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Protocol for a mixed methods study to optimise medication management for polymedicated home-dwelling older adults with multiple chronic conditions

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1   **ABSTRACT**

2   **Introduction:**

3   Optimal medication management is one of the basic conditions necessary for home-dwelling

4   older adults living with multiple chronic conditions (OAMCC) to be able to remain at home

5   and preserve their quality of life. Currently, the reasons for such high numbers of emergency

6   department visits and the very significant rate of hospitalisations for OAMCC, due to

7   medication-related problems, is poorly explored. This study aims to reveal the current state of

8   medication management practices of polymedicated home-dwelling OAMCC and to make

9   proposals for improving clinical and medication pathways through an innovative and integrated

10   model for supporting medication management and preventing adverse health outcomes.

11   **Methods and analysis:** A mixed methods study will address the medication management of

12   polymedicated, home-dwelling OAMCC. Its explanatory sequential design will involve two

13   major phases conducted sequentially over time. The quantitative phase will consist of

14   retrospectively exploiting the last five years of electronic patient records from a local hospital

15   (N ≈ 50,000) in order to identify the different profiles—made up of medication and

16   environment-related factors—of the polymedicated, home-dwelling OAMCC at risk of

17   hospitalisation, emergency department visits, hospital readmission (notably for MRPs),

18   institutionalisation or early death. The qualitative study will involve: a) obtaining and

19   understanding the medication management practices and experiences of the identified profiles

20   extracted from the hospital data of OAMCC who will be interviewed at home (N ≈ 30); b)

21   collecting and analysing the perspectives of the formal and informal caregivers involved in

22   medication management at home in order to cross-reference perspectives about this important

23   dimension of care at home.

24   **Ethics and dissemination :** Ethical approval has been obtained from the Human Research

25   Ethics Committee of the Canton Vaud (2018-02196). Findings will be disseminated in peer-

26   reviewed journals, professional conferences and other knowledge transfer activities with

27   primary healthcare providers, hospital care units, informal caregivers' and patients'

28   associations.

29   **Keywords**

30   Polymedication, home-dwelling older adults, multiples chronic conditions, medication

31   management, mixed methods research, protocol, medication-related problems, hospitalisation,

32   retrospective review

33 **Strengths and limitations of this study**

34 • This mixed methodology will rely on a closely coordinated combination of methods and

35 on the utilization of valuable existing data under-exploited to date (electronic patient

36 records and Resident Assessment Instrument-Home Care data).

37 • The investigation draws upon an interprofessional and interdisciplinary approach,

38 which associates general practitioners, community health care nurses, pharmacists and

39 researchers in health psychology, old age psychiatry, nursing and survey methodology.

40 • Our findings will contribute to the development of an evidence-based and innovative,

41 cooperative model of medication management for polymedicated home-dwelling older

42 adults with chronic conditions.

43 • The study will be conducted in a single canton and its generalizability to other regions

44 should be done with precaution.

45

INTRODUCTION

46

47 The number of older adults living at home with multiple chronic conditions (OAMCC) rises

48 considerably around the world and has been estimated to affect 25.2% of people aged from 65

49 to 79 and 41.3% of those aged 80 and over.[1]

50 These long-term health conditions require taking multiple medications[2], known as

51 polypharmacy (PP) when the daily intake corresponds to five or more medicines.[3]

52 Polypharmacy places older adults at higher risk of medication-related problems (MRPs),

53 including adverse medication reactions, medication errors and potentially inappropriate

54 medications.[4 5] Potentially inappropriate medications are the intake of medicines for which the

55 associated risks outweigh the potential benefits, particularly when more effective alternatives

56 are available.[6] Consequently, MRPs can lead to a degradation of the patient's clinical condition,

57 physical and cognitive decline, an exacerbation of chronic medical conditions and avoidable

58 health costs.[7 8] Moreover, up to 25% of emergency department visits by home-dwelling

59 OAMCC are due to MRPs.[7] However, 60% of MRPs in patients visiting the emergency

60 department with non-specific complaints (such as weakness) may go undiagnosed, whereas

61 83% of those MRPs may be responsible for acute morbidity.[7] MRPs are also a frequent cause

62 of readmission, and they were the most frequent cause in one study that followed older patients

63 for six months after hospital discharge.[9] Care-coordination problems, associated with low or

64 suboptimal medication management, are all the more evident in the sensitive period of

65 discharge home from hospital.[8 10] The complexity of OAMCC' care needs leads them to be

66 significant users of health services and to consult many different health care professionals.[11]

67 The number of health care professionals consulted by home-dwelling OAMCC has been

68 directly associated with fragmented and uncoordinated care.[10] Moreover, different health care

69 professionals may have different treatment preferences. Failure to coordinate care among

70 home-dwelling OAMCC contributes to MRPs.[10]

71 In addition to role of health care professionals in medication management, informal caregivers

72 play a vital role in ensuring safe and appropriate medication use by home-dwelling OAMCC,

73 especially among those who may also have cognitive impairment.[12-14] Despite the important

74 role of informal caregivers in medication management, several complications to do with their

75 activities have been documented in relation to the time spent, anxiety making a mistake and the

76 uncooperative behaviour of the home-dwelling OAMCC.[15] They are also confronted with

77 difficulties in maintaining continuous supplies of medication, assisting with administration,

78 making clinical judgements (e.g. in response to side effects and about over-the-counter

79 medication), and solving conflictual communications or disagreements with the older adult[15],

80 or even with health care professionals, with regards to ineffective and addictive medication

81 practices.[12 15]

82 Nonetheless, many MRPs are preventable.[5 7 16] Studies about medicine-related hospitalisations

83 suggest that up to 58% may be preventable with appropriate primary care.[5] An essential strategy

84 for medicine-related hospitalisations prevention and medication safety is medication

85 reconciliation - the process of creating and maintaining a single list of the patient's current list

86 of medications.[17] This process allows a systematic and comprehensive review of all the

87 medications the patient is taking, reducing medication errors by a consistent communication

88 across transitions of care.[18]

89 Therefore, optimising medication management among home-dwelling OAMCC requires

90 regular monitoring of MRPs, interprofessional collaboration across different health and social

91 care providers, organisations and departments[10] and medication reconciliation at every

92 transition of care including changes in the clinical setting, practitioner, or level of care.[19]

Aim and Objectives

94 The study aim is to document the current state of medication management practices of

95 polymedicated home-dwelling OAMCC and to make proposals for improving clinical and

96 medication evidence-based pathways through an innovative and integrated model intended to

97 support medication management and to prevent adverse health outcomes. To achieve this aim,

98 three main objectives will guide this project:

99 The first objective is to carry out a **retrospective analysis of patients' hospital records**, their

100 medication and environment-related factors in order to identify those that increase the risk of

101 hospitalisation, emergency department visits, hospital readmission (notably due to MRPs),

102 institutionalisation or early death, among home-dwelling polymedicated OAMCC—factors that

103 prevent OAMCC from staying at home.

104 The second objective is to use **a prospective qualitative study** to explore and better understand

105 **the medication experiences and practices of home-dwelling OAMCC with different**

106 **profiles**. We seek to identify the skills and strategies developed by them to manage

107 polymedication within their social contexts and health trajectories despite possible cognitive

108 impairment and particularly after a recent hospitalisation.

109 The third objective is to better understand the **roles and coordination of the different**
110 **caregivers involved in the medication management of home-dwelling OAMCC**. We seek
111 to investigate the perspectives of both professional caregivers (community health care nurses,
112 pharmacists, general practitioners or specialist physicians) and non-professional/informal
113 caregivers (family members, friends or neighbours).

114 **METHODS**

115 **Study design**

116 To enable us to meet our objectives, a mixed method study will address the medication
117 management of polymedicated home-dwelling OAMCC.[20] There will be two major phases
118 conducted sequentially over time: a quantitative data collection phase followed by a qualitative
119 phase. The reasons for using an explanatory sequential design are, firstly, that existing data in
120 electronic patient records from a local hospital will enable us to identify profiles affected by
121 similar medication and environment-related factors among the polymedicated, home-dwelling
122 OAMCC at risk of hospitalisation, emergency department visits, hospital readmission (notably
123 due to MRPs), institutionalisation, or early death. Secondly, the identified profiles extracted
124 from the hospital data will allow proceeding to a purposive sampling—of those polymedicated
125 home-dwelling OAMCC who present with more risk factors—for the qualitative data collection
126 focused on medication management at home.

127 **Phase 1, Retrospective Quantitative Analysis**

128 To fulfil the first objective, the purpose of the quantitative phase is to identify the different
129 profiles—made up of factors related to medication and environment—of the polymedicated
130 home-dwelling OAMCC at risk of hospitalisation, emergency department visits, hospital
131 readmission (notably for MRPs), institutionalisation, or early death. A systematic, retrospective
132 chart analysis of the electronic patient records from a local hospital over the last four years
133 using the evidence-based methodology developed by Vassar & Holzmann will provide
134 substantial clinical information.[21] Motheral et al.'s standardised extraction sheets will be
135 adapted to explore and assess the data of older inpatients or ED-visiting home-dwelling older
136 adult.[22] The four-year period was selected based on the availability of systematic, well-coded
137 patient data using the Swiss-Diagnostic Related Groups (DRG)[23] and the Swiss surgery coding
138 system (CHOP).[24]

139 *Research population*

140 All home-dwelling OAMCC with somatic and/or mental health disorders who were

141 hospitalised, rehospitalised or who consulted the emergency department at the partner hospital

142 between 2015 and 2018 (estimated N= 50,000) will be included. The estimated sample of

143 50,000 older adults' electronic inpatient charts are part of the 40,000 yearly adult inpatients in

144 acute care units and more than 40,000 adult emergency department consultations yearly at the

145 partner hospital.

146 *Data Collection*

147 Sociodemographic data will include age, sex and environmental data such as a rural or urban

148 domicile, and the presence of formal and/or informal caregivers. Clinical and health data will

149 integrate primary ICD-10 diagnosis completed with the reason for hospitalisation or

150 rehospitalisation due to MRPs. Supplementary filters will be added to discriminate

151 polymedication, multi-morbidity (secondary ICD-10 diagnosis), physical and cognitive

152 impairment documented in the clinical data files (Function Independence Measure, Mini-

153 Mental State Examination, and Activities of Daily Living). In addition, data on length of stay,

154 readmissions (number of admissions in the previous year, 30-day readmission and unplanned

155 readmission), death during hospitalisation and medication data (number and types of

156 medication treatments during hospitalisation, discharge and post-discharge medication

157 changes) will be collected. A unique patient identification number will allow us to identify and

158 analyse re-hospitalisation via the emergency department during the period from 2015 to 2018.

159 *Data Analyses*

160 This retrospective investigation will allow us to identify the medication and environment-

161 related factors that can increase the risk of hospitalisation, emergency department visits,

162 readmission (notably due to MRPs), institutionalisation or early death. This retrospective

163 analysis will serve to guide the qualitative study and lead to a purposive sampling of

164 polymedicated home-dwelling OAMCC presenting with more risk factors.

165 The final outcome of the quantitative phase will be the identification of polymedicated home-

166 dwelling OAMCC hospitalised or visiting the emergency department due to MRPs.[25]

167 **Phase 2, Prospective Patient-Centred Qualitative Analysis**

168 To meet the second and third objectives, a qualitative investigation, based on purposive

169 sampling, will draw upon work done in a feasibility study.[26] This qualitative investigation will

170 consist of collecting and understanding the medication practices and experiences of OAMCC
171 presenting with the risk factors identified in the first phase. The focus will be on identified
172 OAMCC who were recently hospitalised and are at risk of hospital readmission. The older adult
173 will be interviewed at home on two separate occasions. This methodology is a way to analyse
174 changes in their medication practises and their experiences following their recent
175 hospitalisation. The data collection tools include a walking-interview[27] based on a medication
176 journal and household photographs of where medication is stored. This allows us to focus on
177 the tangible practices of OAMCC and contextualises them within the private space of their daily
178 lives.

179 To discriminate the older adults' health profile, we will use the Resident Assessment Instrument
180 – Home-Care (RAI-HC) introduced by the Swiss Association for Home Care Services for all
181 home care services in 2004. Based on a comprehensive geriatric assessment, the RAI-HC not
182 only allows for the establishment of an individualised care plan, but it also generates quality
183 indicators, plans resource use, optimises the medication management process by monitoring
184 and documenting the number and types of medication and the persons involved in preparing
185 medication, and regularly assesses adherence to the medication prescribed.[28]

186 Furthermore, we will also collect and analyse the perspectives of the formal and informal
187 caregivers involved in medication management at home, to cross-reference perspectives about
188 this important dimension of care at home.

189 ***Research population***

190 The profiles of the polymedicated OAMCC hospitalised/rehospitalised or consulting the
191 emergency department, as identified in the retrospective investigation, will be used to select
192 participants for the qualitative investigation. A theoretical, purposive sampling will be carried
193 out. Based on Guest et al., we will recruit about 30 polymedicated OAMCC (until saturation of
194 data), all recently hospitalised (within the last 90 days) and at risk of hospital readmission.[29]
195 For each OAMCC participant an informal caregiver will also be integrated into the
196 investigation. We defined informal caregivers as any family member, neighbour or friend
197 assisting a dependent older adult with certain activities in their daily life. That assistance, help,
198 care or physical presence must be given on a regular basis, for at least two basic activities or
199 instrumental activities of daily living or to ensure patient safety, and for six months or more.[30]
200 The informal caregiver will be included in the study if the recruited older adult identifies that

person as being significant in their medication management and if they give informed written consent to participate.

Furthermore, a formal caregiver will be integrated into the investigation for each participant. Professional caregivers are those employed to provide professional home health care services (i.e. nurses, nursing assistants, social assistant). They will be included in the study if the recruited OAMCC identifies them as the professional most involved in their medication management.

Table 1 presents the specific inclusion/exclusion criteria for each group of participants.

Table 1. Inclusion and exclusion criteria of phase 2

Participants	Inclusion criteria	Exclusion criteria
OAMCC	- Aged 65 or above - Man or woman - Hospitalised within the last 90 days - Managing at least five different medications (prescribed and over-the-counter medications explored during recruitment) - Suffering from multiple chronic conditions - Living alone or in a couple, in a rural or urban area - With or without support from a Community Healthcare Centre	- Not able to speak and understand French
Informal caregiver	- Designated by the OAMCC as the most significant informal caregiver involved in medication management - Aged 18 or above	- Not able to speak and understand French
Professional caregiver	- Designated by the OAMCC as having a key role in medication management	- Student - Apprentice

Participant recruitment

Polymedicated home-dwelling OAMCC will be recruited via two paths so that all of the participants meet the eligibility criteria and fit corresponding profiles established in the quantitative phase. Some OAMCC will be receivers of care from Community Healthcare Centres and others will be functioning without that day-to-day support:

- For OAMCC who do not receive support from a Community Healthcare Centre, recruitment will be based on variables in their patient files and carried out in collaboration with different nursing departments from the partner hospital;

- For OAMCC who do receive support from a Community Healthcare Centre, recruitment will be based on the clinical and health data documented in the RAI-HC and carried out in collaboration with community health care nurses from Sion Community Healthcare Centre.

222 Research nurses partnering the project, from a hospital or a Community Healthcare Centre, will

223 briefly explain the study to the patient. Potential participants will be asked for permission to

224 give their name to the researchers. A member of the research team will contact the older adult

225 by telephone during the week following hospital discharge and ask for their agreement to

226 participate in the study. In case of agreement, a first meeting will be organised at the older

227 adult's home in the next few days.

228 ***Data Collection from OAMCC***

229 During the first home meeting with the OAMCC, the researcher will provide all the study details

230 and will suggest two semi-structured interviews, each lasting about an hour, starting on the first

231 meeting and spaced two to three weeks apart. The older adult will be invited to sign the

232 informed written consent form, allowing the researcher to collect sociodemographic and health

233 data (RAI-HC and the patient's hospital records). Eligible home-dwelling OAMCC from both

234 recruitment paths will be screened using the RAI-HC Minimal Data Set (MDS), which includes

235 information on polymedication (section P), multiple chronic conditions (sections J and K) and

236 recent hospitalisation (section Ac). The research team will also carry out this evaluation for

237 participants who do not have a RAI-HC. The following multidimensional clinical data will be

238 retrieved from the RAI-HC MDS: cognitive status, hearing, vision, mood status, functional and

239 physical status, continence, health care problems, and nutritional state.

240 The first semi-structured interview will collect the perspectives of OAMCC with regards to

241 their medication management, the return home, information received about their treatment and

242 its possible modifications, and the informal and professional caregivers involved. Each

243 OAMCC will be interviewed alone. The researcher will then ask the participant to complete a

244 week-long medication journal[31] [32], either alone or with the help from informal or professional

245 caregivers, emphasising that any information on daily medication routines is helpful, even if

246 the OAMCC feels unable to complete the journal for the full seven days. The instructions will

247 mention the importance of noting all the medicines taken—those prescribed by general

248 practitioners or specialist physicians, but also any others taken at their own initiative (over-the-

249 counter medications). This will provide information on the daily routines associated with the

250 participant's medication and will form the basis of the second interview.

251 The second interview will be based on the participant's medication journal and will take the

252 form of a walking-interview[33] using household photographs.[32] The researcher will ask the

253 participant to explain their medication practises while pointing out the locations within their

254 home where drugs are stored, prepared and taken. The hypothesis underlying this methodology

255 is that the physical presence of drugs promotes discussion.[34][35] We will identify and photograph,

256 with the participants' agreement, the places where medication, contact details for medical

257 professionals and other information are stored as well as the locations of any other objects

258 involved in daily care practises. The collection and analysis of photographs provide a better

259 understanding of the complexity of medication management in home settings. They help to

260 capture the interviewee's concerns or strategies when they are pointed out to the interviewer.

261 The interview guide will also investigate the issue of self-medication in order to reveal the

262 extent and influence of this practice.

Data Collection from Informal Caregivers

264 Sociodemographic data and information related to medication management will be collected.

265 When possible and appropriate, a joint third interview[36] with the OAMCC and their principal

266 informal caregiver[31] will be organised at the older adult's home one to two weeks after the

267 walking interview. This type of interview provides access to the interactions between OAMCC

268 and their informal caregivers with regards to medication management. We hypothesise that the

269 main informal caregiver is deeply involved in the older adult's experience of medication

270 management, but the caregiver's ideas about this may be similar to, overlapping with or

271 different from those of an OAMCC.

Data Collection from Professional Caregivers

273 A semi-structured interview of about one hour will be conducted with a professional caregiver

274 in order to explore their point of view on the OAMCC's medication management and other

275 issues associated with the return home after hospitalisation. This will take place at the

276 professional's workplace (Community Healthcare Centre, medical practice office or pharmacy)

277 one to two weeks after the interview with the OAMCC and their informal caregiver.

Qualitative data analyses

279 A database will be prepared using the RedCap® software platform to record and store the

280 participants' sociodemographic, health and interview data. Information on their health statuses

281 will be collected using the RAI-HC data and will be analysed using the IBM-Statistical Package

282 for Social Sciences (IBM-SPSS®), version 25.0.

283 Data collected via the interviews will be examined according to an analytical plan that integrates

284 and compares two different methods. Firstly, thematic content analysis[37][38], using NVivo 12®

285 software, will be used to identify the themes emerging from the data, and this will provide a

286 rich, detailed account of the data set. Themes will be compared by different members of the

287 analysis team until a consensus is reached. Secondly, lexicometric analysis, using Iramuteq

288 software—a technique derived from the Alceste® method[39]—will allow a very fine exploration,

289 both within each interview and across the whole corpus of interviews, of the structures

290 underlying the discourse. Each older adult's medication journal will be analysed and

291 categorised according to the same principles as the interviews. The data collected from these

292 documents will be put into perspective by the analysis of the interviews. In the final data

293 analysis, links will be made between the interviews, the medication journal, the older adult's

294 RAI-HC data, and the photos of the medicines' locations.

295

296 **Ethics and Dissemination**

297 Ethical approval has been obtained from the Human Research Ethics Committee of the Canton

298 Vaud (CER-VD) (2018-02196). With this approval, the medical informatics department of

299 partner hospital will provide the appropriate data for the retrospective phase based on a data

300 extraction protocol. Extracted data will be delivered and stored in the ReDCap® data platform

301 via a secure coded data file. In coherence with the Data Management Plan submitted to the

302 Swiss National Science Foundation (NSF), the collected data will be securely stored for future

303 research.

304 The autonomy of the participants will be respected. Participation in the prospective phase in

305 this research is free. It will be possible for participants to refuse to record the interview or to

306 request the deletion of the recorded data. Participating in a structured effort to understand

307 medication practises and the post-hospital return home experience can contribute to

308 improvements in health management in the community at large, and particularly in the area of

309 home support.

310 Findings will be disseminated in peer-reviewed journals, professional conferences and other

311 knowledge transfer activities with primary healthcare providers, hospital care units, informal

312 caregiver and patient associations.

313

314 **Authors' contributions**

315 FP, PR and HV had the original idea. MSD, AVG, BW and HV provided conceptual and

316 methodological expertise to the design of the research protocol. FP, PR and HV were major

317 contributors to writing the manuscript. All authors read, edited and approved the final

318 manuscript.

319

320 **Funding statement**

321 This work is supported by the Swiss National Science Foundation grant number

322 407440_183434/1.

323

324 **Competing interest statement**

325 None declared.

326

327 **Word Count:** 3'657.

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434

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Protocol for a mixed-methods study to optimise medication management for polymedicated home-dwelling older adults with multiple chronic conditions

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Protocol for a mixed-methods study to optimise medication management for polymedicated home-dwelling older adults with multiple chronic conditions

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1 **ABSTRACT**

2 **Introduction:**

3 Optimal medication management is one of the basic conditions necessary for home-dwelling

4 older adults living with multiple chronic conditions (OAMCC) to be able to remain at home

5 and preserve their quality of life. Currently, the reasons for such high numbers of emergency

6 department visits and the very significant rate of hospitalisations for OAMCC, due to

7 medication-related problems (MRPs), is poorly explored. This study aims to reveal the current

8 state of the medication management practices of polymedicated, home-dwelling OAMCC and

9 to make proposals for improving clinical and medication pathways through an innovative and

10 integrated model for supporting medication management and preventing adverse health

11 outcomes.

12 **Methods and analysis:** A mixed-methods study will address the medication management of

13 polymedicated, home-dwelling OAMCC. Its explanatory sequential design will involve two

14 major phases conducted sequentially over time. The quantitative phase will consist of

15 retrospectively exploiting the last five years of electronic patient records from a local hospital

16 (N ≈ 50,000) in order to identify the different profiles—made up of patient-, medication- and

17 environment-related factors—of the polymedicated, home-dwelling OAMCC at risk of

18 hospitalisation, emergency department visits, hospital readmission (notably for MRPs),

19 institutionalisation or early death. The qualitative study will involve: a) obtaining and

20 understanding the medication management practices and experiences of the identified profiles

21 extracted from the hospital data of OAMCC who will be interviewed at home (N ≈ 30); b)

22 collecting and analysing the perspectives of the formal and informal caregivers involved in

23 medication management at home in order to cross-reference perspectives about this important

24 dimension of care at home. Finally, the mixed-methods findings will enable the development

25 of an innovative, integrated model of medication management based on the Agency for Clinical

26 Innovation framework and Bodenheimer & Sinsky's quadruple aim.

27 **Ethics and dissemination:** Ethical approval has been obtained from the Human Research

28 Ethics Committee of the Canton Vaud (2018-02196). Findings will be disseminated in peer-

29 reviewed journals, professional conferences and other knowledge transfer activities with

30 primary healthcare providers, hospital care units, informal caregivers' and patients'

31 associations.

32

Study strengths and limitations

- This mixed methodology will rely on a closely coordinated combination of methods and on the utilisation of valuable existing data under-exploited to date (patients' electronic hospital records and Resident Assessment Instrument-Home Care (RAI-HC) data).

- The investigation draws upon an interprofessional and interdisciplinary approach, which associates general practitioners, community health care nurses, pharmacists and researchers in health psychology, old age psychiatry, nursing and survey methodology.

- Our findings will contribute to the development of an evidence-based and innovative, cooperative model of medication management for polymedicated, home-dwelling older adults with multiple chronic conditions.

- Although patients' electronic hospital records and RAI-HC data provide a broad range of patient-, medication- and environment-related information, they rarely highlight factors that may influence the occurrence of MRPs.

INTRODUCTION

The number of older adults living at home with multiple chronic conditions (OAMCC) rises considerably around the world and has been estimated to affect 25.2% of people aged from 65 to 79 and 41.3% of those aged 80 and over.[1] Multiple chronic conditions is a comprehensive concept used to properly cover the diverse definitions of multi-morbidity[2][3] and therefore the complexity of older adults' health statuses. The concept encompasses the simultaneous presence of an individual's diseases and their chronic physical, mental or behavioural health problems requiring ongoing management over years or decades.[4]

These long-term health conditions require taking multiple medications[5], known as polypharmacy (PP) when the daily intake corresponds to five or more medicines.[6] Polypharmacy places older adults at higher risk of medication-related problems (MRPs), including adverse medication reactions, medication errors and potentially inappropriate medications.[7][8] Potentially inappropriate medications are the intake of medicines for which the associated risks outweigh the potential benefits, particularly when more effective alternatives are available.[9] Consequently, MRPs can lead to a degradation of the patient's clinical condition, physical and cognitive decline, an exacerbation of chronic medical conditions and avoidable health costs.[10][11] Moreover, up to 25% of emergency department visits by home-dwelling OAMCC are due to MRPs.[10] However, 60% of MRPs in patients visiting the emergency department with non-specific complaints (such as weakness) may go undiagnosed, whereas 83% of those MRPs may be responsible for acute morbidity.[10] MRPs are also a frequent cause of readmission, and they were the most frequent cause in one study that followed older patients for six months after hospital discharge.[12] Care-coordination problems, associated with low or suboptimal medication management, are all the more evident in the sensitive period of discharge home from hospital.[11][13] The complexity of OAMCC' care needs leads them to be significant users of health services and to consult many different health care professionals.[14] The number of health care professionals consulted by home-dwelling OAMCC has been directly associated with fragmented and uncoordinated care.[13] Moreover, different health care professionals may have different treatment preferences. Failure to coordinate care among home-dwelling OAMCC contributes to MRPs.[13]

In addition to role of health care professionals in medication management, informal caregivers play a vital role in ensuring safe and appropriate medication use by home-dwelling OAMCC, especially among those who may also have cognitive impairment.[15-17] Despite the important

83   role of informal caregivers in medication management, several complications to do with their

84   activities have been documented in relation to the time spent, anxiety making a mistake and the

85   uncooperative behaviour of the home-dwelling OAMCC.[18] They are also confronted with

86   difficulties in maintaining continuous supplies of medication, assisting with administration,

87   making clinical judgements (e.g. in response to side effects and about over-the-counter

88   medication), and solving conflictual communications or disagreements with the older adult[18],

89   or even with health care professionals, with regards to ineffective and addictive medication

90   practices.[15 18]

91   Nonetheless, many MRPs are preventable.[8 10 19] Studies about medicine-related hospitalisations

92   suggest that up to 58% may be preventable with appropriate primary care.[8] An essential strategy

93   for medicine-related hospitalisations prevention and medication safety is medication

94   reconciliation - the process of creating and maintaining a single list of the patient's current list

95   of medications.[20] This process allows a systematic and comprehensive review of all the

96   medications the patient is taking, reducing medication errors by a consistent communication

97   across transitions of care.[21]

98   Therefore, optimising medication management among home-dwelling OAMCC requires

99   regular monitoring of MRPs, interprofessional collaboration across different health and social

100   care providers, organisations and departments[13] and medication reconciliation at every

101   transition of care including changes in the clinical setting, practitioner, or level of care.[22]

Aim and Objectives

103   The study aim is to document the current state of medication management practices of

104   polymedicated, home-dwelling OAMCC and to make proposals for improving evidence-based

105   clinical and medication pathways through an innovative, integrated model intended to support

106   medication management and to prevent adverse health outcomes related to MRPs (recurrent

107   hospitalisation, emergency department visits, institutionalisation in nursing homes and early

108   death). To achieve this aim, three main objectives will guide this project:

109   The first objective is to carry out a **retrospective analysis of patients' hospital records**, their

110   medication and environment-related factors in order to identify those that increase the risk of

111   hospitalisation, emergency department visits, hospital readmission (notably due to MRPs),

112   institutionalisation or early death, among home-dwelling polymedicated OAMCC—factors that

113   prevent OAMCC from staying at home.

114   The second objective is to use **a prospective qualitative study** to explore and better understand

115   **the medication experiences and practices of home-dwelling OAMCC with different**

116   **profiles**. We seek to identify the skills and strategies developed by them to manage

117   polymedication within their social contexts and health trajectories despite possible cognitive

118   impairment and particularly after a recent hospitalisation.

119   The third objective is to better understand the **roles and coordination of the different**

120   **caregivers involved in the medication management of home-dwelling OAMCC**. We seek

121   to investigate the perspectives of both professional caregivers (community health care nurses,

122   pharmacists, general practitioners or specialist physicians) and non-professional/informal

123   caregivers (family members, friends or neighbours).

124   **METHODS**

125   **Study design**

126   To enable us to meet our objectives, a mixed-methods study will address the medication

127   management of polymedicated, home-dwelling OAMCC.[23] Two major phases will be

128   conducted sequentially from February 2019 to January 2022: a quantitative data collection

129   phase followed by a qualitative phase. The reasons for using an explanatory sequential design

130   are, firstly, that existing data in electronic patient records from a local hospital will enable us

131   to identify profiles affected by similar patient-, medication- and environment-related factors

132   among the polymedicated, home-dwelling OAMCC at risk of hospitalisation, emergency

133   department visits, hospital readmission (notably due to MRPs), institutionalisation, or early

134   death. Secondly, the identified profiles extracted from the hospital data will allow proceeding

135   to a purposive sampling—of those polymedicated, home-dwelling OAMCC who present with

136   more risk factors—for the qualitative data collection focused on medication management at

137   home. Thus, the analysis of the results from the retrospective quantitative phase will be

138   integrated with the data collected from the prospective qualitative phase. Finally, phase 3 will

139   develop a Medication Management Model based on interpreting the quantitative and qualitative

140   findings.

141   **Phase 1, Retrospective Quantitative Analysis**

142   To fulfil the first objective, the purpose of the quantitative phase is to identify the different

143   profiles—made up of patient-, medication- and environment-related factors—of the

144   polymedicated, home-dwelling OAMCC at risk of hospitalisation, emergency department

145 visits, hospital readmission (notably for MRPs), institutionalisation in nursing homes, or early

146 death (before the average age of death described by the Organisation for Economic Co-

147 operation and Development in 2018).[24] A systematic, retrospective chart analysis of the

148 electronic patient records from a local hospital over the last four years using the evidence-based

149 methodology developed by Vassar & Holzmann will provide substantial clinical information.[25]

150 Motheral et al.'s standardised extraction sheets will be adapted to explore and assess the data

151 of older inpatients or emergency department-visiting home-dwelling older adults.[26] The four-

152 year analysis was selected based on the availability of systematic, well-coded patient data using

153 the Swiss-Diagnostic Related Groups (DRG)[27] and the Swiss Classification of Surgical

154 Interventions (CHOP). [28]

155 *Research population*

156 All home-dwelling OAMCC with somatic and/or mental health disorders who were

157 hospitalised, rehospitalised or who consulted the emergency department (for MRPs or other

158 reasons) at the partner hospital between 2015 and 2018 (estimated N = 50,000) will be included.

159 The estimated sample of 50,000 older adults' electronic inpatient charts are part of the 40,000

160 yearly adult inpatients in acute care units and more than 40,000 adult emergency department

161 consultations yearly at the partner hospital. To explore generalisability, we will compare their

162 sociodemographic and health status characteristics with those of the national sample of

163 hospitalised older adults in Swiss hospitals for the same period.

164 *Data Collection*

165 Data from the hospitalisation and emergency admissions databases will be collected on patient-,

166 medication- and environment-related factors that could have influenced the occurrence of

167 MRPs that resulted in hospitalisation, rehospitalisation or emergency department admission.

168 Patient-related factors comprise sociodemographic characteristics, the International

169 Classification of Diseases 10th version (ICD-10) diagnostics (main diagnosis and co-

170 morbidities), the Swiss Classification of Surgical Interventions (CHOP) category and the reason

171 for hospitalisation, rehospitalisation or emergency department admission. Supplementary filters

172 will be added to discriminate polymedication, multi-morbidity (secondary ICD-10 diagnosis),

173 physical and cognitive impairment documented in the clinical data files (Function

174 Independence Measure, Mini-Mental State Examination, and Activities of Daily Living).

175 Medication-related factors include the number, types and changes in medication at admission,

176 during hospitalisation and at discharge.

177   Environment-related factors include the presence of formal and/or informal caregivers, patient's
178   provenance (rural or urban), hospital pathways (wards and eventual transfers), length of stay,
179   readmissions (number of admissions in the previous year, 30-day readmission and unplanned
180   readmission), discharge destination and, potentially, death during hospitalisation. A unique
181   patient identification number will allow us to analyse re-hospitalisations via the emergency
182   department during the period from 2015 to 2018. Retrospective data collection began in April
183   2019.

184   *Data Analyses*

185   The dataset of polymedicated, home-dwelling OAMCC will be analysed using multivariate
186   regression analysis, in order to identify the patient-, medication- and environment-related
187   factors that can increase the risk of hospitalisation, emergency department visits, readmission
188   (notably due to MRPs), institutionalisation or early death. Furthermore, the profiles of
189   polymedicated, home-dwelling OAMCC hospitalised or visiting the emergency department due
190   to MRPs, and identified via multi-cluster analysis, will serve to guide the qualitative study and
191   lead to a purposive sampling of polymedicated, home-dwelling OAMCC presenting with more
192   risk factors. A draft of the cluster analysis strategy is available as a supplementary file.

193

194   **Phase 2, Prospective Patient-Centred Qualitative Analysis**

195   To meet the second and third objectives, a qualitative investigation, based on purposive
196   sampling, will draw upon work done in a feasibility study.[29] This qualitative investigation will
197   consist of collecting and understanding the medication practices and experiences of OAMCC
198   presenting with the risk factors identified in the first phase. The focus will be on identified
199   OAMCC who were recently hospitalised and are at risk of hospital readmission. The older adult
200   will be interviewed at home on two separate occasions. This methodology is a way to analyse
201   changes in their medication practises and their experiences following their recent
202   hospitalisation. The data collection tools include a walking-interview[30] based on a medication
203   journal and household photographs of where medication is stored. This allows us to focus on
204   the tangible practices of OAMCC and contextualises them within the private space of their daily
205   lives.

206   To discriminate the older adults' health profile, we will use the Resident Assessment Instrument
207   –Home-Care (RAI-HC) introduced by the Swiss Association for Home Care Services for all

208 home care services in 2004. Based on a comprehensive geriatric assessment, the RAI-HC not

209 only allows for the establishment of an individualised care plan, but it also generates quality

210 indicators, plans resource use, optimises the medication management process by monitoring

211 and documenting the number and types of medication and the persons involved in preparing

212 medication, and regularly assesses adherence to the medication prescribed.[31] This instrument

213 will provide information on the patient-, medication- and environment-related factors which

214 may influence the occurrence of MRPs, and it will be used to recruit OAMCC at risk of or

215 already presenting with MRPs.

216 Furthermore, we will also collect and analyse the perspectives of the formal and informal

217 caregivers involved in medication management at home, to cross-reference perspectives about

218 this important dimension of care at home.

219 ***Research population***

220 The profiles of the polymedicated OAMCC hospitalised/rehospitalised or consulting the

221 emergency department, as identified in the retrospective investigation, will be used to select

222 participants for the qualitative investigation. A theoretical, purposive sampling will be carried

223 out. Based on Guest et al., the principal investigator will recruit about 30 polymedicated

224 OAMCC (until saturation of data), all recently hospitalised (within the last 90 days) and at risk

225 of hospital readmission.[32] For each OAMCC participant, an informal caregiver will also be

226 integrated into the investigation. We defined informal caregivers as any family member,

227 neighbour or friend assisting a dependent older adult with certain activities in their daily life.

228 That assistance, help, care or physical presence must be given on a regular basis, for at least

229 two basic activities or instrumental activities of daily living or to ensure patient safety, and for

230 six months or more.[33] The informal caregiver will be included in the study if the recruited older

231 adult identifies that person as being significant in their medication management and if they give

232 informed written consent to participate.

233 Furthermore, a formal caregiver will be integrated into the investigation for each participant.

234 Professional caregivers are those employed to provide professional health care services (i.e.

235 nurses, nursing assistants, general practitioners, pharmacists, social workers). They will be

236 included in the study if the recruited OAMCC identifies them as the professional most involved

237 in their medication management.

238 Table 1 presents the specific inclusion/exclusion criteria for each group of participants.

239

240   **Table 1. Phase 2 inclusion and exclusion criteria**

Participants	Inclusion criteria	Exclusion criteria
OAMCC	- Aged 65 or above - Man or woman - Hospitalised within the last 90 days - Managing at least five different medications (prescribed and over-the-counter medications explored during recruitment) - Suffering from multiple chronic conditions[4] - Living alone or in a couple, in a rural or urban area - With or without support from a Community Healthcare Centre	- Not able to speak and understand French
Informal caregiver	- Designated by the OAMCC as the most significant informal caregiver involved in medication management - Aged 18 or above	- Not able to speak and understand French
Professional caregiver	- Designated by the OAMCC as having a key role in medication management	- Student - Apprentice

241

242   ***Participant recruitment***

243   Polymedicated, home-dwelling OAMCC will be recruited via two paths so that all of the

244   participants meet the eligibility criteria and fit corresponding profiles established in the

245   quantitative phase. Some OAMCC will be receivers of care from Community Healthcare

246   Centres and others will be functioning without that day-to-day support:

247   - For OAMCC who do not receive support from a Community Healthcare Centre, recruitment

248   will be based on variables in their patient files and carried out in collaboration with different

249   nursing departments from the partner hospital;

250   - For OAMCC who do receive support from a Community Healthcare Centre, recruitment will

251   be based on the clinical and health data documented in the RAI-HC and carried out in

252   collaboration with community health care nurses from Sion Community Healthcare Centre.

253   Research nurses partnering the project, from a hospital or a Community Healthcare Centre, will

254   briefly explain the study to the patient. Potential participants will be asked for permission to

255   give their name to the researchers. The principal investigator will contact the older adult by

256   telephone during the week following hospital discharge and ask for their agreement to

257   participate in the study. In case of agreement, a first meeting will be organised at the older

258   adult's home in the next few days. Participant recruitment will start in October 2019.

259

260

261 ***Data Collection from OAMCC***

262 During the first home meeting with the OAMCC, the principal investigator will provide all the

263 study details and will suggest two semi-structured interviews, each lasting about an hour,

264 starting on the first meeting and spaced two to three weeks apart. According to participants'

265 levels of tiredness, it may be necessary to subdivide the interviews. The older adult will be

266 invited to sign the informed written consent form, allowing the researcher to collect

267 sociodemographic and health data (RAI-HC and the patient's hospital records). Eligible home-

268 dwelling OAMCC from both recruitment paths will be screened using the RAI-HC Minimal

269 Data Set (MDS), which includes information on polymedication (section P), multiple chronic

270 conditions (sections J and K) and recent hospitalisation (section Ac). Research team members

271 trained on the RAI-HC will also carry out this evaluation for participants who do not have an

272 RAI-HC. The following multidimensional clinical data will be retrieved from the RAI-HC

273 MDS: cognitive status, hearing, vision, mood status, functional and physical status, continence,

274 health care problems, and nutritional state. The MDS will aid interviews with OAMCC and the

275 exploration of the facilitators and barriers to daily medication management.

276 The first semi-structured interview will collect the perspectives of OAMCC with regards to

277 their medication management, the return home, information received about their treatment and

278 its possible modifications, whether their opinions and preferences were taken into account in

279 the prescription of medications, and the informal and professional caregivers involved.

280 OAMCCs will be interviewed alone or with an informal caregiver, if necessary. The principal

281 investigator will then ask the participant to complete a week-long medication journal[34 35], either

282 alone or with the help from informal or professional caregivers, emphasising that any

283 information on daily medication routines is helpful, even if the OAMCC feels unable to

284 complete the journal for the full seven days. The instructions will mention the importance of

285 noting all the medicines taken—those prescribed by general practitioners or specialist

286 physicians, but also any others taken at their own initiative (over-the-counter medications).

287 Participants will be asked to note their perceptions of and satisfaction with their treatment in a

288 week-long medication journal. This will provide information on the daily routines associated

289 with the participant's medication and will form the basis of the second interview.

290 The second interview will be based on the participant's medication journal and will take the

291 form of a walking-interview[36] using household photographs.[35] The principal investigator will

292 ask the participant to explain their medication practises while pointing out the locations within

293   their home where drugs are stored, prepared and taken. The hypothesis underlying this

294   methodology is that the physical presence of drugs promotes discussion.[37 38] We will identify

295   and photograph, with the participants' agreement, the places where medication, contact details

296   for medical professionals and other information are stored as well as the locations of any other

297   objects involved in daily care practises. The collection and analysis of photographs provide a

298   better understanding of the complexity of medication management in home settings. They help

299   to capture the interviewee's concerns or strategies when they are pointed out to the interviewer.

300   The interview guide will also investigate the issue of self-medication in order to reveal the

301   extent and influence of this practice.

Data Collection from Informal Caregivers

303   Sociodemographic data and information related to medication management will be collected.

304   When possible and appropriate, a joint third interview[39] with the OAMCC and their principal

305   informal caregiver[34] will be organised at the older adult's home one to two weeks after the

306   walking interview. This type of interview provides access to the interactions between OAMCC

307   and their informal caregivers with regards to medication management. We hypothesise that the

308   main informal caregiver is deeply involved in the older adult's experience of medication

309   management, but the caregiver's ideas about this may be similar to, overlapping with or

310   different from those of an OAMCC.

Data Collection from Professional Caregivers

312   A semi-structured interview of about one hour will be conducted with a professional caregiver

313   in order to explore their point of view on the OAMCC's medication management and other

314   issues associated with the return home after hospitalisation. In agreement with the project's

315   field partners and stakeholders, these interviews will take place in professionals' workplaces

316   (Community Healthcare Centre, medical practice office or pharmacy), during working hours,

317   one to two weeks after the interview with the OAMCC and their informal caregiver.

Qualitative data analyses

319   A database will be prepared using the RedCap® software platform to record and store the

320   participants' sociodemographic, health and interview data. Information on their health statuses

321   will be collected using the RAI-HC data and will be analysed using the IBM-Statistical Package

322   for Social Sciences (IBM-SPSS®), version 25.0.

323 Data collected via the interviews will be examined according to an analytical plan that integrates

324 and compares two different methods. Firstly, thematic content analysis[40 41], using NVivo 12®

325 software, will be used to identify the themes emerging from the data, and this will provide a

326 rich, detailed account of the data set. Themes will be compared by different members of the

327 analysis team until a consensus is reached. Secondly, lexicometric analysis, using Iramuteq

328 software—a technique derived from the Alceste® method[42]—will allow a very fine exploration,

329 both within each interview and across the whole corpus of interviews, of the structures

330 underlying the discourse. Each older adult's medication journal will be analysed and

331 categorised according to the same principles as the interviews. The data collected from these

332 documents will be put into perspective by the analysis of the interviews. In the final data

333 analysis, links will be made between the interviews, the medication journal, the older adult's

334 RAI-HC data, and the photos of the medicines' locations.

335

Phase 3, Development of a Medication Management Model

337 Connecting retrospective and prospective findings, using an explanatory sequential design and

338 participants' different perspectives, will contribute to a deep understanding of the current state

339 of medication management practices of polymedicated, home-dwelling OAMCC. This mixed-

340 methods study corresponds to the "diagnostic" phase of the process of developing a Model of

341 Care, as presented by the Agency for Clinical Innovation (ACI).[43] It will guide the "solution

342 design" phase—the next step in the creation of an innovative, integrated model for supporting

343 medication management and preventing adverse health outcomes. In addition to the ACI's

344 framework, the development of a proposed Medication Management Model will consider the

345 quadruple aim of enhancing the patient's experience, improving population health, reducing

346 costs and improving the working lives of health care providers.[44]

347 Finally, our mixed-methods research findings will be completed with those of an ongoing

348 systematic review of Medication Management Models.[45]

349 The study phase outcomes are summarised in Table 2.

Table 2. Outcomes for each study phase

Phase 1 outcomes	Patient-, medication- and environment-related factors which can increase the risk of hospitalisation, emergency department visits, hospital readmission (notably due to MRPs), institutionalisation or early death.
	Profiles of polymedicated, home-dwelling OAMCC hospitalised or visiting the emergency department due to MRPs based on the previously identified patient-, medication- and environment-related factors.

Phase 2 outcomes	For OAMCC participants: • Patient-, medication- and environment-related factors for MRPs (defined by phase 1's outcomes) extracted from the RAI-HC MDS and the patient's electronic hospital records (number and types of medication, multiple chronic conditions, recent hospitalisations, cognitive status, hearing, vision, mood status, functional and physical status, continence, healthcare problems, nutritional state); • Medication practices and experiences of OAMCC following their recent hospitalisation, facilitators/barriers to medication management, informal and professional caregivers involved. For informal caregivers: • Sociodemographic profiles; • Practices and experiences related to medication management. For professional caregivers: • Sociodemographic and professional profiles; • Role and perspectives on OAMCC medication management; • Coordination activities related to returning home after hospitalisation.
Phase 3 outcomes	Three first steps in the process of developing a Model of Care[43]: • "Project Initiation", • "Diagnostic", • "Solution Design" considering the quadruple aim; Proposals for the Medication Management Model's "Implementation" and "Sustainability" steps[43], to support medication management and to prevent adverse health outcomes related to MRPs.

351

Patient and Public Involvement

353 This study and the feasibility study on which it is based were developed in collaboration with
354 representatives from a Community Healthcare Centre, a regional hospital, medical and
355 pharmacy associations, and an informal caregivers association. They shared their expertise on
356 the study's relevance and the feasibility of data collection with the research team. Patients'
357 priorities, experiences and preferences, collected during the feasibility study, were the drivers
358 for the development of the research question and outcome measures.

359 A steering committee will involve these different actors at various stages in the project, both to
360 contribute to data collection and to provide their expertise to the co-construction of a
361 Medication Management Model and its future implementation. As regards data collection, the
362 hospital's medical informatics department will provide the appropriate data based on a data
363 extraction protocol (phase 1) and the Community Healthcare Centre will help with OAMCC
364 recruitment and access to participants' RAI-HC and professional caregivers (phase 2).

365 Results will be disseminated to study participants through presentations to associations of

366 patients and informal caregivers and at professional training sessions.

367 **Ethics and Dissemination**

368 Ethical approval has been obtained from the Human Research Ethics Committee of the Canton

369 Vaud (CER-VD) (2018-02196). With this approval, the medical informatics department of

370 partner hospital will provide the appropriate data for the retrospective phase based on a data

371 extraction protocol. Extracted data will be delivered and stored in the ReDCap® data platform

372 via a secure coded data file. In coherence with the Data Management Plan submitted to the

373 Swiss National Science Foundation (NSF), the collected data will be securely stored for future

374 research.

375 The autonomy of the participants will be respected. Participation in the prospective phase in

376 this research is free. It will be possible for participants to refuse to record the interview or to

377 request the deletion of the recorded data. Participating in a structured effort to understand

378 medication practises and the post-hospital return home experience can contribute to

379 improvements in health management in the community at large, and particularly in the area of

380 home support.

381 Findings will be disseminated in peer-reviewed journals, professional conferences and other

382 knowledge transfer activities with primary healthcare providers, hospital care units, informal

383 caregiver and patient associations.

384

385 **Authors' contributions**

386 FP, PR and HV had the original idea. MSD, AVG, BW, MMM and HV provided conceptual

387 and methodological expertise to the design of the research protocol. FP, PR and HV were major

388 contributors to writing the manuscript. All authors read, edited and approved the final

389 manuscript.

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395 **Competing interest statement**

396 None declared.

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397 **Data sharing statement**

398 The data collected and analysed during the study will be available from the principal

399 investigator on reasonable request.

400

401 **Word Count:** 4'126.

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Rapport de travail - partie quantitative

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July 11, 2019

Contents

1

Introduction

Dataset

Two datasets are available for this study at the moment: one containing the hospitalizations in the Valais hospital and one of the emergency admissions. The former plays a central role in this project and will be used most often in this document.

The hospitalizations data set contains distinct variables, most of which are measured twice: at the admission and at the discharge from the hospital. The total number of variables is then 174. After selecting only the population if interest, i.e. individuals aged 65 or more and living at home before the hospitalization, we finally obtain a sample of 36'792 hospitalizations. All observations have been collected between 2015 and 2018.

These variables are not completely independent and may be regrouped in several groups according to the dimension they are measuring as shown in figure 1. To begin we will analyze only the condition of the individuals **entering** the hospital.

The major groups of information can be split on: somatic/physical condition, psychological condition, number of medicines, diagnose(s), interventions and information on the medical course. Furthermore the precise medications will also be investigated.

Besides these most obvious distinctions between the variables, other underlying subgroups might also be present within these groups. This will be the subject of a complementary analysis within some groups. Therefore we will verify the presence of an interpretable **clustering of the variables** within a group before clustering the individuals.

Clustering approach

The **large number of variables** in the data set makes it difficult to investigate the relations between the different factors and the risk of critical health events. Therefore the possibility to put all variables in the same model may be not an optimal choice of modeling if we consider the multi-dimensionality problem and the dependence between the variables.

An **alternative approach** will be considered in this study. Here we will make use of the important information provided by the experts in healthcare, that is the presence of clear groups within the set of **variables**.

For the cases when this grouping is not very clear, we may rely on the expert's decision. However this is not always sufficient and we also need to employ statistical methods to cluster the variables. The results of these methods will be compared to the experts opinion and will serve as a **validation tool** in order to limit a possible bias from the experts point of view or to propose a solution to an unclear relation. Both methods should pe performed independently.

A hierarchical cluster analysis using the R package "ClustOfVar" is suggested in this paper. As each statistical analysis, its result should not be accepted as they appear, but should be taken as suggestions or questions instead.

2

somatic / physical condition			
Mobility - moving I / O	Perception / vigilance I / O		psychological
Mobility - position change Ent/Exit	Orientation (person, time, place) I / O		
Altered gait I / O	Ability to learn I / O		
Balance disorders I / O	Skill of daily life I / O		
Past falls I / O	Attention		
Recent falls	Medic. inc. Risk of falling / delirium I / O		
Exhaustion I / O	Number of drugs at the entrance		med.
Body Care - Upper Body I / O	Number of drugs on the way out		
Body Care - Lower Body I / O	CIM-10 main diagnosis		diagnoses
Dress and undress - upper body I / O	CIM-10 Comorb1		
Dress and undress - lower body I / O	CIM-10 Comorb2		
Eating I / O	CIM-10 Comorb3		
Drinking I / O	CIM-10 Comorb4		
Micturition I / O	CIM-10 Comorb5		
Defecation I / O	CHOP main intervention		interventions
Hearing I / O	CHOP add. Inter. 1		
View I / O	CHOP add. Inter. 2		
Verbal expression I / O	CHOP add. Inter. 3		
Drowsiness / full nights I / O	CHOP add. Inter. 4		
Sleep rhythm I / O	CHOP add. Inter. 5		
Pain intensity I / O	Emergency service - triage		medical course
Chronic pain I / O	Reason of visit		
bedsores	Loss of consciousness		
Sores	Waiting time		
Self-care index	Destination		
Risk of bedsores (Braden) I / O	Diagnosis		
Risk of malnutrition I / O	Origin		
Risk of falling I / O			
Risk of insufficient post-hospit. care			
BMI			

Figure 1: Structure of the hospitalization variables

When the final set of groups is defined, we will use statistical models to cluster the **individuals** within each group. This will provide one variable from each group, that indicates the type of characteristics that the individual displayed by his answers. For example, if we separate the individuals on three groups according to their psychological indicators, we might obtain a variable indicating that a person belongs to a group with noticeable, small or no psychological issues. This type of aggregated variables will be used in the final analysis of the risk factors.

Further analyses and tests

The approach described above will also be compared to the more typical method of feature selection. A series of regression analyses and tests will follow both approaches to understand which characteristics are the most important risk factors for occurrence of critical health events such as hospitalization, early death etc.

Longitudinal perspective

A longitudinal analyses may complement the research if the data allows (to be continued when we receive the identifiers).

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Chapter 1

Cluster analysis

1.1 Introduction and clustering methods

1.1.1 Methods of clustering of Mixed variables data

A large variety of clustering methods exist in the literature. However the majority are focused on either continuous or nominal data alone. There exist a limited number of techniques and strategies to incorporate both variables types in the same clustering partition (add all the formulas and references later):

- Distance measure. The idea is to be able to create a measure of the distance between individuals (or sequences) that includes nominal and continuous variables. The **Gower distance** is the most used such measure and is defined as: (formulas)

  However because it uses the range of continuous variables to determine the distance and assumes that nominal variables have a distance of either 0 or 1, it may under-estimate the impact of the continuous variables (which reaches 1 much less often than in the nominal variables case). Furthermore, the weights are also arbitrarily selected, however they define the contribution of each data type to the global distance (see **??** for more detailed examples). As all measure distances, Gower should be used as input for clustering methods, such as k-means for instance, to provide clustering results.

- k-means is another algorithm mainly used for continuous variables. Several other implementations, such as the R package KAMILA, integrate different types of variables together. In this particular case, it uses the probabilities of a multinomial distribution for the discrete variables. The continuous variables distribution is estimated by univariate Kernel Densities. The probabilities resulting from the both distribution types are added together to obtain a measure of how close an observation is to the center of each cluster. (formulas)

- k-medoids is a more robust version of k-means. The difference is that in k-medoids a real data points are selected as centers of the clusters, whereas in k-means the centers are the computed averages. The R package PAM is a popular implementation of this approach.

- Normal-Multivariate mixture models are another although a bit more complex but very flexible and useful alternative (to detail with formulas)

- The standard method for clustering of factor variables is the **Multiple Correspondence Analysis (MCA)**. This model is implemented in the R packages "FactoMineR" and "PCAmix". It splits all factors into multiple binary variables. Usually the principle components obtained by MCA are then clustered by a **kmeans** algorithm. (details and formulas)

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In our analysis we tried several different clustering methods. However in the displayed results we most often used the following procedure to cluster the variables:

1. Typically one factor analysis type of model is used (such as MCA, PCA, or other depending on the data type).

2. Then the most important factors are selected. In this case we prefer to select larger number of components if it is necessary in order to keep larger part of the variation of the data. We keep in mind that our aim in this stage is to obtain an accurate clustering, rather than to reduce the dimensionality (this will be done using the final cluster partition).

3. At the end these factors are considered as variables and serve as input of an k-means clustering algorithm.

4. The number of clusters is then selected using the Silhouette statistic, but also by considering the interpretability of the resulting partition.

1.2 Psychological variables (green)

1.2.1 Data overview and strategies

All the **six psychological variables are ordinal**. However, together with many other variables in the data set, most often we will consider them as nominal in our analysis, because of the small number of modalities of each of these variables.

Some observations are excluded from the analysis because they contained only missing values. These are the first subjects in the data set and they have also been excluded from other analyses for the same reason.

The final sample for the following analyses contains 32'484 observations

1.2.2 Clustering of psychological variables

A hierarchical clustering method has been performed on the psychological variables in order to investigate any possible relation and presence of subgroups within these variables. The R package "ClustOfVar" has been used for this purpose.

The results do not suggest any clear interpretable structure within as illustrated by the dendrogram in figure 1.1. They indicate that only single variables clusters (singletons) may be separated one at a time to form separate and not very distinct clusters. This information does not provide any useful solution to our problem because obviously it does not make sense to cluster the individuals over one single variable. Therefore this result, combined with the small total number of variables (only 6), lead us to the conclusion that the six psychological variables should be considered together in the same individual clustering algorithm.

1.2.3 Clustering of individuals

Multiple correspondence analysis has been used to cluster the individuals according to their psychological state because all variables are categorical. Even though the first two principal components do not explain large part of the data (26%), we can observe the four most discriminant variables for the clustering (and the importance of their categories) on figure 1.2.

For further analysis we choose rather large number of principal components (9) because of the relatively low explanatory power (65% of the variance). After that we examined several different clustering partitions with respect to the number of clusters. Some particular groups and features can be systematically found in all the partitions. This allows us to make the following generalizations of the results, regardless the number of clusters:
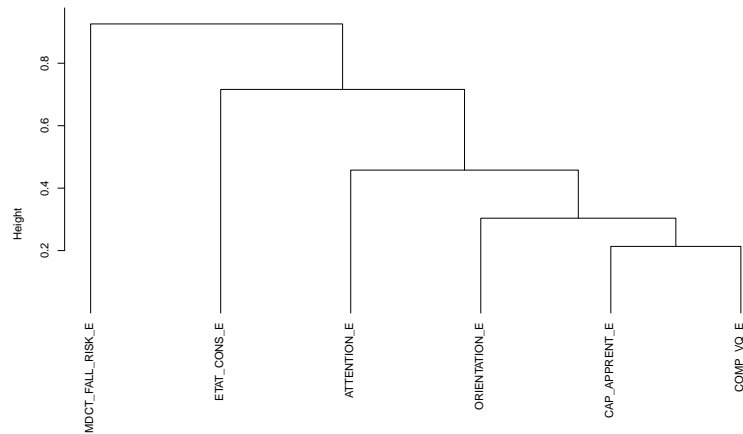
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Figure 1.1: Dendrogram of psychological variables

- The majority of valid observations are displaying good condition in almost all of the variables. They are found in every clustering solution and form always the largest cluter.

- When increasing the number of clusters, the observations with average or "bad" psychological condition are split and nuanced.

- One group of individuals with predominantly missing values have been excluded from the analysis.

The optimal number of clusters is determined here by the silhouette statistic on figure 1.3. This statistic measures how similar each observation is to its own cluster, compared to all other clusters. The results indicates that two or four clusters solution would be the most appropriate in terms of within and between cluster distances. These two solutions will be resumed in this section.

Two cluster soution

The two cluster solution is made of one dominant group of 29913 "healthy" people and one small group of impatients in average and bad condition. On table 1.1 we observe that the two clusters are differently distributed over all 6 variables and the diagnoses (CIM). These differences are also highly significant. It is interesting to mention that much smaller part of the "healthy" group has taken medications increasing the risk of falling or delirium, 15% vs 44% of group 2.

Two other variables (number of medications and primary diagnostic) are added to the analysis for sake of exploration. They do not participate in the clustering model. No difference is observed in the average number of medications, however the primary diagnosis appear to be different among the groups.

Four cluster solution

In the four clustering solution, the results are similar, except that we do not have a single "unhealthy" group, but three clusters with different degree of health issues.

(**INCLUDE THE TABLE FOR 4 GROUPS**)

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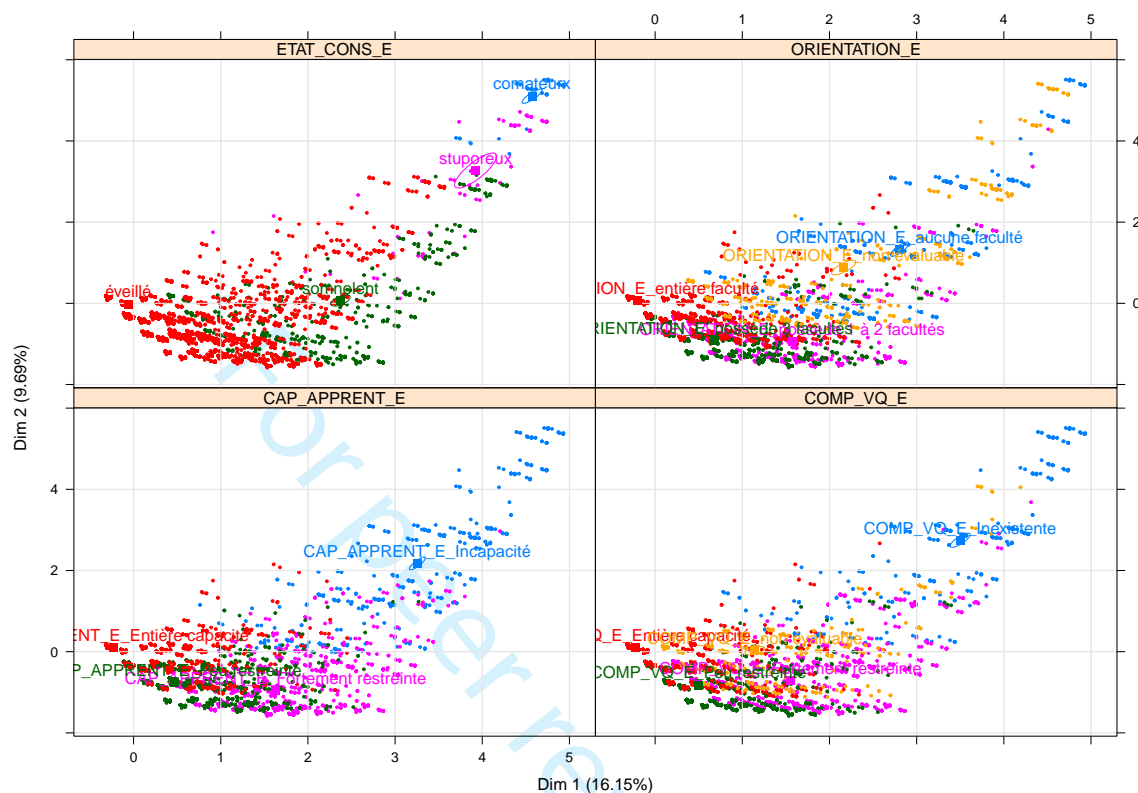
Figure 1.2: Dendrogram of psychological variables

1.3 Somatic/physiologic variables (orange)

1.3.1 Data overview and strategies

Note that several variables have modalities that do not correspond to these described in the list (see the variable description document "summaries age domicile"). These modalities have bean corrected but in an arbitrary manner. Therefore a discussion over all such corrections is necessary.

At least two of the variables from the list should be considered as continuous in this group (Braden risk of sores and risk of falling, probably *"Indice d'autosoins"* and *"risque de déficit de soins post-hospitalisation" may be also continuous*), therefore we dispose with **mixed data**, and will apply the corresponding model. Both continuous variables are finally present in the second sub-group.

1.3.2 Clustering of variables

The number of somatic variables is relatively large to perform a direct clustering on the individuals. Furthermore, the possible presence of similarities between the variables indicate that we must consider a split of these variables in multiple sub-groups.

The initial separation of the variables has been done according to the experts knowledge of the data. However the results from a statistical model for variable clustering have also been used in order to provide an external validation of the experts point of view. These results are summarized

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Figure 1.3: Silhouette statistic for choosing the number of clusters: two or four-cluster solution is suggested.

on figure 1.4. Even though they do not completely match the experts partition, we can observe that many of the variables can be found in the same cluster.
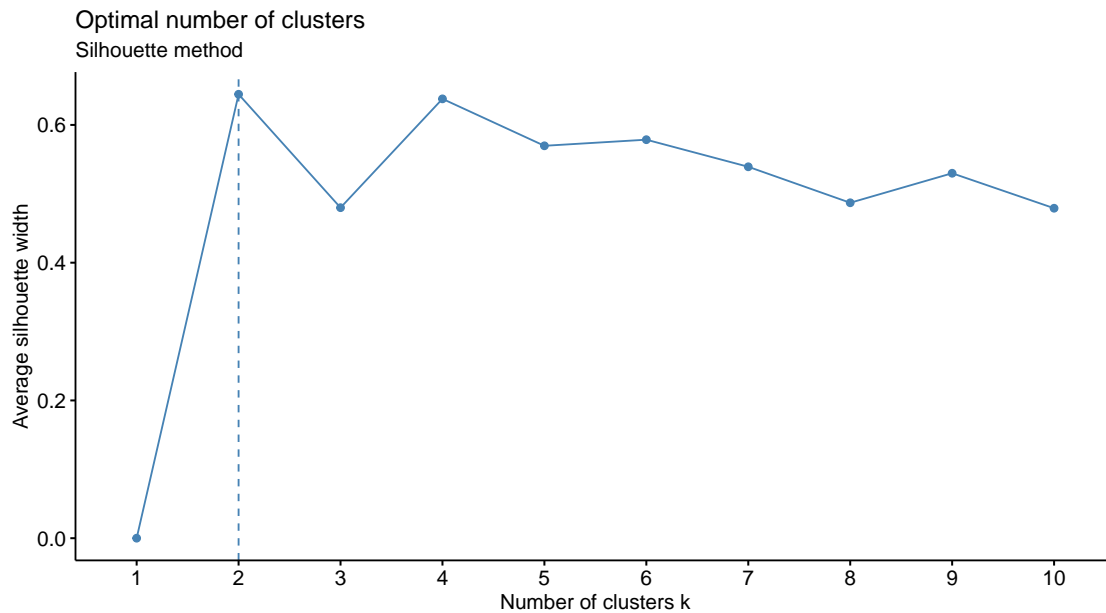
Initially four groups were formed: mobility, health difficulties, support for the daily life activities and other health risks.

As stated before, four groups of variable separation was the initial guess. However on table 1.3 we see that 3 of the variables in the last group "other health risks" present an excessive number of missing values: bedsores, wounds and malnutrition risk.

First, this could be a reason for unreliable results from the variable clustering for these variables, which is a reason to ignore their place in the analysis presented earlier on figure 1.4. But most importantly, it is also a burden for any further clustering of the observations if we keep these variables. Therefore the only solution is to take them out of the analysis.

The two other variables from the group: Braden risk and risk of falling are not sufficient to create an entire group of clustering. Therefore they are attached to the group "health difficulties" for the clustering of individuals. This leads to the following final three sub-groups of physiological/somatic variables displayed on table 1.4.

1.3.3 Clustering of individuals within the physiologic sub-groups

In this section, we will present the results of the 3 separate cluster partitions, one for each of the above-mentioned sub-groups.

Mobility (sub-group 1)

The optimal number of clusters n is unclear according to the silhouette statistic. It suggest rather similar and increasing values as n increases. Therefore we chose two cluster partition because this

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Consciousness	comateurx	stuporeux	somnolent	éveillé		total
group 1	0.00	0.00	0.00	1.00		29913
group 2	0.02	0.03	0.19	0.76		2571
Orientation	aucune faculté	1 à 2 facultés	3 facultés	entière faculté	not measurable	
group 1	0.0	0.01	0.05	0.93	0.00	29913
group 2	0.2	0.34	0.20	0.12	0.14	2571
Learning capacity	Incapacity	severely reduced	slightly reduced	Full capacity		
group 1	0.00	0.01	0.09	0.90		29913
group 2	0.22	0.60	0.12	0.05		2571
Daily life skills	Inexistant	severely reduced	slightly reduced	Full capacity	not measurable	
group 1	0.00	0.01	0.08	0.90	0.01	29913
group 2	0.15	0.57	0.16	0.06	0.07	2571
Attention	perm. reduced	occas. reduced	not affected	not measurable		
group 1	0.01	0	0.98	0.01		29913
group 2	0.61	0	0.30	0.09		2571
Mdc incr. fall risk	yes	no				
group 1	0.15	0.85				29913
group 2	0.44	0.56				2571
Additional variables	(not included)					
Nbr of medications	0	1-3	4-5	6-9	10+	
group 1	0.57	0.12	0.09	0.13	0.09	29913
group 2	0.65	0.04	0.06	0.13	0.12	2571
	mean for gr.1	mean for gr.2				
	2.809748	2.846752				
CodeCim1 REC1	other	cancer	mental	sensory	systemes	
group 1	0.39	0.01	0.13	0.03	0.44	29913
group 2	0.32	0.01	0.08	0.04	0.55	2571

Table 1.1: Two clustering solution: distribution of the groups in all six psychological variables. All distributions are significantly different among clusters (χ^2-tests, p-values<0.01), except the mean number of medications.

Mobility	Health difficulties	Daily life activ. support	Other health risks
Movement	Exhaustion	Body care - upper body	Sores
Changing position	Hearing	Body care - lower body	Wounds
Altered gait	View	Dress and undress - upper b.	Malnutrition risk
Balance disorders	Verbal expression	Dress and undress - lower b.	Risk of falling
Past falls	Drowsiness Full night	Eating	Braden risk (of sores)
Recent falls	Sleep rithm	Drinking	
	Pain intensity	Micturition	
	Chronic pain	Defecation	

Table 1.2: Initial idea for sub-goups of physiological/somatic variables

variable	bedsores	wounds	Braden risk	malnutrition risk	risk of falling
missing values	98.6%	93.6%	0.3%	87.7%	44.9%

Table 1.3: Percentage of missing values in sub-group "other health risks"

is also the best separation in terms of interpretability of the results and implies a clear difference between the groups.

Again in table 1.5 we see that roughly $\frac{2}{3}$ of the subjects have little or no mobility issues (group 2). The remaining individuals exhibit problems in at least one of the 6 dimensions. That number is rather large but not surprising if we consider the advanced age of the selected population.

The χ^2-tests confirm the clear difference between the groups among all variables.
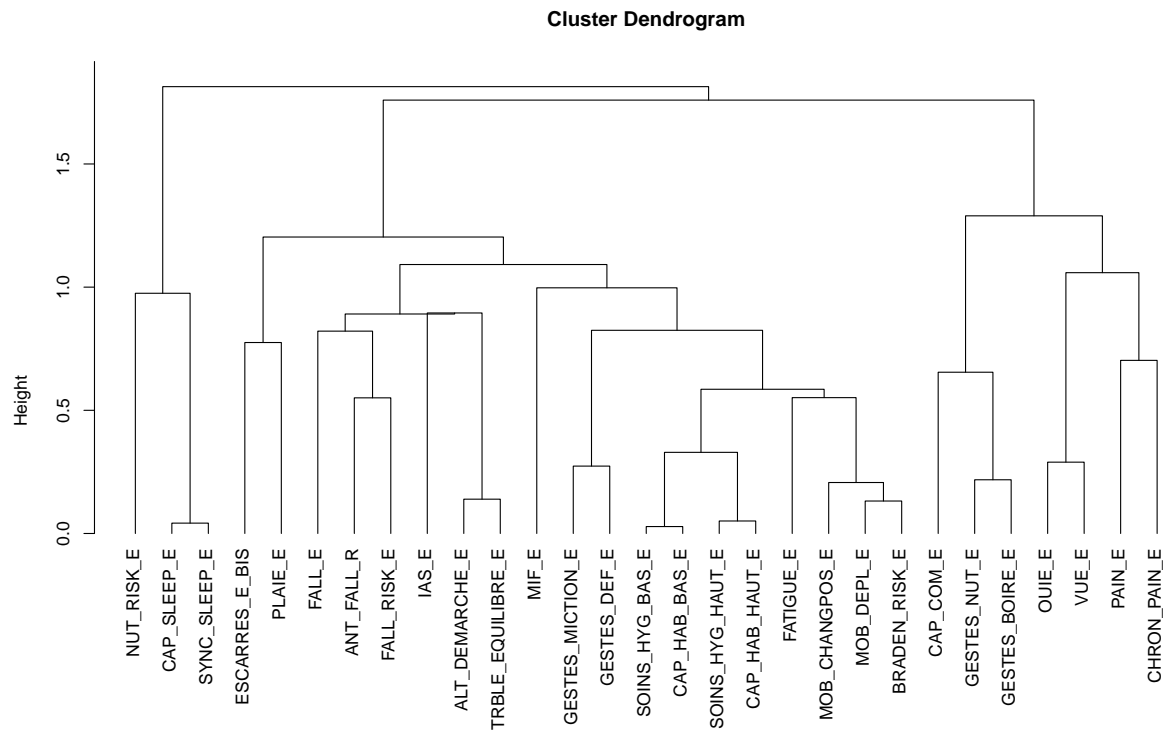
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Figure 1.4: Dendrogram of physiological/somatic variables

Mobility	Health difficulties	Daily life activities support
Movement	Exhaustion	Body care - upper body
Changing position	Hearing	Body care - lower body
Altered gait	View	Dress and undress - upper body
Balance disorders	Verbal expression	Dress and undress - lower body
Past falls	Drowsiness Full night	Eating
Recent falls	Sleep rithm	Drinking
	Pain intensity	Micturition
	Chronic pain	Defecation
	Braden risk (of sores)	
	Risk of falling	

Table 1.4: Final sub-goups of physiological/somatic variables

Health difficulties (sub-group 2)

The objective of our analysis is clustering and not dimension reduction. Therefore it is worth taking into account larger number of principal components in the analysis in order to explain larger part of the variability of the data.

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Movement	Incapacity	severely reduced	slightly reduced	full capacity	total
group 1	0.23	0.37	0.34	0.06	11328
group 2	0.02	0.01	0.16	0.82	21172
Changing position	Incapacity	severely reduced	slightly reduced	full capacity	
group 1	0.08	0.29	0.40	0.23	11329
group 2	0.00	0.00	0.05	0.95	21174
Altered gait	yes	no	not measurable		
group 1	0.56	0.09	0.35		11331
group 2	0.10	0.90	0.01		21172
Balance disorders	yes	no	not measurable		
group 1	0.42	0.21	0.37		11330
group 2	0.06	0.94	0.00		21172
Past falls	yes	no	not measurable		
group 1	0.33	0.59	0.08		11329
group 2	0.05	0.95	0.01		21170
Recent falls	yes	no			
group 1	0.11	0.89			9288
group 2	0.01	0.99			12925

Table 1.5: Two clustering solution of the "mobility" subgroup. All distributions are significantly different among clusters (χ^2-tests, p-values<0.01).

The silhouette statistic suggests 2, 8 or 10 clusters . Our decision is to choose 2 cluster solution for two reasons, first it corresponds to the first and most pronounces peak in the graph 1.5, but it is also more easy to interpret. .
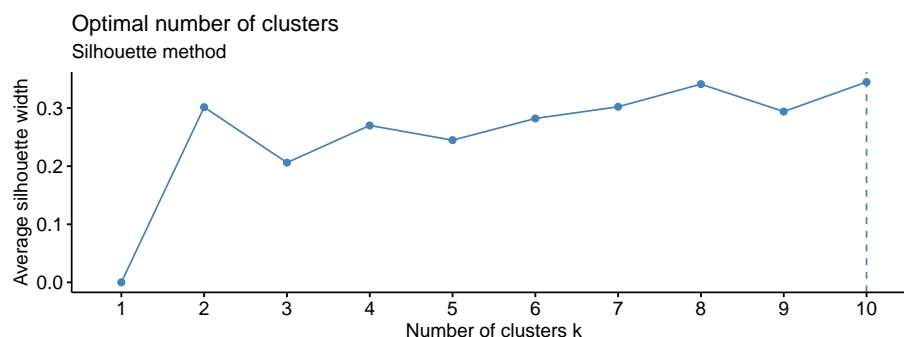

Figure 1.5: Sub-group "Health difficulties": silhouette statistic for choosing the number of clusters. Two or four-cluster solution is suggested.

Before adding the two continuous variables to this sub-group, a **three** cluster solution was the optimal solution, despite the excessively small size of one of the groups ($n_3 = 241$). However this group is the more distinct from the rest. It comprises impatient that were probably unconscious or in very bad condition. Concerning the two other large groups, the only clearly distinctive feature between them was the higher proportion belonging to the group "not measurable" of the variables and therefore they could be merged together.

After adding both continuous variables to the analysis, we observe on figure 1.6 that both solutions are rather similar. The main difference is due to the rather large categories "not measurable" in the variables Drowsiness and Sleep rhythm.

A possible solution to this problem is to **take these variables out of the analysis** and perform a new clustering. Note that both variables are not measurable for the same individuals, which biases the result of the clustering.

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Exhaustion	no activitiy possible	some auton. a. w. recovery	occas. act. possible	good phys./ mental strenght	not meas.	total
group 1	0.01	0.12	0.21	0.65	0.00	24034
group 2	0.04	0.18	0.25	0.50	0.03	8458
Hearing	deafness	auditive problems	no auditive problems	not meas.		
group 1	0	0.1	0.90	0.00		24031
group 2	0	0.1	0.87	0.02		8460
View	blindness	visual problems	no visual problems	not meas.		
group 1	0	0.07	0.93	0.00		24032
group 2	0	0.08	0.88	0.03		8460
Verbal expression	Incapcity	Restricted	entire capacity			
group 1	0.00	0.03	0.96			24030
group 2	0.02	0.07	0.91			8461
Drowsiness	disturbed	no disturbation	not measurable			
group 1	0.15	0.84	0.01			24029
group 2	0.02	0.01	0.97			8459
Sleep rithm	modified	not modified	not measurable			
group 1	0.06	0.94	0.00			24025
group 2	0.02	0.02	0.96			8455
Pain intensity	Signs of pain (3-d p.)	improbable (3-d p.)	intense pain	meduim pain	slight pain	no pain
group 1	0	0	0.03	0.11	0.17	0.69 24017
group 2	0	0	0.03	0.11	0.17	0.69 8460
Chronic pain	yes	no	not meas.			
group 1	0.08	0.92	0.00			23998
group 2	0.07	0.87	0.05			8457

Continuous varibles			
Braden risk sores			
Welch 2 s. t-test:	mean gr.1	mean gr.2	95% conf. int.
	21.1	19.9	(1.08; 1.23)
Risk of falling			
Welch 2 s. t-test:	mean gr.1	mean gr.2	95% conf. int.
	2.11	2.39	(-0.33;-0.24)

Table 1.6: Two clustering solution of the "Health difficulties" subgroup. Nominal and continuous variables results. All distributions are significantly different among clusters (χ^2-tests, p-values<0.01).

The continuous variables have also a significant difference, but it is not a sufficient reason in terms of interpretability to keep this solution.

Daily life activities support (sub-group 3)

The Silhouette statistic is indecisive on figure 1.6, but the two cluster solution appears more appropriate and is our choice.

A brief look on the clusters in figure 1.7 is sufficient to spot the difference between groups. One large cluster of 27'233 observations is formed by mainly healthy individuals that have their full capacity on the majority of the variables. The smaller cluster 1 of 5'268 observations regroups the individuals who have at least one serious problem with their daily life activities. Overall the separation appears interesting for our aim of separating the observations. Once again the distributions of the clusters are significantly different over all variables.
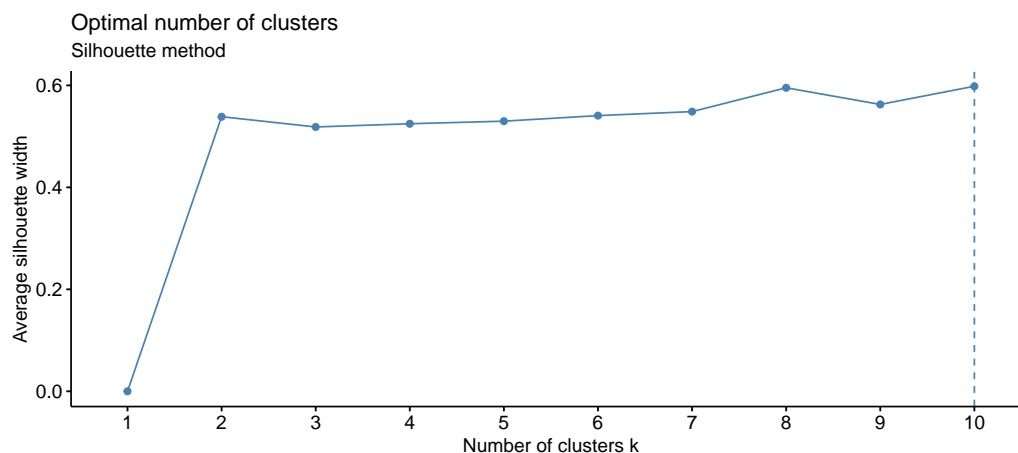
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Optimal number of clusters
Silhouette method

Figure 1.6: Sub-group 3 "Daily life activities support": silhouette statistic for choosing the number of clusters. Two, eight or ten-cluster solution is suggested. Two groups are chosen for sake of simplicity.

Body care - upper b.	incapacity	severely reduced	slightly reduced	full capacity	total
group 1	0.22	0.52	0.23	0.04	5268
group 2	0.00	0.00	0.23	0.76	27233
Body care - lower b.	incapacity	severely reduced	slightly reduced	full capacity	total
group 1	0.53	0.45	0.02	0.00	5268
group 2	0.01	0.09	0.25	0.65	27233
Dress and undress - upper	incapacity	severely reduced	slightly reduced	full capacity	total
group 1	0.26	0.50	0.21	0.03	5268
group 2	0.00	0.01	0.22	0.78	27234
Dress and undress - lower	incapacity	severely reduced	slightly reduced	full capacity	total
group 1	0.53	0.45	0.02	0.00	5268
group 2	0.01	0.08	0.24	0.67	27233
Eating	incapacity	severely reduced	slightly reduced	full capacity	total
group 1	0.13	0.13	0.29	0.45	5268
group 2	0.01	0.00	0.02	0.97	27232
Drinking	incapacity	severely reduced	slightly reduced	full capacity	total
group 1	0.09	0.08	0.18	0.65	5268
group 2	0.01	0.00	0.00	0.99	27229
Micturition	incapacity	severely reduced	slightly reduced	full capacity	total
group 1	0.31	0.24	0.21	0.23	5267
group 2	0.04	0.01	0.08	0.88	27224
Defecation	incapacity	severely reduced	slightly reduced	full capacity	total
group 1	0.17	0.28	0.19	0.36	5267
group 2	0.00	0.00	0.06	0.94	27227

Table 1.7: Two clustering solution of the "Daily life activities support" subgroup. All distributions are significantly different among clusters (χ^2-tests, p-values<0.01).

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Bibliography

[1] A semiparametric method for clustering mixed data. Foss. *Machine Learning*. 2016