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Predictors of health literacy in multimorbid patients in primary care: a cross sectional study in Switzerland.

Running title: Health literacy in multimorbid patients

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Abstract

Objective: To identify factors associated with health literacy in multimorbid patients.

Design: A nationwide cross-sectional study in Switzerland. Univariate and multivariate linear regressions were calculated to identify variables associated with health literacy. A multiple imputation approach was used to deal with missing values.

Participants: Multimorbid patients recruited in primary care settings (N=888), above 18 years old and suffering from at least three of the 75 chronic conditions on a predefined list.

Main measures: Health literacy was assessed using the European Health Literacy Survey project questionnaire (HLS-EU 6). This comprises six items, each with five possible responses (*very difficult* =1, *fairly difficult* =2, *fairly easy* =3, *very easy* =4, and *do not know* =5). The mean health literacy score (sum of answers/number of items) can be computed if at least five of the six items are completed. The score ranges from 1 to 4.

Results: The mean health literacy score (SD) was 2.9 (0.5). Multivariate analyses found significant associations between low health literacy scores and: treatment burden scores (β = -0.004, 95% CI: [-0.006; -0.002]); marital status, predominantly the divorced group (β = 0.136, 95% CI: [0.012; 0.260]); dimensions of the EQ5D3L quality of life assessment, i.e., for moderate problems with mobility (β = -0.086, 95% CI: [-0.157; -0.016]); and with moderate problems (β = -0.129, 95% CI: [-0.198; -0.060]) and severe problems with anxiety/depression (β = -0.343, 95% CI: [-0.500; -0.186]).

Conclusions Multimorbid patients with high treatment burden, problems with mobility, or problems with anxiety or depression, often also have low levels of health literacy. Primary care practitioners should therefore pay particular attention to these patients in their daily practice.

Keywords: Health literacy, Multimorbidity, Primary care, Chronic disease, Switzerland.

Article summary

- This national primary care study enabled the analysis of data from a sample of multimorbid patients
- The first study to assess health literacy in multimorbid patients in primary care settings
- Only multimorbid patients with at least three consulted GPs settings are assessed
- Causal relationships cannot be inferred due to the study design

Introduction

Multimorbidity, defined as the occurrence of multiple chronic medical conditions in one individual (1-3), is a steadily increasing phenomenon due to population ageing (4, 5). Multimorbid patients must face many challenges: more frequent and longer hospitalizations (6, 7), greater use of polypharmacy (causing adverse drug effects) (8, 9), higher expenditure on healthcare (10-12), and the use of a broader range of healthcare services (8, 10). Moreover, as the number of health professionals involved in treatment increases, the more likely patients will be faced with fragmented medical care due to conflicting instructions and care pathways. This makes piecing together and adhering to instructions even more testing and thus prevents patients from participating effectively in their own care (8, 10, 12). Facing all these challenges effectively requires good levels of health literacy. The U.S. Institute of Medicine defines health literacy as "the degree to which individuals have the capacity to obtain, process and understand basic health information and services needed to make appropriate health decisions" (13, 14). Health literacy includes a broad set of skills (i.e., reading, writing, numeracy, communication, and, increasingly, the use of digital technologies) needed to make appropriate health decisions and successfully navigate the healthcare system (15). Health literacy is recognized as an important determinant of health (16-18). Studies have shown that lower health literacy is associated with a lower mental and physical health status, adverse disease-specific outcomes, higher mortality, and more use of healthcare but less use of preventive care (17, 19). Consequently, governments, researchers, clinicians, and patients' associations are paying ever more attention to research into health literacy (20).

Effective patient–clinician communication that ensures patients are able to understand the health information and treatment recommendations they receive and feel comfortable enough to ask

questions or admit when they do not understand something, is vital to the successful management of a chronic illness (21). Healthcare providers should be conscious of their patients' health literacy skills so as to ensure that health information is communicated effectively to help manage long-term conditions. Additionally, health literacy is a prerequisite for patient activation and shared decision making. Thus, identifying factors associated with low health literacy is an important step towards devising effective engagement, prevention, and intervention strategies for multimorbid patients in primary care (20). Studies have assessed health literacy in different ways, for example, the relationships between health literacy and multimorbidity in primary care settings, or the factors influencing health literacy among less well-educated young people and their consequences (14, 17, 22, 23). However, to the best of our knowledge, no study has yet assessed the factors of association between health literacy and multimorbid patients. To fill this gap, the present study aimed to explore factors that might associate low health literacy and multimorbid patients with at least three chronic conditions treated in primary care settings.

Methods

1. *Participants and procedures*

We analyzed data (N = 888) from a national cross-sectional survey conducted in collaboration with Switzerland's five academic institutes of family medicine, between January and September 2015. The study was designed to assess multimorbidity in patients in a primary care setting. The detailed study protocol and dataset description have been published elsewhere (24).

A convenience sample of 100 general practitioners (GPs) randomly enrolled patients from their practices who consulted them during the study period. All multimorbid patients above 18 years old and suffering from at least three of the 75 chronic conditions on a predefined list were considered eligible (25) and signed a written consent to participate to the study. The study protocol (Protocol No 314/15) was approved by the Human Research Ethics Committee of the Canton Vaud, Switzerland.

2. *Measures*

2.1 Health literacy

Health literacy was assessed using the validated six-item questionnaire from the European Health Literacy Survey project (HLS-EU 6) (26, 27). The HLS-EU was a Europe-wide project developed to gather data on health literacy (26). The six items for the survey instrument were selected from the full 47-question survey (HLS-EU 47) (26, 28). We used the shorter, validated questionnaire (HLS-EU-6) because the present study's main objective was to measure overall levels of health literacy in multimorbid patients, not to assess health literacy in detail. The HLS-

EU 6 scale consists of six items with five possible responses. Participants were asked to respond to the following questions. How easy or difficult is it for you to: (a) judge when you may need to get a second opinion from another doctor? (b) use information the doctor gives you to make decisions about your illness? (c) find information on how to manage mental health problems like stress or depression? (d) judge whether the information on health risks in the media is reliable? (e) find out about activities that are good for your mental wellbeing? and (f) understand information in the media on how to get healthier? The possible responses were as follows: *very difficult* = 1, *fairly difficult* = 2, *fairly easy* = 3, *very easy* = 4, and a fifth alternative for when participants did not answer or did not have a definite answer. This was labelled as *do not know*. All other values, including *do not know* answers, that were optional for personal interviews were coded as missing values. Patients' responses were considered incomplete if at least one of the six items was missing a response. The mean health literacy score (sum of answers/number of items) was computed if at least five of the six items had been completed, and the scores thus ranged from 1 to 4 (27).

2.2 Covariates

Demographic covariates included:

- age
- sex (female/male)
- marital status (single, married, divorced, or widowed)
- educational level (primary, secondary, and tertiary)
- number of chronic conditions
- number of drugs (0–4, 5–6, 7–9, or ≥ 10)

- number of medical visits in the last year
- number of hospitalizations in the last year
- Dipcare questionnaire for deprivation assessment, containing 16 items examining the three dimensions of deprivation (material, social, and health), and validated for the Swiss population and published elsewhere in detail (29)
- treatment burden questionnaire (TBQ), recently developed to produce a score for the overall burden related to the treatment of chronic conditions (30); it consists of 13 questions to rate with an answer between 0 and 10, with 0 corresponding to *no burden* and 10 to *a very important/considerable burden*
- nurse (yes/no)
- paramedical therapist grouped together physiotherapist and/or occupational therapist (yes/no)
- homecare (yes/no)
- number of specialists involved in patient's care
- EQ5D3L composed of five dimensions of health (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) and using a visual analogue scale
- the severity index (SI) derived from the cumulative illness rating scale (CIRS), a validated questionnaire published elsewhere in detail (31). The SI, (32-34) was obtained by dividing the total CIRS score by the number of categories with morbidities.

3. Statistical analyses

On collecting the questionnaires, the number of values missing from our variable of interest (health literacy score) was considered too high (i.e. the health literacy score could not be computed in full for 577 participants) to reasonably consider each participant's case in its entirety for analysis. We first considered computing the health literacy scores for all participants with at least five non-missing items. However, even then, the number of missing scores remained too high (377 participants), and comparisons between complete and the incomplete sets of responses showed significant differences in several covariates (data not shown). We therefore opted for the imputation of the values missing from the health literacy items and demographic covariates by using the multiple imputation approach developed by Rubin (35).

We calculated means and standard deviations for quantitative variables, and frequencies and proportions for categorical ones. Univariate and multivariate linear regressions were carried out to identify predictors of health literacy. Using sensitivity analysis, we checked whether a model without imputations would produce the same results as the model with multiple imputations: analysis with and without imputation gave similar results.

All analyses were performed using R software version 3.3.2, (36) and the mice package version 2.29, (37).

Results

Descriptive analyses

Cases with at least one missing value among the six items were considered incomplete. The *do not know* alternative generated a lot of missing values (239, 18, 417, 168, 252, and 175 for questions (a) to (f), respectively), making the health literacy score incomputable for 577 patients. The mean age (SD) of the participants was 72.9 (12.0) years old; 52.0% were women. Almost half of the participants were married (49.0%), and 40.0% had a tertiary level of education. The mean (SD) number of chronic conditions was 7.20 (2.9), and the mean (SD) number of medical visits in the last year was 12.90 (8.7). The mean health literacy score (SD) of the participants was 2.9 (0.5). Descriptive statistics are summarized in Table 1.

Insert table 1 about here

In bivariate analyses with imputation, we found significant relationships between health literacy and almost all the covariates except for the number of chronic conditions, number of drugs, number of medical visits in the last year, number of hospitalizations in the last year, homecare, nurse, and severity index (Table 2).

Insert table 2 about here

The multivariate analyses showed significant relationships between health literacy and: the treatment burden score (β = -0.004, 95% CI: [-0.006; -0.002]); marital status, but particularly for the divorced group (β = 0.136, 95% CI: [0.012; 0. 260]); dimensions of the EQ5D3L quality of life assessment, i.e. moderate problems with mobility and moderate and severe problems with anxiety/depression (β = -0.086, 95% CI: [-0.157; -0.016]), (β = -0.129, 95% CI: [-0.198; -0.060], and (β = -0.343, 95% CI: [-0.500; -0.186]), respectively. Table 3 shows the results of these multivariate analyses.

Insert table 3 about here

Discussion

The present study showed that the mean (SD) health literacy score in our multimorbid primary care patient sample was 2.9 (0.5). In multimorbid patients, a high treatment burden and effects on patients' quality of life due to problems with mobility and anxiety/depression were negatively associated with health literacy. Although several studies have assessed health literacy, to the best of our knowledge, little is known about which factors are associated with low health literacy in multimorbid patients.

The present study's main finding was that the treatment burden facing multimorbid primary care patients was negatively associated with health literacy. In other words, the higher the treatment burden found in multimorbid patients, the lower their health literacy. This could be explained by the fact that multimorbid patients facing a high treatment burden and several associated diseases at once are so concerned about simply coping with their care procedures and treatment that they do not have time to improve their literacy and truly understand those medical acts. This is a common result of polypharmacy, several different treatment procedures and care regimens, and numerous administrative procedures. When we look at all of these elements together, patients faced with the complex situation of a high treatment burden may well become confused: there are too many things happening at the same time for them to be able to understand and manage them effectively. They therefore have neither the time nor the energy to improve their health literacy from its initial low level. Moreover, low health literacy was found to be associated with a reduced ability to identify medication in adults with coronary heart disease (38), poor health outcomes (14, 19, 39), and a more significant use of healthcare (40). As these three factors can also be linked to multimorbidity and may have an impact on the overall treatment burden, this could explain the association between the treatment burden and low health literacy.

This finding is very interesting, and although the β coefficient is small, we believe that this result is clinically relevant and allows us to identify treatment burden as an element to take into account for potentially low literacy in multimorbid patients. It should be noted that due to the study's design, this result could also be seen from another angle, i.e., that low literacy is negatively associated with a high treatment burden. Indeed, individuals with low health literacy are usually less well educated and therefore belong to lower socioeconomic groups. Multimorbidity is higher in these groups and patients in them are more likely to suffer from more severe diseases – this leads to a higher treatment burden.

Another important finding was that patients whose quality of life had been altered by problems related to anxiety/depression or mobility were more likely to have low levels of health literacy. One explanation for the association between problems of anxiety/depression and low health literacy could be that these syndromes can impair cognitive focus, energy, and patient motivation. They might also be expected to affect patients' motivation and ability (41) to seek out and understand information about their diseases and treatment, resulting in a lower level of health literacy, especially in the complex context of multimorbidity. We could suggest that anxious, depressed patients should expend their energies on dealing with their treatment difficulties and reduced quality of life rather than worrying about improving their level of health literacy. Moreover, anxiety and depression may well be higher when patients have to face up to more numerous health problems, especially in multimorbidity. This result is not concordant with the study by Green et al. (42), however, which found no association between limited health literacy and depression in patients treated with chronic hemodialysis, but this difference might be explained by the differences in the study populations and how health literacy was assessed.

Concerning the association between mobility problems and low health literacy, one explanation might be that patients with mobility problems are more dependent on their relatives. Their lack of physical energy may reduce their motivation and interest in searching out and understanding information about their health and how to manage their health concerns: their over-reliance on relatives results in a low level of health literacy. Thus, multimorbid patients with mobility problems would be less inclined to actively search for of health information and might have a tendency to somewhat give up their independence. Moreover, problems of mobility could exacerbate problems of anxiety/depression, resulting in combined effects and explanations for low levels of health literacy in multimorbid patients. However, we can only speculate as to whether there is any precise explanation of these associations and, due to its design, the study's findings could be interpreted the other way (i.e., that health literacy influences anxiety/depression).

The present study found no association between the health literacy of multimorbid primary care patients and their use of healthcare services, especially with regards to the number of consultations with their GP or the number of hospitalizations in the past year. This result agreed with the study by Vandenbosch et al. (40) who also found no significant associations between health literacy and the number of medical visits or hospitalizations. However, a study by Duong et al. (43) did find an association between health literacy and healthcare use. These results are inconsistent due to differences in the study populations (i.e. our study population was composed of multimorbid patients in primary care settings) and methodologies. Indeed, we suggest that health literacy in multimorbid patients is different from that in the general population and should be assessed differently. Further research should aim to clearly confirm or invalidate our results with multimorbid patients.

Strengths and limitations

This national primary care study enabled the analysis of data from a relatively representative sample of multimorbid patients suffering from at least three chronic conditions and enrolled in GPs' practices across Switzerland. Although several studies have previously assessed health literacy, to the best of our knowledge, this was the first to have assessed factors associated with health literacy in multimorbid patients in a primary care setting.

However, this study had some limitations. First, the beta coefficients were small, making clinical interpretation difficult, despite the fact that the study gives an overall view of the factors associated with health literacy. Further studies should be done to confirm these trends.

Second, our sample might not be perfectly representative of all multimorbid patients. GPs only recruited patients who came to their practices and who were suffering from at least three chronic conditions from a list of 75 provided to them. The most impaired multimorbid patients, therefore, those with the most extensive mobility problems (i.e., those cared for via homecare visits, in nursing homes, or hospitalized) were not included (selection bias). Our results concerning the health literacy in multimorbid patients should thus be interpreted with caution, taking into consideration multimorbid patients who cannot attend GPs' practices or who have rare chronic conditions.

Third, due to the study's cross-sectional design, causal relationships cannot be inferred.

Conclusion

The present study highlights the factors associated with health literacy in multimorbid patients. It provides useful information which could guide GPs in their daily practice and help them to pay more attention to patients at risk of having low health literacy. With the knowledge that multimorbidity increases the risks of poor health outcomes, it is particularly important to note that low health literacy is associated with poor health outcomes too. Indeed, despite a greater use of healthcare services, there is less use of preventive care. Even though, with the current state of knowledge, we cannot demonstrate causal relationships between multimorbidity and the treatment burden or quality of life, GPs should carefully weigh up how best to transmit clinical information to their patients in an understandable manner so that they may comprehend it without too much complexity. Moreover, with ageing populations and the likely increase in the numbers of multimorbid patients, it will be important to develop new strategies to improve their health literacy and, in so doing, improve their treatment and patient management in primary care settings.

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Conflict of interest:

The authors declare no conflicts of interest.

Authors' contributions

AAN, ADL, BB, DMH, AZ, LH, and PB developed the protocol for the MMFM study. LH, AZ, and DMH ensured the recruitment of participating GPs. AAN was primarily responsible for planning the analysis and drafting the manuscript. JP was responsible for the analyses. PB, JP, and LH helped to improve the manuscript during this process. BB, AD, DMH, SS, SNJ, AZ, PB, and LH made contributions to the interpretation of the findings and the content of the final manuscript. All authors read and approved the final manuscript.

Data Sharing Statement

Data are available at family medicine institute of Lausanne.

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Table 1: Descriptive statistics of the sample of multimorbid patients, N = 888.

Variable	**mean**‡	**sd**‡
Age	72.93	12.00
Health literacy score (577 missing values)	2.87	0.45
Material deprivation score	0.50	1.27
Social deprivation score	1.93	1.38
Health deprivation score	0.48	0.68
Number of medical visits last year (1 missing value)	12.90	8.70
Number of hospitalizations (3 missing values)	0.54	0.99
Number of chronic conditions (4 missing values)	7.20	2.86
TBQ* score	26.77	18.60
Number of specialists (141 missing values)	2.23	1.27
Severity index	1.75	0.38
Visual analogue scale (EQ5D3L)	63.19	19.25
Variable	**count**	**prop**
Sex		
Male	428	0.48
Female	460	0.52
Educational level (1 missing value)		
Primary	195	0.22
Secondary	337	0.38
Tertiary	355	0.40
Marital status		
Single	85	0.10
Married	437	0.49
Divorced	150	0.17
Widowed	216	0.24
Number of drugs		
0–4	156	0.18
5–6	212	0.24
7–9	276	0.31
≥ 10	244	0.27
Nurse (1 missing value)		
No	798	0.90
Yes	89	0.10
Paramedical † (12 missing values)		
No	572	0.65
Yes	304	0.35

Homecare (1 missing value)		
No	755	0.85
Yes	132	0.15
EQ5D3L five dimensions		
Mobility		
No problems	497	0.56
Moderate problems	386	0.43
Severe problems	5	0.01
Self-care		
No problems	785	0.88
Moderate problems	92	0.10
Severe problems	11	0.01
Usual activities		
No problems	543	0.61
Moderate problems	328	0.37
Severe problems	17	0.02
Pain/discomfort		
No problems	211	0.24
Moderate problems	591	0.67
Severe problems	86	0.10
Anxiety/depression		
No problems	516	0.58
Moderate problems	329	0.37
Severe problems	43	0.05

* TBQ: treatment burden questionnaire

† Paramedical includes physiotherapists/occupational therapists

‡ With multiple imputation

Table 2: Results of bivariate analyses with multiple imputation.

Variable	**β**	**95% CI**		**p-value**
Age	0.0053	0.0027	0.0079	0.0001
Sex	-0.1008	-0.1643	-0.0372	0.0019
Deprivation				
Material deprivation	-0.0786	-0.1034	-0.0537	0.0000
Social deprivation	-0.0485	-0.0707	-0.0263	0.0000
Health deprivation	-0.1407	-0.1853	-0.0961	0.0000
Educational level (ref: Primary)				
Secondary	0.0408	-0.0464	0.1280	0.3579
Tertiary	0.0880	0.0034	0.1726	0.0415
Number of medical visits last year	-0.0023	-0.0060	0.0014	0.2285
Number of hospitalizations	-0.0283	-0.0598	0.0033	0.0789
Number of chronic conditions	0.0042	-0.0076	0.0160	0.4820
Number of drugs (ref: 0–4)				
5–6	-0.0249	-0.1238	0.0741	0.6217
7–9	0.0025	-0.0926	0.0976	0.9588
≥ 10	-0.0601	-0.1579	0.0377	0.2279
TBQ* score	-0.0071	-0.0086	-0.0055	0.0000
Nurse	-0.1016	-0.2133	0.0100	0.0743
Paramedical †	-0.0843	-0.1489	-0.0198	0.0105
Homecare	-0.0772	-0.1698	0.0153	0.1016
Number of specialists	-0.0284	-0.0544	-0.0024	0.0322
Severity index	-0.0457	-0.1258	0.0344	0.2630
Visual analogue scale (EQ5D3L)	0.0048	0.0032	0.0064	0.0000
EQ5D3L five dimensions				
Mobility (ref: No problems)				
Moderate problems	-0.1507	-0.2131	-0.0882	0.0000
Severe problems	-0.1404	-0.5589	0.2781	0.5100
Self-care (ref: No problems)				
Moderate problems	-0.1965	-0.3045	-0.0884	0.0004
Severe problems	-0.1464	-0.4724	0.1795	0.3755
Usual activities (ref: No problems)				
Moderate problemss	-0.1729	-0.2371	-0.1086	0.0000
Severe problems	-0.4167	-0.6521	-0.1813	0.0006
Pain/discomfort (ref: No problems)				
Moderate problems	-0.1174	-0.1970	-0.0378	0.0040
Severe problems	-0.2760	-0.3961	-0.1558	0.0000
Anxiety/depression (ref: No problems)				
Moderate problems	-0.2211	-0.2839	-0.1584	0.0000
Severe problems	-0.5390	-0.6788	-0.3991	0.0000

Marital status (ref: Single)				
Married	0.1596	0.0484	0.2709	0.0050
Divorced	0.0947	-0.0315	0.2208	0.1412
Widowed	0.1128	-0.0057	0.2313	0.0619

* TBQ: treatment burden questionnaire

† Paramedical includes physiotherapists/occupational therapists

Table 3: Results of multivariate analyses with multiple imputation.

Variables	**β**	**95% CI**		**p-value**
Age	0.0007	-0.0027	0.0041	0.6889
Sex	-0.0361	-0.1043	0.0320	0.2981
Deprivation				
Material deprivation	-0.0245	-0.0533	0.0043	0.0954
Social deprivation	-0.0235	-0.0480	0.0010	0.0606
Health deprivation	0.0221	-0.0364	0.0806	0.4577
Educational level (ref: Primary)				
Secondary	0.0070	-0.0763	0.0903	0.8688
Tertiary	0.0560	-0.0284	0.1405	0.1929
Number of medical visits last year	0.0009	-0.0029	0.0048	0.6302
Number of hospitalizations	-0.0183	-0.0503	0.0136	0.2603
Number of chronic conditions	0.0096	-0.0032	0.0224	0.1399
Number of drugs (ref: 0–4)				
5–6	-0.0278	-0.1210	0.0653	0.5577
7–9	0.0276	-0.0647	0.1199	0.5568
≥ 10	0.0110	-0.0905	0.1125	0.8318
TBQ* score	-0.0038	-0.0058	-0.0018	0.0002
Nurse	0.0228	-0.1120	0.1577	0.7390
Paramedical †	-0.0327	-0.0968	0.0314	0.3172
Homecare	0.0057	-0.1069	0.1183	0.9205
Number of specialists	-0.0235	-0.0513	0.0043	0.0967
Severity index	0.0385	-0.0420	0.1190	0.3480
Visual analogue scale (EQ5D3L)	0.0000	-0.0019	0.0019	0.9722
EQ5D3L five dimensions				
Mobility (ref: No problem)s				

Moderate problems	-0.0864	-0.1567	-0.0161	0.0161
Severe problems	0.1663	-0.3459	0.6786	0.5230
Self-care (ref: No problems)				
Moderate problems	-0.0440	-0.1552	0.0673	0.4379
Severe problems	-0.0661	-0.4830	0.3508	0.7532
Usual activities (ref: No problems)				
Moderate problems	-0.0244	-0.0998	0.0509	0.5242
Severe problems	-0.1912	-0.4453	0.0630	0.1402
Pain/discomfort (ref: No problems)				
Moderate problems	-0.0033	-0.0847	0.0780	0.9356
Severe problems	0.0073	-0.1297	0.1444	0.9161
Anxiety/depression (ref: No problems)				
Moderate problems	-0.1288	-0.1978	-0.0598	0.0003
Severe problems	-0.3426	-0.4996	-0.1857	0.0000
Marital status (ref: Single)				
Married	0.0953	-0.0146	0.2053	0.0890
Divorced	0.1360	0.0122	0.2599	0.0314
Widowed	0.0780	-0.0477	0.2037	0.2233

* TBQ: treatment burden questionnaire

† Paramedical includes physiotherapists/occupational therapists

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	**Item #**	**Recommendation**	**Reported on page #**
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Page 1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 5
Objectives	3	State specific objectives, including any prespecified hypotheses	Page 6
Methods			
Study design	4	Present key elements of study design early in the paper	Page 7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	Page7
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Pages 7, 8 & 9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Pages 7, 8 & 9
Bias	9	Describe any efforts to address potential sources of bias	
Study size	10	Explain how the study size was arrived at	Page 7. cf. Published protocol study
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Pages 7, 8 & 9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	Pages 9 & 10
		(*b*) Describe any methods used to examine subgroups and interactions	Pages 9 & 10
		(*c*) Explain how missing data were addressed	Pages 9 & 10
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	Pages 9 & 10
		(*e*) Describe any sensitivity analyses	Pages 9 & 10

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	CF. published protocol study
		(b) Give reasons for non-participation at each stage	CF. published protocol study
		(c) Consider use of a flow diagram	CF. published protocol study
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Page 11
		(b) Indicate number of participants with missing data for each variable of interest	Page 25 & 26
Outcome data	15*	Report numbers of outcome events or summary measures	Page 25 & 26
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Page 27 & 28
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	Page 13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Page 16
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Page 16
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Page 17

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Predictors of health literacy in multimorbid patients in primary care: a cross sectional study in Switzerland

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Predictors of health literacy in multimorbid patients in primary care: a cross-sectional study in Switzerland.

Running title: Health literacy in multimorbid patients

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Abstract

Objective: To identify factors associated with health literacy in multimorbid patients.

Design: A nationwide cross-sectional study in Switzerland. Univariate and multivariate linear regressions were calculated to identify variables associated with health literacy. A multiple imputation approach was used to deal with missing values.

Participants: Multimorbid patients recruited in primary care settings (N=888), above 18 years old and suffering from at least three of the 75 chronic conditions on a predefined list based on the ICPC-2.

Main measures: Health literacy was assessed using the European Health Literacy Survey project questionnaire (HLS-EU 6). This comprises six items scored from 1 to 4 (*very difficult* = 1, *fairly difficult* = 2, *fairly easy* = 3, *very easy* = 4), and the total health literacy score is computed as their mean. As we wished to understand the determinants associated with lower health literacy, the HLS-EU 6 score was the only dependent variable; all other covariates were considered independent.

Results: The mean health literacy score (SD) was 2.9 (0.5). Multivariate analyses found significant associations between low health literacy scores and: treatment burden scores (β = -0.004, 95% CI: [-0.006; -0.002]); marital status, predominantly the divorced group (β = 0.136, 95% CI: [0.012; 0.260]); dimensions of the EQ5D3L quality of life assessment, i.e. for moderate problems with mobility (β = -0.086, 95% CI: [-0.157; -0.016]); and with moderate problems (β = -0.129, 95% CI: [-0.198; -0.060]) and severe problems with anxiety/depression (β = -0.343, 95% CI: [-0.500; -0.186]).

Conclusions Multimorbid patients with a high treatment burden, problems with mobility, or problems with anxiety or depression, often also have low levels of health literacy. Primary care practitioners should therefore pay particular attention to these patients in their daily practice.

Keywords: Health literacy, Multimorbidity, Primary care, Chronic disease, Switzerland.

Article summary

- This national primary care study enabled the analysis of data from a sample of multimorbid patients
- The first study to understand the determinants associated with health literacy in multimorbid patients in primary care settings
- Only multimorbid patients with at least three chronic conditions were assessed
- Causal relationships could not be inferred due to the study design

Strengths and limitations

This national primary care study enabled the analysis of data from a relatively representative sample of multimorbid patients suffering from at least three chronic conditions and enrolled in GPs' practices across Switzerland. Although several studies have previously assessed health literacy, to the best of our knowledge, this was the first to have assessed factors associated with health literacy in multimorbid patients in a primary care setting.

However, this study had some limitations. First, the beta coefficients were small, making clinical interpretation difficult, despite the fact that the study gives an overall view of the factors associated with health literacy. Further studies should be done to confirm these trends.

Second, our sample might not be perfectly representative of all multimorbid patients. GPs only recruited patients who came to their practices and who were suffering from at least three chronic conditions from a list of 75 provided to them. The most impaired multimorbid patients, therefore, those with the most extensive mobility problems (i.e. those cared for via homecare visits, in nursing homes, or hospitalised) were not included (selection bias). Our results concerning health literacy in multimorbid patients should thus be interpreted with caution, taking into consideration multimorbid patients who cannot attend GPs' practices or who have rare chronic conditions. Furthermore, we cannot exclude a potential selection bias, as patients who consulted more frequently had a higher chance of being included. However, we found no association between the frequency of consultations and health literacy in our final model.

Third, the health literacy score contained a lot of missing values, and we cannot exclude that the cause of that missing data was related to health literacy itself. However, we examined whether the mean of the available HL items was associated with the number of missing HL items, and this was not the case.

Fourth, due to the study's cross-sectional design, causal relationships cannot be inferred.

Introduction

Multimorbidity, defined as the occurrence of multiple chronic medical conditions in one individual (1-3), is a steadily increasing phenomenon due to population ageing (4, 5). Multimorbid patients must face many challenges: more frequent and longer hospitalisations (6, 7), greater use of polypharmacy (causing adverse drug effects) (8, 9), higher expenditure on healthcare (10-12) and the use of a broader range of healthcare services (8, 10). Moreover, as the number of health professionals involved in treatment increases, the more likely patients will be faced with fragmented medical care due to conflicting instructions and care pathways. This makes piecing together and adhering to instructions even more testing and thus prevents patients from participating effectively in their own care (8, 10, 12). Facing all these challenges effectively requires good levels of health literacy. The U.S. Institute of Medicine defines health literacy as "the degree to which individuals have the capacity to obtain, process and understand basic health information and services needed to make appropriate health decisions" (13, 14). Health literacy includes a broad set of skills (i.e. reading, writing, numeracy, communication and, increasingly, the use of digital technologies) needed to make appropriate health decisions and successfully navigate the healthcare system (15). Health literacy is recognized as an important determinant of health (16-18). Studies have shown that lower health literacy is associated with a lower mental and physical health status, adverse disease-specific outcomes, higher mortality, and more use of healthcare but less use of preventive care (17, 19). Consequently, governments, researchers, clinicians and patients' associations are paying ever more attention to research into health literacy (20).

Effective patient–clinician communication that ensures patients are able to understand the health information and treatment recommendations they receive and feel comfortable enough to ask

questions or admit when they do not understand something, is vital to the successful management of a chronic illness (21). Healthcare providers should be conscious of their patients' health literacy skills so as to ensure that health information is communicated effectively to help manage long-term conditions (22, 23). Additionally, health literacy is a prerequisite for patient activation and shared decision-making. Thus, identifying factors associated with low health literacy is an important step towards devising effective engagement, prevention and intervention strategies for patients in primary care (20). The literature shows that health literacy has been assessed in different ways and with contrasting conclusions: e.g. different studies looking at the factors influencing health literacy among less well-educated young people showed a relationship between low health literacy and socioeconomic factors (17, 24, 25). One study evaluating relevant associations between health literacy and multimorbidity (defined as two or more chronic diseases from a list of 11 conditions) in primary care, found none (14). To better understand the determinants associated with low health literacy, the present study aimed to explore all the factors that might be associated with low health literacy in multimorbid patients in primary care with at least three chronic conditions.

Methods

1. Participants and procedures

We analysed data (N = 888) from a national cross-sectional survey conducted in collaboration with Switzerland's five academic institutes of family medicine, between January and September 2015. The study was designed to assess multimorbidity in patients in a primary care setting in order to target a population whose management is more challenging to general practitioners (GPs). The detailed study protocol, dataset description and initial results have been published elsewhere (26, 27).

A convenience sample of 100 GPs randomly enrolled patients from their practices who consulted them during the study period. All multimorbid patients above 18 years old and suffering from at least three of the 75 chronic conditions on a predefined list, based on the International Classification of Primary Care 2 (ICPC-2), were considered eligible (28, 29) and gave written informed consent to participate in the study. The study protocol (Protocol No 314/15) was approved by the Human Research Ethics Committee of the Canton Vaud, Switzerland.

2. Measures

2.1 Health literacy

Health literacy was assessed using the validated six-item questionnaire from the European Health Literacy Survey project (HLS-EU 6) (30, 31). The HLS-EU was a Europe-wide project developed to gather data on health literacy (30). The original HLS-EU 47 explored three domains: 1. healthcare; 2. disease prevention; and 3. health promotion. Each domain explored four matrices: accessing/obtaining information; understanding information; processing/

appraising information; and applying/using information. The HLS-EU 6 is a validated short form with two of the original questions remaining in each domain (30-32). Validated French and German versions of the HLS-EU 6 were available. We used this shorter, validated questionnaire because the present study's main objective was to measure overall levels of health literacy in multimorbid patients, not to assess health literacy in detail. The HLS-EU 6 scale consists of six items with five possible responses. Participants were asked to respond to the following questions. How easy or difficult is it for you to: (a) judge when you may need to get a second opinion from another doctor? (b) use information the doctor gives you to make decisions about your illness? (c) find information on how to manage mental health problems like stress or depression? (d) judge whether the information on health risks in the media is reliable? (e) find out about activities that are good for your mental wellbeing? and (f) understand information in the media on how to get healthier? The possible responses and their scores were as follows: *very difficult* = 1, *fairly difficult* = 2, *fairly easy* = 3, *very easy* = 4, and a fifth alternative for when participants did not answer or did not have a definite answer, coded as a missing value. The health literacy score was thus calculated as the mean of the six health literacy items, scored from 1 to 4, after imputation of the missing values (see the Statistical Analyses section below) (31).

2.2 Covariates

All the variables have been described elsewhere (26). Briefly, our analyses used the following variables:

2.2.1 Dependent variable: as we wished to understand the determinants associated with lower health literacy scores, we chose the HLS-EU as the dependent variable.

2.2.2 Independent variables: Includes all other variables as:

- age
- sex (female/male)
- marital status (single, married, divorced or widowed)
- educational level (primary, secondary and tertiary)
- number of chronic conditions (based on ICPC 2)
- number of drugs (0–4, 5–6, 7–9, or ≥ 10)
- number of medical visits in the last year (based on GPs' medical records)
- number of hospitalisations in the last year
- Dipcare questionnaire for deprivation assessment, containing 16 items examining the three dimensions of deprivation (material, social and health), and validated for the Swiss population and published elsewhere in detail (33)
- treatment burden questionnaire (TBQ), recently developed to produce a score for the overall burden related to the treatment of chronic conditions (34); it consists of 13 questions to rate with an answer between 0 and 10, with 0 corresponding to *no burden* and 10 to *a very important/considerable burden*
- medical help from a home nurse
- *paramedical therapist* grouped together physiotherapist and/or occupational therapist (yes/no)
- homecare (yes/no)
- number of specialists involved in patient's care
- EQ5D3L composed of five dimensions of health (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) and used a visual analogue scale

- the severity index (SI) (35-37) was derived by dividing the total cumulative illness rating scale (CIRS) score, a validated questionnaire published elsewhere in detail (38), by the number of categories with morbidities.

3. *Statistical analyses*

On collecting the questionnaires, the number of values missing from our variable of interest (health literacy score) was considered too high (i.e. the health literacy score could not be computed in full for 577 participants) to reasonably analyse each participant’s case in its entirety. We first considered computing the health literacy scores for all participants with at least five non-missing items. However, even then, the number of missing scores remained too high (377 participants), and comparisons between complete and the incomplete sets of responses showed significant differences in several covariates (data not shown). We therefore opted for the imputation of the values missing from the health literacy items and demographic covariates by using the multiple imputation approach developed by Rubin (39). As a sensitivity analysis, we carried out a complete case analysis, and this gave similar results.

We calculated means and standard deviations for quantitative variables, and frequencies and proportions for categorical ones. Univariate and multivariate linear regressions were carried out to identify predictors of health literacy. Using sensitivity analysis, we checked whether a model without imputations would produce the same results as the model with multiple imputations: analysis with and without imputation gave similar results.

All analyses were performed using R software version 3.3.2 (40) and the MICE package version 2.29 (41).

Results

Descriptive analyses

Cases with at least one missing value among the six items were considered incomplete (239, 18, 417, 168, 252 and 175 missing values for questions (a) to (f), respectively). Of the original 888 patients, 200, 175, 117, 59, 24 and 2 had, respectively, 1, 2, 3, 4, 5 and 6 missing HL variables. Thus a complete HL score was only computable for 311 respondents (35%), and we therefore chose to impute the missing values.

The mean age (SD) of the participants was 72.9 (12.0) years old; 52.0% were women. Almost half of the participants were married (49.0%), and 40.0% had a tertiary level of education. The mean (SD) number of chronic conditions was 7.20 (2.9), and the mean (SD) number of medical visits in the last year was 12.90 (8.7). The mean health literacy score (SD) of the participants was 2.9 (0.5). Descriptive statistics are summarized in Table 1.

Insert table 1 about here

In bivariate analyses with imputation, we found significant relationships between health literacy and almost all the covariates except for the number of chronic conditions, number of drugs, number of medical visits in the last year, number of hospitalisations in the last year, homecare, nurse, and severity index (Table 2).

Insert table 2 about here

The multivariate analyses showed significant relationships between health literacy and: the treatment burden score (β = -0.004, 95% CI: [-0.006; -0.002]); marital status, but particularly for the divorced group (β = 0.136, 95% CI: [0.012; 0. 260]); dimensions of the EQ5D3L quality of life assessment, i.e. moderate problems with mobility and moderate and severe problems with anxiety/depression (β = -0.086, 95% CI: [-0.157; -0.016]), (β = -0.129, 95% CI: [-0.198; -0.060], and (β = -0.343, 95% CI: [-0.500; -0.186]), respectively. Table 3 shows the results of these multivariate analyses.

Insert table 3 about here

Discussion

The present study showed that the mean (SD) health literacy score in our multimorbid primary care patient sample was 2.9 (0.5). In multimorbid patients, a high treatment burden and effects on patients' quality of life due to problems with mobility and anxiety/depression were negatively associated with health literacy. However, our study revealed no association between HL and age. Although several studies have assessed health literacy, to the best of our knowledge, little is known about which factors are associated with low health literacy in multimorbid patients in primary care.

The present study's main finding was that the treatment burden facing multimorbid primary care patients was negatively associated with health literacy. In other words, the higher the treatment burden found in multimorbid patients, the lower their health literacy. This could be explained by the fact that multimorbid patients, facing a high treatment burden and several associated diseases at once, are so concerned about simply coping with their care procedures and treatment that they do not have time to improve their literacy and truly understand those medical acts. This is a common result of polypharmacy, several different treatment procedures and care regimens, and numerous administrative procedures. When we look at all of these elements together, patients faced with the complex situation of a high treatment burden may well become confused: there are too many things happening at the same time for them to be able to understand and manage them effectively. They therefore have neither the time nor the energy to improve their health literacy from its initial low level.

This is a very interesting finding, and although the β coefficient is small, we believe that this result is clinically relevant and allows us to identify treatment burden as an element to take into account for potentially low literacy in multimorbid patients.

However, our exploratory study was unable to determine any causal association between the treatment burden and health literacy. But our results could also be considered from another angle, that has been taken in other analyses”. Indeed, individuals with low health literacy are usually less well educated and belong to lower socioeconomic groups. Multimorbidity is higher in these groups and patients in them are likely to suffer more severely and from more diseases, leading to a higher treatment burden. Furthermore, low health literacy, used as an independent variable, has been found to be associated with a reduced ability of adults with coronary heart disease to identify medication (42), poor health outcomes (14, 19, 43), and a more significant use of healthcare (44). These three factors can also be linked to multimorbidity and may have an impact on the overall treatment burden.

Another important finding was that patients whose quality of life had been altered by problems related to anxiety/depression or mobility were more likely to have low levels of health literacy. One explanation for the association between problems of anxiety/depression and low health literacy could be that these syndromes can impair cognitive focus, energy and patient motivation. They might also be expected to affect patients' motivation and ability (45) to seek out and understand information about their diseases and treatment, resulting in a lower level of health literacy, especially in the complex context of multimorbidity. We could suggest that anxious, depressed patients should expend their energies on dealing with their treatment difficulties and reduced quality of life rather than worrying about improving their level of health literacy. Moreover, anxiety and depression may well be higher when patients have to face up to more numerous health problems, especially in multimorbidity. This result is not concordant with the study by Green et al. (46), however, which found no association between limited health literacy and depression in patients receiving chronic hemodialysis treatment, but this difference might be explained by the differences in the study populations, how health literacy was assessed and the fact that his study used health literacy as independent variable.

Concerning the association between mobility problems and low health literacy, one explanation might be that patients with mobility problems are more dependent on their relatives. Their lack of physical energy may reduce their motivation and interest in searching out and understanding information about their health and how to manage their health concerns: their over-reliance on relatives results in a low level of health literacy. Thus, multimorbid patients with mobility problems would be less inclined to actively search for of health information and might have a tendency to give up their independence somewhat. Moreover, problems of mobility could exacerbate problems of anxiety/depression, resulting in combined effects and explanations for low levels of health literacy in multimorbid patients. However, we can only speculate as to whether there is any precise explanation of these associations and, due to its design, the study's findings could be interpreted the other way (i.e. that health literacy influences anxiety/depression).

The present study found no association between the level of health literacy of multimorbid primary care patients and their use of healthcare services, especially with regards to the number of consultations with their GP or the number of hospitalisations in the past year. Results in the literature are inconsistent. The study by Vandenbosch et al. (44) found no significant associations between health literacy and the number of medical visits or hospitalisations, whereas a study by Duong et al. (47) described an association between health literacy and healthcare use. These results are inconsistent due to differences in the study populations (i.e. our study population was composed of multimorbid patients in primary care settings) and methodologies (other studies considered health literacy as an independent variable). Indeed, we suggest that health literacy in multimorbid patients is different from that in the general population and should be assessed differently. Further research should aim to clearly confirm or invalidate our results with multimorbid patients.

Strengths and limitations

This national primary care study enabled the analysis of data from a relatively representative sample of multimorbid patients suffering from at least three chronic conditions and enrolled in GPs' practices across Switzerland. Although several studies have previously assessed health literacy, to the best of our knowledge, this was the first to have assessed factors associated with health literacy in multimorbid patients in a primary care setting.

However, this study had some limitations. First, the beta coefficients were small, making clinical interpretation difficult, despite the fact that the study gives an overall view of the factors associated with health literacy. Further studies should be done to confirm these trends.

Second, our sample might not be perfectly representative of all multimorbid patients. GPs only recruited patients who came to their practices and who were suffering from at least three chronic conditions from a list of 75 provided to them. The most impaired multimorbid patients, therefore, those with the most extensive mobility problems (i.e. those cared for via homecare visits, in nursing homes, or hospitalised) were not included (selection bias). Our results concerning health literacy in multimorbid patients should thus be interpreted with caution, taking into consideration multimorbid patients who cannot attend GPs' practices or who have rare chronic conditions. Furthermore, we cannot exclude a potential selection bias, as patients who consulted more frequently had a higher chance of being included. However, we found no association between the frequency of consultations and health literacy in our final model.

Third, the health literacy score contained a lot of missing values, and we cannot exclude that the cause of that missing data was related to health literacy itself. However, we examined whether the mean of the available HL items was associated with the number of missing HL items, and this was not the case.

Fourth, due to the study's cross-sectional design, causal relationships cannot be inferred.

Conclusion

The present study highlights the factors associated with health literacy in multimorbid patients. It provides useful information that could guide GPs in their daily practice and help them to pay more attention to patients at risk of having low health literacy. With the knowledge that multimorbidity increases the risks of poor health outcomes, it is particularly important to note that low health literacy is associated with poor health outcomes too. Indeed, despite a greater use of healthcare services, there is less use of preventive care. Even though, with the current state of knowledge, we cannot demonstrate causal relationships between multimorbidity and the treatment burden or quality of life, GPs should carefully weigh up how best to transmit clinical information to their patients, in an understandable manner, so that they may comprehend it without too much complexity. Moreover, with ageing populations and the likely increase in the numbers of multimorbid patients, it will be important to develop new strategies to improve their health literacy and, in so doing, improve their treatment and patient management in primary care settings.

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Conflict of interest:

The authors declare no conflicts of interest.

Authors' contributions

AAN, ADL, BB, DMH, AZ, LH and PB developed the protocol for the MMFM study. LH, AZ and DMH ensured the recruitment of participating GPs. AAN was primarily responsible for planning the analysis and drafting the manuscript. JP was responsible for the analyses. PB, JP and LH helped to improve the manuscript during this process. BB, AD, DMH, SS, SNJ, AZ, PB and LH made contributions to the interpretation of the findings and the content of the final manuscript. All authors read and approved the final manuscript.

Data Sharing Statement

Data are available at family medicine institute of Lausanne.

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Table 1: Descriptive statistics of the sample of multimorbid patients, N = 888.

Variable	**mean**‡	**sd**‡
Age	72.93	12.00
Health literacy score (577 missing values)	2.87	0.45
Material deprivation score	0.50	1.27
Social deprivation score	1.93	1.38
Health deprivation score	0.48	0.68
Number of medical visits last year (1 missing value)	12.90	8.70
Number of hospitalisations (3 missing values)	0.54	0.99
Number of chronic conditions (4 missing values)	7.20	2.86
TBQ* score	26.77	18.60
Number of specialists (141 missing values)	2.23	1.27
Severity index	1.75	0.38
Visual analogue scale (EQ5D3L)	63.19	19.25
Variable	**count**	**prop**
Sex		
Male	428	0.48
Female	460	0.52
Educational level (1 missing value)		
Primary	195	0.22
Secondary	337	0.38
Tertiary	355	0.40
Marital status		
Single	85	0.10
Married	437	0.49
Divorced	150	0.17
Widowed	216	0.24
Number of drugs		
0–4	156	0.18
5–6	212	0.24
7–9	276	0.31
≥ 10	244	0.27
Home Nurse (1 missing value)		
No	798	0.90
Yes	89	0.10
Paramedical † (12 missing values)		
No	572	0.65
Yes	304	0.35

Homecare (1 missing value)		
No	755	0.85
Yes	132	0.15
EQ5D3L five dimensions		
Mobility		
No problems	497	0.56
Moderate problems	386	0.43
Severe problems	5	0.01
Self-care		
No problems	785	0.88
Moderate problems	92	0.10
Severe problems	11	0.01
Usual activities		
No problems	543	0.61
Moderate problems	328	0.37
Severe problems	17	0.02
Pain/discomfort		
No problems	211	0.24
Moderate problems	591	0.67
Severe problems	86	0.10
Anxiety/depression		
No problems	516	0.58
Moderate problems	329	0.37
Severe problems	43	0.05

* TBQ: treatment burden questionnaire

† Paramedical includes physiotherapists/occupational therapists

‡ With multiple imputation

Table 2: Results of bivariate analyses with multiple imputation.

Independent variable	**β**	**95% CI**		**p-value**
Age	0.0053	0.0027	0.0079	0.0001
Sex	-0.1008	-0.1643	-0.0372	0.0019
Deprivation				
Material deprivation	-0.0786	-0.1034	-0.0537	0.0000
Social deprivation	-0.0485	-0.0707	-0.0263	0.0000
Health deprivation	-0.1407	-0.1853	-0.0961	0.0000
Educational level (ref: Primary)				
Secondary	0.0408	-0.0464	0.1280	0.3579
Tertiary	0.0880	0.0034	0.1726	0.0415
Number of medical visits last year	-0.0023	-0.0060	0.0014	0.2285
Number of hospitalisations	-0.0283	-0.0598	0.0033	0.0789
Number of chronic conditions	0.0042	-0.0076	0.0160	0.4820
Number of drugs (ref: 0–4)				
5–6	-0.0249	-0.1238	0.0741	0.6217
7–9	0.0025	-0.0926	0.0976	0.9588
≥ 10	-0.0601	-0.1579	0.0377	0.2279
TBQ* score	-0.0071	-0.0086	-0.0055	0.0000
Home nurse	-0.1016	-0.2133	0.0100	0.0743
Paramedical †	-0.0843	-0.1489	-0.0198	0.0105
Homecare	-0.0772	-0.1698	0.0153	0.1016
Number of specialists	-0.0284	-0.0544	-0.0024	0.0322
Severity index	-0.0457	-0.1258	0.0344	0.2630
Visual analogue scale (EQ5D3L)	0.0048	0.0032	0.0064	0.0000
EQ5D3L five dimensions				
Mobility (ref: No problems)				
Moderate problems	-0.1507	-0.2131	-0.0882	0.0000
Severe problems	-0.1404	-0.5589	0.2781	0.5100
Self-care (ref: No problems)				
Moderate problems	-0.1965	-0.3045	-0.0884	0.0004
Severe problems	-0.1464	-0.4724	0.1795	0.3755
Usual activities (ref: No problems)				
Moderate problemss	-0.1729	-0.2371	-0.1086	0.0000
Severe problems	-0.4167	-0.6521	-0.1813	0.0006
Pain/discomfort (ref: No problems)				
Moderate problems	-0.1174	-0.1970	-0.0378	0.0040
Severe problems	-0.2760	-0.3961	-0.1558	0.0000
Anxiety/depression (ref: No problems)				
Moderate problems	-0.2211	-0.2839	-0.1584	0.0000

Severe problems	-0.5390	-0.6788	-0.3991	0.0000
Marital status (ref: Single)				
Married	0.1596	0.0484	0.2709	0.0050
Divorced	0.0947	-0.0315	0.2208	0.1412
Widowed	0.1128	-0.0057	0.2313	0.0619

Table 3: Results of multivariate analyses with multiple imputation.

Independent variables	**β**	**95% CI**		**p-value**
Age	0.0007	-0.0027	0.0041	0.6889
Sex	-0.0361	-0.1043	0.0320	0.2981
Deprivation				
Material deprivation	-0.0245	-0.0533	0.0043	0.0954
Social deprivation	-0.0235	-0.0480	0.0010	0.0606
Health deprivation	0.0221	-0.0364	0.0806	0.4577
Educational level (ref: Primary)				
Secondary	0.0070	-0.0763	0.0903	0.8688
Tertiary	0.0560	-0.0284	0.1405	0.1929
Number of medical visits last year	0.0009	-0.0029	0.0048	0.6302
Number of hospitalisations	-0.0183	-0.0503	0.0136	0.2603
Number of chronic conditions	0.0096	-0.0032	0.0224	0.1399
Number of drugs (ref: 0–4)				
5–6	-0.0278	-0.1210	0.0653	0.5577
7–9	0.0276	-0.0647	0.1199	0.5568
≥ 10	0.0110	-0.0905	0.1125	0.8318
TBQ* score	-0.0038	-0.0058	-0.0018	0.0002
Nurse	0.0228	-0.1120	0.1577	0.7390
Paramedical †	-0.0327	-0.0968	0.0314	0.3172
Homecare	0.0057	-0.1069	0.1183	0.9205
Number of specialists	-0.0235	-0.0513	0.0043	0.0967
Severity index	0.0385	-0.0420	0.1190	0.3480
Visual analogue scale (EQ5D3L)	0.0000	-0.0019	0.0019	0.9722

EQ5D3L five dimensions				
Mobility (ref: No problem)s				
Moderate problems	-0.0864	-0.1567	-0.0161	0.0161
Severe problems	0.1663	-0.3459	0.6786	0.5230
Self-care (ref: No problems)				
Moderate problems	-0.0440	-0.1552	0.0673	0.4379
Severe problems	-0.0661	-0.4830	0.3508	0.7532
Usual activities (ref: No problems)				
Moderate problems	-0.0244	-0.0998	0.0509	0.5242
Severe problems	-0.1912	-0.4453	0.0630	0.1402
Pain/discomfort (ref: No problems)				
Moderate problems	-0.0033	-0.0847	0.0780	0.9356
Severe problems	0.0073	-0.1297	0.1444	0.9161
Anxiety/depression (ref: No problems)				
Moderate problems	-0.1288	-0.1978	-0.0598	0.0003
Severe problems	-0.3426	-0.4996	-0.1857	0.0000
Marital status (ref: Single)				
Married	0.0953	-0.0146	0.2053	0.0890
Divorced	0.1360	0.0122	0.2599	0.0314
Widowed	0.0780	-0.0477	0.2037	0.2233

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract **Title: Predictors of health literacy in multimorbid patients in primary care: a cross-sectional study in Switzerland.**
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found **p. 3 -4**
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported **p.5**
Objectives	3	State specific objectives, including any prespecified hypotheses **pp. 6**
Methods		
Study design	4	Present key elements of study design early in the paper **p. 7**
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection **p. 7**
Participants	6	*Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants **p.7**
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable **p. 7-10**
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group **pp. 7-10**
Bias	9	Describe any efforts to address potential sources of bias **p. 7**
Study size	10	Explain how the study size was arrived at **p. 7**
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why **p. 8**
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding **pp. 10**
		(*b*) Describe any methods used to examine subgroups and interactions **pp. 10**
		(*c*) Explain how missing data were addressed **p. 10**
		(*e*) Describe any sensitivity analyses **p. 10**

Continued on next page

Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed **p. p.10**
		(b) Give reasons for non-participation at each stage **p. 10**
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders **Table 1**
		(b) Indicate number of participants with missing data for each variable of interest **Table 1 and p 11**
Outcome data	15*	
		Cross-sectional study—Report numbers of outcome events or summary measures **P 11**
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included **Table 1**
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses **Tables 2 and 3**
Discussion		
Key results	18	Summarise key results with reference to study objectives **p. 13**
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias **p. 16**
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence **pp. 17**
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based **p. 18**

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Factors associated with health literacy in multimorbid patients in primary care: a cross sectional study in Switzerland

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Factors associated with health literacy in multimorbid patients in primary care: a cross-sectional study in Switzerland.

Running title: Health literacy in multimorbid patients

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Abstract

Objective: To identify factors associated with health literacy in multimorbid patients.

Design: A nationwide cross-sectional study in Switzerland. Univariate and multivariate linear regressions were calculated to identify variables associated with health literacy. A multiple imputation approach was used to deal with missing values.

Participants: Multimorbid patients recruited in primary care settings (N=888), above 18 years old and suffering from at least three of the 75 chronic conditions on a predefined list based on the ICPC-2.

Main measures: Health literacy was assessed using the European Health Literacy Survey project questionnaire (HLS-EU 6). This comprises six items scored from 1 to 4 (*very difficult* = 1, *fairly difficult* = 2, *fairly easy* = 3, *very easy* = 4), and the total health literacy score is computed as their mean. As we wished to understand the determinants associated with lower health literacy, the HLS-EU 6 score was the only dependent variable; all other covariates were considered independent.

Results: The mean health literacy score (SD) was 2.9 (0.5). Multivariate analyses found significant associations between low health literacy scores and: treatment burden scores (β = -0.004, 95% CI: [-0.006; -0.002]); marital status, predominantly the divorced group (β = 0.136, 95% CI: [0.012; 0.260]); dimensions of the EQ5D3L quality of life assessment, i.e. for moderate problems with mobility (β = -0.086, 95% CI: [-0.157; -0.016]); and with moderate problems (β = -0.129, 95% CI: [-0.198; -0.060]) and severe problems with anxiety/depression (β = -0.343, 95% CI: [-0.500; -0.186]).

Conclusions: Multimorbid patients with a high treatment burden, altered quality of life by problems with mobility, anxiety or depression, often also have low levels of health literacy. Primary care practitioners should therefore pay particular attention to these patients in their daily practice.

Keywords: Health literacy, Multimorbidity, Primary care, Chronic disease, Switzerland.

Article summary, Strengths and limitations

- This national primary care study enabled the analysis of data from a sample of multimorbid patients
- The first study to understand factors associated with health literacy in multimorbid patients in primary care settings
- Only multimorbid patients with at least three chronic conditions were assessed
- Causal relationships could not be inferred due to the study design

Introduction

Multimorbidity, defined as the occurrence of multiple chronic medical conditions in one individual (1-3), is a steadily increasing phenomenon due to population ageing (4, 5). Multimorbid patients must face many challenges: more frequent and longer hospitalisations (6, 7), greater use of polypharmacy (causing adverse drug effects) (8, 9), higher expenditure on healthcare (10-12) and the use of a broader range of healthcare services (8, 10). Moreover, as the number of health professionals involved in treatment increases, the more likely patients will be faced with fragmented medical care due to conflicting instructions and care pathways. This makes piecing together and adhering to instructions even more testing and thus prevents patients from participating effectively in their own care (8, 10, 12). Facing all these challenges effectively requires good levels of health literacy. The U.S. Institute of Medicine defines health literacy as "the degree to which individuals have the capacity to obtain, process and understand basic health information and services needed to make appropriate health decisions" (13, 14). Health literacy includes a broad set of skills (i.e. reading, writing, numeracy, communication and, increasingly, the use of digital technologies) needed to make appropriate health decisions and successfully navigate the healthcare system (15). Health literacy is recognized as an important determinant of health (16-18). Studies have shown that lower health literacy is associated with a lower mental and physical health status, adverse disease-specific outcomes, higher mortality, and more use of healthcare but less use of preventive care (17, 19). Consequently, governments, researchers, clinicians and patients' associations are paying ever more attention to research into health literacy (20).

Effective patient–clinician communication that ensures patients are able to understand the health information and treatment recommendations they receive and feel comfortable enough to ask

questions or admit when they do not understand something, is vital to the successful management of a chronic illness (21). Healthcare providers should be conscious of their patients' health literacy skills so as to ensure that health information is communicated effectively to help manage long-term conditions (22, 23). Additionally, health literacy is a prerequisite for patient activation and shared decision-making (24-26). Thus, identifying factors associated with low health literacy is an important step towards devising effective engagement, prevention and intervention strategies for patients in primary care (20). The literature shows that health literacy has been assessed in different ways and with contrasting conclusions: e.g. different studies looking at the factors influencing health literacy among less well-educated young people showed a relationship between low health literacy and socioeconomic factors (17, 27, 28). One study evaluating relevant associations between health literacy and multimorbidity (defined as two or more chronic diseases from a list of 11 conditions) in primary care, found none (14). To better understand the determinants associated with low health literacy, the present study aimed to explore all the factors that might be associated with low health literacy in multimorbid patients in primary care with at least three chronic conditions.

Methods

1. *Participants and procedures*

We analysed data (N = 888) from a national cross-sectional survey conducted in collaboration with Switzerland's five academic institutes of family medicine, between January and September 2015. The study was designed to assess multimorbidity in patients in a primary care setting in order to target a population whose management is more challenging to general practitioners (GPs). The detailed study protocol, dataset description and initial results have been published elsewhere (29, 30).

A convenience sample of 100 GPs randomly enrolled patients from their practices who consulted them during the study period. Each GP was provided with a randomisation calendar specifying which patients to enroll on each half-day during the recruitment weeks. All multimorbid patients above 18 years old and suffering from at least three of the 75 chronic conditions on a predefined list, based on the International Classification of Primary Care 2 (ICPC-2), were considered eligible (31, 32) and gave written informed consent to participate in the study. GPs completed a paper-based questionnaire for each included patient (patient-related variables assessed through the GP survey). Patients enrolled completed a telephone-based questionnaire. The study protocol (Protocol No 314/15) was approved by the Human Research Ethics Committee of the Canton Vaud, Switzerland.

2. *Measures*

2.1 *Health literacy*

Health literacy was assessed using the validated six-item questionnaire from the European Health Literacy Survey project (HLS-EU 6) (33, 34). The HLS-EU was a Europe-wide project developed to gather data on health literacy (33). The original HLS-EU 47 explored three domains: 1. healthcare; 2. disease prevention; and 3. health promotion. Each domain explored four matrices: accessing/obtaining information; understanding information; processing/ appraising information; and applying/using information. The HLS-EU 6 is a validated short form with two of the original questions remaining in each domain (33-35). Validated French and German versions of the HLS-EU 6 were available by the authors (34). We used this shorter, validated questionnaire because the present study's main objective was to measure overall levels of health literacy in multimorbid patients, not to assess health literacy in detail. The HLS-EU 6 scale consists of six items with five possible responses. Participants were asked to respond to the following questions. How easy or difficult is it for you to: (a) judge when you may need to get a second opinion from another doctor? (b) use information the doctor gives you to make decisions about your illness? (c) find information on how to manage mental health problems like stress or depression? (d) judge whether the information on health risks in the media is reliable? (e) find out about activities that are good for your mental wellbeing? and (f) understand information in the media on how to get healthier? The possible responses and their scores were as follows: *very difficult* = 1, *fairly difficult* = 2, *fairly easy* = 3, *very easy* = 4, and a fifth alternative for when participants did not answer or did not have a definite answer, coded as a missing value. The health literacy score was thus calculated as the mean of the six health literacy items, scored from 1 to 4, after imputation of the missing values (see the Statistical Analyses section below) (34).

2.2 Covariates

All the variables have been described elsewhere previously (29). Briefly, our analyses used the following variables:

2.2.1 Dependent variable: as we wished to understand the determinants associated with lower health literacy scores, we chose the HLS-EU as the dependent variable.

2.2.2 Independent variables: included all other variables (based on GP and patient questionnaires).

- Age
- Sex (female/male)

GP's questionnaire, based on his medical records:

- number of chronic conditions based on a predefined list of 75 chronic conditions relevant to multimorbidity and coded according to the ICPC 2
- number of drugs (0–4, 5–6, 7–9 or ≥ 10) listed by organic system (general, blood, immune, digestive, cardiovascular, respiratory, neurological, endocrine, eye, ear, psychological, musculoskeletal) and by substance
- number of medical visits in the last year
- number of hospitalisations in the last year
- the severity index (SI) (36-38) was derived by dividing the total cumulative illness rating scale (CIRS) score, a validated questionnaire published elsewhere in detail (39), by the number of categories with morbidities

Patient interview (based on a questionnaire):

- marital status (single, married, divorced or widowed)

- educational level (primary, secondary and tertiary)
- Dipcare questionnaire for deprivation assessment, containing 16 items examining the three dimensions of deprivation (material, social and health), and validated for the Swiss population and published elsewhere in detail (40)
- treatment burden questionnaire (TBQ), recently developed to produce a score for the overall burden related to the treatment of chronic conditions (41); it consists of 13 questions to rate with an answer between 0 and 10, with 0 corresponding to *no burden* and 10 to *a very important/considerable burden*
- medical help from a home nurse
- *paramedical therapist* grouped together physiotherapist and/or occupational therapist (yes/no)
- homecare (yes/no)
- number of specialists involved in patient's care
- EQ5D3L composed of five dimensions of health (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) and used a visual analogue scale

3. *Statistical analyses*

On collecting the questionnaires, the number of values missing from our variable of interest (health literacy score) was considered too high (i.e. the health literacy score could not be computed in full for 577 participants) to reasonably analyse each participant's case in its entirety. We first considered computing the health literacy scores for all participants with at least five non-missing items. However, even then, the number of missing scores remained too high (377 participants), and comparisons between complete and the incomplete sets of responses showed significant differences in several covariates (data not shown). We therefore opted for the imputation of the values missing from the health literacy items and demographic covariates by using the multiple imputation approach developed by Rubin (42). As a sensitivity analysis, we carried out a complete case analysis, and this gave similar results.

We calculated means and standard deviations for quantitative variables, and frequencies and proportions for categorical ones. Univariate and multivariate linear regressions were carried out to identify variables of health literacy. Using sensitivity analysis, we checked whether a model without imputations would produce the same results as the model with multiple imputations: analysis with and without imputation gave similar results.

All analyses were performed using R software version 3.3.2 (43) and the MICE package version 2.29 (44).

Results

Descriptive analyses

Cases with at least one missing value among the six items were considered incomplete (239, 18, 417, 168, 252 and 175 missing values for questions (a) to (f), respectively). Of the original 888 patients, 200, 175, 117, 59, 24 and 2 had, respectively, 1, 2, 3, 4, 5 and 6 missing HL variables. Thus a complete HL score was only computable for 311 respondents (35%), and we therefore chose to impute the missing values.

The mean age (SD) of the participants was 72.9 (12.0) years old; 52.0% were women. Almost half of the participants were married (49.0%), and 40.0% had a tertiary level of education. The mean (SD) number of chronic conditions was 7.20 (2.9), and the mean (SD) number of medical visits in the last year was 12.90 (8.7). The mean health literacy score (SD) of the participants was 2.9 (0.5). Descriptive statistics are summarized in Table 1.

Insert table 1 about here

In bivariate analyses with imputation, we found significant relationships between health literacy and almost all the covariates except for the number of chronic conditions, number of drugs, number of medical visits in the last year, number of hospitalisations in the last year, homecare, nurse, and severity index (Table 2).

Insert table 2 about here

The multivariate analyses showed significant relationships between health literacy and: the treatment burden score (β = -0.004, 95% CI: [-0.006; -0.002]); marital status, but particularly for the divorced group (β = 0.136, 95% CI: [0.012; 0. 260]); dimensions of the EQ5D3L quality of life assessment, i.e. moderate problems with mobility and moderate and severe problems with anxiety/depression (β = -0.086, 95% CI: [-0.157; -0.016]), (β = -0.129, 95% CI: [-0.198; -0.060], and (β = -0.343, 95% CI: [-0.500; -0.186]), respectively. Table 3 shows the results of these multivariate analyses.

Insert table 3 about here

Discussion

The present study showed that the mean (SD) health literacy score in our multimorbid primary care patient sample was 2.9 (0.5). In multimorbid patients, a high treatment burden and effects on patients' quality of life due to problems with mobility and anxiety/depression were negatively associated with health literacy. However, our study revealed no association between HL and age. Although several studies have assessed health literacy, to the best of our knowledge, little is known about which factors are associated with low health literacy in multimorbid patients in primary care.

The present study's main finding was that the treatment burden facing multimorbid primary care patients was negatively associated with health literacy. In other words, the lower a multimorbid patient's health literacy, the higher the treatment burden. This is a very interesting finding, and although the β coefficient is small, we believe that this result is clinically relevant and allows us to identify treatment burden as an element to take into account for potentially low literacy in multimorbid patients.

There are no specific references to explain the association found between health literacy and the burden of treatment. As a proxy for treatment burden, some authors have described an association between low health literacy and treatment adherence (45, 46), however, others found no evidence for such an association (47, 48). Our exploratory study was unable to determine any causal association between the treatment burden and health literacy. But our results could also be considered from another angle, that has been taken in other analyses. Indeed, individuals with low health literacy are usually less well educated and belong to lower socioeconomic groups (18). Multimorbidity is higher in these groups and patients in them are likely to suffer more severely and from more diseases, leading to a higher treatment burden. Furthermore, low health literacy, used as an independent variable, has been found to be associated with a reduced ability of adults with coronary heart disease to identify medication (49), poor health outcomes (14, 19, 50), and a more significant use of healthcare (51). These three factors can also be linked to multimorbidity and may have an impact on the overall treatment burden.

Another important finding was that patients whose quality of life had been altered by problems related to anxiety/depression or mobility were more likely to have low levels of health literacy.. As described by DiMatteo, anxiety and depression may affect patients' motivation and ability (52) to seek out and understand information about their diseases and treatment, resulting in a lower level of health literacy, especially in the complex context of multimorbidity. Moreover, anxiety and depression may well be higher when patients have to face up to more numerous health problems, especially in multimorbidity. This result is not concordant with the study by Green et al. (53), which found no association between limited health literacy and depression in patients receiving chronic hemodialysis treatment, but this difference might be explained by the differences in the study populations, how health literacy was assessed and the fact that his study used health literacy as independent variable.

Concerning the association between mobility problems and low health literacy, Matsumoto et al. describes a relationship with different social determinants of health such as housing, employment, transport or social support (54). On the other hand, in a very different population, there was a strong association between low health literacy and obesity in young children with a described lack of physical activity (55). However, we can only speculate as to whether there is any precise explanation of the associations between anxiety, depression, mobility and health literacy. Furthermore, due to its design, the study's findings cannot determine a causal association.

Anxiety, depression and mobility are just some of the detereminants of quality of life, and the literature reveals very controversial results concerning the association between health literacy and quality of life. It seems that such associations may depend on certain other aspects, such as specific chronic diseases or the cultural characteristics of the population studied (56). Thus, although we found that some of the determinants of quality of life are factors associated with low health literacy, we believe that further studies are necessary to better understand the underlying reasons for the controversial results in the literature. However, it nevertheless seems important to describe factors associated with low health literacy, thus allowing GPs to better identify such patients and to adapt how they inform them about medical problems.

The present study found no association between the level of health literacy of multimorbid primary care patients and their use of healthcare services, especially with regards to the number of consultations with their GP or the number of hospitalisations in the past year. Results in the literature are inconsistent. The study by Vandenbosch et al. (51) found no significant associations between health literacy and the number of medical visits or hospitalisations, whereas a study by Duong et al. (57) described an association between health literacy and healthcare use. These results are inconsistent due to differences in the study populations (i.e. our study population was composed of multimorbid patients in primary care settings) and methodologies (other studies considered health literacy as an independent variable). Indeed, we suggest that health literacy in multimorbid patients is different from that in the general population and should be assessed differently. Further research should aim to clearly confirm or invalidate our results with multimorbid patients.

Strength and limitations:

This national primary care study enabled the analysis of data from a relatively representative sample of multimorbid patients suffering from at least three chronic conditions and enrolled in GPs' practices across Switzerland. Although several studies have previously assessed health literacy, to the best of our knowledge, this was the first to have assessed factors associated with health literacy in multimorbid patients in a primary care setting.

However, this study had some limitations. First, the beta coefficients were small, making clinical interpretation difficult, despite the fact that the study gives an overall view of the factors associated with health literacy. Further studies should be done to confirm these trends.

Second, our sample might not be perfectly representative of all multimorbid patients. GPs only recruited patients who came to their practices and who were suffering from at least three chronic conditions from a list of 75 provided to them. The most impaired multimorbid patients, therefore, those with the most extensive mobility problems (i.e. those cared for via homecare visits, in nursing homes, or hospitalised) were not included (selection bias). Our results concerning health literacy in multimorbid patients should thus be interpreted with caution, taking into consideration multimorbid patients who cannot attend GPs' practices or who have rare chronic conditions. Furthermore, we cannot exclude a potential selection bias, as patients who consulted more frequently had a higher chance of being included. However, we found no association between the frequency of consultations and health literacy in our final model.

Third, the health literacy score contained a lot of missing values, and we cannot exclude that the cause of that missing data was related to health literacy itself. However, we examined whether the mean of the available HL items was associated with the number of missing HL items, and this was not the case.

Fourth, due to the study's cross-sectional design, causal relationships cannot be inferred.

Conclusion

The present study highlights factors associated with health literacy in multimorbid patients in primary care: a high treatment burden, altered quality of life by problems with anxiety or depression and poor mobility were associated with a low level of health literacy. This is a useful information that could guide GPs in their daily practice and help them to better identify patients at risk of having low health literacy. Even though, with the current state of knowledge, we cannot demonstrate causal relationships between multimorbidity and the treatment burden, GPs should carefully weigh up how best to transmit clinical information to patients whom they believe to be at risk of low health literacy.

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Conflict of interest:

The authors declare no conflicts of interest.

Authors' contributions

AAN, ADL, BB, DMH, AZ, LH and PB developed the protocol for the MMFM study. LH, AZ and DMH ensured the recruitment of participating GPs. AAN was primarily responsible for planning the analysis and drafting the manuscript. JP was responsible for the analyses. PB, JP and LH helped to improve the manuscript during this process. BB, AD, DMH, SS, SNJ, AZ, PB and LH made contributions to the interpretation of the findings and the content of the final manuscript. All authors read and approved the final manuscript.

Data Sharing Statement

Data are available at family medicine institute of Lausanne.

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Table 1: Descriptive statistics of the sample of multimorbid patients, N = 888.

Variable	**mean**‡	**sd**‡
Age	72.93	12.00
Health literacy score (577 missing values)	2.87	0.45
Material deprivation score	0.50	1.27
Social deprivation score	1.93	1.38
Health deprivation score	0.48	0.68
Number of medical visits last year (1 missing value)	12.90	8.70
Number of hospitalisations (3 missing values)	0.54	0.99
Number of chronic conditions (4 missing values)	7.20	2.86
TBQ* score	26.77	18.60
Number of specialists (141 missing values)	2.23	1.27
Severity index	1.75	0.38
Visual analogue scale (EQ5D3L)	63.19	19.25
Variable	**count**	**prop**
Sex		
Male	428	0.48
Female	460	0.52
Educational level (1 missing value)		
Primary	195	0.22
Secondary	337	0.38
Tertiary	355	0.40
Marital status		
Single	85	0.10
Married	437	0.49
Divorced	150	0.17
Widowed	216	0.24
Number of drugs		
0–4	156	0.18
5–6	212	0.24
7–9	276	0.31
≥ 10	244	0.27
Home Nurse (1 missing value)		
No	798	0.90
Yes	89	0.10
Paramedical † (12 missing values)		
No	572	0.65
Yes	304	0.35

Homecare (1 missing value)		
No	755	0.85
Yes	132	0.15
EQ5D3L five dimensions		
Mobility		
No problems	497	0.56
Moderate problems	386	0.43
Severe problems	5	0.01
Self-care		
No problems	785	0.88
Moderate problems	92	0.10
Severe problems	11	0.01
Usual activities		
No problems	543	0.61
Moderate problems	328	0.37
Severe problems	17	0.02
Pain/discomfort		
No problems	211	0.24
Moderate problems	591	0.67
Severe problems	86	0.10
Anxiety/depression		
No problems	516	0.58
Moderate problems	329	0.37
Severe problems	43	0.05

* TBQ: treatment burden questionnaire

† Paramedical includes physiotherapists/occupational therapists

‡ With multiple imputation

Table 2: Results of bivariate analyses with multiple imputation.

Independent variable	**β**	**95% CI**		**p-value**
Age	0.0053	0.0027	0.0079	0.0001
Sex	-0.1008	-0.1643	-0.0372	0.0019
Deprivation				
Material deprivation	-0.0786	-0.1034	-0.0537	0.0000
Social deprivation	-0.0485	-0.0707	-0.0263	0.0000
Health deprivation	-0.1407	-0.1853	-0.0961	0.0000
Educational level (ref: Primary)				
Secondary	0.0408	-0.0464	0.1280	0.3579
Tertiary	0.0880	0.0034	0.1726	0.0415
Number of medical visits last year	-0.0023	-0.0060	0.0014	0.2285
Number of hospitalisations	-0.0283	-0.0598	0.0033	0.0789
Number of chronic conditions	0.0042	-0.0076	0.0160	0.4820
Number of drugs (ref: 0–4)				
5–6	-0.0249	-0.1238	0.0741	0.6217
7–9	0.0025	-0.0926	0.0976	0.9588
≥ 10	-0.0601	-0.1579	0.0377	0.2279
TBQ* score	-0.0071	-0.0086	-0.0055	0.0000
Home nurse	-0.1016	-0.2133	0.0100	0.0743
Paramedical †	-0.0843	-0.1489	-0.0198	0.0105
Homecare	-0.0772	-0.1698	0.0153	0.1016
Number of specialists	-0.0284	-0.0544	-0.0024	0.0322
Severity index	-0.0457	-0.1258	0.0344	0.2630
Visual analogue scale (EQ5D3L)	0.0048	0.0032	0.0064	0.0000
EQ5D3L five dimensions				
Mobility (ref: No problems)				
Moderate problems	-0.1507	-0.2131	-0.0882	0.0000
Severe problems	-0.1404	-0.5589	0.2781	0.5100
Self-care (ref: No problems)				
Moderate problems	-0.1965	-0.3045	-0.0884	0.0004
Severe problems	-0.1464	-0.4724	0.1795	0.3755
Usual activities (ref: No problems)				
Moderate problemss	-0.1729	-0.2371	-0.1086	0.0000
Severe problems	-0.4167	-0.6521	-0.1813	0.0006
Pain/discomfort (ref: No problems)				
Moderate problems	-0.1174	-0.1970	-0.0378	0.0040
Severe problems	-0.2760	-0.3961	-0.1558	0.0000
Anxiety/depression (ref: No problems)				
Moderate problems	-0.2211	-0.2839	-0.1584	0.0000

Severe problems	-0.5390	-0.6788	-0.3991	0.0000
Marital status (ref: Single)				
Married	0.1596	0.0484	0.2709	0.0050
Divorced	0.0947	-0.0315	0.2208	0.1412
Widowed	0.1128	-0.0057	0.2313	0.0619

Table 3: Results of multivariate analyses with multiple imputation.

Independent variables	**β**	**95% CI**		**p-value**
Age	0.0007	-0.0027	0.0041	0.6889
Sex	-0.0361	-0.1043	0.0320	0.2981
Deprivation				
Material deprivation	-0.0245	-0.0533	0.0043	0.0954
Social deprivation	-0.0235	-0.0480	0.0010	0.0606
Health deprivation	0.0221	-0.0364	0.0806	0.4577
Educational level (ref: Primary)				
Secondary	0.0070	-0.0763	0.0903	0.8688
Tertiary	0.0560	-0.0284	0.1405	0.1929
Number of medical visits last year	0.0009	-0.0029	0.0048	0.6302
Number of hospitalisations	-0.0183	-0.0503	0.0136	0.2603
Number of chronic conditions	0.0096	-0.0032	0.0224	0.1399
Number of drugs (ref: 0–4)				
5–6	-0.0278	-0.1210	0.0653	0.5577
7–9	0.0276	-0.0647	0.1199	0.5568
≥ 10	0.0110	-0.0905	0.1125	0.8318
TBQ* score	-0.0038	-0.0058	-0.0018	0.0002
Nurse	0.0228	-0.1120	0.1577	0.7390
Paramedical †	-0.0327	-0.0968	0.0314	0.3172
Homecare	0.0057	-0.1069	0.1183	0.9205
Number of specialists	-0.0235	-0.0513	0.0043	0.0967
Severity index	0.0385	-0.0420	0.1190	0.3480
Visual analogue scale (EQ5D3L)	0.0000	-0.0019	0.0019	0.9722

EQ5D3L five dimensions				
Mobility (ref: No problem)s				
Moderate problems	-0.0864	-0.1567	-0.0161	0.0161
Severe problems	0.1663	-0.3459	0.6786	0.5230
Self-care (ref: No problems)				
Moderate problems	-0.0440	-0.1552	0.0673	0.4379
Severe problems	-0.0661	-0.4830	0.3508	0.7532
Usual activities (ref: No problems)				
Moderate problems	-0.0244	-0.0998	0.0509	0.5242
Severe problems	-0.1912	-0.4453	0.0630	0.1402
Pain/discomfort (ref: No problems)				
Moderate problems	-0.0033	-0.0847	0.0780	0.9356
Severe problems	0.0073	-0.1297	0.1444	0.9161
Anxiety/depression (ref: No problems)				
Moderate problems	-0.1288	-0.1978	-0.0598	0.0003
Severe problems	-0.3426	-0.4996	-0.1857	0.0000
Marital status (ref: Single)				
Married	0.0953	-0.0146	0.2053	0.0890
Divorced	0.1360	0.0122	0.2599	0.0314
Widowed	0.0780	-0.0477	0.2037	0.2233

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract **Title: Factors associated with health literacy in multimorbid patients in primary care: a cross-sectional study in Switzerland.**
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found **p. 3 -4**
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported **p.5**
Objectives	3	State specific objectives, including any prespecified hypotheses **pp. 6**
Methods		
Study design	4	Present key elements of study design early in the paper **p. 7**
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection **p. 7**
Participants	6	*Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants **p.7**
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable **p. 7-10**
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group **pp. 7-10**
Bias	9	Describe any efforts to address potential sources of bias **p. 7**
Study size	10	Explain how the study size was arrived at **p. 7**
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why **p. 8**
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding **pp. 10**
		(*b*) Describe any methods used to examine subgroups and interactions **pp. 10**
		(*c*) Explain how missing data were addressed **p. 10**
		(*e*) Describe any sensitivity analyses **p. 10**

Continued on next page

Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed **p. p.10**
		(b) Give reasons for non-participation at each stage **p. 10**
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders **Table 1**
		(b) Indicate number of participants with missing data for each variable of interest **Table 1 and p 11**
Outcome data	15*	
		Cross-sectional study—Report numbers of outcome events or summary measures **P 11**
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included **Table 1**
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses **Tables 2 and 3**
Discussion		
Key results	18	Summarise key results with reference to study objectives **p. 13**
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias **p. 16**
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence **pp. 17**
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based **p. 18**

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.