss at the next meeting.

- *Action 12.5: **SK** to produce a plan for a paper on the approaches taken for validation by the DAs.*

3.8 The Chair confirmed that the model would be updated, particularly as new data is received, including Test & Trace, vaccination and antibody data. Members were requested to bear in mind that validation data sets should be maintained for use with future versions of the model.

3.9 The policy priorities for the tool would be confirmed by DHSC and CMO's office. The tool has been produced as an academic research version, and a clinical version for use by GPs is in progress. It is understood that a public facing version will also be produced. It is important that all of the different versions use the same basis, to ensure consistency in approach for the patient. The use of the same tool across the DAs will also help ensure consistency.

4.0 Preparation of report/paper for publication and journal for submission

4.1 The Chair advised members that the aim was to submit the validation paper as soon as possible. The paper would focus on the ONS validation, but additional analyses could be included if available. Those validations not included would be published in separate papers. The Chair agreed to circulate an authorship form for the ONS validation paper.

- *Action 12.6:* ***JHC*** *to circulate an authorship form to members.*

5.0 Timelines

5.1 Members discussed the potential timings for producing validations and also statistical approaches to use in the validations.

6.0 Next steps

6.1 It was agreed that the next meeting would be held in January 2021, with the date and time to be confirmed.

7.0 AOB

7.1 No items were raised. The Chair thanked members for their attendance. The meeting closed at 15:18.