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### Appendix 1. PROSPERO protocol

#### PROSPERO

International prospective register of systematic reviews

NHS National Institute for Health Research

Multiple health risk behaviours and multimorbidity risk: a systematic review and metaanalysis Konstantinos Spyropoulos, Christopher Gidlow, Naomi Ellis, Ian Lahart

#### Citation

Konstantinos Spyropoulos, Christopher Gidlow, Naomi Ellis, Ian Lahart. Multiple health risk behaviours and multimorbidity risk: a systematic review and meta-analysis. PROSPERO 2018 CRD42018111026 Available from:

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#### Review question

What is the impact of multiple health risk behaviours in the development of multimorbidity risk of the adult population?

#### Searches

The search strategy will be applied using the following electronic databases MEDLINE, Scopus, PubMed, Cochrane Library, CINAHL and PsycINFO.

The keyword Multimorbidity will mainly be used to describe this health issue, alongside the Medical Subject Heading (MeSH) term of "Comorbidity". Furthermore, terms like multiple diseases, multiple conditions, multiple long-term disease, concomitant diseases or multiple non-communicable disease will also be used to add up the all-inclusive process.

Regarding the health risk behaviours , Medical Subject Heading (MeSH) terms, like "Diet", "Fruit", "Vegetables", "Exercise", "Leisure activities", "Sedentary lifestyle", "Smoking", "Alcohol drinking" accompanied by keywords like healthy/unhealthy diet, physical (in)activity, tobacco, alcohol abuse or excessive drinking will be applied to cover as much as possible the spectrum of the lifestyles under investigation.

Several refinements will also be applied to filter the search results:

 Only the studies that have examined the combined effect of the four most common (smoking, alcohol, drinking, diet) health risk behaviours (HRB) on the development of Multimorbidity issue will be included in the final systematic review.

and only those studies that have examined the combined effect of health risk behaviours on noncommunicable Multimorbidity

 Cancer survivors will be treated as chronic patients only if their survivorship does not exceed the five years' time from the initial diagnosis

 Smoking, alcohol, diet and physical activity will be treated as health risk behaviours even when studies have aimed to examine the associated psychological disorders.

 Obesity will be treated as chronic condition, rather than a health risk behaviour. This is in accordance with current clinical suggestions that obesity is a complex phenomenon comprising behavioural, epidemiologic and molecular/metabolic factors.

Randomized Control Trials (RCT) will be included only when the control groups have zero or one chronic condition.

#### Types of study to be included

Retrospective and prospective cross-sectional and/or cohort studies.

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#### PROSPERO

#### International prospective register of systematic reviews

#### Condition or domain being studied

Multimorbidity is defined as the co-existence of two or more chronic conditions within the same individual with or without indexing. Health Risk Behaviours (HRBs) are defined as any behaviour that influence the health of the engaging individuals increasing the likelihood of developing a disease. For the systematic review, the health risk behaviours will be:

- Smoking (current, ex-smoker, never smoker)
- Excessive Alcohol consumption (relative to recommended guidelines)
- (Un)healthy diet (based on daily portions of fruit/vegetables relative to recommended guidelines)
- Physical (in)activity (relative to recommended guidelines).

Participants/population All adults (aged?18 yr.).

#### Intervention(s), exposure(s)

The four most common Health Risk Behaviours such as smoking, excessive alcohol consumption, (un)healthy diet and physical (in)activity.

#### Comparator(s)/control

People exposed to the aforementioned Health Risk Behaviours and people not exposed

Context

#### Main outcome(s)

The main outcome concerns the examination of the joint effect of multiple health risk behaviours in the development of multimorbidity (Any measures of multimorbidity will be taken under consideration such as, Quality and Outcomes Framework (QOF), Adjusted Clinical Group (ACG) system, Simple disease count system).

#### Additional outcome(s)

None.

#### Data extraction (selection and coding)

The present systematic review reflects the partial requirements of PhD. KS (PhD student) will screen, extract the data and assess the quality of included studies. CG will act as second reviewer verifying the quality of screening and data extraction. NE and IL will resolve discrepancies between CG and KS.

#### Risk of bias (quality) assessment

Articles that meet the inclusion criteria will be assessed for methodological quality (ROBINS-I tool).

#### Strategy for data synthesis

Statistical analysis will be implemented using RevMan 5, while the pooled estimated effect of multiple health risk behaviours on Multimorbidity will be presented in odds ratios (OR) with 95% confidence intervals (CI).

#### Analysis of subgroups or subsets

If the specific data is available then the following subgroups will be analysed:

 The pooled estimate effect of multiple health risk behaviours on Multimorbidity risk (when the latter is defined as 3+CC)

- Gender
- · Socioeconomic status (area of living, education, etc)

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PROSPERO

#### International prospective register of systematic reviews

NHS National Institute for Health Research

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Language English

Country England

Stage of review Review\_Ongoing

Subject index terms status Subject indexing assigned by CRD

Subject index terms Comorbidity; Health Risk Behaviors; Humans; Multimorbidity; Risk

Date of registration in PROSPERO 12 November 2018

Date of publication of this version 12 November 2018

Details of any existing review of the same topic by the same authors

Stage of review at time of this submission

PROSPERO International prospective register of systematic reviews NHS National Institute for Health Research

Stage	Started	Completed
Preliminary searches	Yes	No
Piloting of the study selection process	Yes	No
Formal screening of search results against eligibility criteria	Yes	No
Data extraction	Yes	No
Risk of bias (quality) assessment	Yes	No
Data analysis	No	No
Versions		

12 November 2018

PROSPERO

This information has been provided by the named contact for this review. CRD has accepted this information in good faith and registered the review in PROSPERO. CRD bears no responsibility or liability for the content of this registration record, any associated files or external websites.

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### Appendix 2. Multimorbidity – Multibehaviours – review search strategy

- 1. Comorbidity/
- 2. TI Multiple comorbid\*
- 3. AB Multiple comorbid\*
- 4. TI Multimorbid\*
- 5. AB Multimorbid\*
- 6. TI Multi morbidity
- 7. AB Multi morbidity
- 8. TI Multiple diseas\*
- 9. AB Multiple diseas\*
- 10. TI Multiple condition\*
- 11. AB Multiple condition\*
- 12. TI Multiple patholog\*
- 13. AB Multiple patholog\*
- 14. TI Multiple chronic condition\*
- 15. AB Multiple chronic condition\*
- 16. TI Multiple chronic diasese\*
- 17. AB Multiple chronic disease\*
- 18. TI Multiple non-communicable disease\*
- 19. AB Multiple non-communicable disease\*
- 20. TI Multiple long-term condition\*
- 21. AB Multiple long-term condition\*
- 22. TI Multiple long-term disease\*
- 23. AB Multiple long-term disease\*
- 24. TI Multiple long-term patholog\*
- 25. AB Multiple long-term patholog\*
- 26. TI Coexist\* patholog\*
- 27. AB Coexist\* patholog\*
- 28. TI Coexist\* chronic condit\*
- 29. AB Coexist\* chronic condit\*
- 30. TI Coexist\* chronic diseas\*
- 31. AB Coexist\* chronic diseas\*
- 32. TI Coexist\* diseas\*
- 33. AB Coexist\* diseas\*
- 34. TI Coexist\* condition\*
- 35. AB Coexist\* condition\*
- 36. TI Coexist\* long-term patholog\*
- 37. AB Coexist\* long-term patholog\*
- 38. TI Coexist\* long-term condition\*
- 39. AB Coexist\* long-term condition\*
- 40. TI Coexist\* long-term disease\*
- 41. AB Coexist\* long-term disease\*
- 42. TI Coexist\* non-communicable disease\*
- 43. AB Coexist non-communicable disease\*
- 44. TI Concomitant patholog\*
- 45. AB Concomitant patholog\*
- 46. TI Concomitant disease\*
- 47. AB Concomitant disease\*
- 48. TI Concomitant chronic disease\*
- 49. AB Concomitant chronic disease\*
- 50. TI Concomitant long-term disease\*
- 51. AB Concomitant long-term disease\*
- 52. TI Concomitant condition\*
- 53. AB Concomitant condition\*
- 54. TI Concomitant chronic condition\*
- 55. AB Concomitant chronic condition\*
- 56. TI Concomitant non-communicable disease\*
- 57. AB Concomitant non-communicable disease\*

- 58. 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 OR 38 OR 39 OR 40 OR 41 OR 42 OR 43 OR 44 OR 45 OR 46 OR 47 OR 48 OR 49 OR 50 OR 51 OR 52 OR 53 OR 54 OR 55 OR 56 OR 57 OR 58
- 59. Diet/
- 60. Exp Healthy Diet/
- 61. Exp Fruit/
- 62. Exp Vegetables/
- 63. TI Health\* eat\*
- 64. AB Health\* eat\*
- 65. TI Health\* food\*
- 66. AB Health\* food\*
- 67. TI Unhealth\* diet
- 68. AB Unhealth\* diet
- 69. TI Unhealth\* eat\*
- 70. AB Unhealth\* eat\*
- 71. TI Unhealth\* food\*
- 72. AB Unhealth\* food\*
- 73. TI Unhealth\* nutrition
- 74. AB Unhealth nutrition
- 75. TI Poor eat\*
- 76. AB Poor eat\*
- 77. TI Poor nutrition
- 78. AB Poor nutrition
- 79. TI Poor diet
- 80. AB Poor diet
- 81. 59 OR 60 OR 61 OR 62 OR 63 OR 64 OR 65 OR 66 OR 67 OR 68 OR 69 OR 70 OR 71 OR 72 OR 73 OR 74 OR 75 OR 76 OR 77 OR 78 OR 79 OR 80
- 82. exp Exercise/
- 83. leisure activities/
- 84. exp Sedentary lifestyle/
- 85. TI Physical activ\*
- 86. AB Physical activ\*
- 87. TI Physical inactiv\*
- 88. AB Physical inactivt\*
- 89. TI Sedentary behav\*
- 90. AB Sedentary behav\*
- 91. 82 OR 83 OR 84 OR 85 OR 86 OR 87 OR 88 OR 89 OR 90
- 92. Smoking/
- 93. TI chew\* Tobacco
- 94. AB chew\* Tobacco
- 95. TI water pipe tobacco
- 96. AB water pipe tobacco
- 97. TI electronic cigarette smoking
- 98. AB electronic cigarette smoking
- 99. 92 OR 93 OR 94 OR 95 OR 96 OR 97 OR 98
- 100. Alcohol drinking/
- 101.TI alcohol abuse
- 102.AB alcohol abuse
- 103.TI Excessive drink\*
- 104.AB Excessive drink\*
- 105.TI Heavy Drink\*
- 106.AB Heavy Drink\*
- 107.TI harm drink\*
- 108. AB harm drink\*
- 109. 100 OR 101 OR 102 OR 103 OR 104 OR 105 OR 106 OR 107 OR 108
- 110.81 OR 91 OR 99 OR 109
- 111.58 AND 110
- 112. Limit 112 to yr="1990-Current"

## Appendix 3. ROBINS-E tool for assessment of internal validity of SR-META included studies

# Preliminary tool for risk of bias in exposure studies (1): At protocol stage

Specify the research question by defining a generic target experiment: What is the accumulated impact of multiple health risk behaviours in the development of Multimorbidity risk in adult population?

Participants	Adults aged≥18 yr. with zero or one chronic condition
Experimental exposure	Engaged with two or more HRBs (smoking, alcohol abuse, physical inactive, less than 5 a day fruits/vegetable
Control exposure	Engage with none or one HRBs

#### List the confounding domains relevant to all or most studies

SES - AGE - GENDER - AREA OF LIVING - ETHNICITY

#### List the possible co-exposures that could differ between exposure groups and could have an impact on study outcomes

OBESITY

#### List the criteria used to determine the accuracy of exposure measurement

OFFICIAL GUIDELINES (SMOKING -1 CIGARETTE PER DAY, PHYSICAL ACTIVITY – 150 min MODERTE or 60 min VIGOROUS ACTIVITY PER WEEK, ALCOHOL CONSUMPTION 14UNITS ALCOHOL PER WEEK, FRUITS/VEGETABLES – 5 PER DAY)

#### Factors to consider when evaluating health outcome assessment

MM is defined as the co-existence of two or more chronic conditions in the same individual. Ideally at least 12 morbidities must be included in MM measurement tool

### Preliminary tool for risk of bias in exposure studies (2): For each study

Specify a target experiment specific to the study.

		Participant	Outpatient general population age 18-75 years old
The protocol-specified target experiment fully applies	OR	Experimental exposure Control exposure	Exposure at least on two Health Risk Behaviours (smoking, alcohol drinking, unhealthy diet, physical inactivity) Non-exposure to the above-mentioned Health Risk Behaviours of outpatient

#### Specify the outcome

Specify which outcome is being assessed for risk of bias (typically from among those earmarked for the Summary of Findings table). Specify whether this is a proposed benefit or harm of exposure.

The combined effect of two and three Health Risk Behaviours (sedentary lifestyle, inadequate fruit and vegetable consumption) in development of cardiometabolic multimorbidity (at least 2 of diabetes, heart disease, stroke) risk

#### Is your aim for this study...?

- □ to assess the effect of initiating intervention (as in an intention-to-treat analysis)
- □ to assess the effect of initiating and adhering to intervention (as in a per-protocol analysis)
- $\sqrt{}$  other To assess the effect of multiple exposure statues (smoking, alcohol drinking, diet, physical activity) of the participants in cardiometabolic multimorbidity risk: Harm exposure (specify)

#### Specify the numerical result being assessed

In case of multiple alternative analyses being presented, specify the numeric result (e.g. RR = 1.52 (95% CI 0.83 to 2.77) and/or a reference (e.g. to a table, figure or paragraph) that uniquely defines the result being assessed.

2RF OR1.51 95%CI (1.28-1.79 p<0.05), ≥3RF OR1.91 95%CI (1.57-2.33 p<0.05), Table 1

#### Preliminary consideration of confounders

Complete a row for each important confounding area (i) listed in the review protocol; and (ii) relevant to the setting of this particular study, or which the study authors identified as potentially important.

"Important" confounding areas are those for which, in the context of this study, adjustment is expected to lead to a clinically important change in the estimated effect of the exposure. "Validity" refers to whether the confounding variable or variables fully measure the area, while "reliability" refers to the precision of the measurement (more measurement error means less reliability).

(i) <b>Confou</b>	(i) Confounding areas listed in the review protocol				
Confounding area	Measured variable(s)	Is there evidence that controlling for this variable was unnecessary?*	Is the confounding area measured validly and reliably by this variable (or these variables)?	OPTIONAL: Is adjusting for this variable (alone) expected to move the effect estimate up or down?	
			Yes / No / No information	Favor intervention / Favor control / No information	
Age	18-75	No	Yes	No information	
Socio-economic status	Carstairs index of deprivation based on census results for four indicators of socioeconomic status (car ownership, male unemployment, overcrowding, and low social class) for residents of each postcode sector	No	Yes	No information	
gender	Male -female	No	Yes	No information	
ethnicity	White- Indian	No	Yes	No information	

(ii) Additional confounding areas relevant to the setting of this particular study, or which the study authors identified as important

Confounding area	variable(s)	Is there evidence that controlling for this variable was unnecessary?*	validly and reliably by this variable (or these variables)?	OPTIONAL: Is adjusting for this variable (alone) expected to move the effect estimate up or down?
			Yes / No / No information	Favor intervention / Favor control / No information

\* In the context of a particular study, variables can be demonstrated not to be confounders and so not included in the analysis: (a) if they are not predictive of the outcome; (b) if they are not predictive of exposure; or (c) because adjustment makes no or minimal difference to the estimated effect of the primary parameter. Note that "no statistically significant association" is not the same as "not predictive".

### Preliminary consideration of criteria used to determine the accuracy of measurement of exposure and outcome

Complete a row for each measure listed in the study for the (i) exposure and (ii) outcome. Of the measures listed in the protocol, consider the sensitivity, specificity, and confidence in the methods used in the study.

Exposure measurement method listed in the study				
Method of measurement	Measured exposure	Is the exposure measured validly and reliably by this method (or these methods)?		
surveys administered using standardised protocols	smoking status, respondents were classified into: never smoker, ex-smoker, and current smoker	Yes / No / No information		
surveys administered using standardised protocols	Two measures of alcohol intake were created: exceeding existing weekly recommended maximum guidelines and exceeding daily recommended maximum guidelines (binge drinking) in the previous week. Males exceeded weekly guidelines if they consumed more than 21 units of alcohol a week, and exceeded binge drinking guidelines if they consumed more than 10 units in one session. Equivalent figures for females were 14 and 7 respectively	Yes		
surveys administered using standardised protocols	Diet was classified on the basis of frequency of fruit and vegetable consumption in the 7 days prior to inter- view into: ate fruit or vegetables every day; ate fruit or	Yes		

	vegetables some days; had not eaten fruit or vegetables.	
surveys administered using standardised protocols	Exercise was estimated by number of days per week of activity lasting at least 20 minutes which made the respondent out of breath or sweaty, categorised into: none, 1– 3, and >3 days.	Yes

Outcome measurement method lis	sted in the study	
Method of measurement	Measured outcome	Is the outcome measured validly and reliably by this method (or these methods)?
surveys administered using standardised protocols	Multimorbidity is typically characterised by the presence of two or more chronic conditions respondents who had two or more of the 40 relevant conditions were classed as having multimorbidity.	Yes. We defined chronic conditions on the basis of those used by Barnett and colleagues in their landmark study, whose work was informed by a previous systematic review of multimorbidity indices [15]. Self-reported conditions were coded based on the Royal College of General Practitioners' Morbidity classification

### Preliminary consideration of co-exposures

Complete a row for each important co-intervention (i) listed in the review protocol; and (ii) relevant to the setting of this particular study, or which the study authors identified as important.

"Important" co-interventions are those for which, in the context of this study, adjustment is expected to lead to a clinically important change in the estimated effect of the intervention.

(i) Co-exposures listed in th	e review protocol	
Co-exposure	Is there evidence that controlling for this co-exposure was unnecessary (e.g., because it was not administered)?	Is presence of this co-exposure likely to favor outcomes in the experimental or the control group
Obesity	it was not administered	No information
(ii) Additional co-exposures	relevant to the setting of this particular study, or which the	e study authors identified as important
Co-exposure	Is there evidence that controlling for this co-exposure was unnecessary (e.g., because it was not administered)?	Is presence of this co-exposure likely to favor outcomes in the experimental or the control group

# Risk of bias assessment (cohort-type studies)

Bias due to confounding	1.1 Is there potential for confounding of the effect of exposure in this study? If N or PN to 1.1: the study can be considered to be at low risk of bias due to confounding and no further signaling questions need be considered	РҮ	Most of the known important confounders have been controlled (i.e. age, income, education, gender, age, ethnicity). However, the risk of bias due to confounding still exist mainly due to NRSI nature of the study.
	If Y/PY to 1.1, answer 1.2 and 1.3 to determine whether there is a need to assess time-varying confounding:		
	<ul> <li>1.2. <u>If Y or PY to 1.1</u>: Was the analysis based on splitting follow up time according to exposure received?</li> <li>If N or PN to 1.2, answer questions 1.4 to 1.6, which relate to baseline confounding</li> </ul>	Y	"Twenty-07 employed a two-stage stratified random sample of respondents from three cohorts, born in the early 1930s, 1950s and 1970s (baseline approximate age 15, 35, 55 years) and residing in the west of Scotland."
	1.3. If Y or PY to 1.2: Were exposure discontinuations or switches likely to be related to factors that are prognostic for the outcome?	Ν	"To understand how multimorbidity prevalence has changed over time, we modelled prevalence across the lifecourse by predicting the probability of having multimorbidity. For the main longitudinal analysis, the outcome at each wave was modelled based on deprivation and risk factor predictors from the previous wave, effectively me. For example, multimorbidity outcomes at wave 5 were modelled using deprivation and risk factor predictors measured at wave 4"
	If N or PN to 1.3, answer questions 1.4 to 1.6, which relate to baseline confounding		
	1.4. Did the authors use an appropriate analysis method that adjusted for all the critically important confounding areas?	Y	Modelled rather than crude prevalence was assessed to account for potential bias arising from attrition. For the main longitudinal analysis, the outcome at each wave was modelled based on deprivation and risk factor predictors from the previous wave. The modelling strategy meant that each wave was conditional on data being available at

		the previous wave, hence outcomes at baseline (wave 1 for the 1950s and 1930s cohort and waves 1 and 2 for the 1970s cohort) were not modelled.
1.5. <b>If Y or PY to 1.4</b> : Were confounding areas that were adjusted for measured validly and reliably by the variables available in this study?	РҮ	"Interactions between cohort, sex, and age, and with all risk factor and socioeconomic status variables were tested using the global Wald test; final models included significant interactions. There were no significant inter- actions between risk factors and age, sex, or cohort. Interactions between sex and cohort were statistically significant and are included in all analyses."
1.6. Did the authors avoid adjusting for post-exposure variables?	Υ	"to illustrate the results, we present predicted probabilities for developing multimorbidity across the lifecourse. Stata's margins command was used. he sample was restricted to those who were not multimorbid at the prior wave and the fixed part of the regression models used for prediction. Separate curves were drawn for each covariate
If Y or PY to 1.3, answer questions 1.7 and 1.8, which relate to time-varying confounding		

	1.7. Did the authors use an appropriate analysis method that adjusted for all the critically important confounding areas and for time-varying confounding?	Y / PY / PN / N / NI	[Description]
	1.8. If Y or PY to 1.7: Were confounding areas that were adjusted for measured validly and reliably by the variables available in this study?	NA / Y / PY / PN / N / NI	[Description]
Ris	sk of bias judgement	Moderate	Although most important confounders have been controlled there is still the risk of bias due to confounding due to NRSI nature of the study

	Optional: What is the predicted direction of bias due to confounding?	Favors experimental / Favors comparator / Unpredictable	[Rationale]
Bias in selection of participants into the study	<ul> <li>2.1. Was selection of participants into the study (or into the analysis) based on variables measured after the start of the exposure?</li> <li><u>If N or PN to 2.1 go to 2.4</u></li> </ul>	N	Twenty-07 employed a two-stage stratified random sample of respondents from three cohorts, born in the early 1930s, 1950s and 1970s in 1987 of 15, 35, 55 years that have been follow up for almost 20 years. There were four data collection waves on same variables as those when they started.
	2.2. If Y/PY to 2.1: Were the post-exposure variables that influenced selection associated with exposure?	Y / PY / PN / N / NI	[Description]
	2.3. If Y/PY to 2.2: Were the post-exposure variables that influenced eligibility selection influenced by the outcome or a cause of the outcome?	NA / Y / PY / PN / N / NI	[Description]
	2.4 Do start of follow-up and start of exposure coincide for most participants?	Y	Yes, this is a cohort study where at baseline, participants responded to a questionnaire and underwent a structured clinical evaluation and as such comparing groups follow up in terms of their baseline health and exposure statues
	2.5 If Y/PY to 2.2 and 2.3, or N/PN to 2.4: Were adjustment techniques used that are likely to correct for the presence of selection biases?	NA / Y / PY / PN / N / NI	[Description]
	Risk of bias judgement	Moderate	[Support for judgement]
	Optional: What is the predicted direction of bias due to selection of participants into the study?	Favors experimental / Favors comparator / Towards null /Away from null / Unpredictable	[Rationale]
Bias in classification of exposures	3.1 Is exposure status well defined?	pY	"Diet was classified on the basis of frequency of fruit and vegetable consumption in the 7 days prior to inter- view. Exercise was estimated by number of days per week of activity lasting at

		least 20 minutes which made the respondent out of breath or sweaty, categorised into: none, 1–3, and >3 days. For smoking status, respondents were classified into: never smoker, ex-smoker, and current smoker. For alcohol measure based on thealcoholic drinks consumed in the week prior to interview, and units of alcohol were calculated based on amount and type. Two measures of alcohol intake were created: exceeding existing weekly recommended maximum guidelines, and exceeding daily recommended maximum guidelines (binge drinking) in the previous week. Males exceeded weekly guidelines if they consumed more than 21 units of alcohol a week, and exceeded binge drinking guidelines if they consumed more than 10 units in one session. Equivalent figures for females were 14 and 7 respectively. <b>However</b> ,
3.2 Did entry into the study begin with start of the exposure?	Y	Twenty-07 study, an ongoing cohort study where at baseline, participants responded to a questionnaire and underwent a structured clinical evaluation
3.3 Was information used to define exposure status recorded prior to outcome assessment?	Ν	""
3.4 Could classification of exposure status have been affected by knowledge of the outcome or risk of the outcome?	PN	Twenty-07 study, an ongoing cohort study where at baseline, participants responded to a questionnaire and underwent a structured clinical evaluation. This process has been repeated other four times in corresponding data collection waves.
3.5 Were exposure assessment methods robust (including methods used to input data)?	РҮ	"Daily units of alcohol intake were not available for all cohorts at all waves and were therefore used only in supplementary analyses. Lastly, a count score was created by adding up the number of adverse risk factors.

	Risk of bias judgement	Moderate	[Support for judgement]
	Optional: What is the predicted direction of bias due to measurement of outcomes or exposures?	Favors experimental / Favors comparator / Towards null /Away from null / Unpredictable	[Rationale]
Bias due to departures from intended exposures	<ul> <li>4.1. Is there concern that changes in exposure status occurred among participants?</li> <li>If your aim for this study is to assess the effect of initiating and adhering to an exposure (as in a per-protocol analysis), answer questions 4.2 and 4.3, otherwise continue to 4.4 if Y or PY to 4.1.</li> </ul>	N	Any possible change in exposure status would have followed a normal part of prevention usual practice and as such do not lead to bias.
	4.2. Did many participants switch to other exposures?	NI	[Description]
	4.3. Were the critical co-exposures balanced across exposure groups?	РҮ	Obesity, has been measured within Multimorbidity measurement as one of its included morbidities rather than a risk co- exposure
	4.4. <u>If NY/PN PY to 4.1, or Y/PY to 4.2, or 4.3:</u> Were adjustment techniques used that are likely to correct for these issues?	Y	"Multilevel logistic regression models were used to assess the relationship between multimorbidity and potential socioeconomic and health-related risk factor. Models were constructed in Stata version 13 using three levels: measurement points ( $n = 9277$ ), within individuals ( $n = 3466$ ), and within sampling units ( $n = 62$ ). Modelled rather than crude prevalence was assessed to account for potential bias arising from attrition. modelling strategy meant that each wave was conditional on data being available at the previous wave, hence outcomes at baseline (wave 1 for the 1950s and 1930s cohort and waves 1 and 2 for the

			1970s cohort) were not modelled Finally, although some missing data appeared in measured variables this has been addressed through multiple imputation.".
	Risk of bias judgement	Moderate	[Support for judgement]
	Optional: What is the predicted direction of bias due to departures from the intended exposures?	Favors experimental / Favors comparator / Towards null /Away from null / Unpredictable	[Rationale]
Bias due to	5.1 Were there missing outcome data?	Y	[Description]
missing data	5.2 Were participants excluded due to missing data on exposure status?	Y	"To understand how multimorbidity prevalence has changed over time, we modelled prevalence across the lifecourse by predicting the probability of having multi- morbidity. To illustrate the results, we present predicted probabilities for developing multimorbidity across the lifecourse. Stata's margins command was used, and for these graphs only, the sample was restricted to those who were not multimorbid at the prior wave and the fixed part of the regression models used for prediction. Separate curves were drawn for each covariate
	5.3 Were participants excluded due to missing data on other variables needed for the analysis?	Ν	"" …
	5.4 If Y/PY to 5.1, 5.2 or 5.3: Are the proportion of participants and reasons for missing data similar across exposures?	NI	
	5.5 If Y/PY to 5.1, 5.2 or 5.3: Were appropriate statistical methods used to account for missing data?	Y	"To minimise potential bias arising from missing data we used multiple imputation with chained equations to

			address both item and wave missingness. Imputed data for covariates were not used when there was attrition from the study. Imputed outcome data were used when covariates were available at the previous wave."
	Risk of bias judgement	Low	[Support for judgement]
	Optional: What is the predicted direction of bias due to missing data?	Favors experimental / Favors comparator / Towards null /Away from null / Unpredictable	[Rationale]
Bias in measurement of outcomes	6.1 Could the outcome measure have been influenced by knowledge of the exposure received?	РҮ	Self-reported measures have been used. So, knowledge of the exposure inevitably existed to outcome assessors which in this case are the study's participant, though seems minimally influential.
	6.2 Was the outcome measure sensitive?	РҮ	[Description]
	6.3 Were outcome assessors unaware of the exposure received by study participants?	PN	This is a study where self reports have been used. So, in that case participants can thought as the outcome assessors of the study
	6.4 Were the methods of outcome assessment comparable across exposure groups?	Y NI	Data collection methods involve same outcome detection methods, thresholds, within the same point in time with same definition using same measurements
	6.5 Were any systematic errors in measurement of the outcome unrelated to exposure received?	PN	It is expected that any error in measuring outcome is minimally related with level of participants' exposure apart from alcohol which may had caused reverse causation

	Risk of bias judgement	Moderate	[Support for judgement]
	Optional: What is the predicted direction of bias due to measurement of outcomes?	Favors experimental / Favors comparator / Towards null /Away from null / Unpredictable	[Rationale]
Bias in selection of	Is the reported effect estimate likely to be selected, on the basis of the results, from?		
the reported result	7.1 multiple outcome <i>measurements</i> within the outcome domain?	Ν	All measurements were well presented for all effect estimates
	7.2 multiple <i>analyses</i> of the exposure-outcome relationship?	Ν	
	7.3 different <i>subgroups</i> ?	Ν	
	Risk of bias judgement	Low	[Support for judgement]
	Optional: What is the predicted direction of bias due to selection of the reported result?	Favors experimental / Favors comparator / Towards null /Away from null / Unpredictable	[Rationale]
Overall bias	Risk of bias judgement	Moderate	[Support for judgement]
	Optional: What is the overall predicted direction of bias for this outcome?	Favors experimental / Favors comparator / Towards null /Away from null / Unpredictable	[Rationale]

# Appendix 4. Forest plots of various Multimorbidity – Multibehaviours meta-analyses

### Table A4.1. Forest plot of 2+ health risk behaviours in Multimorbidity risk

				Odds Ratio		Odds	Ratio	
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI		IV, Rando	om, 95% Cl	
1.1.1 MM+2								
Adams 2017	0.7419	0.0511	12.4%	2.10 [1.90, 2.32]			+	
Agrawal 2016	0.8372	0.2544	6.4%	2.31 [1.40, 3.80]			— <b>-</b>	
Balto 2017	0.5878	0.2513	6.5%	1.80 [1.10, 2.95]			<b>-</b>	
de Almeida,2020	0.0862	0.0977	11.2%	1.09 [0.90, 1.32]		-	<b>-</b>	
deAlmeida,2020b	0.1044	0.107	10.9%	1.11 [0.90, 1.37]		-	<b>-</b>	
Fortin,2014b	0.6678	0.3158	5.1%	1.95 [1.05, 3.62]				
Fortin 2014	0.8065	0.6008	1.9%	2.24 [0.69, 7.27]				
Katikireddi 2017	0.4121	0.0843	11.6%	1.51 [1.28, 1.78]			-	
Linardakis,2015b	0.6206	0.1907	8.2%	1.86 [1.28, 2.70]			— <b>-</b>	
Linardakis 2015	0.5188	0.2546	6.4%	1.68 [1.02, 2.77]			<b>—</b> •—	
Loprinzi 2015	0.5766	0.1969	8.0%	1.78 [1.21, 2.62]			— <b>•</b> —	
Shao, 2021	0.5878	0.093	11.3%	1.80 [1.50, 2.16]			+	
Subtotal (95% CI)			100.0%	1.65 [1.38, 1.97]			•	
Heterogeneity: Tau <sup>2</sup> =	= 0.06; Chi <sup>2</sup> = 58.19	, df = 11	(P < 0.00	001); I² = 81%				
Test for overall effect	Z = 5.48 (P < 0.00	001)						
Total (95% CI)			100.0%	1.65 [1.38, 1.97]			•	
Heterogeneity: Tau <sup>2</sup> =	= 0.06; Chi <sup>2</sup> = 58.19	. df = 11	(P < 0.00	001); I² = 81%	<u> </u>		<u>.</u>	
Test for overall effect	•	•			0.01	0.1 Evenues desease MM risk	1 10 Evenenus increases MM rick	100
Test for subgroup dif	•					Expouse decrease MM fisk	Exposure increase MM risk	

## Table A4.2. Forest plot sensitivity analysis of 2+ health risk behaviours in

### Multimorbidity risk

Study or Subgroup	log[Odds Ratio]	SF	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio Cl IV, Random, 95% Cl
1.1.1 MM+2	log[oudo hudo]	02	Trongine	in financial control	
Adams 2017	0.7419	0.0511	15.3%	2.10 [1.90, 2.32]	2] -
Agrawal 2016	0.8372	0.2544	8.5%	2.31 [1.40, 3.80]	0] ———
Balto 2017	0.5878	0.2513	0.0%	1.80 [1.10, 2.95]	5]
de Almeida,2020	0.0862	0.0977	14.0%	1.09 [0.90, 1.32]	2] +
deAlmeida,2020b	0.1044	0.107	13.7%	1.11 [0.90, 1.37]	7]
Fortin,2014b	0.6678	0.3158	6.8%	1.95 [1.05, 3.62]	2]
Fortin 2014	0.8065	0.6008	2.7%	2.24 [0.69, 7.27]	7]
Katikireddi 2017	0.4121	0.0843	14.4%	1.51 [1.28, 1.78]	8] 🗕
Linardakis,2015b	0.6206	0.1907	0.0%	1.86 [1.28, 2.70]	0]
Linardakis 2015	0.5188	0.2546	0.0%	1.68 [1.02, 2.77]	7]
Loprinzi 2015	0.5766	0.1969	10.4%	1.78 [1.21, 2.62]	2]
Shao, 2021 Subtotal (95% CI)	0.5878	0.093	14.2% 100.0%	1.80 [1.50, 2.16] 1.62 [1.31, 2.00]	-
	0.00:062-67.00				· ·
Heterogeneity: Tau <sup>2</sup> =	•		~ ~ 0.0000	JT), I" = 00%	
Test for overall effect:	Z = 4.40 (F < 0.00)	01)			
Total (95% CI)			100.0%	1.62 [1.31, 2.00]	0]
Heterogeneity: Tau <sup>2</sup> =	0.08; Chi <sup>2</sup> = 57.89	, df = 8 (F	° < 0.000	01); <b>I<sup>2</sup> =</b> 86%	0.01 0.1 1 10 100
Test for overall effect:	Z = 4.40 (P < 0.00)	01)			Expouse decrease MM risk Exposure increase MM risk
Test for subgroup diff	erences: Not appli	cable			Expose decrease will have Exposule increase will have

# Table A4.3. Forest plot Subgroups analysis by Multimorbidity definition

0			147-1-1-4	Odds Ratio		Odds Ratio
Study or Subgroup 1.1.1 MM+2	log[Odds Ratio]	SE.	weight	IV, Random, 95% CI		IV, Random, 95% Cl
Adams 2017	0.7419			2.10 [1.90, 2.32]		*
Agrawal 2016		0.2544		2.31 [1.40, 3.80]		<b>_</b>
Linardakis,2015b	0.6206	0.1907	8.2%	1.86 [1.28, 2.70]		
Linardakis 2015	0.5188	0.2546	6.4%	1.68 [1.02, 2.77]		+
Shao, 2021	0.5878	0.093		1.80 [1.50, 2.16]		
Subtotal (95% CI)			81.7%	1.61 [1.29, 2.00]		+
Heterogeneity: Tau <sup>2</sup> =	: 0.08; Chi <sup>z</sup> = 57.28	, df = 8 (F	° < 0.000	01); I² = 86%		
Test for overall effect:	$Z = 4.24 (P \le 0.00)$	01)				
1.1.4 MM+3						•
Balto 2017	0.5878	0.2513		1.80 [1.10, 2.95]		
de Almeida,2020	0.0862	0.0977		1.09 [0.90, 1.32]		
deAlmeida,2020b	0.1044	0.107		1.11 [0.90, 1.37]		
Fortin,2014b	0.6678	0.3158		1.95 [1.05, 3.62]		
Fortin 2014	0.8065	0.6008		2.24 [0.69, 7.27]		<b>_</b>
Katikireddi 2017	0.4121	0.0843		1.51 [1.28, 1.78]		
Loprinzi 2015		0.1969		1.78 [1.21, 2.62]		+
Subtotal (95% CI)			18.3%	1.82 [1.53, 2.16]		●
Heterogeneity: Tau <sup>2</sup> =	: 0.00 <sup>:</sup> Chi <sup>2</sup> = 0.18	df = 2 (P)	= 0.91); P			
Test for overall effect:		•	0.01/11	0.0		
restion overall effect.	2 = 0.73 (1 < 0.00)	001,				
Total (95% CI)			100.0%	1.65 [1.38, 1.97]		◆
Heterogeneity: Tau <sup>2</sup> =	: 0.06; Chi <sup>2</sup> = 58.19	, df = 11 i	(P < 0.00	001); I² = 81%		
Test for overall effect:	Z = 5.48 (P < 0.00)	001)	-		0.01	
Test for subaroup diff	· ·	· ·	/D = 0.00	N IZ = 0.96		Expouse decrease MM risk Exposure increase MM risk

# Table A4.4. Forest plot Subgroups analysis by sampling age

				Odds Ratio		Odds Ratio	
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI		IV, Random, 95% Cl	
1.1.1 ≥ 45							
Adams 2017	0.7419	0.0511		2.10 [1.90, 2.32]			
Agrawal 2016	0.8372	0.2544		2.31 [1.40, 3.80]		+	
Linardakis,2015b	0.6206	0.1907	8.2%	1.86 [1.28, 2.70]			
Linardakis 2015	0.5188	0.2546	6.4%	1.68 [1.02, 2.77]			
Shao, 2021 Subtotal (95% CI)	0.5878	0.093	11.3% 61.6%	1.80 [1.50, 2.16] 1.52 [1.22, 1.89]			
Heterogeneity: Tau <sup>2</sup> =	- 0.06 <sup>,</sup> Chi <b>z</b> - 24.04	df = 7 /6					
Test for overall effect		• •	0.001,	1,1 - 71.20		-	
restion overall ellect	. Z = 3.73 (F = 0.00)	02)					
1.1.4 <45						•	
Balto 2017	0.5878	0.2513		1.80 [1.10, 2.95]			
de Almeida,2020	0.0862	0.0977		1.09 [0.90, 1.32]			
deAlmeida,2020b	0.1044	0.107		1.11 [0.90, 1.37]			
Fortin,2014b	0.6678	0.3158		1.95 [1.05, 3.62]		•	
Fortin 2014	0.8065	0.6008		2.24 [0.69, 7.27]		│ — <b>-</b>	
Katikireddi 2017	0.4121	0.0843		1.51 [1.28, 1.78]		+	
Loprinzi 2015	0.5766	0.1969		1.78 [1.21, 2.62]			
Subtotal (95% CI)			38.4%	1.86 [1.48, 2.32]		●	
Heterogeneity: Tau <sup>2</sup> =	= 0.03; Chi <sup>2</sup> = 11.87	, df = 3 (F	P = 0.008)	); I² = 75%			
Test for overall effect	: Z = 5.43 (P < 0.00)	001)					
Total (95% CI)			100.0%	1.65 [1.38, 1.97]		◆	
Heterogeneity: Tau <sup>2</sup> :	= 0.06; Chi <sup>2</sup> = 58.19	, df = 11	(P < 0.00)	001); I² = 81%			
Test for overall effect					0.01		10
Test for subaroup dif	ferences: Chi <sup>2</sup> = 1.9	57. df = 1	(P = 0.21	), I² = 36.2%		Expouse decrease MM risk Exposure increase MM risk	

### Table A4.5. Forest plot Subgroups analysis by number of morbidities

				Odds Ratio			Ratio	
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI		IV, Rando	m, 95% Cl	
1.1.1 ≤12CC								
Adams 2017		0.0511	12.4%	2.10 [1.90, 2.32]			-	
Agrawal 2016	0.8372	0.2544	6.4%	2.31 [1.40, 3.80]			—•—	
Linardakis,2015b	0.6206	0.1907	8.2%	1.86 [1.28, 2.70]			—•—	
Linardakis 2015	0.5188	0.2546	6.4%	1.68 [1.02, 2.77]				
Shao, 2021	0.5878	0.093	11.3%	1.80 [1.50, 2.16]				
Subtotal (95% CI)			44.8%	2.01 [1.85, 2.19]			•	
Heterogeneity: Tau <sup>2</sup> =	= 0.00; Chi <sup>2</sup> = 3.10,	df = 4 (P	= 0.54); l <sup>a</sup>	'= 0%				
Test for overall effect	: Z = 16.53 (P < 0.0)	0001)						
1.1.4 ≥ 12 CC								
Balto 2017	0.5878	0.2513	6.5%	1.80 [1.10, 2.95]			<b>-</b>	
de Almeida,2020	0.0862	0.0977	11.2%	1.09 [0.90, 1.32]		-	<b>-</b> -	
deAlmeida,2020b	0.1044	0.107	10.9%	1.11 [0.90, 1.37]		-	<b>-</b> -	
Fortin,2014b	0.6678	0.3158	5.1%	1.95 [1.05, 3.62]				
Fortin 2014	0.8065	0.6008	1.9%	2.24 [0.69, 7.27]				
Katikireddi 2017	0.4121	0.0843	11.6%	1.51 [1.28, 1.78]			-	
Loprinzi 2015	0.5766	0.1969	8.0%	1.78 [1.21, 2.62]			— <b>•</b> —	
Subtotal (95% CI)			55.2%	1.40 [1.16, 1.70]			◆	
Heterogeneity: Tau <sup>2</sup> :	= 0.03; Chi <sup>2</sup> = 15.13	, df = 6 (F	P = 0.02);	I² = 60%				
Test for overall effect								
Total (95% CI)			100.0%	1.65 [1.38, 1.97]			•	
Heterogeneity: Tau <sup>2</sup> :	= 0.06: Chi <sup>2</sup> = 58.19	. df = 11	(P < 0.00)	001):   <b>*</b> = 81%	<u> </u>	t.	l	
Test for overall effect		•			0.01	0.1	1 10	100
Test for subgroup dif			1 (P = 0.0	006), I² = 91.5%		Expouse decrease MM risk	Exposure increase MM risk	

### Table A4.6. Forest Plot of <12CC Multimorbidity and 2 SNAP-HRB

				Odds Ratio		Odds Ratio	
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI		IV, Random, 95% Cl	
Adams 2017	0.6419	0.0567	64.1%	1.90 [1.70, 2.12]			
Agrawal 2016	0.8372	0.2544	3.2%	2.31 [1.40, 3.80]			
Linardakis,2015b	0.5188	0.2546	3.2%	1.68 [1.02, 2.77]			
Linardakis 2015	0.6206	0.1907	5.7%	1.86 [1.28, 2.70]			
Shao, 2021	0.5878	0.093	23.8%	1.80 [1.50, 2.16]		+	
Total (95% CI)			100.0%	1.88 [1.72, 2.05]		•	
Heterogeneity: Tau² = Test for overall effect:			= 0.89); lª	²= 0%	0.01	0.1 1 10 Exposure decrease MM risk	100

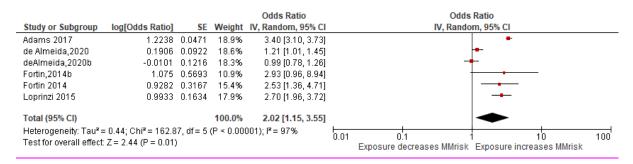
### Table A4.7. Forest Plot of ≥12CC Multimorbidity and 2 SNAP-HRB

				Odds Ratio		Odds	Ratio	
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI		IV, Rando	om, 95% Cl	
Adams 2017	0.7419	0.0511	19.0%	2.10 [1.90, 2.32]			+	
de Almeida,2020	0.1044	0.107	17.4%	1.11 [0.90, 1.37]		-	<b>-</b>	
deAlmeida,2020b	0.0862	0.0977	17.7%	1.09 [0.90, 1.32]		-	<b>-</b> -	
Fortin,2014b	0.8065	0.6008	4.2%	2.24 [0.69, 7.27]		—		
Fortin 2014	0.6678	0.3158	9.6%	1.95 [1.05, 3.62]				
Katikireddi 2017	0.4121	0.0843	18.1%	1.51 [1.28, 1.78]			-	
Loprinzi 2015	0.5766	0.1969	13.9%	1.78 [1.21, 2.62]				
Total (95% CI)			100.0%	1.53 [1.17, 2.01]			•	
Heterogeneity: Tau <sup>2</sup> =	: 0.10; Chi <sup>2</sup> = 55.74	, df = 6 (F	< 0.000	01); I <sup>z</sup> = 89%				400
Test for overall effect:	Z = 3.09 (P = 0.00)	2)			0.01	0.1 Exposure decrease MM risk	1 10 Exposure increase MM risk	100

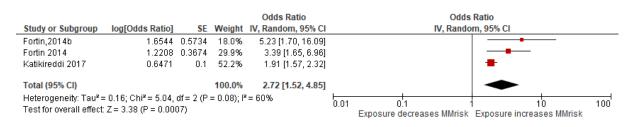
#### Table A4.8. Forest Plot of ≥12CC Multimorbidity and 3 SNAP-HRB

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% Cl			Ratio m, 95% Cl	
Adams 2017	1.0986	0.0538	32.0%	3.00 [2.70, 3.33]			-	
Agrawal 2016	0.8796	0.2673	12.8%	2.41 [1.43, 4.07]			— <b></b>	
Linardakis,2015b	0.5188	0.2546	13.6%	1.68 [1.02, 2.77]				
Linardakis 2015	0.6206	0.1907	18.4%	1.86 [1.28, 2.70]			_ <b></b>	
Shao, 2021	1.1939	0.1417	23.2%	3.30 [2.50, 4.36]				
Total (95% CI)			100.0%	2.52 [1.99, 3.20]			•	
Heterogeneity: Tau <sup>2</sup> = 0.04; Chi <sup>2</sup> = 11.67, df = 4 (P = 0.02); l <sup>2</sup> = 66% Test for overall effect: Z = 7.68 (P < 0.00001)						0.1 Exposure decrease MM risk	10 Exposure increase MM risk	100

#### Table A4.9. Forest Plot of <12CC Multimorbidity and 3 SNAP-HRB



#### Table A4.10. Forest Plot of ≥12CC Multimorbidity and all 4 SNAP-HRB



#### Table A4.11. Forest plot of 2 health risk behaviours in (MM3+) Multimorbidity risk

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% Cl			Ratio m, 95% Cl	
Fortin,2014b	0.8065	0.6008	3.1%	2.24 [0.69, 7.27]				
Fortin 2014	0.6678	0.3158	11.1%	1.95 [1.05, 3.62]				
Katikireddi 2017	0.6419	0.1595	43.7%	1.90 [1.39, 2.60]				
Shao, 2021	0.7885	0.1625	42.1%	2.20 [1.60, 3.03]				
Total (95% CI)			100.0%	2.04 [1.66, 2.50]			•	
Heterogeneity: Tau² = Test for overall effect:			= 0.93); lª	²= 0%	0.01	0.1 Exposure decrease MM risk	10 Exposure increase MM risk	100

#### Table A4.12. Forest Plot of 2 health risk behaviours in (MM2+) Multimorbidity risk

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI			Ratio om, 95% Cl	
Adams 2017	0.7419	0.0511	16.7%	2.10 [1.90, 2.32]			+	
Agrawal 2016	0.8372	0.2544	9.6%	2.31 [1.40, 3.80]			— <b>•</b> —	
de Almeida,2020	0.1044	0.107	15.1%	1.11 [0.90, 1.37]		-	<b>-</b>	
deAlmeida,2020b	0.0862	0.0977	15.4%	1.09 [0.90, 1.32]		-	<b>-</b> -	
Katikireddi 2017	0.4121	0.0843	15.9%	1.51 [1.28, 1.78]			-	
Loprinzi 2015	0.5766	0.1969	11.6%	1.78 [1.21, 2.62]			— <b></b>	
Shao, 2021	0.5878	0.093	15.6%	1.80 [1.50, 2.16]			-	
Total (95% CI)			100.0%	1.58 [1.26, 1.99]			•	
Heterogeneity: Tau <sup>2</sup> =	: 0.08; Chi <sup>z</sup> = 57.46	, df = 6 (F	- < 0.000	01); I <sup>z</sup> = 90%			<u> </u>	100
Test for overall effect:					0.01	0.1 Exposure decrease MM risk	1 10 Exposure increase MM risk	100

#### Table A4.13. Forest Plot of 3 health risk behaviours in (MM2+) Multimorbidity risk

				Odds Ratio			Ratio	
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI		IV, Rando	om, 95% Cl	
Adams 2017	1.2238	0.0471	13.5%	3.40 [3.10, 3.73]			+	
Agrawal 2016	0.8796	0.2673	11.1%	2.41 [1.43, 4.07]				
de Almeida,2020	0.1906	0.0922	13.3%	1.21 [1.01, 1.45]			<b>+-</b>	
deAlmeida,2020b	-0.0101	0.1216	13.0%	0.99 [0.78, 1.26]		-	<b>↓</b>	
Linardakis,2015b	0.5188	0.2546	11.3%	1.68 [1.02, 2.77]				
Linardakis 2015	0.6206	0.1907	12.2%	1.86 [1.28, 2.70]				
Loprinzi 2015	0.9933	0.1634	12.6%	2.70 [1.96, 3.72]			_ <b>_</b>	
Shao, 2021	0.9933	0.1282	13.0%	2.70 [2.10, 3.47]				
Total (95% CI)			100.0%	1.96 [1.31, 2.96]			•	
Heterogeneity: Tau <sup>2</sup> =	0.32; Chi <sup>z</sup> = 167.7	1, df = 7	(P < 0.00	001); I <b>²</b> = 96%	01	0.1	1 10	100
Test for overall effect:	Z = 3.24 (P = 0.00)	1)			I.01 Exposur	0.1 re increase MM risk	Exposure decrease MM risk	100

### Table A4.14. Forest plot of 3 health risk behaviours in (MM3+) Multimorbidity risk

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI		Odds Ratio IV, Random, 95% Cl
Fortin,2014b	1.075	0.5693	4.9%	2.93 [0.96, 8.94]		
Fortin 2014	0.9282	0.3167	15.9%	2.53 [1.36, 4.71]		<b></b>
Shao, 2021	1.1939	0.1417	79.2%	3.30 [2.50, 4.36]		
Total (95% CI)			100.0%	3.15 [2.46, 4.03]		•
Heterogeneity: Tau² = Test for overall effect			= 0.74); P	*= 0%	0.01	0.1 1 10 10 Exposure decrease MM risk Exposure increase MM risk

#### Table A4.15. Forest Plot of 4 health risk behaviours in (MM2+) Multimorbidity risk

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% Cl			s Ratio om, 95% Cl	
Agrawal 2016	1.0543	0.3204	22.1%	2.87 [1.53, 5.38]				
Katikireddi 2017	0.6471	0.1	77.9%	1.91 [1.57, 2.32]			■	
Total (95% CI)			100.0%	2.09 [1.50, 2.91]			•	
Heterogeneity: Tau² = Test for overall effect:			= 0.23); l <sup>a</sup>	²= 32%	0.01	0.1 Exposure decrease MM risk	1 10 Exposure increase MM risk	100

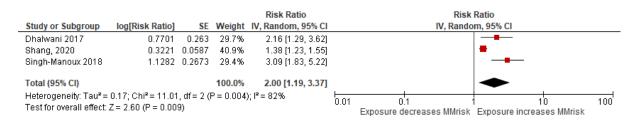
### Table A4.16. Forest Plot of 4 health risk behaviours in (MM3+) Multimorbidity risk

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% Cl			Ratio m, 95% Cl	
Fortin,2014b	1.6544	0.5734	6.9%	5.23 [1.70, 16.09]			<b>-</b>	
Fortin 2014	1.2208	0.3674	16.9%	3.39 [1.65, 6.96]			<b>_</b>	
Katikireddi 2017	1.0367	0.1728	76.2%	2.82 [2.01, 3.96]				
Total (95% CI)			100.0%	3.04 [2.26, 4.08]			•	
Heterogeneity: Tau² = Test for overall effect:			= 0.56); l²	²= 0%	⊢ 0.01	0.1 Exposure decrease MM risk	10 Exposure increase MM risk	100

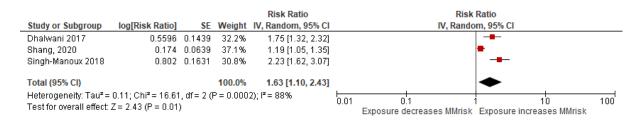
#### Table A4.17. Forest Plot of Multimorbidity progression from Multibehaviours exposure

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% Cl			Ratio om, 95% Cl	
Dhalwani 2017	0.3507	0.1032	7.8%	1.42 [1.16, 1.74]				
Freinling, 2020	0.2852	0.0399	23.1%	1.33 [1.23, 1.44]			-	
Freinling,2020b	0.174	0.0355	24.9%	1.19 [1.11, 1.28]			-	
Freinling,2020c	0.1906	0.0349	25.1%	1.21 [1.13, 1.30]			•	
Shang, 2020	0.174	0.0639	15.0%	1.19 [1.05, 1.35]			+	
Singh-Manoux 2018	0.5068	0.1488	4.2%	1.66 [1.24, 2.22]				
Total (95% CI)			100.0%	1.26 [1.18, 1.34]			•	
Heterogeneity: Tau² =			° = 0.05);	I² = 54%	0.01	0.1	1 10	100
Test for overall effect: .	Z = 7.11 (P < 0.00	001)			0.01		Exposure increases MMrisk	100

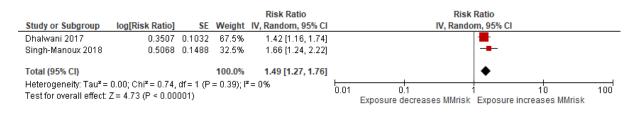
#### Table A4.18. Forest Plot of Multimorbidity progression from all 4 SNAP-HRB



#### Table A4.19. Forest Plot of Multimorbidity progression from 3 SNAP-HRB



#### Table A4.20. Forest Plot of Multimorbidity progression from 2 SNAP-HRB



#### Table A4.21. Forest Plot of Mortality in presence of Multimorbidity and all four SNAP-

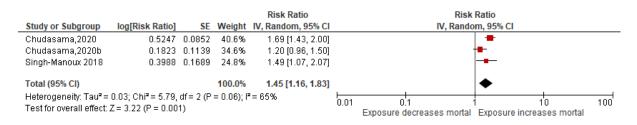
#### HRB

				Risk Ratio		Risk	Ratio	
Study or Subgroup	log[Risk Ratio]	SE	Weight	IV, Random, 95% CI		IV, Rando	om, 95% Cl	
Chudasama,2020	0.7975	0.0636	38.9%	2.22 [1.96, 2.51]			-	
Chudasama,2020b	0.9163	0.0841	35.8%	2.50 [2.12, 2.95]			-	
Singh-Manoux 2018	1.292	0.1505	25.3%	3.64 [2.71, 4.89]				
Total (95% CI)			100.0%	2.63 [2.09, 3.29]			•	
Heterogeneity: Tau² = Test for overall effect: 2			= 0.009);	I <sup>z</sup> = 79%	0.01	0.1 Exposure decreases mortal	1 10 Exposure increases mortal	100

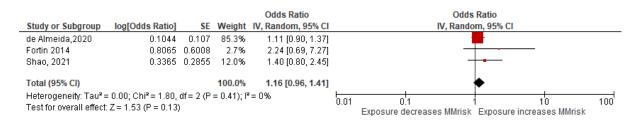
#### Table A4.22. Forest Plot of Mortality in presence of Multimorbidity and 3 SNAP-HRB

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% Cl			Ratio m, 95% Cl	
Chudasama,2020	0.5596	0.0586	38.8%	1.75 [1.56, 1.96]			-	
Chudasama,2020b	0.7514	0.0807	32.8%	2.12 [1.81, 2.48]				
Singh-Manoux 2018	0.8065	0.0976	28.5%	2.24 [1.85, 2.71]			+	
Total (95% CI)			100.0%	2.00 [1.71, 2.34]			•	
Heterogeneity: Tau² = Test for overall effect:			= 0.04); P	²= 69%	0.01	0.1 Exposure decreases mortal	10 Exposure increases mortal	100

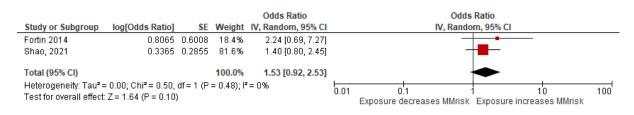
#### Table A4.23. Forest Plot of Mortality in presence of Multimorbidity and 2 SNAP-HRB



#### Table A4.24. Forest Plot of Men- 2 SNAP-HRB and (MM2+) Multimorbidity risk



#### Table A4.25. Forest Plot of Men- 2 SNAP-HRB and (MM3+) Multimorbidity risk



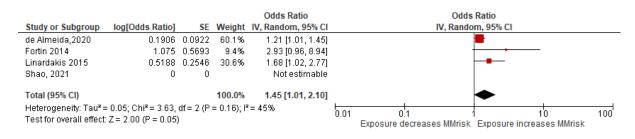
#### Table A4.26. Forest Plot of Women- 2 SNAP-HRB and (MM2+) Multimorbidity risk

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI			Ratio om, 95% Cl	
de Almeida,2020	0.0862	0.0977	39.1%	1.09 [0.90, 1.32]		-	-	
Fortin 2014	0.6678	0.3158	23.3%	1.95 [1.05, 3.62]			<b>-</b>	
Shao, 2021	0.6419	0.1206	37.6%	1.90 [1.50, 2.41]			-	
Total (95% CI)			100.0%	1.54 [0.98, 2.41]			•	
Heterogeneity: Tau² = Test for overall effect:			P = 0.000!	9); I² = 86%	0.01	0.1 Exposure decreases MMrisk	1 10 Exposure increases MMrisk	100

#### Table A4.27. Forest Plot of Women- 2 SNAP-HRB and (MM3+) Multimorbidity risk

				Odds Ratio		Odds	Ratio	
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI		IV, Rando	om, 95% Cl	
Fortin 2014	0.6678	0.3158	19.3%	1.95 [1.05, 3.62]				
Shao, 2021	0.8329	0.1542	80.7%	2.30 [1.70, 3.11]				
Total (95% CI)			100.0%	2.23 [1.70, 2.92]			•	
Heterogeneity: Tau² = Test for overall effect			= 0.64); l <sup>a</sup>	²= 0%	0.01	0.1 Exopsure decreases MMrisk	1 10 Exposure increases MMrisk	100

#### Table A4.28. Forest Plot of Men- 3 SNAP-HRB and (MM2+) Multimorbidity risk



#### Table A4.29. Forest Plot of Men- 3 SNAP-HRB and (MM3+) Multimorbidity risk

Study or Subgroup	log[Odds Ratio]	<b>S</b> E	Weight	Odds Ratio IV, Random, 95% CI		Odds Ratio IV, Random, 95% Cl	
Fortin 2014	1.075	0.5693	38.5%	2.93 [0.96, 8.94]			
Shao, 2021	1.0647	0.4502	61.5%	2.90 [1.20, 7.01]		<b></b>	
Total (95% CI)			100.0%	2.91 [1.46, 5.82]		-	
Heterogeneity: Tau² = Test for overall effect			= 0.99); I <sup>z</sup>	<sup>2</sup> = 0%	⊢ 0.01	0.1 1 10 Exposure decreases MMrisk Exposure increases MMrisk	100

#### Table A4.30. Forest Plot of Women- 3 SNAP-HRB and (MM2+) Multimorbidity risk

Study or Subgroup	log[Odds Ratio]	<b>S</b> E	Weight	Odds Ratio IV, Random, 95% Cl	Odds Ratio IV, Random, 95% Cl	
de Almeida,2020	-0.0101	0.1216	38.0%	0.99 [0.78, 1.26]	+	
Fortin 2014	0.9282	0.3167	27.4%	2.53 [1.36, 4.71]	│ <b></b>	
Linardakis 2015	0.6206	0.1907	34.6%	1.86 [1.28, 2.70]		
Shao, 2021	0	0		Not estimable		
Total (95% CI)			100.0%	1.59 [0.90, 2.80]	•	
Heterogeneity: Tau <sup>2</sup> = Test for overall effect			° = 0.002)	; I² = 85%	0.01 0.1 1 10 Exposure decreases MMrisk Exposure increases MMris	100 sk

#### Table A4.31. Forest Plot of Women- 3 SNAP-HRB and (MM3+) Multimorbidity risk

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI			Ratio m, 95% Cl	
Fortin 2014	0.9282	0.3167	21.6%	2.53 [1.36, 4.71]			<b>-</b>	
Shao, 2021	1.2809	0.166	78.4%	3.60 [2.60, 4.98]				
Total (95% CI)			100.0%	3.34 [2.50, 4.45]			•	
Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.97, df = 1 (P = 0.32); l <sup>2</sup> = 0% Test for overall effect: Z = 8.19 (P < 0.00001)					0.01	0.1 Exposure decreases MMrisk	10 Exposure increases MMrisk	100

Appendix 5. CSU Proposal for providing data for epidemiological studies



MIDLANDS AND LANCASHIRE COMMISSIONING SUPPORT UNIT

# Proposal Pilot Scheme Multi-morbidities Reporting



NHS





# **Document Control**

# Purpose

The purpose of this document is to provide a proposal of work for completion by NHS Midlands and Lancashire CSU's Data Quality team on behalf of Faculty of Health Science at, Staffordshire University.

# **Version History**

Version	Issue Date	Brief Summary of Change	Author
0.1	16/11/2017	First draft	Jonathan Vause
0.2	20/11/2017	Revised Draft	Jonathan Vause
Etc			

# Sign Off

Name	Position	Date	Signature
Catherine Smith	Senior Data Quality and Training Manager	20/11/2017	





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# Background

Multi-morbidity patients (MMP) constitute the main users of primary and secondary health care with annual estimations indicating that 78% of primary care consultations concern of people having two or more morbidities (Salisbury et al. 2011).

Faculty of Health Science at, Staffordshire University, wish to further understand the local picture and are looking to NHS Midlands and Lancashire CSU to provide primary care data.

# **Objectives**

The objectives of the project sit within two principal areas:

- The design of a suite of EMIS Web clinical system searches to extract details of patients with multi-morbidities.
- Data extraction from five GP practices participating in the pilot to allow further investigation by public health commissioners.

Key aims

- Provide access to five Pilot GP clinical systems
- Extract pseudonymised datasets using bespoke local searches from the five pilot GP practices
- Use 5-byte Read codes within search specifications
- Deliver requested pseudonymised data to public health commissioners

# Approach

With access to Primary Care data from GP Practices across Staffordshire, along with a wealth of knowledge, skills and experience held within the Data Quality Team we are confident that we can fulfil the requirement as requested.

NHS Midlands and Lancashire Commissioning Support Unit (MLCSU) is an accredited Safe Haven with our own DSCRO services; we have a strong IG team who have achieved **80%** compliance in our latest IG toolkit return, assurances that personal information is dealt with legally, securely, efficiently and effectively.

The DQT will author EMIS Web system searches to extract the relevant multi-morbidities data

MLCSU will collect, process and manage this data on behalf of the five GP Practices identified by the Faculty of Health Science at, Staffordshire University as being within the Pilot Scheme. Extracts from the practices will be made using the EMIS Web integrated search and reporting tools.





On receipt of acceptance of the quotation, the data quality team aim to complete the work detailed within this proposal in no more than 90 working days.

# Dependencies

- Availability of and consent from pilot practices to allow access their EMIS Web Clinical System,
- Data Sharing Agreements being in place between the Faculty of Health Science at, Staffordshire University and GP practices participating in the Pilot for the requested data.

# Deliverables

- A suite of clinical system searches for EMIS Web as detailed in Appendix A
- A single Excel workbook report containing the output from the General Practice systems of
  results from the above searches to be provided to the client.

# Governance

The project will be overseen by:

Jonathan Vause, Data Quality Manager (Staffordshire) J.vause@nhs.net Tel. 07730-617371

In the event of dispute or where escalation to senior management is required please contact:

Catherine Smith, Senior Data Quality and Training Manager. catherine.smith36@nhs.net

# Resourcing

The searches will be authored by a team of Data Quality Specialists based in Staffordshire.

The primary contact for search authoring and data provision is Amanda Howell, Data Quality Specialist <u>amandahowell@nhs.net</u> Tel. 07816-661633

# Proposed costs

Proposed costs are detailed within the attached Quotation.

## Appendix 6. CSU-Staffordshire University agreement for data provision



## NHS

Midlands and Lancashire Commissioning Support Unit

Midlands & Lancashire CSU Kingston House 438–450 High Street West Midlands B70 9LD

Tel: 0121 612 3895 Email: midlands.lancashire@nhs.net www.midlandsandlancashirecsu.nhs.uk.uk

Quotation

Date of Quote: 16/11/2017

Staffordshire University

Leek Road

Stoke-on-Trent

Staffordshire ST4 2DF

Faculty of Health Sciences Brindley Building

Internal Ref:

Requested by: Chris Gidlow Prepared by: Jonathan Vause

Item	Description	Quantity	Value	Cost
1	Authoring of EMIS Web Multi-	1		
	Morbidities Searches (as per			
	Appendix 1 to Proposal document)			
2	Remote Extraction of Multi-	5 Sites		
	Morbidities Data			
3	Collation of data & compile report	1		
			Total	£1,339

(all prices quoted excl VAT)

#### Quote acceptance:

To proceed with delivery and invoicing for the above quotation please have an authorised signatory complete below.

Name:

Position:

Signature:

For and on behalf of (Organisation Name):

Date Signed

#### Midlands and Lancashire CSU Kingston House 438-450 High Street West Midlands 870 9LD

www.midlandsandlancashirecsu.nhs.uk

# Appendix 7. Data Specification for CSU relating to CHAD multi-morbidity work

# Scientific background & rationaile of the study

Evidence mainly derived from behavioural science showed that the vast majority of people tend to expose themselves in Multiple Health Risk Behaviours(Prochaska, Spring, Nigg. 2008), a phenomenon called Multibehaviours (MB) increasing sharply their risk for developing a chronic condition (CC) (Prochaska, 2008). Furthermore, epidemiological research have shown a close interrelation between MB and Multimorbidity (MM) (Loprinzi, 2015; Fortin et al. 2014) implying that MB may stand of equally importance MM risk factors as others more projective ones, such as aging (Marengoni et al. 2011; Fortin et al. 2012) urban living (Violán et al. 2014) low of socioeconomic status (Barnett et al. 2012).

This is an important area for research given the considerable challenges that MB and MM pose to the health service, which is unprepared for dealing with multiple conditions (Prochaska, 2008; Shadmi, 2013). MM impact is extended from individual to societal level affecting dramatically individuals' health status and daily quality of life as well as families and governmental health care costs (Smith et al. 2010; Mann, et al.2016; Lindvall et al. 2016; Orueta et al. 2013; Wister et al. 2016; Prochaska, 2008). For example, studies have shown that MM burden transcends MMp affecting also their formal caregivers (Shadmi, 2013). For this burdensome situation the fragmented healthcare system plays crucial role since Multimorbidity patients (MMp) consist the main users of primary and secondary health care with annually estimations to indicate that the 78% of primary care consultations concern of people having two or more morbidities (Salisbury et al. 2011).

In conjunction, both constructs of MB and MM can provide a new person-centred framework, linking treatment and preventive medicine (Loprinzi, 2015), introducing MB processes complementary to medical processes to embed sustainable behaviour change in MM management (Prochaska, 2008). As such, providing further evidence on the association between MB and MM risk, within primary care settings of urban and deprived areas will have important theoretical and practical implications, for both health care delivery and preventive health care policies.

# **MM Measurement**

Since there is no standard approach regarding the measurement of Multimorbidity, the selection of included morbidities will be based on the methodology recommended by a UK study (Barnett et al. 2012). As such 40 chronic morbidities are presented at the Appendix 1 (as those presented by Barnett et al. (2012) study). Among them the 12 most common (cancer, diabetes mellitus, depression, hypertension, myocardial infarction, chronic ischemic heart disease, heart arrhythmias, heart insufficiency, stroke, COPD, and arthritis); the core of any MM measure as have been suggested by two systematic reviews (Diederichs et al. 2011; Fortin et al. 2014). These recommendations have found a general appeal and been followed by several other studies.

# **Operational definition of MM**

Mutimorbidity is be defined as the coexistence of 2+ chronic conditions in the same individual with or without indexing disorder

# Practice sample:

Data are requested from a sample of three General Practices (GP) in Staffordshire – these will be appraoched and recuited by CHAD.

## Patient sample:

Population will be all adults (aged  $\geq$ 18 yr.) registered with the participating general practices.

## Data fields:

All data requested will used existing Read codes. Provisional data fields required are listed in Table 1.

## Socio-demographic data:

- Age
- Gender
- Eethnicity
- Postcode or Lower Super Output Area of home address (to derive urban rural area, deprivation of living area)
- Employment status (if available)

### Health Risk/Enhancing Behaviours:

- Smoking / tobacco use
- Level of alcohol consumption
- Physical activity (if any fields available)
- Diet (if any fields available)

### Table 1. Requested data fields

Condition	Variable definition	Mental/physical health condition
Hypertension	Read code ever recorded	Physical
Depression	Read code recorded in last 12 months OR ≥4 anti-depressant prescriptions (excluding low dose tricyclics) in last 12 months	Mental
Painful condition	≥4 prescription only medicine analgesic prescriptions in last 12 months OR ≥4 specified anti-epileptics in the absence of an epilepsy Read code in last 12 months	Physical
Asthma (currently treated)	Read code ever recorded AND any prescription in last 12 months	Physical
Coronary heart disease	Read code ever recorded	Physical
Treated dyspepsia	≥ 4 prescriptions in last 12 months BNF 0103% excluding antacids AND NOT (≥4 NSAIDS OR ≥4 aspirin/clopidogrel)	Physical
Diabetes	Read code ever recorded	Physical
Thyroid disorders	Read code ever recorded	Physical
Rheumatoid arthritis, other inflammatory polyarthropathies & systematic connective tissue disorders	Read code ever recorded	Physical
Hearing loss	Read code ever recorded	Physical

Chronic obstructive	Read code ever recorded	Physical
pulmonary disease		
Anxiety & other neurotic,	Read code in last 12 months OR ≥ 4 anxiolytic/hypnotic	Mental
stress related & somatoform	prescriptions in last 12 months $OR \ge 4 \ 10/25 mg$ amitriptyline	
disorders	in last 12 months & do not meet the criteria for 'Pain'	
Irritable bowel syndrome	Read code ever recorded OR ≥ 4 prescription only medicine	Physical
	antispasmodic prescription in last 12 months	
New diagnosis of cancer in	Read code first recorded in last 5 years	Physical
last five years		
Alcohol problems	Read code ever recorded Mental 2·4	Mental
Other psychoactive	Read code ever recorded	Mental
substance misuse		
Treated constipation	≥4 laxative prescriptions in last year	Physical
Stroke & transient ischemic	Read code ever recorded 1	Physical
attack		
Chronic kidney disease	Read code ever recorded	Physical
Diverticular disease of	Read code ever recorded	Physical
intestine		
Atrial fibrillation	Read code ever recorded	Physical
Peripheral vascular disease	Read code ever recorded	Physical
Heart failure	Read code ever recorded	Physical
Prostate disorders	Read code ever recorded	Physical
Glaucoma 9	Read code ever recorded	Physical
Epilepsy (currently treated)	Read code ever recorded AND antiepileptic prescription in	Physical
	last 12 months	-
Dementia	Read code ever recorded	Mental
Schizophrenia (and related	Read code ever recorded/recorded in last 12 months (code	Mental
non-organic psychosis) or	dependent) OR Lithium prescribed in last 168 days	
bipolar disorder		
Psoriasis or eczema	Read code ever recorded AND $\geq$ 4 related prescriptions in last	Physical
	12 months (excluding simple emollients)	
Inflammatory bowel disease	Read code ever recorded	Physical
Migraine 6	M≥ 4 prescription only medicine anti-migraine prescriptions	Physical
	in last year	
Blindness & low vision	Read code ever recorded	Physical
Chronic sinusitis	Read code ever recorded	Physical
Learning disability	Read code ever recorded	Mental
Anorexia or bulimia	Read code ever recorded	Mental
Bronchiectasis	Read code ever recorded	Physical
Parkinson's disease	Read code ever recorded	Physical
Multiple sclerosis	Read code ever recorded	Physical
Viral Hepatitis	Read code ever recorded	Physical
Chronic liver disease	Read code ever recorded	Physical

Barnett Barnett et al. Lancet. 2012 Jul 7;380(9836):37-43

Konstantinos Spyropoulos

PhD Candidate

Staffordshire University Faculty of Health Sciences Brindley Building Leek Road Stoke-on-Trent Staffordshire



# Appendix 8. Summary of Index of Multiple Deprivation 2019 (MHCLG 2019)

#### **English Indices of Deprivation 2019**

#### File 1 Index of Multiple Deprivation (IMD2019)

The 'IMD2019' worksheet in this file contains the ranks and deciles for the Index of Multiple Deprivation 2019 (IMD 2019) at Lower-layer Super Output Area (LSOA) level.

The LSOA with a rank of 1 is the most deprived and the LSOA with a rank of 32,844 is the least deprived.

The **deciles** are calculated by ranking the 32,844 LSOAs in England from most deprived to least deprived and dividing them into 10 equal groups. LSOAs in decile 1 fall within the most deprived 10% of LSOAs nationally and LSOAs in decile 10 fall within the least deprived 10% of LSOAs nationally.

The Index of Multiple Deprivation (IMD) is an overall relative measure of deprivation constructed by combining seven domains of deprivation according to their respective weights, as described below.

LSOAs (Lower-layer Super Output Areas) are small areas designed to be of a similar population size, with an average of approximately 1,500 residents or 650 households. There are 32,844 Lower-layer Super Output Areas (LSOAs) in England. They were produced by the Office for National Statistics for the reporting of small area statistics.

Following the 2011 Census, the geography of Lower-layer Super Output Areas was revised and the number of areas has increased from 32,482 (as used for the Indices of Deprivation 2010, 2007 and 2004) to 32,844 (as used for the Indices of Deprivation 2015 and 2019).

#### About the English Indices of Deprivation 2019 (IoD2019)

The Indices of Deprivation 2019 provide a set of relative measures of deprivation for small areas (Lower-layer Super Output Areas) across England, based on seven domains of deprivation. The domains were combined using the following weights to produce the overall Index of Multiple Deprivation:

- Income Deprivation (22.5%)
- Employment Deprivation (22.5%)
- Education, Skills and Training Deprivation (13.5%)
- Health Deprivation and Disability (13.5%)
- Crime (9.3%)
- Barriers to Housing and Services (9.3%)
- Living Environment Deprivation (9.3%)

In addition to the Index of Multiple Deprivation and the seven domain indices, there are two supplementary indices: the Income Deprivation Affecting Older People Index.

A range of summary measures are available for higher-level geographies including local authority districts and upper-tier local authorities, local enterprise partnerships, and clinical commissioning groups.

The Index of Multiple Deprivation, domain indices and the supplementary indices, together with the higher-level geography summaries, are collectively referred to as the Indices of Deprivation.

As far as is possible, the data sources used in each indicator were based on data from the most recent time point available. For the highest weighted domains, indicators in the Indices of Deprivation 2019 relate to a 2015/16 time point.

Annex A of the Technical Report provides more detail on the data sources used and section 3.3 of the Research Report provides advice on using and interpreting the data.

All of the data files and supporting documents for the English Indices of Deprivation 2019 are available from: <u>www.gov.uk/government/statistics/english-indices-of-deprivation-2019</u>

The Indices of Deprivation 2019 have been published using the Open Government License (OGL) version 3.0, see <a href="http://www.nationalarchives.gov.uk/doc/open-government-licence/version/3/">www.nationalarchives.gov.uk/doc/open-government-licence/version/3/</a>

The Indices of Deprivation 2019 have been constructed for the Ministry of Housing, Communities & Local Government (MHCLG) by Oxford Consultants for Social Inclusion (OCSI) and Deprivation.org.

For statistical enquiries, please contact: indices.deprivation@communities.gov.uk

# Appendix 9. Data extraction tool – Multimorbidity index

# Practice:

# Name of lead contact:

Condition	Variable definition	Mental/physical health condition
Hypertension	Read code ever recorded	Physical
Depression	Read code recorded in last 12 months OR ≥4 anti- depressant prescriptions (excluding low dose tricyclics) in last 12 months	Mental
Painful condition	≥4 prescription only medicine analgesic prescriptions in last 12 months OR ≥4 specified anti-epileptics in the absence of an epilepsy Read code in last 12 months	Physical
Asthma (currently treated)	Read code ever recorded AND any prescription in last 12 months	Physical
Coronary heart disease	Read code ever recorded	Physical
Treated dyspepsia	≥ 4 prescriptions in last 12 months BNF 0103% excluding antacids AND NOT (≥4 NSAIDS OR ≥4 aspirin/clopidogrel)	Physical
Diabetes	Read code ever recorded	Physical
Thyroid disorders	Read code ever recorded	Physical
Rheumatoid arthritis, other inflammatory polyarthropathies & systematic connective tissue disorders	Read code ever recorded	Physical
Hearing loss	Read code ever recorded	Physical
Chronic obstructive pulmonary disease	Read code ever recorded	Physical
Anxiety & other neurotic, stress related & somatoform disorders	Read code in last 12 months $OR \ge 4$ anxiolytic/hypnotic prescriptions in last 12 months $OR \ge 4$ 10/25mg amitriptyline in last 12 months & do not meet the criteria for 'Pain'	Mental
Irritable bowel syndrome	Read code ever recorded OR ≥ 4 prescription only medicine antispasmodic prescription in last 12 months	Physical
New diagnosis of cancer in last five years	Read code first recorded in last 5 years	Physical
Alcohol problems	Read code ever recorded Mental 2-4	Mental
Other psychoactive substance misuse	Read code ever recorded	Mental
Treated constipation Stroke & transient ischaemic attack	≥4 laxative prescriptions in last year Read code ever recorded 1	Physical Physical
Chronic kidney disease	Read code ever recorded 1	Physical
Diverticular disease of intestine	Read code ever recorded	Physical
Atrial fibrillation	Read code ever recorded	Physical
Peripheral vascular disease	Read code ever recorded	Physical
Heart failure	Read code ever recorded	Physical
Prostate disorders	Read code ever recorded	Physical
Glaucoma 9	Read code ever recorded	Physical
Epilepsy (currently treated)	Read code ever recorded AND antiepileptic prescription in last 12 months	Physical
Dementia	Read code ever recorded	Mental
Schizophrenia (and related non-organic psychosis) or bipolar disorder	Read code ever recorded/recorded in last 12 months (code dependent) OR Lithium prescribed in last 168 days	Mental
Psoriasis or eczema	Read code ever recorded AND ≥ 4 related prescriptions in last 12 months (excluding simple emollients)	Physical
Inflammatory bowel disease	Read code ever recorded	Physical
Migraine 6	M≥ 4 prescription only medicine anti-migraine prescriptions in last year	Physical
Blindness & low vision	Read code ever recorded	Physical
Chronic sinusitis	Read code ever recorded	Physical
Learning disability	Read code ever recorded	Mental
Anorexia or bulimia	Read code ever recorded	Mental
Bronchiectasis	Read code ever recorded	Physical
Parkinson's disease	Read code ever recorded	Physical
Multiple sclerosis Viral Hepatitis	Read code ever recorded Read code ever recorded	Physical Physical

# List of the 40 morbidities that will be included in the study

Barnett et al. Lancet. 2012 Jul 7;380(9836):3

Adjustment of the list of 40 morbidities from Barnett et al. (2012) Multimorbidity Index to the corresponding domain in the Cumulative Illness Rating Scale (CIRS):

- 1. Hypertension: Physical (Cardiovascular: Vascular)
- 2. Depression: Mental (Psychiatric)
- 3. Painful condition: Physical (Musculoskeletal)
- 4. Asthma (currently treated): Physical (Respiratory)
- 5. Coronary heart disease: Physical (Cardiovascular: cardiac)
- 6. Treated dyspepsia: Physical (Gastrointestinal)
- 7. Diabetes: Physical (Endocrine)
- 8. Thyroid disorders: Physical (Endocrine)
- 9. Rheumatoid arthritis, other inflammatory polyarthropathies & systematic connective tissue disorders: Physical (Musculoskeletal)
- 10. Hearing loss: Physical (Sensory)
- 11. Chronic obstructive pulmonary disease: Physical (Respiratory)
- 12. Anxiety & other neurotic, stress-related & somatoform disorders: Mental (Psychiatric)
- 13. Irritable bowel syndrome: Physical (Gastrointestinal)
- 14. New diagnosis of cancer in the last five years: Physical (Oncological)
- 15. Alcohol problems: Mental (Psychiatric)
- 16. Other psychoactive substance misuse: Mental (Psychiatric)
- 17. Treated constipation: Physical (Gastrointestinal)
- 18. Stroke & transient ischaemic attack: Physical (Neurological)
- 19. Chronic kidney disease: Physical (Renal)
- 20. Diverticular disease of the intestine: Physical (Gastrointestinal)
- 21. Atrial fibrillation: Physical (Cardiovascular)
- 22. Peripheral vascular disease: Physical (Cardiovascular: Vascular)
- 23. Heart failure: Physical (Cardiovascular: Cardiac)
- 24. **Prostate disorders**: Physical (Genitourinary)
- 25. Glaucoma: Physical (Ophthalmological)
- 26. Epilepsy (currently treated): Physical (Neurological)
- 27. Dementia: Mental (Neurological)
- 28. Schizophrenia (and related non-organic psychosis) or bipolar disorder: Mental (Psychiatric)

- 29. Psoriasis or eczema: Physical (Dermatological)
- 30. Inflammatory bowel disease: Physical (Gastrointestinal)
- 31. Migraine: Physical (Neurological)
- 32. Blindness & low vision: Physical (Ophthalmological)
- 33. Chronic sinusitis: Physical (Otolaryngological)
- 34. Learning disability: Mental (Psychiatric)
- 35. Anorexia or bulimia: Mental (Psychiatric)
- 36. Bronchiectasis: Physical (Respiratory)
- 37. Parkinson's disease: Physical (Neurological)
- 38. Multiple sclerosis: Physical (Neurological)
- 39. Viral Hepatitis: Physical (Hepatological)
- 40. Chronic liver disease: Physical (Hepatological)

# Appendix 10. Data extraction and categorisation of smoking status from Electronic health records

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Data extraction and categorisation of	of smoking statu	s from Electronic health records	
Smoking status derived from			
Electronic Health Records	Advice	Categorisation of smoking status	
	Health ed		
Tobacco consumption unknown	smoking	0=Never smoked	
	Health		
	education -	1=Smoker	
Date ceased smoking	smoking		
	Smoking		
	cessation	2=Ex smoker	
Current non-smoker	advice		
Ex cigar smoker			
Ex pipe smoker			
Ex smoker			
Ex-Cigarette Smoker			
Ex-heavy smoker (20-39/day)			
Ex-light smoker (1-9/day)			
Ex-moderate smoker (10-19/day)			
Ex-smoker			
Ex-smoker - amount unknown			
Ex-trivial smoker (<1/day)			
Ex-very heavy smoker (40+/day)			
I used to smoke			
Stopped smoking			
Never smoked tobacco			
No			
Non-smoker			
I have never smoked			
Passive smoker			
Light smoker - 1-9 cigs/day			
Moderate smoker - 10-19 cigs/d			
Not interested in stop smoking			
Not interested in stopping smoking			
Occasional cigarette smoker			
Occasional smoker			
Pipe smoker			
Ready to stop smoking			
Rolls own cigarettes			
Smoker			
Smoking restarted			
Smoking started			
Thinking about stopping smoking			

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Tobacco consumption	
Total time smoked	
Trivial smoker - < 1 cig/day	
Trying to give up smoking	
Very heavy smoker - 40+cigs/d	
Yes	
Failed attempt to stop smoking	
Heavy smoker - 20-39 cigs/day	
I currently smoke	
Cigar smoker	
Cigarette consumption	
Cigarette pack-years	
Cigarette smoker	
Current smoker	

# Appendix 11. Data extraction and categorisation of nutrition status from Electronic health records

Nutrition status derived from Electronic Health Records	Advice	Categorisation of nutrition status
Diet - low in fat	Health ed diet	0=Poor
Diet good	High fat diet {Ub02O}	1=Average
Dietary sodium - low	Healthy eating advice	2=Good
Healthy diet	Patient advised about weight-reducing diet	
Intake of fruit and vegetables at least 5 portions daily	Patient advised re diet	
Normal diet	Patient advised re low cholesterol diet	
Number of portions of fruit and vegetables daily	Patient advised to lose weight	
Dietary salt intake NOS	Pt advised re diabetic diet	
Dietary sodium - average	Pt advised re low fat diet	
Diet average	Pt advised re low salt diet	
Dietary sodium - high	Pt advised re wt reducing diet	
	Patient advised about	
Diet poor	diet NOS	
High fat diet		
High fat diet {Ub02O}		
Dietary history		

# Appendix 12. Data extraction and categorisation of alcohol status from Electronic health records

Alcohol status derived from Electronic Health Records	Advices	Categorisation of alcohol status
Teetotaller	Advice on alcohol consumption	0=Never
Current non drinker	Health ed alcohol	1=Normal
	Health education -	
Lower risk drinking	alcohol	2=Excessive
	Lifestyle advice regarding	
Non drinker alcohol	alcohol	
Alcohol intake within recommended	Patient advised about	
sensible limits	alcohol	
	Advice on alcohol	
Drinks occasionally	consumption	
Light drinker - 1-2u/day	Health ed alcohol	
	Health education -	
Occasional drinker	alcohol	
	Lifestyle advice regarding	
Social drinker	alcohol	
Stopped drinking alcohol	Alcohol health	
Stopped drinking alcohol	promotion	
Trivial drinker - <1u/day		
Alcohol abuse		
Alcohol consumption		
Alcohol intake		
Alcohol misuse		
Binge drinker		
Harmful alcohol use		
Hazardous alcohol use		
Moderate drinker - 3-6u/day		
Problem drinker		
Alcohol units per week {Ub173}*		
Alcohol Intake, 0 units/week		
Alcohol Intake, 1 units/week		
Alcohol Intake, 2 units/week		
Alcohol Intake, 3 units/week		
Alcohol Intake, 4 units/week		
Alcohol Intake, 5 units/week		
Alcohol Intake, 6 units/week		
Alcohol Intake, 7 units/week		
Alcohol Intake, 8 units/week		
Alcohol Intake, 9 units/week		
Alcohol Intake, 10 units/week		
Alcohol Intake, 11 units/week		
Alcohol Intake, 12 units/week		
Alcohol Intake, 13 units/week		
Alcohol Intake, 14 units/week		
Alcohol Intake, 15 units/week		

Alcohol Intake, 20 units/week	
Alcohol Intake, 21 units/week	
Alcohol Intake, 30 units/week	

# Appendix 13. Data extraction and categorisation of physical activity status from Electronic health records

Physical activity status derived from Electronic Health Records	Advices	Categorisation of physical activity status
Avoids even trivial exercise	Health ed exercise	0=Inactive
Declined referral to physical exercise programme	Health education - exercise	1=Moderately Active
Exercise physically impossible	Patient advised about exercise	2=Active
FITT activity level 0; no mod/vig activity	Patient advised re	
of 20 mins duratn	exercise	
Gets no exercise	Health ed exercise	
	Health education -	
GPPAQ physical activity index: inactive	exercise	
Takes inadequate exercise		
FITT activity level 2; 5-11 occas of		
mod/vig activt in 4 wks		
Enjoys light exercise		
Enjoys moderate exercise		
GPPAQ physical activity index:		
moderately inactive		
GPPAQ physical activity index:		
moderately active		
Aerobic exercise 3+ times/week		
Aerobic exercise three or more times		
per week		
Average duration of mod intensity		
physicl activty per day active		
GPPAQ physical activity index: active		
FITT activity level 3; 12+ occas of mod		
activity in 4 weeks		
FITT activity level 4; 12+ occas of		
mod/vig activit in 4 wks		
Competitive athlete		

Appendix 14. Approval of Staffordshire University Independent Peer Review



### INDEPENDENT PEER REVIEW APPROVAL FEEDBACK

Status of approval:	Approved
Award Pathway	sectional study PhD
Title of Study	Examining the association between Multiple Health Risk/Enhancing Behaviours and Multimorbidity risk: A cross
Researcher Name	Konstantinos Spyropoulos

Thank you for forwarding the amendments requested by the Independent Peer Review Panel (IPR)

#### Action now needed:

You must now apply to the Local NHS Research Ethics Committee (LREC) for approval to conduct your study. You must not commence the study without this second approval.

Please forward a copy of the letter you receive from the LREC by email to <u>HealthScienceEthics@staffs.ac.uk</u> as soon as possible after you have received approval.

Once you have received LREC approval you can commence your study. You should be sure to do so in consultation with your supervisor.

You should note that any divergence from the approved procedures and research method will invalidate any insurance and liability cover from the University. You should, therefore, notify the Panel of any significant divergence from this approved proposal.

When your study is complete, please send the Ethics Committee an end of study report. A template can be found on the ethics BlackBoard site.

Comments for your consideration:

Signed: Dr Roozbeh Naemi

Date: 05.10.2017

Chair of the Health Sciences Ethics Panel



East of England - Essex Research Ethics Committee The Old Chapel Royal Standard Place Nottingham

NG16ES

<u>Please note</u>: This is the favourable opinion of the REC only and does not allow you to start your study at NHS sites in England until you receive HRA Approval

17 January 2018

Dr C Gidlow Staffordshire University Leek Road Stoke-on- Trent Staffordshire ST4 2DF

Dear Dr Gidlow

Study title:	Examining the association between Multiple Health Risk/Enhancing Behaviours and Multi-morbidity risk: A cross sectional study
REC reference:	17/EE/0469
IRAS project ID:	233239

Thank you for your letter of 14 December 2018, responding to the Proportionate Review Sub-Committee's request for changes to the documentation for the above study.

The revised documentation has been reviewed and approved by the sub-committee.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this favourable opinion letter. The expectation is that this information will be published for all studies that receive an ethical opinion but should you wish to provide a substitute contact point, wish to make a request to defer, or require further information, please contact please contact hra.studyregistration@nhs.net outlining the reasons for your request.

Under very limited circumstances (e.g. for student research which has received an unfavourable opinion), it may be possible to grant an exemption to the publication of the study.

#### Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised.

#### Conditions of the favourable opinion

The REC favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements. Each NHS organisation must confirm through the signing of agreements and/or other documents that it has given permission for the research to proceed (except where explicitly specified otherwise).

Guidance on applying for HRA Approval (England)/ NHS permission for research is available in the Integrated Research Application System, <u>www.hra.nhs.uk</u> or at <u>http://www.rdforum.nhs.uk</u>.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of management permissions from host organisations.

#### Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database. This should be before the first participant is recruited but no later than 6 weeks after recruitment of the first participant.

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g. when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non-clinical trials this is not currently mandatory.

If a sponsor wishes to request a deferral for study registration within the required timeframe, they should contact <u>hra.studyregistration@nhs.net</u>. The expectation is that all clinical trials will

be registered, however, in exceptional circumstances non registration may be permissible with prior agreement from the HRA. Guidance on where to register is provided on the HRA website.

# It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

#### Ethical review of research sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" above).

#### Approved documents

The documents reviewed and approved by the Committee are:

Document	Version	Date
Evidence of Sponsor insurance or indemnity (non NHS Sponsors		
only)		
IRAS Application Form [IRAS_Form_30102017]		30 October 2017
Letter from sponsor		
Letters of invitation to participant		11 October 2017
Letters of invitation to participant [Revised_Appendix 1_GP's e-mail invitation]	2	12 December 2017
Other [Public Liability Staffordshire University]		12 October 2017
Other [Employers Liability Staffordshire University]		12 October 2017
Other [Appendix 2. Eligibility assessment for GP]		
Other [Appendix 3. Third party Aggreement]		16 October 2017
Other [Appendix 4. Data extraction Tool]		16 October 2017
Other [Independent_Peer_Reviewer's_1stReport_AH]	1	12 December 2017
Other [Independent_Peer_Reviewer's_1stReport_HB]	1	12 December 2017
Other [Independent_Peer_Reviewers'_Approval feedback]	1	12 December 2017
Other [Cover Letter _HRA's amendments]		12 December 2017
Participant consent form		11 October 2017
Participant information sheet (PIS) [Revised_Appendix 1_GP's e-mail invitation]	2	12 December 2017
Research protocol or project proposal [Revised_Research protocol]	2	12 December 2017
Summary CV for Chief Investigator (CI) [C. Gidlow CV]		11 October 2017
Summary CV for student [CV_Konstantinos Spyropoulos]		12 October 2017
Summary CV for supervisor (student research) [C. Gidlow CV]		11 October 2017
Summary CV for supervisor (student research) [N. Ellis_CV]		11 October 2017

#### Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

#### After ethical review

#### Reporting requirements

The attached document "After ethical review – guidance for researchers" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- · Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The HRA website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

#### Feedback

You are invited to give your view of the service that you have received from the Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website: <u>http://www.hra.nhs.uk/about-the-hra/governance/guality-assurance</u>

We are pleased to welcome researchers and R & D staff at our RES Committee members' training days – see details at <a href="http://www.hra.nhs.uk/hra-training/">http://www.hra.nhs.uk/hra-training/</a>

## 17/EE/0469 Please quote this number on all correspondence

With the Committee's best wishes for the success of this project.

Yours sincerely

pp & Swow Date

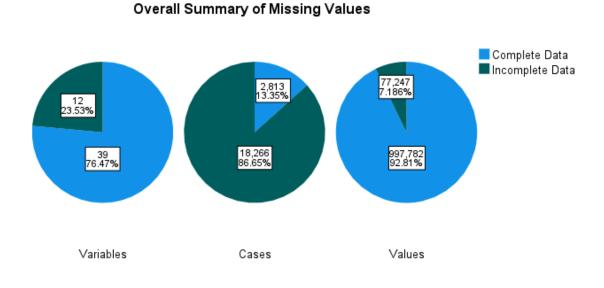
Dr Niki Bannister Chair

Email: NRESCommittee.EastofEngland-Essex@nhs.net

Enclosures: "After ethical review – guidance for researchers"

Copy to:

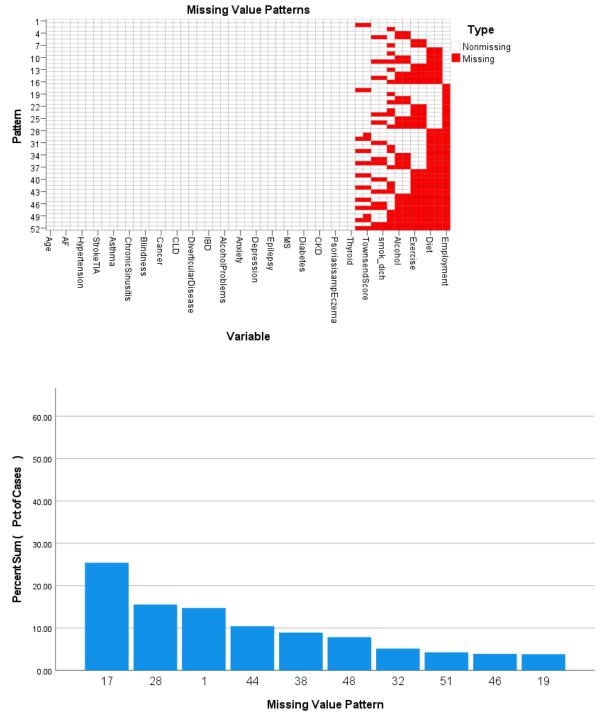
Professor Nachi Chockalingam Chockalingam



Variable Summary <sup>a,b</sup>				
	Mis	sing		
	N	Percent	Valid N	
Employment	18047	85.6%	3032	
diet_dich	11717	55.6%	9362	
Diet	11717	55.6%	9362	
excers_dich	8288	39.3%	12791	
Exercise	8288	39.3%	12791	
alc_dich	5505	26.1%	15574	
Alcohol	5505	26.1%	15574	
Ethnicity (Category 5/5)	4925	23.4%	16154	
smok_dich	1598	7.6%	19481	
Smoking	1598	7.6%	19481	
Townsend Score	31	0.1%	21048	
IMD	28	0.1%	21051	

a. Maximum number of variables shown: 51

b. Minimum percentage of missing values for variable to be included: .0%



The 10 most frequently occurring patterns are shown in the chart.

Imputati	on Specifications
Imputation Method	Automatic
Number of Imputations	5
Model for Scale Variables	Linear Regression
Interactions Included in Models	(none)
Maximum Percentage of Missing Values	100.0%
Maximum Number of Parameters in Imputation Model	100

	Imputation Resu	lts
Imputation Method		Fully Conditional Specification
Fully Conditional Specifi	cation Method Iterations	10
Dependent Variables	Imputed	EthnicityCategory55,TownsendScore ,IMD,Employment,Smoking,Alcohol, Exercise,Diet,smok_dich,alc_dich,ex cers_dich,diet_dich
	Not Imputed(Too Many Missing Values)	
	Not Imputed(No Missing Values)	Age,Gender,AF,HeartFailure,Hypert ension,PVD,StrokeTIA,CHD,Asthma, Bronchiectasis,ChronicSinusitis,COP D,Blindness,Glaucoma,AnorexiaorBu limia,Cancer,ProstateDisorders,CLD, Constipation,DiverticularDisease,Dys pepsia,IBD,IBS,AlcoholProblems,Anx iety,Dementia,Depression,Schizofre nia,Epilepsy,Migraine,MS,Parkinsons Disease,Diabetes,HearingLoss,CKD,P ainfulCondition,PsoriasisampEczema ,RheumatoidArthiritis,Thyroid
Imputation Sequence		Age,Gender,AF,HeartFailure,Hypert ension,PVD,StrokeTIA,CHD,Asthma, Bronchiectasis,ChronicSinusitis,COP D,Blindness,Glaucoma,AnorexiaorBu limia,Cancer,ProstateDisorders,CLD, Constipation,DiverticularDisease,Dys pepsia,IBD,IBS,AlcoholProblems,Anx iety,Dementia,Depression,Schizofre nia,Epilepsy,Migraine,MS,Parkinsons Disease,Diabetes,HearingLoss,CKD,P ainfulCondition,PsoriasisampEczema ,RheumatoidArthiritis,Thyroid,IMD,T ownsendScore,Smoking,smok_dich, EthnicityCategory55,Alcohol,alc_dic h,Exercise,excers_dich,Diet,diet_dic h,Employment

		Imputation Models		
	_	Model	Missing	Imputed
	Туре	Effects	Values	Values
IMD	Logistic Regression	Age,Gender,AF,HeartFailure,Hypertension, PVD,StrokeTIA,CHD,Asthma,Bronchiectasis, ChronicSinusitis,COPD,Blindness,Glaucoma, AnorexiaorBulimia,Cancer,ProstateDisorde rs,CLD,Constipation,DiverticularDisease,Dys pepsia,IBD,IBS,AlcoholProblems,Anxiety,De mentia,Depression,Schizofrenia,Epilepsy,M igraine,MS,ParkinsonsDisease,Diabetes,He aringLoss,CKD,PainfulCondition,Psoriasisa mpEczema,RheumatoidArthiritis,Thyroid,T ownsendScore,Smoking,smok_dich,Ethnicit yCategory55,Alcohol,alc_dich,Exercise,exce rs_dich,Diet,diet_dich,Employment	28	140
Townsend Score	Logistic Regression	Age,Gender,AF,HeartFailure,Hypertension, PVD,StrokeTIA,CHD,Asthma,Bronchiectasis, ChronicSinusitis,COPD,Blindness,Glaucoma, AnorexiaorBulimia,Cancer,ProstateDisorde rs,CLD,Constipation,DiverticularDisease,Dys pepsia,IBD,IBS,AlcoholProblems,Anxiety,De mentia,Depression,Schizofrenia,Epilepsy,M igraine,MS,ParkinsonsDisease,Diabetes,He aringLoss,CKD,PainfulCondition,Psoriasisa mpEczema,RheumatoidArthiritis,Thyroid,I MD,Smoking,smok_dich,EthnicityCategory 55,Alcohol,alc_dich,Exercise,excers_dich,Di et,diet_dich,Employment	31	155
Smoking	Logistic Regression	Age,Gender,AF,HeartFailure,Hypertension, PVD,StrokeTIA,CHD,Asthma,Bronchiectasis, ChronicSinusitis,COPD,Blindness,Glaucoma, AnorexiaorBulimia,Cancer,ProstateDisorde rs,CLD,Constipation,DiverticularDisease,Dys pepsia,IBD,IBS,AlcoholProblems,Anxiety,De mentia,Depression,Schizofrenia,Epilepsy,M igraine,MS,ParkinsonsDisease,Diabetes,He aringLoss,CKD,PainfulCondition,Psoriasisa mpEczema,RheumatoidArthiritis,Thyroid,I MD,TownsendScore,smok_dich,EthnicityCa tegory55,Alcohol,alc_dich,Exercise,excers_ dich,Diet,diet_dich,Employment	1598	7990
smok_dich	Logistic Regression	Age,Gender,AF,HeartFailure,Hypertension, PVD,StrokeTIA,CHD,Asthma,Bronchiectasis, ChronicSinusitis,COPD,Blindness,Glaucoma, AnorexiaorBulimia,Cancer,ProstateDisorde rs,CLD,Constipation,DiverticularDisease,Dys pepsia,IBD,IBS,AlcoholProblems,Anxiety,De mentia,Depression,Schizofrenia,Epilepsy,M igraine,MS,ParkinsonsDisease,Diabetes,He aringLoss,CKD,PainfulCondition,Psoriasisa mpEczema,RheumatoidArthiritis,Thyroid,I MD,TownsendScore,Smoking,EthnicityCate gory55,Alcohol,alc_dich,Exercise,excers_di ch,Diet,diet_dich,Employment	1598	7990

Ethnicity (Category 5/5)	Logistic Regression	Age,Gender,AF,HeartFailure,Hypertension, PVD,StrokeTIA,CHD,Asthma,Bronchiectasis, ChronicSinusitis,COPD,Blindness,Glaucoma, AnorexiaorBulimia,Cancer,ProstateDisorde rs,CLD,Constipation,DiverticularDisease,Dys pepsia,IBD,IBS,AlcoholProblems,Anxiety,De mentia,Depression,Schizofrenia,Epilepsy,M igraine,MS,ParkinsonsDisease,Diabetes,He aringLoss,CKD,PainfulCondition,Psoriasisa mpEczema,RheumatoidArthiritis,Thyroid,I MD,TownsendScore,Smoking,smok_dich,Al cohol,alc_dich,Exercise,excers_dich,Diet,di et_dich,Employment	4925	24625
Alcohol	Logistic Regression	Age,Gender,AF,HeartFailure,Hypertension, PVD,StrokeTIA,CHD,Asthma,Bronchiectasis, ChronicSinusitis,COPD,Blindness,Glaucoma, AnorexiaorBulimia,Cancer,ProstateDisorde rs,CLD,Constipation,DiverticularDisease,Dys pepsia,IBD,IBS,AlcoholProblems,Anxiety,De mentia,Depression,Schizofrenia,Epilepsy,M igraine,MS,ParkinsonsDisease,Diabetes,He aringLoss,CKD,PainfulCondition,Psoriasisa mpEczema,RheumatoidArthiritis,Thyroid,I MD,TownsendScore,Smoking,smok_dich,Et hnicityCategory55,alc_dich,Exercise,excers _dich,Diet,diet_dich,Employment	5505	27525
alc_dich	Logistic Regression	Age,Gender,AF,HeartFailure,Hypertension, PVD,StrokeTIA,CHD,Asthma,Bronchiectasis, ChronicSinusitis,COPD,Blindness,Glaucoma, AnorexiaorBulimia,Cancer,ProstateDisorde rs,CLD,Constipation,DiverticularDisease,Dys pepsia,IBD,IBS,AlcoholProblems,Anxiety,De mentia,Depression,Schizofrenia,Epilepsy,M igraine,MS,ParkinsonsDisease,Diabetes,He aringLoss,CKD,PainfulCondition,Psoriasisa mpEczema,RheumatoidArthiritis,Thyroid,I MD,TownsendScore,Smoking,smok_dich,Et hnicityCategory55,Alcohol,Exercise,excers_ dich,Diet,diet_dich,Employment	5505	27525
Exercise	Logistic Regression	Age,Gender,AF,HeartFailure,Hypertension, PVD,StrokeTIA,CHD,Asthma,Bronchiectasis, ChronicSinusitis,COPD,Blindness,Glaucoma, AnorexiaorBulimia,Cancer,ProstateDisorde rs,CLD,Constipation,DiverticularDisease,Dys pepsia,IBD,IBS,AlcoholProblems,Anxiety,De mentia,Depression,Schizofrenia,Epilepsy,M igraine,MS,ParkinsonsDisease,Diabetes,He aringLoss,CKD,PainfulCondition,Psoriasisa mpEczema,RheumatoidArthiritis,Thyroid,I MD,TownsendScore,Smoking,smok_dich,Et hnicityCategory55,Alcohol,alc_dich,excers_ dich,Diet,diet_dich,Employment	8288	41440

excers_dich	Logistic Regression	Age,Gender,AF,HeartFailure,Hypertension, PVD,StrokeTIA,CHD,Asthma,Bronchiectasis, ChronicSinusitis,COPD,Blindness,Glaucoma, AnorexiaorBulimia,Cancer,ProstateDisorde rs,CLD,Constipation,DiverticularDisease,Dys pepsia,IBD,IBS,AlcoholProblems,Anxiety,De mentia,Depression,Schizofrenia,Epilepsy,M igraine,MS,ParkinsonsDisease,Diabetes,He aringLoss,CKD,PainfulCondition,Psoriasisa mpEczema,RheumatoidArthiritis,Thyroid,I MD,TownsendScore,Smoking,smok_dich,Et hnicityCategory55,Alcohol,alc_dich,Exercis e,Diet,diet_dich,Employment	11717	41440
Diet	Logistic Regression	Age,Gender,AF,HeartFailure,Hypertension, PVD,StrokeTIA,CHD,Asthma,Bronchiectasis, ChronicSinusitis,COPD,Blindness,Glaucoma, AnorexiaorBulimia,Cancer,ProstateDisorde rs,CLD,Constipation,DiverticularDisease,Dys pepsia,IBD,IBS,AlcoholProblems,Anxiety,De mentia,Depression,Schizofrenia,Epilepsy,M igraine,MS,ParkinsonsDisease,Diabetes,He aringLoss,CKD,PainfulCondition,Psoriasisa mpEczema,RheumatoidArthiritis,Thyroid,I MD,TownsendScore,Smoking,smok_dich,Et hnicityCategory55,Alcohol,alc_dich,Exercis e,excers_dich,diet_dich,Employment	11717	58585
diet_dich	Logistic Regression	Age,Gender,AF,HeartFailure,Hypertension, PVD,StrokeTIA,CHD,Asthma,Bronchiectasis, ChronicSinusitis,COPD,Blindness,Glaucoma, AnorexiaorBulimia,Cancer,ProstateDisorde rs,CLD,Constipation,DiverticularDisease,Dys pepsia,IBD,IBS,AlcoholProblems,Anxiety,De mentia,Depression,Schizofrenia,Epilepsy,M igraine,MS,ParkinsonsDisease,Diabetes,He aringLoss,CKD,PainfulCondition,Psoriasisa mpEczema,RheumatoidArthiritis,Thyroid,I MD,TownsendScore,Smoking,smok_dich,Et hnicityCategory55,Alcohol,alc_dich,Exercis e,excers_dich,Diet,Employment	11717	58585
Employment	Logistic Regression	Age,Gender,AF,HeartFailure,Hypertension, PVD,StrokeTIA,CHD,Asthma,Bronchiectasis, ChronicSinusitis,COPD,Blindness,Glaucoma, AnorexiaorBulimia,Cancer,ProstateDisorde rs,CLD,Constipation,DiverticularDisease,Dys pepsia,IBD,IBS,AlcoholProblems,Anxiety,De mentia,Depression,Schizofrenia,Epilepsy,M igraine,MS,ParkinsonsDisease,Diabetes,He aringLoss,CKD,PainfulCondition,Psoriasisa mpEczema,RheumatoidArthiritis,Thyroid,I MD,TownsendScore,Smoking,smok_dich,Et hnicityCategory55,Alcohol,alc_dich,Exercis e,excers_dich,Diet,diet_dich	18047	90235

5.	EthnicityCat			
Data	Imputation	Category	N	Percent
Original Data		1	6735	41.7
		2	6996	43.3
		3	703	4.4
		4	120	.7
		5	1600	9.9
Imputed Values	1	1	1652	33.5
		2	1941	39.4
		3	255	5.2
		4	352	7.1
		5	725	14.7
	2	1	1668	33.9
		2	1951	39.6
		3	269	5.5
		4	426	8.6
		5	611	12.4
	3	1	1639	33.3
		2	1852	37.6
		3	292	5.9
		4	515	10.5
		5	627	12.7
	4	1	1618	32.9
	7	2	1955	39.7
		3	262	5.3
		4	473	9.6
		5	617	12.5
	5	1	1539	31.2
		2	1907	38.7
		3	275	5.6
		4	514	10.4
		5	690	14.0
Complete Data After	1	1	8387	39.8
Imputation		2	8937	42.4
		3	958	4.5
		4	472	2.2
		5	2325	11.0
	2	1	8403	39.9
		2	8947	42.4
		3	972	4.6
		4	546	2.6
		5	2211	10.5
	3	1	8374	39.7
		2	8848	42.0
		3	995	4.7
		4	635	3.0
		5	2227	10.6
	4	1	8353	39.6
		2	8951	42.5
		3	965	4.6
		4	593	2.8
		5	2217	10.5
	5	1	8274	
	5			39.3
		2	8903	42.2
		3	978	4.6

4	634	3.0
5	2290	10.9

	Townsend	dScore		
Data	Imputation	Category	Ν	Percent
Original Data		1	7335	34.8
		2	4374	20.8
		3	3038	14.4
		4	4153	19.7
		5	2148	10.2
Imputed Values	1	1	4	12.9
		2	6	19.4
		3	3	9.7
		4	3	9.7
		5	15	48.4
	2	1	12	38.7
		2	9	29.0
		3	8	25.8
		4	1	3.2
		5	1	3.2
	3	1	2	6.5
	Ū.	2	2	6.5
		3	2	6.5
		4	3	9.7
		5	22	71.0
	4	1	13	41.9
	7	2	3	9.7
		3	10	32.3
		4	10	3.2
		5	4	12.9
	5	1	5	12.9
	5	2	7	22.6
			3	
		3	5	9.7
		4 		16.1
Campalata Data Aftan	1	5	11	35.5
Complete Data After	1	1	7339	34.8
Imputation		2	4380	20.8
		3	3041	14.4
		4	4156	19.7
	2	5	2163	10.3
	2	1	7347	34.9
		2	4383	20.8
		3	3046	14.5
		4	4154	19.7
		5	2149	10.2
	3	1	7337	34.8
		2	4376	20.8
		3	3040	14.4
		4	4156	19.7
		5	2170	10.3
	4	1	7348	34.9
		2	4377	20.8
		3	3048	14.5
		4	4154	19.7

	5	2152	10.2
5	1	7340	34.8
	2	4381	20.8
	3	3041	14.4
	4	4158	19.7
	5	2159	10.2

	IMD	)		
Data	Imputation	Category	Ν	Percent
Original Data		1	1736	8.2
		2	1626	7.7
		3	1754	8.3
		4	918	4.4
		5	677	3.2
		6	1745	8.3
		7	1600	7.6
		8	2294	10.9
		9	1986	9.4
		10	6715	31.9
Imputed Values	1	2	3	10.7
		4	1	3.6
		5	3	10.7
		6	4	14.3
		7	2	7.1
		8	10	35.7
		9	3	10.7
		10	2	7.1
	2	3	1	3.6
		7	2	7.1
		8	13	46.4
		9	1	3.6
		10	11	39.3
	3	1	1	3.6
		3	3	10.7
		4	2	7.1
		5	1	3.6
		6	2	7.1
		7	1	3.6
		8	5	17.9
		9	9	32.1
		10	4	14.3
	4	3	1	3.6
		5	1	3.6
		9	26	92.9
	5	1	2	7.1
		2	3	10.7
		3	1	3.6
		4	2	7.1
		5	1	3.6
		6	3	10.7
		7	1	3.6
		8	7	25.0
		9	8	28.6
	1	1	1736	8.2

Complete Data After		2	1629	7.7
Imputation		3	1754	8.3
Inputation		4	919	4.4
		5	680	3.2
		6	1749	8.3
		7	1602	7.6
		8	2304	10.9
		9	1989	9.4
		10	6717	31.9
	2	10	1736	8.2
	2	2	1626	7.7
		3	1755	8.3
		4	918	4.4
		5	677	3.2
		6	1745	8.3
		7	1602	7.6
		8	2307	10.9
		9	1987	9.4
	2	10		31.9
	3	1		8.2
		2		7.7
		3		8.3
		4		4.4
		5		3.2
		6	1737         1626         1757         920         678         1747         1601         2299         1995         6719         1736	8.3
		7		7.6
		8		10.9
		9		9.5
		10		31.9
	4	1		8.2
		2	1626	7.7
		3	1755	8.3
		4	918	4.4
		5	678	3.2
		6	1745	8.3
		7	1600	7.6
		8	2294	10.9
		9	2012	9.5
		10	6715	31.9
	5	1	1738	8.2
		2	1629	7.7
		3	1755	8.3
		4	920	4.4
		5	678	3.2
		6	1748	8.3
		7	1601	7.6
		8	2301	10.9
		9	1994	9.5
		10	6715	31.9

Employment										
Data Imputation Category N Percen										
Original Data		0	575	19.0						
		1	316	10.4						

		2	1340	44.2
		3	801	26.4
Imputed Values	1	0	2383	13.2
		1	7683	42.6
		2	6348	35.2
		3	1633	9.0
	2	0	2365	13.1
		1	8360	46.3
		2	5807	32.2
		3	1515	8.4
	3	0	2959	16.4
		1	1034	5.7
		2	9496	52.6
		3	4558	25.3
	4	0	2035	11.3
		1	1154	6.4
		2	8470	46.9
		3	6388	35.4
	5	0	3460	19.2
		1	7840	43.4
		2	4758	26.4
		3	1989	11.0
Complete Data After	1	0	2958	14.0
Imputation		1	7999	37.9
		2	7688	36.5
		3	2434	11.5
	2	0	2940	13.9
		1	8676	41.2
		2	7147	33.9
		3	2316	11.0
	3	0	3534	16.8
		1	1350	6.4
		2	10836	51.4
		3	5359	25.4
	4	0	2610	12.4
		1	1470	7.0
		2	9810	46.5
		3	7189	34.1
	5	0	4035	19.1
	0	1	8156	38.7
		2	6098	28.9
		3	2790	13.2

Smoking											
Data	Imputation	Category	Ν	Percent							
Original Data		0	3925	20.1							
		1	2962	15.2							
		2	12594	64.6							
Imputed Values	1	0	901	56.4							
		1	46	2.9							
		2	651	40.7							
	2	0	709	44.4							
		1	446	27.9							
		2	443	27.7							

	3	0	574	35.9
		1	778	48.7
		2	246	15.4
	4	0	286	17.9
		1	77	4.8
		2	1235	77.3
	5	0	1113	69.6
		1	94	5.9
		2	391	24.5
Complete Data After	1	0	4826	22.9
Imputation		1	3008	14.3
		2	13245	62.8
	2	0	4634	22.0
		1	3408	16.2
		2	13037	61.8
	3	0	4499	21.3
		1	3740	17.7
		2	12840	60.9
	4	0	4211	20.0
		1	3039	14.4
		2	13829	65.6
	5	0	5038	23.9
		1	3056	14.5
		2	12985	61.6

Diet

Diet										
Data	Imputation	Category	N	Percent						
Original Data		0	5084	54.3						
		1	2226	23.8						
		2	2052	21.9						
Imputed Values	1	0	1530	13.1						
		1	5192	44.3						
		2	4995	42.6						
	2	0	4811	41.1						
		1	1469	12.5						
		2	5437	46.4						
	3	0	1920	16.4						
		1	4257	36.3						
		2	5540	47.3						
	4	0	2735	23.3						
		1	5036	43.0						
		2	3946	33.7						
	5	0	3905	33.3						
		1	2720	23.2						
		2	5092	43.5						
Complete Data After	1	0	6614	31.4						
Imputation		1	7418	35.2						
		2	7047	33.4						
	2	0	9895	46.9						
		1	3695	17.5						
		2	7489	35.5						
	3	0	7004	33.2						
		1	6483	30.8						
		2	7592	36.0						

4	0	7819	37.1
	1	7262	34.5
	2	5998	28.5
5	0	8989	42.6
	1	4946	23.5
	2	7144	33.9

excers_dich
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Data	Imputation	Category	N	Percent
Original Data		0	9396	73.5
		1	3395	26.5
Imputed Values	1	0	3983	48.1
		1	4305	51.9
	2	0	3255	39.3
		1	5033	60.7
	3	0	5241	63.2
		1	3047	36.8
	4	0	5116	61.7
		1	3172	38.3
	5	0	2681	32.3
		1	5607	67.7
Complete Data After	1	0	13379	63.5
Imputation		1	7700	36.5
	2	0	12651	60.0
		1	8428	40.0
	3	0	14637	69.4
		1	6442	30.6
	4	0	14512	68.8
		1	6567	31.2
	5	0	12077	57.3
		1	9002	42.7

### diet\_dich

diet_diefi										
Data	Imputation	Category	Ν	Percent						
Original Data		0	7310	78.1						
		1	2052	21.9						
Imputed Values	1	0	7709	65.8						
		1	4008	34.2						
	2	0	7136	60.9						
		1	4581	39.1						
	3	0	6102	52.1						
		1	5615	47.9						
	4	0	5200	44.4						
		1	6517	55.6						
	5	0	7746	66.1						
		1	3971	33.9						
Complete Data After	1	0	15019	71.3						
Imputation		1	6060	28.7						
	2	0	14446	68.5						
		1	6633	31.5						
	3	0	13412	63.6						
		1	7667	36.4						
	4	0	12510	59.3						

	1	8569	40.7
5	0	15056	71.4
	1	6023	28.6

									95% C.I.fo	r EXP(B)	Fraction	Relative Increase	Relative
Imputation Nu	mber		В	S.E.	Wald	df	Sig.	Exp(B)	Lower	Upper	Missing Info.	Variance	Efficiency
Original data	Step 1 <sup>a</sup>	Alcohol			74.316	2	<.001						
		Alcohol(1)	.487	.102	22.872	1	<.001	1.627	1.333	1.987			
		Alcohol(2)	326	.149	4.807	1	.028	.722	.540	.966			
		Constant	-1.329	.100	176.003	1	<.001	.265					
1	Step 1 <sup>a</sup>	Alcohol			252.828	2	<.001						
		Alcohol(1)	1.018	.069	218.159	1	<.001	2.767	2.418	3.168			
		Alcohol(2)	.317	.126	6.329	1	.012	1.374	1.073	1.759			
		Constant	-2.093	.067	982.469	1	<.001	.123					
2	Step 1 <sup>a</sup>	Alcohol			159.058	2	<.001						
		Alcohol(1)	.865	.076	128.608	1	<.001	2.375	2.045	2.758			
		Alcohol(2)	.221	.131	2.837	1	.092	1.247	.965	1.612			
		Constant	-1.972	.074	703.154	1	<.001	.139					
3	Step 1 <sup>a</sup>	Alcohol			431.410	2	<.001						
		Alcohol(1)	.784	.065	144.586	1	<.001	2.190	1.927	2.489			
		Alcohol(2)	830	.110	56.714	1	<.001	.436	.352	.541			
		Constant	-1.801	.063	820.998	1	<.001	.165					
4	Step 1 <sup>a</sup>	Alcohol			158.914	2	<.001						
		Alcohol(1)	.890	.076	138.367	1	<.001	2.434	2.099	2.823			
		Alcohol(2)	.342	.132	6.710	1	.010	1.408	1.087	1.825			
		Constant	-1.997	.074	734.044	1	<.001	.136					
5	Step 1 <sup>a</sup>	Alcohol			660.451	2	<.001						
		Alcohol(1)	.866	.097	80.034	1	<.001	2.378	1.967	2.875			
		Alcohol(2)	838	.117	51.587	1	<.001	.432	.344	.544			
		Constant	-1.824	.095	366.585	1	<.001	.161					
Pooled	Step 1 ª	Alcohol(1)	.885	.121			<.001	2.422	1.859	3.155	.646	1.437	.88
		Alcohol(2)	158	.689			.830	.854	.132	5.529	.977	30.151	.83
	Constant	-1.937	.154			<.001	.144	.100	.208	.810	3.189	.86	

Variables in the Equation

a. Variable(s) entered on step 1: Alcohol.

					v	ariables i	n the Equ	ation					
		95% C.I.for EXP(B)								Fraction	Relative Increase	Relative	
Imputation Nur	Imber		в	S.E.	Wald	df	Sig.	Exp(B)	Lower	Upper	Missing Info.	Variance	Efficiency
Original data	Step 1 <sup>a</sup>	Smoking			259.765	2	<.001						
		Smoking(1)	003	.043	.006	1	.938	.997	.915	1.085			
		Smoking(2)	.680	.043	244.639	1	<.001	1.973	1.812	2.149			
		Constant	-1.197	.021	3216.745	1	.000	.302					
1	Step 1 <sup>a</sup>	Smoking			354.792	2	<.001						
		Smoking(1)	186	.042	19.323	1	<.001	.831	.765	.902			
		Smoking(2)	.722	.043	279.585	1	<.001	2.060	1.892	2.242			
		Constant	-1.260	.021	3621.118	1	.000	.284					
2	Step 1 <sup>a</sup>	Smoking			201.810	2	<.001						
		Smoking(1)	160	.042	14.220	1	<.001	.852	.784	.926			
		Smoking(2)	.520	.042	152.356	1	<.001	1.682	1.549	1.827			
		Constant	-1.241	.021	3492.462	1	.000	.289					
3	Step 1 <sup>a</sup>	Smoking			109.078	2	<.001						
		Smoking(1)	140	.043	10.752	1	.001	.870	.800	.945			
		Smoking(2)	.364	.041	77.026	1	<.001	1.439	1.327	1.561			
		Constant	-1.222	.021	3369.229	1	.000	.295					
4	Step 1 <sup>a</sup>	Smoking			324.800	2	<.001						
		Smoking(1)	.027	.043	.387	1	.534	1.027	.944	1.117			
		Smoking(2)	.760	.043	311.651	1	<.001	2.138	1.965	2.326			
		Constant	-1.312	.021	3980.164	1	.000	.269					
5	Step 1 <sup>a</sup>	Smoking			349.511	2	<.001						
		Smoking(1)	264	.042	39.464	1	<.001	.768	.707	.834			
		Smoking(2)	.670	.043	241.845	1	<.001	1.955	1.796	2.127			
		Constant	-1.234	.021	3454.597	1	.000	.291					
Pooled	Step 1 <sup>a</sup>	Smoking(1)	145	.124			.297	.865	.630	1.189	.912	7.603	.84
		Smoking(2)	.607	.184			.026	1.835	1.123	3.000	.961	17.730	.83
		Constant	-1.254	.044			<.001	.285	.257	.317	.822	3.450	.85

Variables in the Equation

Constant -1
a. Variable(s) entered on step 1: Smoking.

### Variables in the Equation

									95% C.I.for EXP(B)		Fraction Missing Info.	Relative Increase Variance	Relative Efficiency
Imputation Number		В	S.E.	Wald	df	Sig.	Exp(B)	Lower	Upper				
Original data	Step 1 ª	Exercise			601.008	3	<.001						
		Exercise(1)	1.435	.060	580.241	1	<.001	4.201	3.738	4.722			
		Exercise(2)	.531	.063	71.409	1	<.001	1.700	1.503	1.923			
		Exercise(3)	.670	.054	153.078	1	<.001	1.955	1.758	2.174			
		Constant	-1.450	.044	1098.632	1	<.001	.235					
1	Step 1 <sup>a</sup>	Exercise			520.941	3	<.001						
		Exercise(1)	.996	.045	488.983	1	<.001	2.708	2.479	2.958			
		Exercise(2)	.585	.052	124.846	1	<.001	1.796	1.620	1.990			
		Exercise(3)	.726	.044	272.618	1	<.001	2.067	1.897	2.253			
		Constant	-1.730	.032	2848.534	1	.000	.177					
2	Step 1 <sup>a</sup>	Exercise			1079.359	3	<.001						
		Exercise(1)	1.526	.049	973.988	1	<.001	4.601	4.180	5.063			
		Exercise(2)	.350	.048	54.132	1	<.001	1.420	1.293	1.559			
		Exercise(3)	.835	.043	370.744	1	<.001	2.305	2.117	2.510			
		Constant	-1.739	.031	3170.642	1	.000	.176					
3	Step 1 <sup>a</sup>	Exercise			904.560	3	<.001						
		Exercise(1)	1.445	.050	819.954	1	<.001	4.243	3.843	4.684			
		Exercise(2)	.522	.054	94.890	1	<.001	1.686	1.518	1.872			
		Exercise(3)	.282	.042	44.909	1	<.001	1.325	1.221	1.439			
		Constant	-1.605	.033	2393.751	1	.000	.201					
4	Step 1 <sup>a</sup>	Exercise			812.695	3	<.001						
		Exercise(1)	1.307	.050	679.311	1	<.001	3.694	3.348	4.076			
		Exercise(2)	.272	.052	26.878	1	<.001	1.312	1.184	1.454			
		Exercise(3)	.133	.042	10.014	1	.002	1.142	1.052	1.240			
		Constant	-1.489	.032	2105.928	1	.000	.226					
5	Step 1 <sup>a</sup>	Exercise			143.353	3	<.001						
		Exercise(1)	.345	.045	58.870	1	<.001	1.412	1.293	1.543			
		Exercise(2)	.424	.054	61.454	1	<.001	1.527	1.374	1.698			
		Exercise(3)	.532	.045	137.173	1	<.001	1.703	1.558	1.861			
		Constant	-1.506	.035	1903.109	1	.000	.222					
Pooled	Step 1 <sup>a</sup>	Exercise(1)	1.124	.528			.099	3.077	.717	13.198	.994	120.070	.83
		Exercise(2)	.431	.148			.032	1.538	1.056	2.241	.907	7.093	.84
		Exercise(3)	.502	.326			.196	1.651	.677	4.028	.987	55.315	.83
		Constant	-1.614	.134			<.001	.199	.139	.284	.957	15.894	.83

a. Variable(s) entered on step 1: Exercise.

#### Variables in the Equation

						variable	s in the L	quation					
									95% C.I.for EXP(B)		Fraction	Relative Increase	Relative
Imputation Nu	mber		В	S.E.	Wald	df	Sig.	Exp(B)	Lower	Upper	Missing Info.	Variance	Efficiency
Original data	Step 1 <sup>a</sup>	Diet			182.820	2	<.001						
		Diet(1)	.545	.055	99.565	1	<.001	1.725	1.550	1.920			
		Diet(2)	069	.065	1.125	1	.289	.933	.821	1.061			
		Constant	698	.047	221.545	1	<.001	.498					
1	Step 1 <sup>a</sup>	Diet			1342.517	2	<.001						
		Diet(1)	1.150	.040	814.128	1	<.001	3.158	2.918	3.418			
		Diet(2)	171	.045	14.217	1	<.001	.843	.771	.921			
		Constant	-1.567	.032	2471.080	1	.000	.209					
2	Step 1 <sup>a</sup>	Diet			395.303	2	<.001						
		Diet(1)	.719	.038	361.754	1	<.001	2.053	1.906	2.211			
		Diet(2)	.217	.051	17.984	1	<.001	1.242	1.124	1.373			
		Constant	-1.585	.031	2655.449	1	.000	.205					
3	Step 1 <sup>a</sup>	Diet			990.356	2	<.001						
		Diet(1)	1.116	.040	780.825	1	<.001	3.051	2.822	3.300			
		Diet(2)	.140	.045	9.615	1	.002	1.150	1.053	1.256			
		Constant	-1.658	.031	2805.313	1	.000	.191					
4	Step 1 <sup>a</sup>	Diet			769.750	2	<.001						
		Diet(1)	.689	.040	297.274	1	<.001	1.991	1.841	2.153			
		Diet(2)	387	.046	70.793	1	<.001	.679	.621	.743			
		Constant	-1.358	.032	1799.851	1	.000	.257					
5	Step 1 <sup>a</sup>	Diet			284.082	2	<.001						
		Diet(1)	.561	.038	217.644	1	<.001	1.752	1.626	1.887			
		Diet(2)	.023	.047	.240	1	.624	1.023	.933	1.122			
		Constant	-1.444	.030	2301.041	1	.000	.236					
Pooled	Step 1 <sup>a</sup>	Diet(1)	.847	.296			.044	2.332	1.036	5.250	.987	56.069	.835
		Diet(2)	036	.272			.902	.965	.461	2.019	.978	32.638	.836
		Constant	-1.522	.135			<.001	.218	.152	.313	.961	17.756	.839

a. Variable(s) entered on step 1: Diet.

# Appendix 17. Data extraction and categorisation of Ethnicity from Electronic health records

Ethnicity labels derived from Electronic Health Records	Categorisation of ethnicity
	White
African - ethnic category 2001 census	Mixed/Multiple ethnic
Bangladeshi	Asian/Asian British
	Blck/African/ Caribbean/Black
Bangladeshi or British Bangladeshi - ethn categ 2001 census	British
Black African	Other/ Arabs
Black African and White	not specified/ missing
Black and Asian - ethnic category 2001 census	
Black British	
Black Caribbean	
Black Caribbean and White	
British Asian - ethnic category 2001 census	
British or mixed British - ethnic category 2001 census	
Caribbean - ethnic category 2001 census	
English - ethnic category 2001 census	
Ethnic category - 2001 census	
Ethnic category not stated - 2001 census	
Ethnic group not recorded	
Ethnicity and other related nationality data	
Indian or British Indian - ethnic category 2001 census	
Irish - ethnic category 2001 census	_
Italian - ethnic category 2001 census	
Oth White European/European unsp/Mixed European 2001 census	
Other - ethnic category 2001 census	
Other Asian background - ethnic category 2001 census	
Other Asian ethnic group	
Other ethnic group	
Other ethnic group: Arab - NI ethnic category 2011 census	
Other European (NMO)	
Other Mixed background - ethnic category 2001 census	
Other White background - ethnic category 2001 census	
Other white ethnic group	
Other White or White unspecified ethnic category 2001 census	
Pakistani	
Pakistani or British Pakistani - ethnic category 2001 census	
Polish - ethnic category 2001 census	
Turkish - ethnic category 2001 census	
Vietnamese - ethnic category 2001 census White	
White and Asian - ethnic category 2001 census	
White and Black African - ethnic category 2001 census	
White British	
White British - ethnic category 2001 census	
White British	
White Irish White Irish - ethnic category 2001 census	

White: Polish - Scotland ethnic category 2011 census	
White:Eng/Welsh/Scot/NI/Brit - England and Wales 2011 census	

# Appendix 18. Resources for Situational Analysis

# Websites

https://klinikhealthcaresolutions.com/how-a-new-type-of-online-triage-solution-istransforming-some-of-uks-gp-practices/

https://www.fom.ac.uk/

https://www.england.nhs.uk/new-care-models/

https://webarchive.nationalarchives.gov.uk/ukgwa/20080818004700/http://www.dh.g ov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH 40 09653

https://www.who.int/news-room/questions-and-answers/item/social-determinants-ofhealth-key-concepts

# Articles, case studies and guidelines

RSPH. (2015). Rethinking the Public Health Workforce. In *Royal Society for public health vision, voice and practice*.

Local Health and Care Record Exemplars A summary, (2018).

Bower, P., Macdonald, W., Harkness, E., Gask, L., Kendrick, T., Valderas, J. M., Dickens, C., Blakeman, T., & Sibbald, B. (2011). Multimorbidity, service organization and clinical decision making in primary care: A qualitative study. *Family Practice*, *28*(5), 579–587. https://doi.org/10.1093/fampra/cmr018

Garg, R., Shen, C., Sambamoorthi, N., Kelly, K., & Sambamoorthi, U. (2016). Type of Multimorbidity and Patient-Doctor Communication and Trust among Elderly Medicare Beneficiaries. *International Journal of Family Medicine*, 2016, 1–13. https://doi.org/10.1155/2016/8747891

Chipidza, F. E., Wallwork, R. S., & Stern, T. A. (2015). Impact of the doctor-patient relationship. *Primary Care Companion to the Journal of Clinical Psychiatry*, *17*(5), 360. https://doi.org/10.4088/PCC.15f01840

NICE. (2016). Community engagement: improving health and wellbeing and reducing health inequalities. *NICE Guideline, March 2016*, 33.

https://www.nice.org.uk/guidance/ng44/resources/community-engagementimproving-health-and-wellbeing-and-reducing-health-inequalities-1837452829381

NICE. (2014). National Institute for Health and Care Excellence Scope. *National Institute for Health and Care Excellence, May*, 1–9. https://doi.org/10.1016/j.apmr.2004.03.032

NICE. (2016). Multimorbidity : clinical assessment and management. 2016, September, 1–18. https://doi.org/10.1016/j.annepidem.2006.10.010

Levenstein, J. H., McCracken, E. C., Mcwhinney, I. A. N. R., & Stewart, M. A. (1986). The patient-centred clinical method 1 a model for the doctor-patient interaction in family medicine. *Family Practice*, *3*(1), 24–30. https://doi.org/10.1093/fampra/3.1.24



#### School of Health, Science and Wellbeing

#### ETHICAL APPROVAL FEEDBACK

Researcher name:	Konstantinos Spyropoulos
Title of Study:	SU_22_033 'Examining the interrelation of Multimorbidity and Multibehaviours in patient complexity.'
Award Pathway:	PhD
Status of approval:	Approved

Thank you for resubmitting your application and addressing the reviewer comments. This was reviewed as an Independent Peer Review application and has now been transferred to a University Ethics application.

Your project *proposal has been approved* by the Ethics Panel and you may commence the implementation phase of your study. You should note that any divergence from the approved procedures and research method will invalidate any insurance and liability cover from the University. You should, therefore, notify the Panel of any significant divergence from this approved proposal. This approval is only valid for as long as you are registered as a student at the University.

You should arrange to meet with your supervisor for support during the process of completing your study and writing your dissertation.

When your study is complete, please send the ethics committee an end of study report. A template can be found on the ethics BlackBoard site.

The Ethics Committee wishes you well with your research.

Signed:

Date: 09.11.2022

& tol

Dr Edward Tolhurst Ethics Co-coordinator for Health, Science and Wellbeing

# Appendix 20. Participant Consent Form

# Title of Project: The role of Multimorbidity and multiple health risk behaviours in patient complexity care

Please tick the appropriate box(es) on the right if you agree with the correspondent statement(s):

-		
1	I confirm that I have read and understood the information sheet for	
	the above study and have had the opportunity to ask questions.	
2	I understand that my personal data are confidential and only the	
	research team involved in the study will have access to it.	
3	I understand and accept that any data collected during the study will	
	be used in scientific reports in an anonymised form.	
4	I confirm that I read and understand the information sheet and I	
	declare that I am eligible to take part.	
5	I understand that my participation is voluntary and that I am free to	
	withdraw at any time (for up to 1 week after my participation),	
	without giving any reason, without my legal rights being affected	
	and requesting that any information I have already given to be	
	destroyed	
6	I agree that the semi structured interviews will be audio-recorded. I	
	understand that this data will be treated confidentially and stored	
	securely	
7	I agree to take part in the above study.	
8	I consent to be contact in future regarding with this or related researc	

Name of participant

Date

Signature

Researcher

Date

Signature

#### **Konstantinos Spyropoulos**

PhD Researcher
Centre for Health and Development (CHAD)
Staffordshire University
☎+44(0) 1785353402
☑ konstantinos. spyropoulos@research.staffs.ac.uk



# Appendix 21. Email invitation for healthcare professionals

Dear colleagues,

This email is coming to you on behalf of Kostas Spyropoulos from our research team at the Centre for Health and Development (CHAD), who is researching multimorbidity, health-risk behaviours and their management.

This research aims to understand the experiences and opinions of health care professionals regarding how people with multiple chronic conditions are managed, and the role of health-risk behaviours, such as smoking, physical inactivity and unhealthy eating. As someone with relevant knowledge and experience, we would be delighted if you would be willing to speak with the research team. Taking part would involve an interview lasting up to 45 minutes over the telephone or MS Teams.

If this might be of interest, or if you would like to know more, please contact Kostas on konstantinos.spyropoulos@staffs.ac.uk .

With very best wishes

#### **Konstantinos Spyropoulos**

PhD Researcher Centre for Health and Development (CHAD) Staffordshire University The +44(0) 1785353402 Konstantinos. spyropoulos@research.staffs.ac.uk

## Appendix 22. Participant Information Sheet (healthcare providers)

### Exploring multimorbidity and multiple health risk behaviours

I am a researcher and PhD student at the Centre of Health and Development (CHAD), Staffordshire University. I am undertaking a study to understand the complexities of providing care and support for people with two or more chronic conditions (otherwise called multimorbidity) who also engage with health risk behaviours (e.g., smoking, physical inactivity).

This information sheet is designed to tell you the purpose of the study, why you have been invited to participate and what would be involved. I would be very grateful if you would take the time to read the following information. Please feel free to contact me if you would like to discuss anything further.

What is the purpose of the study? The purpose of this study is to speak with a range of individuals to better understand the complexities of providing care and support to people with two or more chronic conditions (otherwise called multimorbidity), and who also engage with several health risk behaviours (e.g., smoking, physical inactivity). I will also be speaking with people who have experience of multimorbidity and health risk behaviours, to understand their perspectives.

**Why have I been contacted?** You have been contacted because you are a healthcare professional (e.g., General or Specialist practitioner or Public health doctor, or Nurse) who is likely to have relevant experience and knowledge.

What will I be asked to do if I decide to take part? Initially you will be contacted to check eligibility (ideally, we would like to speak with healthcare professionals with five or more years of experience). If you are willing and eligible, we would ask you to take part in an informal semi-structured interview over the telephone or through MS Teams, lasting up to 45 minutes. During the interview you would be asked questions to help us to understand your experience and perceptions of healthcare and related support for people with multimorbidity and multiple health risk behaviours.

If you are happy to proceed, the researcher will arrange a convenient day/time to speak. Interviews will be audio recorded to ensure that the information has been collected accurately.

**Do I have to take part?** Taking part is voluntary. It is up to you whether to take part. If you decide to participate, then you will be asked to keep this information sheet. Even if you agree to participate you are still free to withdraw from the study at any time (up to 1 week after your participation, when analysis has started) without stating a reason. If you decide to withdraw, then all information already gathered from you will be either kept securely and confidentially or destroyed if you wish. After 1 week, when analysis is underway, it would not be possible to remove data from the overall analysis.

#### Will my data be kept confidential?

All information you provide will be stored securely. Only the researcher and his supervisors will have access to the data collected. To ensure the anonymity of participants, each person who takes part will be assigned a unique identifier. No participants will be identifiable from the results of this work. All electronic data will be stored securely on a password-protected computer at Staffordshire University and any hard copies will be kept in a locked room at the university. All

data will be held for 10 years and treated in accordance with the General Data Protection Regulation (GDPR).

#### What will happen with the results of the study?

This study will provide insight on the the relationship between a healthcare provider and recipient of care when dealing with multimorbidity and multibehaviours. The results of the study will be written up as part of the researcher's PhD and they may be published in academic journals or presented in academic conferences. All results will be reported anonymously so no individuals can be identified. Participants may request to see the study's main results.

#### Who can I contact if I have any questions after taking part?

Participation poses a minimal risk of causing emotional distress. However, if you feel that you have been negatively affected by the study and wish to speak with someone, you can contact an external organization such as Samaritans (08457 90 90 90, <u>jo@samaritans.org</u>) or you can contact the researcher (see contact details below).

#### If you would like any further information, please contact me using the following details:

#### **Konstantinos Spyropoulos**

PhD Researcher Centre for Health and Development (CHAD) Staffordshire University ☎+44(0) 1785353402 ⋈ konstantinos. spyropoulos@research.staffs.ac.uk centre for centre

# Appendix 23. Email invitations (provisional text)

#### a. For members of the public (email to CHAD colleagues in relevant organisations)

Dear XXXX,

I am emailing you to ask if you could help identify potential participants an interview study that I am leading at the Centre for Health and Development (CHAD). This project is about people who have two or more health conditions (multimorbidity) and who might engage in lifestyle behaviours that could be improved (e.g., smoking, being physically inactive, unhealthy eating).

I am keen to interview people in this position to understand their general experiences, experiences of health care and related support for their health problems, and/or support with changing their lifestyle behaviours. Given your links with members of the local community, I had hoped that you might know people in this position who might be willing to speak with me to share their experiences. All those who take part will be offered a **£30 retail voucher** in appreciation of their time.

I would be hugely grateful if you would share the email (below) with any such individuals so that they can contact me directly to learn more about the study, ask questions and perhaps take part (konstantinos.spyropoulos@staffs.ac.uk).

With very best wishes

\*\*\*

#### b. Email /text to be shared with members of the public by organisations

Participants needed

I am a researcher at the Centre of Health and Development (CHAD), Staffordshire University. I am undertaking a study to understand the experiences of healthcare and related support for people who have more than one health condition and perhaps have areas of their lifestyle that they think could be healthier (such as smoking, not being physically active, unhealthy eating).

I am keen to speak with people in this position through an informal interview over the phone or via a video call (Microsoft Teams) to ask about their experiences and thoughts. Including experiences of healthcare and related support. Everyone who takes part will be offered a £30 retail voucher as an appreciation for their time.

If this sounds of interest and you would like to know more, please email me at

konstantinos.spyropoulos@research.staffs.ac.uk

#### With very best wishes

#### **Konstantinos Spyropoulos**

Centre for Health and Development (CHAD) Staffordshire University 2 +44(0) 1785353402 Konstantinos. spyropoulos@research.staffs.ac.uk



# Appendix 24. Participant (members of the public) Information Sheet

### Exploring multimorbidity and health risk behaviours

Thank you for taking the time to read this information sheet. I am a PhD researcher at the Centre of Health and Development (CHAD), Staffordshire University. I would like to invite you to take part in a study that involves speaking with people who have two or more health conditions (also called multimorbidity) and who engage in several behaviours like smoking, physical inactivity, or unhealthy eating.

This information sheet is designed to tell you the purpose of the study, why you have been invited to participate and what would be involved. I would be very grateful if you would take the time to read the following information. Please feel free to contact me if you would like to discuss anything further.

What is the purpose of the study? The purpose of this study is to better understand the experiences and thoughts of people who have several health conditions and explore areas of their lifestyle that can be improved, and to understand their experiences of healthcare and related support. It is hoped that this information can be used to better understand how services could better support people's health and related behaviours.

Why have I been contacted? You have been contacted because you might have relevant experiences in this area. To be eligible you need to be aged at least 18 years old, have more than one health condition and take part in more than one health risk behaviours. I would check this with you by email or over the phone.

What will I be asked to do if I decide to take part? You will be asked to take part in an informal semi-structured interview lasting up to 45 minutes. The purpose is to explore your thoughts and experiences of healthcare and related support for people with multimorbidity and multiple health risk behaviours. Everyone who takes part will be offered a£30 retail voucher in appreciation of your time.

If you are happy to proceed the PhD researcher will arrange a convenient day/time for having an online or telephone interview. Interviews will be audio recorded to ensure that the information has been collected accurately.

**Do I have to take part?** Taking part is voluntary. It is up to you whether to take part. If you decide to participate, then you will be asked to keep this information sheet. Before proceeding, I will contact you to check your eligibility by email or telephone. Even if you agree to participate you are still free to withdraw from the study at any time (up to 1 week after your participation, when analysis has started) without stating a reason. If you decide to withdraw, then all information already gathered from you will be either kept securely and confidentially or destroyed if you wish.

#### Will my data be kept confidential?

All information you provide will be stored securely. Only the researcher and his supervisors will have access to data collected. To ensure the anonymity of participants, each person who takes part will be assigned a unique identifier. No participants will be identifiable from the results of this work. All electronic data will be stored securely on a password-protected computer at Staffordshire University and any hard copies will be kept in a locked room at the university. All

data will be held for 10 years and treated in accordance with the General Data Protection Regulation (GDPR).

#### What will happen with the results of the study?

The findings of this study will help to better understand the complexities that surround the healing relationship between a healthcare provider and recipient under the involvement of the combined effect of multimorbidity and multibehaviours. The results of the study will be written up as part of researcher's PhD and they may be published in academic journals or presented in academic conferences. All results will be reported anonymously so no individuals can be identified. Participants may request to see the study's main results.

#### Who can I contact if I have any questions after taking part?

Participation poses a minimal risk of causing emotional distress. However, if you feel that you have been negatively affected by the study and wish to speak with someone, you can contact an external organization such as Samaritans (08457 90 90 90, jo@samaritans.org) or you can contact the researcher (see contact details below).

#### If you would like any further information, please contact me using the following details:

#### **Konstantinos Spyropoulos**

PhD Researcher Centre for Health and Development (CHAD) Staffordshire University ☎+44(0) 1785353402 ☑ konstantinos. spyropoulos@research.staffs.ac.uk



# Appendix 25. Provisional semi-structured interview topic guide (members of the public)

#### Introduction

Thank you for participating in this interview. Before we start, I would like to explain some aspects of the process.

Our discussion, in a semi-structured interview form, will cover various topics that relate to your health, lifestyle and related treatment or support. If anything is unclear as we go through, or if you need further clarification, please let me know. There are no right or wrong answers.

Finally, to ensure that I can reflect our discussion accurately and do not miss anything, the interview will be audio recorded.

#### Interview Schedule:

- Multimorbidity: Illness perception
- Could you tell (as a brief story) how is your health?
- What are your main health issues? When did they develop? (prompt: how long, causes (genetic, lifestyle, etc.)
- How do these conditions affect you on a daily basis (if at all?)
   (prompt: combined effect, different priorities between treatment of your chronic diseases?)

#### • Multimorbidity treatments and management

- Could you tell me what treatments you are on or have been recommended by your doctor or other health/medical professionals?
- Do these treatments affect your life? How?
- Multimorbidity -Multibehaviours and/or other sources of complexity
- What changes to your lifestyle behaviours have you made (if any) to try to manage your conditions? Please explain.
- How does the need to adapt your behaviour affect you?
- Do you experience any difficulties when trying to implement your doctor's or other health/medical professionals self-care recommendations? What sort of challenges?
- What do you do when these difficulties appear?
- Are there any other issues that may intervene and complicate your efforts to manage your health conditions, the progression of your treatment or your efforts toward the acquisition of healthier lifestyle(s)? Please explain (example prompts if needed: financial, employment, educational, familial, political neighbourhood, town/city)
- How your doctor or other medical health professionals support you to confront these or other issues that complex your treatment further?

#### • Healthcare provider-recipient relationship

- What else can you tell about your relationship with your doctor or other medical health/medical professionals in relation to your health conditions and/or efforts to adapt your lifestyle behaviours?
- Are there any areas in which you would like more support? Prompts: perhaps from your healthcare professional, perhaps others if they are not able to help with all aspects.
- Is there anything else that you would like your healthcare providers to support you with, that they currently do not (or cannot)? Please explain=

# Appendix 26. Provisional semi-structured interview topic guide for (healthcare providers)

#### Introduction

Thank you for participating in this interview. Before we start, I would like to explain some aspects of the process. Our discussion, in a semi-structured interview form, will cover various topics that relate to multimorbidity and lifestyle and how these two independently and combined complex care and progress of treatment. If anything is unclear as we go through, or if you need further clarification, please let me know. There are no right or wrong answers.

Finally, to ensure that I can reflect our discussion accurately and do not miss anything, the interview will be audio recorded.

#### **Interview Schedule:**

- Patient complexity Healthcare provider-recipient relationship
- What issues in your experience can intervene within the healing relationship, between healthcare provider and recipient with multimorbidity that still engage with multiple health risk behaviours, that complicate the treatment process ?
- Multimorbidity multibehaviours and patient complexity treatments and management
- How, in your experience, the need for a change towards a healthier lifestyle in a patient with multimorbidity, (e.g., stop smoking and improve dietary behaviours affects multimorbidity treatment? Do you have any examples?
- Does the combination of the medical and behavioural support needs of patients complicate their care provision?
- What are the difficulties in managing this?
- What do you do when these difficulties appear?
- Multimorbidity Multibehaviours and/or other sources of complexity
- Are there any parts of this that are outside your remit or go beyond your healthcare professional patient relationship?
- How could this be improved?
- Are they any other issues that complicate your efforts to deal with your patients' multimorbidity, the progression of their treatment or their efforts change their behaviour(s)? Please explain

# Appendix 27. Participant debrief form

Dear Participant,

Thank you for participating in this study. The aim of this study is to help us understand how multimorbidity (the acquisition of 2+ chronic diseases) and multibehaviours (the involvement of someone with two or more health risk behaviours such as smoking, physical inactivity, bad diet and excess alcohol usage) complex the healthcare provision and treatment.

Your name will be replaced with a pseudonym (replacement name) where appropriate. Your details of participation will not be shared with anyone else. In case of the research being published, pseudonym will be used in placement of your real name so that you are not identifiable.

As stated in the participant information sheet, you still have the right to withdraw from the research at any time (up to 1 week after your participation, when analysis has started) without stating a reason. If you would like to withdraw from the research, please email the researcher on the contact details below and your information will be destroyed.

If you would like to know more about my results or you have any questions/concerns about the research, you can email me on: <u>konstantinos.spyropoulos@research.staffs.ac.uk</u>

Furthermore, contact details of an external counselling organisation have been provide to you (in Participant information sheet) as further support in a case you feel that you have been negatively affected by your participation and you need to seek further counselling advice.

## **Konstantinos Spyropoulos**

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# Appendix 28. Focus group topic guide (members of the public)

#### Introduction

Thank you for participating in this interview. Before we start, I would like to explain some aspects of the process.

Our discussion will cover various topics that relate to your health, lifestyle and related treatment or support. If anything is unclear as we go through, or if you need further clarification, please let me know. There are no right or wrong answers.

Finally, to ensure that I can reflect our discussion accurately and do not miss anything, the interview will be audio recorded.

**Q1** What are they key factors that still makes you to engage with health risk behaviours and how healthcare professional try to address them? (do they checked only your health conditions? Do they ask about health risk behaviours, advices etc)

**Q2** How do you perceive the role of healthcare professionals in relation to the support they provide to manage your health conditions and your involvement with health risk behaviours? In short you experiences with healthcare professionals

(advice, felt judged, stigmatised, supportive, humane with genuine interest)

Do they and how establish a trusting and supportive relationship with you

Do they manage to balance the need to advice toward needed behavioural change respecting your autonomy and self-determination?

**Q3** Do multiple chronic conditions change health risk behaviors relative to your conditions? (otherwise, what barriers you face that prevent you from initiating behaviour change) Are there any other issues that may intervene and complicate your efforts (prompts: financial, employment, educational, familial, political neighbourhood, town/city)

**Q4** How support (if at all) to overcome these challenges. (e.g., what are the most effective strategies that they apply to promote behaviour change)

Q5 how healthcare professionals help you to prioritise and manage your health risk behaviours.

In your experience what were the most effective ways that healthcare professionals apply to you in order to motivate you to make change. For example, do they adjust their professional language -terminology and support (e.g. more time) to

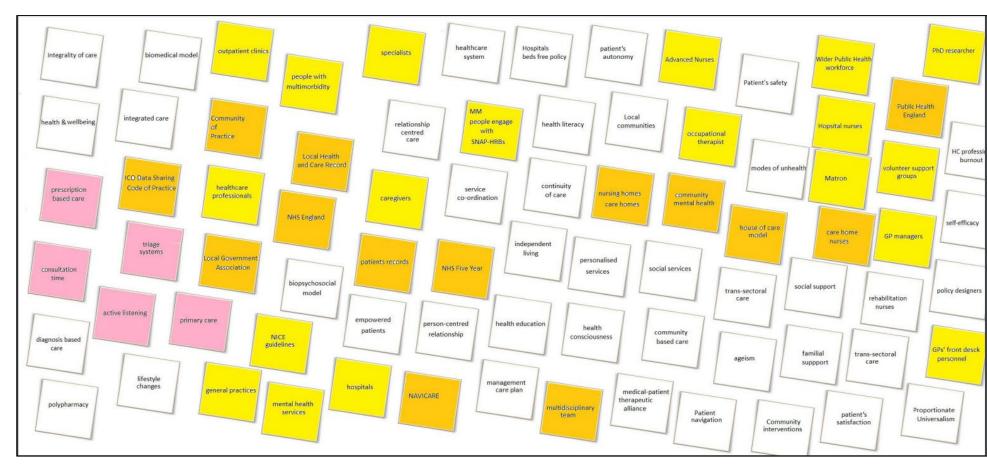
**Q6** How, healthcare professionals (if at all) evaluate the effectiveness of their recommended interventions

**Q7** How if at all healthcare professionals coordinate care and services in order to support the best possible management of your conditions and/or your need to manage the acquisition of healthier lifestyle (as part of your health behaviour change)

**Q8** In your opinion, what changes could be made to the healthcare system to better support patients with multiple chronic conditions and health risk behaviors?

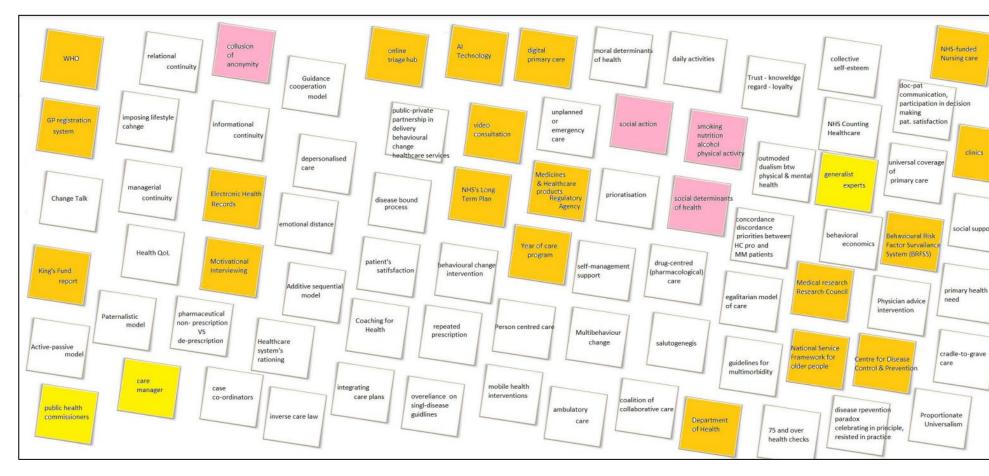
٨	В	C Desistificing stability of VC	D	E	F	G	н	1	J	к	L	м	N	0	P	۵	R	
t integrality of care VS symptomatology		B prioritizing problems ¥S additive sequential decision making		C continuity of care VS triage access		D comprehensive VS disease base care		E prognosis VS diagnosis based	care	F integrated care VS fragmented		G drug based vs well-b	eing car	proactive vs reactive care		social vs moral determinants		
ntegration patient's needs that merge during interview to orvision of care		short visits make patients feel that doctor do not provide all information		Establishment of Long term relationships		Integrality in medicine: committed to the total person rather than particular body of knowledge, group, disease or special technique		Focus on prognosis as marker of psycho-social factors		Multidisciplinary team		rationalization of pharmacological prescription						
Interview as a means to reconstruct MM patient's life to uncover the root of pathology		Common understanding on master problems		Consideration of barriers to optimal care and educaiton		Focus on collaboration (co- evaluaiton of knowledge and health patterns)		The course of disease is influence concurrently by psychosocial factors		GP must lead patient's care team and be responsible for its care co-ordination		pharmacological non- prescription and pharmacological de- prescription						
No contact a sick person but live expertise		not being perceived in hurry		regular s vs emergeno <del>g</del> appointment		single based HC system		porgnosis of disease depends more on psychosocial rather than biomedical factors				relation to a drug centred one masking other significant access of medical						
comprehensive vision of the patient (take into account the interrelatinships of df dimensions of person. See the whole greater than the sum bio- psgeho-social				BAD COMMUNICATION				Prognosis is determined by more than disease diagnosis (people with same diagnosis have df porgnosis)				poypharmacy not to lead to docot absent ot doctor to be seen as drug itself						
disease from biomedical point of view masking other equally important issues for MM patient								no diagnosis driven										
Important issues for MM patient Avoid focusing on complete remission of symptoms but on achieving a good level of autonomy and QoL																		
assess-advice consulation model																		
P13(A3/A7) P112(A7)	A7 A7 A7		B1 B1	P11(C3) P12(C2) P14-5(C1)	C3 C2 C1	P1(D1)	01	P19(E5) P10(E5)	E5	P117 (F) P118 (F)	F	P117 (G)	G	P115 (01)	0	P123Q P114Q	Q	P120
P112(A7) P128 A P116(A7)	A7 A7	P126B	B1 B1		CT C			P111(E5) P113-14(E5)	E5 E5 E5 E5	P117 (F) P118 (F) P125 F P127F	F							
				P121C P122C	000													P1 sees that HRB change is basic
P21(A3)	A3	P2 27 (B2)	B2			P2 43 (D2) D2 P2 36 (D1) D1	02	P28(E2)	E2	P2 9(F1)	FI	P26(G)	G			P24(Q)		P2 sees that HRB change is bas
P2 2 (A3) P2 13 (A7)	A3 A7	P2 30 (B2) P2 31(B2) P2 32 (B2)	B2 B2 B2 B2	P2 20 (C2) P2 37 (C2)	C2 C2 C2	P2 36 (D1)	01	P211(E2) P214(E-Q) P215(E)	E2 E2 E2 E E	P12 (F1) P2 28 (F1) P2 29 (F1)	F1 F1	P2 21(G) P2 23(G)	G G			P210(Q) P214(E-Q)		
		P2 35 (B2)	B2					P2 32 (E) P2 33 (E)	E									
P32(A2) P33(A3) P311(A6) P312(A7)	A2 A3	P3 13 (B2-D1)	B2	P31(C1) P34(C1) P310(C2)	C1 C1	P3 13 (B2-D1) P3 18 (D1-Q)	01 01	P314 (CI-E-Q)	E							P314(C1-E-Q) P318(D1-Q) P318(D1-Q)	0000	P3 - 8 sees that HRB change is b P3 - 16 Generation pattern, older p
P312(A7) P315(A7)	A6 A7 A7			P314 (C1-E-Q) P317 (C1)	C2 C1 C1											1310(044)	a.	
	A4				C2			P4 15 (E3)	E3	P413(F)		P4 20 (G)	G			P418(Q)	Q	SNAP so age of patient and the P4 12 12 HBBs are common det
				P43(C2)	C2					P4 16 (C1 - F)	F							patient. Feeling despair on how t P4 21 The major challenge is to those who do not, that will proto
				P43(C2)	C2					P4 19 (F) P4 29,30,31,33 (F)	F							as they will have bad prognosis to give them more time.
				P46(C1) P46(C1) P48(C2) P49(C1)	C2 C1 C2 C2 C1 C1 C1			P511(E)	Е	P4 29,30,31,33 (F) P5 12 (F) P5 13 (F)	F							
				P4 9 (C1) P4 16 (C1 - F) P4 34 (C2)	C1 C1													
				P4 35 (C2) P4 37 (C2) P4 38 (C2)	C2 C2 C2 C2 C2 C2 C2 C2													
P51(A2)	A2			P5 15,16 C2 P5 19 C1	C2 C1			P56E P517E P521E	E E	P5 5,8,9 (F) P5 18 (F)	F			P5220	0			P52,3 MM is common and ME
P61A2	A2	P612B2	B2	P67C1	C1	Pp6 D	)		E	P63b	5					P6	Q	P65 only MM patients
P63A7	1	P6 43 B2 P6 47 B1	B2 B1	P6 8, 9,10 C1 P6 16 C1	C1 C1			P6 17E P6 31, 32	E	P64 P628F	$\vdash$							p6 btw 5-6 the conjunction of se are responsible for the increase P6 comorbidity preferable termi
		P6 48 B1	BI							P6 29 F1	F1 F1							P6 13 Small proportion of patier and still they don't want to apply
				P6 27 C2 P6 30 C2 P6 37,38	C2 C2 C2 C					p6 45 f1 P6 46 F P6 49 F	F							P6 14 Intervention process for th HC system is enough to provide
P73A1,A4	A1,A4	P712B2	B2 B2	P6 40, 42 C		P710D D	)	P711E	E	P77F	F	P723G	G	P7 39	0	P7 btw 16-17	Q	p7 Comorbidity as terminology P7 13 Motivation is seen as the
P74A2 P745A3-B	A2 A3	P715B2	-		C1 C					P724F P744F	F			P740	0	P734	Q	moving forwards, I'll learn by I'm
TTURA B	A3	PTROATE	62	P7 18 C1	C1						-							cases very unhelpful. P7 39 not necessary that all MM to secondary gains linking to beh
				P7 22 C2	C2													comorbidity preferable term

# Appendix 29. Screenshot to illustrate coding system



## Appendix 30. Situational Analysis messy map

#### ... continued.



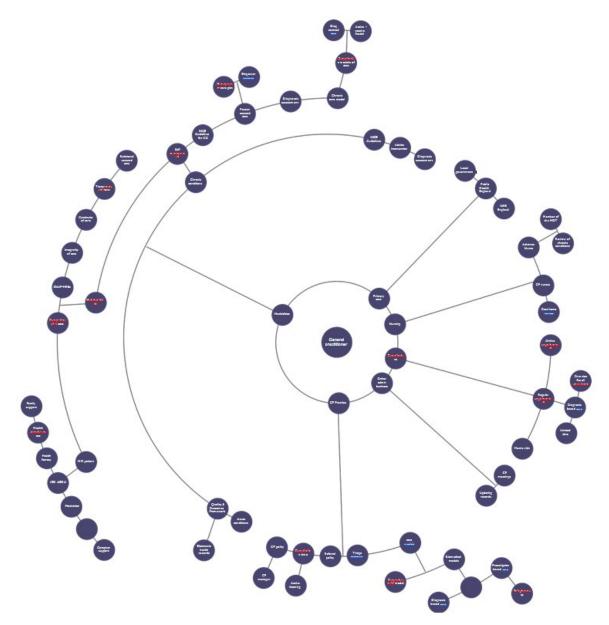
Individual Human Elements/Actors	Nonhuman Elements/Actants
e.g., key individuals and significant	e.g. technologies; material infrastructures;
(unorganized people in situation, including	specialized information and/or knowledges;
the researcher(s)	material "things"
	Quality & Outcomes Framework
People with Multimorbidity	Chronic care model
People engage with SNAP-HRBs	Electronic Health records
Multimorbidity patients	NICE guidelines
(still engaged with SNAP or need MB	Motivational Interviewing
change)	Behavioural change interventions
Caregivers	General Practices
Families of people with MM	Hospitals
PhD researcher	Mental health clinics
	Outpatients' clinics
	Care & nursing homes
	ICO Data Sharing Code of Practice
	King's Fund reports
	NHS England
	Public Health England
	NHS Five Years program
	AI Technology
	Online triage hub
	Digital primary care
	NHS Long Term Plan
	Year of Care program
	Behavioural Risk Factor Surveillance
	System
	Local Health Records
	Multidisciplinary Teams
	NAVICARE
	House of Care model
	GP registration system
	Medical Research Council
	National Service Framework for older
	people Centre for Disease Control & Prevention
	NHS - Funded Nursing care
Collective Human /Actors	Community of Practice training
Collective Human/Actors	Implicated/Silent Actors/Actant As found in the situation
e.g., particular groups; specific	
organizations	Family members
	Family members
General practitioners (experts)	Caregivers
GP managers	Digital and phone care
Specialists	SNAP-HRBs
Occupational therapists	Social media
Advanced nurses	
Hospital nurses	
Care home nurses	
Rehabilitation nurses	
policy designers	
Matron	

# Appendix 31. Situational Analysis Ordered map

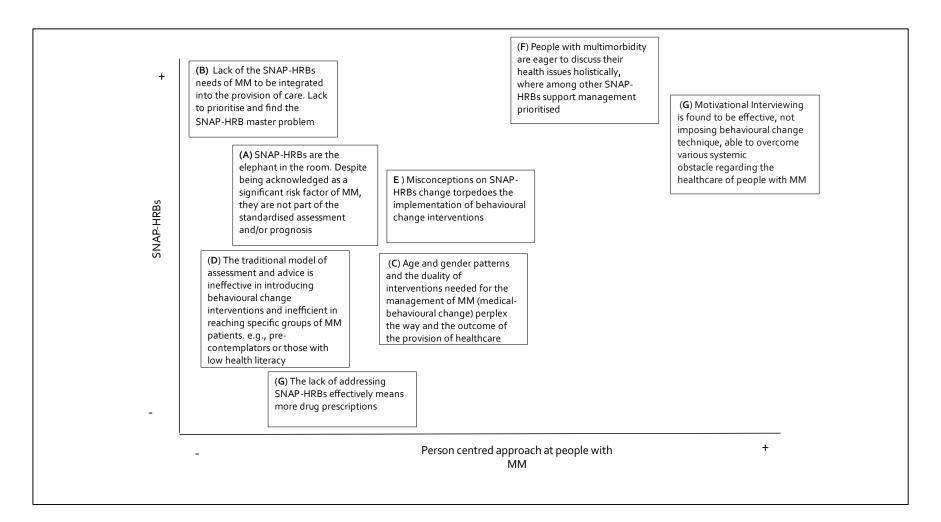
GP managers	
GP front desk personnel	
Volunteer support groups	
Wider Public health workforce (Housing	
Associations, allied health professionals,	
community pharmacists, Sports/fitness	
professionals, volunteer sector support	
groups)	
Pharmacists	
Public health commissioners	
Care manager	
Local Government Association	
Medicines & Healthcare Regulatory	
Agency	
WHO Demonstrate of Health	
Department of Health	
Royal College of General Practitioners Discursive Constructions of Individual	Discursive Constructions of Nonhuman
	Discursive Constructions of Nonnuman
and/or Collective Human Actors	
As found in situation	As found in the situation House of care model
Patient	
Co-production	Local and Health care records
Therapeutical Alliances	Pharmaceutical non-prescription VS de-
Preventative – curative medicine	prescription
Stigma & marginalization Mental health	Online triage
	Joined preventative and curative medicine framework
Social support	Social Action
Individualization (accountability –	
responsibility)	Salutogenesis Iatrogenesis
	Healthism
	inverse care law
	collusion of anonymity
Delitical / Feenemie Flaments	Sociocultural / Symbolic Elements
Political / Economic Elements	
e.g., the state, particular industry/ies;	e.g., religion; race; sexuality; gender;
e.g., the state, particular industry/ies; local/regional/global orders; political	e.g., religion; race; sexuality; gender; ethnicity; nationality; logos; icons; other
e.g., the state, particular industry/ies;	e.g., religion; race; sexuality; gender;
e.g., the state, particular industry/ies; local/regional/global orders; political parties; NGOs; politicized issues	e.g., religion; race; sexuality; gender; ethnicity; nationality; logos; icons; other visual and/or aural symbols
e.g., the state, particular industry/ies; local/regional/global orders; political parties; NGOs; politicized issues Healthcare in Staffordshire	e.g., religion; race; sexuality; gender; ethnicity; nationality; logos; icons; other visual and/or aural symbols Equality & inclusion strategy 2015-2017
e.g., the state, particular industry/ies; local/regional/global orders; political parties; NGOs; politicized issues Healthcare in Staffordshire Hospital discharge (beds free) policy	e.g., religion; race; sexuality; gender; ethnicity; nationality; logos; icons; other visual and/or aural symbols Equality & inclusion strategy 2015-2017 Care Act 2014
e.g., the state, particular industry/ies; local/regional/global orders; political parties; NGOs; politicized issues Healthcare in Staffordshire Hospital discharge (beds free) policy NICE	e.g., religion; race; sexuality; gender; ethnicity; nationality; logos; icons; other visual and/or aural symbols Equality & inclusion strategy 2015-2017 Care Act 2014 Social determinants of health
e.g., the state, particular industry/ies; local/regional/global orders; political parties; NGOs; politicized issues Healthcare in Staffordshire Hospital discharge (beds free) policy NICE Public Health England	e.g., religion; race; sexuality; gender; ethnicity; nationality; logos; icons; other visual and/or aural symbols Equality & inclusion strategy 2015-2017 Care Act 2014 Social determinants of health Triage accessing system
e.g., the state, particular industry/ies; local/regional/global orders; political parties; NGOs; politicized issues Healthcare in Staffordshire Hospital discharge (beds free) policy NICE Public Health England Coalition for collaborative care	e.g., religion; race; sexuality; gender; ethnicity; nationality; logos; icons; other visual and/or aural symbols Equality & inclusion strategy 2015-2017 Care Act 2014 Social determinants of health
e.g., the state, particular industry/ies; local/regional/global orders; political parties; NGOs; politicized issues Healthcare in Staffordshire Hospital discharge (beds free) policy NICE Public Health England	e.g., religion; race; sexuality; gender; ethnicity; nationality; logos; icons; other visual and/or aural symbols Equality & inclusion strategy 2015-2017 Care Act 2014 Social determinants of health Triage accessing system
e.g., the state, particular industry/ies; local/regional/global orders; political parties; NGOs; politicized issues Healthcare in Staffordshire Hospital discharge (beds free) policy NICE Public Health England Coalition for collaborative care King's Fund WHO	e.g., religion; race; sexuality; gender; ethnicity; nationality; logos; icons; other visual and/or aural symbols Equality & inclusion strategy 2015-2017 Care Act 2014 Social determinants of health Triage accessing system
e.g., the state, particular industry/ies; local/regional/global orders; political parties; NGOs; politicized issues Healthcare in Staffordshire Hospital discharge (beds free) policy NICE Public Health England Coalition for collaborative care King's Fund	e.g., religion; race; sexuality; gender; ethnicity; nationality; logos; icons; other visual and/or aural symbols Equality & inclusion strategy 2015-2017 Care Act 2014 Social determinants of health Triage accessing system
e.g., the state, particular industry/ies; local/regional/global orders; political parties; NGOs; politicized issues Healthcare in Staffordshire Hospital discharge (beds free) policy NICE Public Health England Coalition for collaborative care King's Fund WHO Local Government Association NHS	e.g., religion; race; sexuality; gender; ethnicity; nationality; logos; icons; other visual and/or aural symbols Equality & inclusion strategy 2015-2017 Care Act 2014 Social determinants of health Triage accessing system
e.g., the state, particular industry/ies; local/regional/global orders; political parties; NGOs; politicized issues Healthcare in Staffordshire Hospital discharge (beds free) policy NICE Public Health England Coalition for collaborative care King's Fund WHO Local Government Association NHS Department of Health	e.g., religion; race; sexuality; gender; ethnicity; nationality; logos; icons; other visual and/or aural symbols Equality & inclusion strategy 2015-2017 Care Act 2014 Social determinants of health Triage accessing system
e.g., the state, particular industry/ies; local/regional/global orders; political parties; NGOs; politicized issues Healthcare in Staffordshire Hospital discharge (beds free) policy NICE Public Health England Coalition for collaborative care King's Fund WHO Local Government Association NHS	e.g., religion; race; sexuality; gender; ethnicity; nationality; logos; icons; other visual and/or aural symbols Equality & inclusion strategy 2015-2017 Care Act 2014 Social determinants of health Triage accessing system
e.g., the state, particular industry/ies; local/regional/global orders; political parties; NGOs; politicized issues Healthcare in Staffordshire Hospital discharge (beds free) policy NICE Public Health England Coalition for collaborative care King's Fund WHO Local Government Association NHS Department of Health Pharmaceutical companies	e.g., religion; race; sexuality; gender; ethnicity; nationality; logos; icons; other visual and/or aural symbols Equality & inclusion strategy 2015-2017 Care Act 2014 Social determinants of health Triage accessing system
e.g., the state, particular industry/ies; local/regional/global orders; political parties; NGOs; politicized issues Healthcare in Staffordshire Hospital discharge (beds free) policy NICE Public Health England Coalition for collaborative care King's Fund WHO Local Government Association NHS Department of Health Pharmaceutical companies National Voices	e.g., religion; race; sexuality; gender; ethnicity; nationality; logos; icons; other visual and/or aural symbols Equality & inclusion strategy 2015-2017 Care Act 2014 Social determinants of health Triage accessing system
e.g., the state, particular industry/ies; local/regional/global orders; political parties; NGOs; politicized issues Healthcare in Staffordshire Hospital discharge (beds free) policy NICE Public Health England Coalition for collaborative care King's Fund WHO Local Government Association NHS Department of Health Pharmaceutical companies National Voices	e.g., religion; race; sexuality; gender; ethnicity; nationality; logos; icons; other visual and/or aural symbols Equality & inclusion strategy 2015-2017 Care Act 2014 Social determinants of health Triage accessing system
e.g., the state, particular industry/ies; local/regional/global orders; political parties; NGOs; politicized issues Healthcare in Staffordshire Hospital discharge (beds free) policy NICE Public Health England Coalition for collaborative care King's Fund WHO Local Government Association NHS Department of Health Pharmaceutical companies National Voices	e.g., religion; race; sexuality; gender; ethnicity; nationality; logos; icons; other visual and/or aural symbols Equality & inclusion strategy 2015-2017 Care Act 2014 Social determinants of health Triage accessing system

Temporal Elements	Spatial Elements
e.g., historical, seasonal, crisis, and/or	e.g., space in the situation, geographical
trajectory aspects	aspects, local, regional, national. Global
	spatial issues
Single (acute) disease based healthcare	
system	Healthcare in Staffordshire
Biomedical model	NHS policy of universal coverage of
Bio-psycho-social model	primary care
Person centred approach	
Chronic care model	
Kaiser Permanente's Pyramid model	
Disease based approach	
Single-appointment policy	
75+ health checks	
Major Issues /Debates (Usually Contested)	Related Discourses (Historical, Narrative, and/or Visual)
As found in the situation; and see positional	e.g., normative expectations of actors,
map	actant, and/or other specified elements;
	moral/ethical elements; mass media and
Healthcare system's rationing	other popular cultural discourses; situation-
Diagnosis VS prognosis	specific discourses
Patients' safety and satisfaction	
Person centred care VS disease centred	emotional intelligence of healthcare
care	providers
Preventative & curative medicine	social media peer groups
Non-prescription VS de-prescription	Proportionate Universalism
Inverse care law	Social support
Depersonalized care	Empathy
Fragmented care	Social action
Cradle-to-grave care	Change Talk
Individualization of responsibility	Collusion of anonymity
Lack of accountability	Health related QoL
Reliance of single-disease guidelines	Salutogenesis VS latrogenesis
Stigma - blaming	Healthism
Patient complexity	
Multimorbidity management complexity	
Self-management	
Other Kinds of Elements	
As found in the situation	
AI healthcare	

Appendix 32. Situational Analysis Relational map



#### **Appendix 33. Situational Analysis Positional Maps**



	(A) Market and commercial world advertisements are more effective than health messages advertised by NHS	( <b>D</b> ) When proper consultation time allows the implementation of more person-centred care and acts as a damage control
	(B) MM pat and socially constructed narratives such as "the magic pill" and "quick fix and furthermore sabotaging any form of behavioural health innervation	mechanism to the systemic failures of the healthcare system that people with multimorbidity experience in their contact with it
<ul> <li>(D) Limited consultation time <ul> <li>a) Focus on diagnosis rather than prognosis,</li> <li>prioritisation of master problem</li> <li>a) Based on the single-disease guidelines instead to comprehensively addressing the needs of people with MM</li> <li>d) Depends on referral policy and perpetuates fragmented care</li> <li>e) Increase MM pat unsafety (perpetuating polypharmacy)- decreasing their engagement (leaving the responsibility of MM management and SNAP-HRB change solely to MM pat)</li> <li>f) transformation of healthcare relationship between doctor and MM patient to drug relationship- perpetuating the un-healthiness of</li> </ul> </li> </ul>	(C) Consultation has been transformed into a ticking box exercise that alienates both parts of the healing relationship and torpedoed the establishment of any therapeutic alliance while leaving the responsibility for self management to MM pat	
Per	son centred approach at people with MM	+

-	D) Shift treatment toward the idea of treating people rather than their morbidities. Emphasising that the improvement of their wellbeing will be reflected in health outcomes.	A) An emerging trend of MM pat. and HC pro (mostly community specialists) challenge the overreliance on medication prescription resisting to prolonged use of medication and/or polypharmacy advocating for de prescription especially in addressing mental health concerns	D) A subtle role of politics and pharmaceutical companies, that run the current system, to perpetuate this model of unhealth for financial reasons, it perpetuates the construct of "responsible patient", diminish accountability from healthcare system systemic failures C)Internalizationof medicalization sabotages the implementation of any person-centred approach, shifting healthcare relationships to drug relationships, increasing the risk to patient safety through polypharmacy.
	-	latrogenesis	т

+ Care	Shift treatment of MM-MB pat toward Salutogenesis, the idea of treating people rather than their morbidities. Emphasising that the improvement of their well-being will be reflected in health outcomes. In this sense MM-MB integrated framework must be a primarily focus - RCC the medium	Medicalisation overshadows forms of interventions (e.g., SNAP-HRBs that mostly to well-being) to be part of an equivalent standardised perpetuating the construct of "responsible patient", taking accountability form services and leaving the burden of self- management to people with multimorbidity	A subtle role of politics and pharmaceutical companies, that run the current system, to perpetuate this model of unhealth for financial reasons
-		Monomorbit HC system unable to provide proper level of care and cure able to address the needs of M-MB pat. Perpetuating the power imbalances between Secondary care and Primary care and doctors-MM patients relationships	Limited time sabotage the implementation of person-centred and Integrality care leading to overreliance to prescription as main MM treatment approach with twofold consequences. A) turning most of HC relationship to drug relationships, B) it leads to polypharmacy and consequences of iatrogenesis by risking patient safety
			+
	-	Cure	