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Low Health Literacy is Associated with the Onset of CKD during the Life Course

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ABSTRACT

Background Health literacy, the ability to deal with information related to one's health, is a predictor of health outcomes in CKD. However, research has not explored whether low health literacy predicts the onset of CKD.

Methods We used data from participants of Lifelines, a prospective population-based cohort study of individuals living in The Netherlands, to assess the share of individuals with low health literacy by eGFR category, whether low health literacy is associated with CKD onset in the general population and in the subgroup of older adults, and whether established CKD risk factors mediate this association.

Results In the total sample of 93,885 adults (mean follow-up 3.9 years), low health literacy was more likely among individuals in worse eGFR categories, increasing from 26.4% in eGFR category 1 to 50.0% in category 5 (P=0.02). Low health literacy, compared with adequate health literacy, was associated with the onset of CKD in the total sample (3.0% versus 2.1%) and in the subgroup of older adults (13.4% versus 11.3%), with odds ratios (ORs) of 1.44 (95% confidence interval (95% CI), 1.31 to 1.59) and 1.21 (95% CI, 1.04 to 1.41), respectively. After adjustment for sex, age, education, and income, health literacy was associated with CKD onset only in older adults (OR, 1.25; 95% CI, 1.04 to 1.50). This association was mediated by hypertension and high body mass index (BMI) in the crude model, but only by BMI after adjustment (with BMI explaining 18.8% of the association).

Conclusions Low health literacy is a risk factor for CKD onset among older adults, which suggests that CKD prevention might benefit from strategies to address low health literacy.

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Health literacy plays an important role in the management of health,[1] and it might be associated with the onset of diseases, such as CKD. Health literacy is defined 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."[2] Low health literacy is a highly prevalent problem worldwide,[3,4] and has been associated with higher hospitalization and mortality rates.[1] Low health literacy has similar effects on CKD,[5] a global health problem that stands out for its burdening complications[6] and for having a high prevalence that has increased enormously during the last decades.[7]

CKD is a progressive disease that can be divided into five categories on the basis of the patient's eGFR.[6] More severe categories demand more complex disease management skills, which are known to be negatively influenced by low health literacy.[8] The etiology of CKD varies across different age groups, being diabetes and hypertension the most

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prominent causes in older adults.[6] Because these causes of CKD are more dependent on health behaviors than those more prominent in younger populations,[9] the effects of low health literacy are probably stronger among older individuals. The study of this group is of special interest given the number of older adults and the prevalence of chronic diseases among them is expected to increase.[10,11] Moreover, low health literacy is also associated with several CKD risk factors, namely the presence of hypertension,[5] diabetes,[5] high body mass index (BMI),[12] lower levels of physical activity,[13] and the use of nonsteroidal anti-inflammatory drugs,[14] tobacco,[5] and alcohol.[15] These risk factors could, therefore, be mediators in the association between low health literacy and CKD.

Although low health literacy is known to be associated with the deterioration of renal function,[16] research has not explored whether low health literacy predicts the onset of CKD, or the associated pathways. Studying health literacy is important because it is an actionable target, different from other predictors of worse renal function, such as age, educational level, and income. Furthermore, studies on health literacy and CKD focus primarily on ESKD,[17,18] notably patients on dialysis, whereas little attention has been paid to individuals with milder renal impairment. Finally, the prevalence of low health literacy and its effects on the CKD community-dwelling population are unknown, as all previous studies were carried out in nephrology clinics or with patients who were hospitalized.[5,19] Thus, understanding how health literacy relates to CKD in the community-dwelling population would be a critical step for improving medical practice and public health policies toward disease prevention.

This study focused on better understanding the effect of low health literacy on CKD. First, we assessed the share of individuals with low health literacy in the different eGFR categories. Second, using a longitudinal design, we assessed whether low health literacy is associated with the onset of CKD in the total population and in the subgroup of older adults. Finally, we tested whether these associations were mediated by known CKD risk factors.

Significance Statement

Low health literacy, the decreased ability to deal with information related to one's health, has been associated with poor outcomes in patients with CKD, but research has not explored whether low health literacy is associated with the onset of CKD. Using data from a prospective cohort study of 93,885 community-dwelling adults living in The Netherlands, the authors showed that low health literacy was associated with the onset of CKD in older adults, and that this association was partially explained by the presence of a high body mass index (BMI). Moreover, individuals with worse renal function were more likely to have low health literacy. These results suggest that measures to address low health literacy, notably over the control of BMI, might help prevent the development of CKD.

METHODS

Sample and Procedures

The study sample was derived from the first (T1) and second (T2) assessment waves of the Lifelines study. Lifelines is a multidisciplinary prospective population-based cohort study examining, in a unique three-generation design, the health and health-related behaviors of 167,729 persons living in the north of The Netherlands. It employs a broad range of investigative procedures in assessing the biomedical, sociodemographic, behavioral, physical, and psychologic factors that contribute to the health and disease of the general population, with a special focus on multimorbidity and complex genetics. Data collection was performed between November 2006 and December 2013 for T1 (n=152,737) and between January 2014 and July 2018 for T2 (n=111,915). The recruitment and collection of the data have been described elsewhere.[20] The Lifelines Cohort Study is conducted in accordance with the principles of the Declaration of Helsinki and the research code of the University Medical Center Groningen.[20] Exclusion criteria for our study included pregnancy and a history of kidney transplantation, due to the changes in renal function and prognosis that these conditions entail.[21,22]

We performed two analyses, cross-sectional and longitudinal. First, to assess the share of low and adequate health literacy, we used data on participants who were aged 18 years or older, completed the health literacy questionnaire, and had their renal function measured at T1. To assess CKD onset, participants had to also have a measurement of renal function at T2. The derivation of our sample is described in Supplemental Appendix 1.

Measurements

Health Literacy

Health literacy was measured at T1, using self-reported answers to the three validated questions from Chew *et al.*[23]

1. How often do you have trouble understanding your medical situation because you have difficulty with the written information?

2. How sure are you of yourself when you fill out medical forms?

3. How often does someone help you with reading information materials from the hospital or another healthcare provider?

Participants answered these questions on a Likert scale ranging from 1 (*Never/Not at all)* to 5 (*Always/Very*). We reversed the scores of the first and third questions and then added up the scores of all questions, resulting in a health literacy scale ranging from 3 to 15. This was dichotomized as low (3–12) versus adequate health literacy (≥13). This cutoff point is in accordance with that used in previous studies using the same database[24] and leads to percentages of low and adequate health literacy comparable to those found in large-scale health literacy surveys in The Netherlands.[25]

Renal Function, eGFR Categories, and CKD Onset

Renal function was assessed at T1 and T2 using the eGFR, calculated with the CKD- Epidemiology Collaboration formula,[6] on the basis of the results of laboratory tests performed on fasting blood samples. According to this renal function, participants were divided into five different eGFR categories.[6] Moreover, participants who had an eGFR ≥60 ml/min per 1.73 m^2 at T1 that dropped to an eGFR <60 ml/min per 1.73 m^2 at T2, and whose eGFR decline was equal or higher than 10% of the baseline eGFR were considered positive for CKD onset (yes/no; y/n).

CKD Risk Factors

We assessed the CKD risk factors of hypertension, diabetes, high BMI, high use of anti-inflammatory drugs (NSAIDs), inadequate physical activity, smoking, and the use of alcohol. A previous diagnosis of hypertension (y/n) and diabetes (y/n), the presence of current smoking (y/n), the use of NSAIDs, and the amount of physical activity were reported by the participants in a questionnaire. High use of NSAIDs (y/n) was defined as taking more than 200 pills a year. Participants were considered to have inadequate physical activity (y/n) if they reported <30 minutes of moderate to vigorous physical activity during at least 5 days a week.[26] Alcohol intake was measured as usual alcohol consumption in grams per day, on the basis of a food frequency questionnaire. It was dichotomized into low or high alcohol intake, using the cutoff of 40 g/d (four standard drinks/day).[27] Height and weight for the calculation of BMI were measured at one of the Lifelines research sites. BMI was dichotomized and considered high if above 25 kg/m^2. This is the threshold cited in current CKD guidelines,[6] and is the earliest BMI abnormality associated with CKD development and complications.[28,29] All variables were measured at T1.

Other Variables

Sex, age, educational level, and monthly household income were treated as potential confounders because of their association with health literacy.[30] Age was divided into categories of 10 years to decrease the possibility of residual error. For the subgroup analyses, participants over 65 years of age were considered as older adults. Educational level was measured with an eight-item ordinal scale (from no education to university education). The answers to this questionnaire were categorized as low (consisting of no education or only complete primary education), intermediate (consisting of complete secondary education), and high (consisting of higher vocational education or university education). Monthly household income was measured with an eight-item ordinal scale (from <€750 to >€3500), and *I do not know* or *I would rather not answer this question*. The answers were clustered into four categories: <€1000, €1000–3000, >€3000, and information not given. Cardiovascular disease (y/n) is a composite outcome consisting of the self-reported history (y/n) of myocardial infarction, heart failure, and/or stroke. Information on the confounders, cardiovascular disease, and atherosclerosis (y/n) was reported by the participants in a questionnaire. All variables were collected at T1.

Statistical Analyses

First, we calculated descriptive statistics for the total sample and the subgroup of older adults and evaluated differences between the low- and adequate-health-literacy groups using Pearson's chi-squared tests, independent samples *t* tests, or Mann–Whitney tests. Second, we assessed the share of participants with low and adequate health literacy by eGFR category and compared them using Pearson's chi-squared linear-by-linear association. To verify whether the association between low health literacy and the eGFR categories remained significant after adjustment for confounders, we performed an ordinal logistic regression. Third, we assessed if low health literacy was associated with the onset of CKD in the total sample and in the subgroup of older adults at T2, using logistic regression. Fourth, we assessed whether the CKD risk factors mediated the relationship between low health literacy and the onset of CKD. We did so by using probit structural equation modeling to explore the direct and indirect, *i.e.* mediated, association between health literacy and CKD onset. The strength of the mediation effect was expressed in terms of percentage of the association explained by the mediator. The models above were adjusted for age, sex, educational level, and income. The analyses were conducted with IBM SPSS Statistics version 22 and R version 3.4.2 (package lavaan) for Windows, and the results of all models were considered statistically significant if $P<0.05$.

Sensitivity Analysis

We performed two sensitivity analyses. To account for the possible effect of cognitive dysfunction on low health literacy, we repeated the analyses excluding individuals with mild, moderate, and severe cognitive impairment. We did that by excluding individuals with a Mini Mental State Examination total score below 24. To account for the possible effect of other renal conditions, we repeated the analyses excluding individuals who reported contracted kidney, hydronephrosis, narrowing of a renal artery, renal vessel balloon angioplasty, or kidney removal for donation or because of medical problems. The Mini Mental State Examination was applied by a trained interviewer at one of the Lifelines research sites at T1. The other renal conditions were self-reported by participants in a questionnaire applied at T1. The results of the sensitivity analyses did not differ from the main results (Supplemental Appendix 2).

RESULTS

Sample Characteristics

Our total sample consisted of 93,885 eligible participants (59.7% females, mean age of 45.7 years). Among these,

77,531 also had values of eGFR at T2. A comparison between participants with and without missing values of eGFR at T2 showed no important differences between the two groups. The mean follow-up time was 3.9 years (SD, 1.2 years). More than 99% of the eligible participants had initial eGFR compatible with categories 1, 2, or 3, and 27.5% of them had low health literacy. Among the older adults ($n=7754$), 38.6% had low health literacy. Low health-literate participants in both groups were older, had a lower educational level and income, and had higher rates of hypertension, diabetes, and high BMI (Table 1). A total of 14% of the respondents did not provide their income, but there were no important differences between these and the rest of the sample. The incidence of CKD (positive CKD onset from T1 to T2) was 2.5% for the total sample and 12.8% for the subgroup of older adults.

The Share of Individuals with Low Health Literacy in the Different eGFR Categories

Within the total sample, the share of low health literacy was higher for individuals with more severe renal impairment, increasing from 26.4% in category 1 to 50.0% in category 5 (Figure 1). A similar pattern was present when the sample was stratified by age (Supplemental Appendix 3). The differences in the percentages across categories were statistically significant before ($P<0.01$) and after adjustment for confounders ($P=0.02$).

The Association Between Low Health Literacy and the Onset of CKD

Low health literacy was associated with CKD onset in the crude models both in the total sample and in the subgroup of older adults (Table 2). In other words, participants with low

Table 1. Comparison of baseline characteristics between participants with low and adequate health literacy in the total sample and in the subgroup of older adults

Variables	Total Sample			Subgroup of Older Adults		
	Adequate Health Literacy	Low Health Literacy	*N*	Adequate Health Literacy	Low Health Literacy	*N*
Demographic characteristics						
Sex, % of females	59.6	60.0	93,830	49.0	57.0	7754
Age, mean (SD)	44.9 (12.5)	47.8 (13.5)[a]	93,830	69.2 (4.1)	70.2 (4.7)[a]	7754
Education, %						
Low	1.1	4.9[a]	91,757	4.8	15.4[a]	7268
Intermediate	61.5	79.7[a]		64.2	74.3[a]	
High	37.4	15.5[a]		31.0	10.3[a]	
Monthly household income, %						
<€1000	5.7	7.7[a]	91,478	2.1	4.9[a]	7577
€1000–3000	48.1	56.2[a]		59.3	65.6[a]	
>€3000	33.5	18.4[a]		24.3	11.0[a]	
Information not given	12.7	17.7[a]		14.3	18.6[a]	
Clinical characteristics						
Hypertension, %	24.5	30.3[a]	80,592	46.2	49.3[a]	7275
Diabetes mellitus, %	2.0	3.5[a]	93,632	7.7	10.1[a]	7716
High BMI[b], %	52.3	61.2[a]	93,801	66.7	73.7[a]	7750
High NSAID intake, %	2.2	3.4[a]	93,830	9.9	10.6	7754
Inadequate physical activity, %	45.4	38.0[a]	87,031	11.4	13.6[a]	7113
Current smoking, %	18.1	21.1[a]	92,910	7.4	8.1	7709
High alcohol intake[c], %	0.9	0.8	51,510	0.8	0.9	4309
Cardiovascular disease, %	1.8	3.2[a]	92,156	9.0	10.6[a]	7535
Atherosclerosis, %	0.4	0.7[a]	93,830	2.2	2.4	7754
Albumin 24 h urine[d], median (IQR)	3.8 (4.4)	3.9 (4.7)[a]	43,132	5.1 (6.1)	5.3 (7.3)	2997
eGFR[e], mean (SD)	95.8 (14.8)	94.4 (15.5)[a]	93,830	78.4 (12.2)	77.4 (12.6)[a]	7754
eGFR[e] categories, %						
1	65.9	62.3[a]	93,830	18.7	15.8[a]	7754
2	33.0	36.0[a]		72.9	75.1[a]	
3	1.0	1.6[a]		8.3	8.8[a]	
4	0.02	0.03[a]		0.1	0.2[a]	
5	<0.01	0.01[a]		0.0	0.03[a]	

[a]Statistically significant difference between groups with low and adequate health litearcy with $P<0.05$.
[b]High BMI defined as BMI above 25 kg/m^2.
[c]High alcohol intake defined as more than 40 g of alcohol per day.
[d]Measured at baseline in mg per 24 h.
[e]eGFR in ml/min per 1.73 m^2.

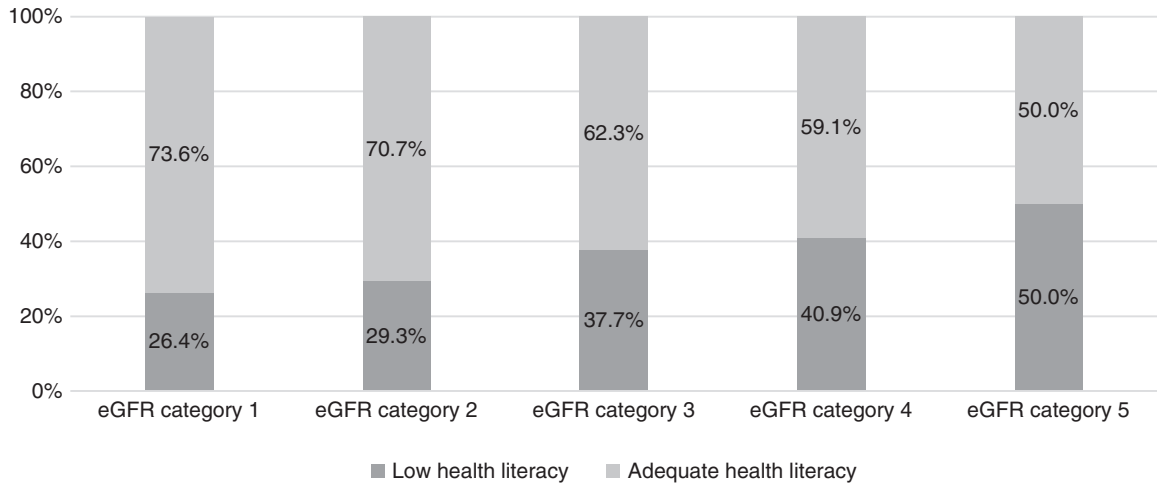

Figure 1. Share of low health literacy across the different eGFR categories in the total sample. The differences between groups with low and adequate health literacy were significant across all categories with a Pearson's chi-squared linear-by-linear association of $P<0.05$.

health literacy were more likely to develop CKD from T1 to T2 in the total sample (3.0% versus 2.1%) and among the older adults (13.4% versus 11.3%). After adjustment for confounders, health literacy was still associated with CKD onset in the older adults, but not in the total sample.

The Mediation Between Low Health Literacy and the Onset of CKD

Hypertension, diabetes, high BMI, high NSAID intake, inadequate physical activity, and smoking were, separately, significant mediators of the association between health literacy and CKD onset in the total sample, in the crude models. For the older adults, hypertension and BMI were mediators in the crude models, and only BMI in the adjusted models (Table 3).

DISCUSSION

Main Findings

This study detected that the share of low health literacy is higher among individuals with worse renal function. Furthermore, low health literacy was associated with the onset of CKD in the crude analyses. After adjustment for confounders, this association remained only among older adults. The association in older adults was mediated by hypertension and high BMI in the crude analyses, but only by high BMI after adjustment.

We found that the share of individuals with low health literacy was higher among the group with a worse renal function. This confirms previous findings that populations with more severe CKD have higher levels of low health literacy,[16] but now in a much larger sample. Although the cross-sectional nature of this analysis does not allow us to infer causality, this result suggests that low health literacy might have a negative effect on the deterioration of renal function.

Low health literacy was positively associated with the onset of CKD in older adults, but not in the total sample. This complements the findings of previous cross-sectional studies, which showed a relationship between low health literacy and worse renal function.[16,31] These studies mostly included older adults (average age over 60 years), but ours was the first to analyze a wider age range. Two main reasons could explain why we found an association in older adults but not in the total sample. First, the etiology of CKD is typically different in younger and older people. Whereas young individuals' CKD is normally primary, or secondary to vasculitis,[7] CKD in older adults is more likely to stem from chronic diseases, such as hypertension and diabetes.[6] These diseases are more likely to be influenced by health behaviors and, *via* this pathway, by health literacy. Second, low health literacy might have a

Table 2. Association between low health literacy and the onset of CKD

Model	Total Sample				Subgroup of Older Adults			
	OR[a]	95% CI	*P* value	*N*	OR[a]	95% CI	*P* value	*n*
Crude model[b]	1.44	1.31 to 1.59	<0.001[c]	77,531	1.21	1.04 to 1.41	0.01[c]	6528
Adjusted model[d]	1.06	0.94 to 1.19	0.37	63,767	1.25	1.04 to 1.50	0.02[c]	5091

[a]Values for health literacy considering adequate health literacy as the reference.
[b]Model with only health literacy.
[c]Statistically significant.
[d]Model with health literacy and the confounders (age, sex, educational level, and income).

Table 3. Percentage of the association between low health literacy and CKD onset explained by individual mediators in the subgroup of older adults

Variables	Percentage of the Association Explained, %					
	Crude Model[a]	*P* Value	*N*	Adjusted Model[b]	*P* Value	*N*
Hypertension	6.8	0.039[c]	7676	2.5	0.489	7676
Diabetes	1.0	0.850	7746	1.3	0.756	7746
High BMI[d]	20.4	0.001[c]	7753	18.8	0.003[c]	7753
High NSAID intake	2.0	0.424	7754	0.0	0.678	7754
Inadequate physical activity[e]	2.9	0.456	7643	0.0	0.717	7643
Smoking	1.0	0.516	7743	5.0	0.319	7743
High alcohol intake[f]	1.0	0.922	7241	16.3	0.579	7241

[a]Model with only health literacy.
[b]Model with health literacy and the confounders (age, sex, educational level, and income).
[c]Statistically significant.
[d]High BMI defined as BMI above 25 kg/m^2.
[e]Participant does not meet Dutch healthy exercise norm.
[f]High alcohol intake defined as more than 40 g of alcohol per day.

cumulative effect on health over time and, consequently, its effect would only be clearly noticed in older adults. Accordingly, it might be important to target people with low health literacy at younger ages to diminish the negative effects of low health literacy on the development of CKD along the life course.

We found that the association between low health literacy and CKD onset in older adults was positively mediated by hypertension and BMI (but not by diabetes, NSAIDs, inadequate physical activity, alcohol, or smoking) in the crude analyses, and only by BMI after adjustment. Individuals with low health literacy are more likely to have difficulties in maintaining a healthy diet and engaging in physical activity.[13,32] This worse lifestyle may cause a higher BMI, which might, in turn, lead to the development of CKD. The retention of only BMI as a mediator, and not of various other health behaviors that relate to CKD, might be due to a high BMI being a result of several unfavorable health behaviors, such as poor physical activity and nutrition. A high BMI might, therefore, represent a wide set of health behaviors that are prejudicial to older adults with low health literacy, making it an overall indicator of poor lifestyle. Previous research already suggested a direct effect of BMI on CKD development.[33] BMI being a more general indicator might explain why it is a stronger mediator than hypertension. Evidently, this requires further study. Our results suggest, nevertheless, that the control of BMI could be an important target to decrease the incidence of CKD in the older population.

Strengths and Limitations

The main strength of this study is its large sample with longitudinal design in the general population. Another strength is the community-dwelling nature of our sample, with a majority of participants having milder renal impairment. These characteristics enable the evaluation of disease-related factors focused on earlier stages of CKD, where prevention measures might be more efficient, and enhances the external validity of the results. Furthermore, sensitivity analyses demonstrated the robustness of our results, which did not change after extra adjustment for cognitive impairment and other renal conditions. A final strength of our study is the objective measurement of renal function used in the analysis. This allowed us to circumvent a biased measurement of CKD due to the use of questionnaires,[34] and ensured the inclusion of patients who had no symptoms and were unaware of their disease, given CKD is very frequently asymptomatic in its first stages.[6]

Some limitations of our study should also be taken into account. First, the possibility of selection bias cannot be excluded as there was a loss in follow-up of 17% of the participants. However, as further analyses showed, no important differences were found between this group and the rest of the participants. Second, we measured health literacy and comorbidities on the basis of self-report, which could have led to misclassification and, thus, to a larger measurement error. Our health literacy questionnaire, however, is a validated tool[23] that has been used in other studies.[24,35] Third, we could not use albuminuria as an extra criterion to define CKD because it was not available in the second wave of Lifelines. Albuminuria is responsible for a larger proportion of the CKD diagnoses when compared with the eGFR alone,[36,37] and CKD patients with albuminuria usually have a more severe disease.[38,39] Consequently, the absence of albuminuria might have led to an underestimation of the strength of our associations.

Implications

Our study may have important implications for policy and practice. Policymakers and clinicians should be aware of the importance of health literacy, because low health literacy is present in a large portion of adults. The large share of low health literacy among patients with CKD indicates that strategies to approach these patients should cover difficulties inherent to low health literacy, such as remaining motivated and taking part in shared decision making.[40] Moreover, although our design does not yield conclusions on causality, the results point toward the possibility that low health literacy may increase the risk of developing CKD in older adults. The issue of low health literacy, notably on the control of BMI, could be

tackled on several levels, namely the patients, their social context, and the professionals and health care organizations.[41] On the patient level, older adults might be empowered by interventions that promote the acquisition of health-related skills and the feeling of self-efficacy.[42] These interventions should be tailored to the patient's characteristics, such as economical and educational context, to ensure the intervention's success and to maintain motivation. Regarding the patients' social context, support networks could help them to feel more motivated and self-confident.[43] On the level of professionals and health care organizations, various strategies could be used, such as clearer communication techniques and low-health-literacy–tailored educational materials. This is in accordance with the concept of organizational health literacy, which indicates that the patients' ability to understand health information is related to the demands that health care systems place on them and that the organizational context where care is provided should compensate for patients' low health literacy.[44] Combinations of these interventions may have a positive effect on various aspects related to CKD development and care, thereby reducing the risk of CKD in older adults. This study shows that low health literacy is associated with the occurrence of CKD in older adults, and that this association is partially explained by a high BMI. Moreover, the share of low health literacy was higher among individuals with worse renal function. These results suggest a need to increase awareness on the topic of low health literacy, notably on the control of BMI and related health behaviors, and to create effective strategies to tackle it. Such strategies may help to reduce the major public health problems related to the effect of low health literacy on CKD and to promote healthier ageing of the population.

DISCLOSURES

G.J. Navis reports being a scientific advisor or member as Chair on the Scientific Board Dutch Kidney Foundation and as a Member of the Health Council of The Netherlands. All remaining authors have nothing to disclose.

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SUPPLEMENTAL MATERIAL

This article contains the following supplemental material online at http://jasn.asnjournals.org/lookup/suppl/doi:10.1681/ASN.2020081155/-/DCSupplemental.

Supplemental Appendix 1. Flow of participants in the study.

Supplemental Appendix 2. Sensitivity analyses.

Supplemental Appendix 3. Share of low health literacy across the different eGFR categories for adults below and above the age of 65.

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