Syndemic approach to chronic kidney disease, cardiovascular disease and educational level: a longitudinal cohort study in northwest Italy

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ABSTRACT

Introduction Chronic kidney disease (CKD) and end-stage renal disease (ESRD) represent significant public health challenges, linked to an elevated risk of cardiovascular disease (CVD) and influenced by socioeconomic disparities. This longitudinal study investigates the interplay between socioeconomic position (SEP), measured as educational level, CKD/ESRD and CVD using the syndemic framework.

Methods We used data from the Piedmont Longitudinal Study to establish CKD and ESRD cohorts and to identify incident CVD between January 2013 and December 2017. The educational level was retrieved from census data. We applied an accelerated failure time model to explore the relationships between CKD/ESRD, CVD and educational level with all-cause mortality and emergency room (ER) acuity.

Results The CKD cohort included 44 220 individuals, with 12 341 deaths and 15 440 ER admissions. The ESRD cohort included 4021 subjects, experiencing 1303 deaths and 1640 ER admissions. After adjusting for confounders, the combination of CKD, low educational level and incident CVD was associated with increased all-cause mortality (time ratios (TR) 0.07, 95% CI 0.05 to 0.08) and ER acuity (TR 0.16, 95% CI 0.14 to 0.17) compared with those with higher education. Instead, patients with ESRD with incident CVD and high educational level had the highest increase in mortality (TR 0.08, 95% CI 0.05 to 0.14) and ER acuity (TR 0.20, 95% CI 0.1 to 0.30).

Conclusions Patients with CKD with low educational levels and incident CVD may represent a 'syndemic', associated with higher mortality and ER acuity. Our study highlights a potential link between these conditions and socioeconomic disparities, suggesting the need for multifaceted approaches.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Chronic kidney disease is known to be associated with cardiovascular risk, as well as socioeconomic disparities. However, the impact of the co-occurrence of chronic kidney disease, cardiovascular diseases and socioeconomic position on health remains understudied. Employing the syndemic framework can offer a valuable analytical tool to investigate this interaction.

WHAT THIS STUDY ADDS

⇒ Low educational level and incident cardiovascular disease were associated with increased all-cause mortality and access to the emergency room in individuals with chronic kidney disease, whereas the educational level alone did not significantly elevate this risk in subjects with end-stage renal disease.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Effective management of chronic kidney disease and cardiovascular disease requires multidisciplinary approaches that take into account socioeconomic factors to ensure equitable health.

INTRODUCTION

Chronic kidney disease (CKD) is defined as a long-term condition characterised by the progressive loss of kidney function over time.[1] In its advanced form, end-stage renal disease (ESRD), the kidneys have lost almost all their ability to function effectively, requiring renal replacement therapy such as dialysis or transplantation. Both CKD and ESRD are recognised as urgent public health concerns worldwide with an increasing incidence of CKD and a substantial financial burden.[2] The global prevalence of CKD was estimated to be approximately 9.1% in 2017.[3] Similarly, the prevalence of ESRD is rising, with a 107% increase from 2000 to 2019 in the USA alone.[4]

Individuals with CKD, and particularly those with ESRD, are prone to several comorbidities. One of the most significant is cardiovascular disease (CVD), which is acknowledged as a major contributor to early morbidity and mortality in individuals with CKD, particularly in patients with ESRD.[5 6] CKD and CVD share common risk factors such as obesity, diabetes, hypertension and smoking, as well as specific pathogenic mechanisms.[2 5 7 8] However, understanding the relationship between CKD and CVD remains challenging because it goes beyond pathophysiological interactions.

According to Krieger and colleagues,[9] socioeconomic position (SEP) is the term used to describe the economic and social factors that may influence an individual or a group's position within society.[10] Several indicators have been used to measure SEP,[11 12] including the educational level. Socioeconomic inequalities exist in the prevalence of CKD and CVD common risk factors.[13–15] However, there is limited direct evidence of the complex interplay among CVD, CKD and SEP, leaving a gap in our understanding of these relationships.

The syndemic framework, previously described by Singer in medical anthropological studies, goes beyond the traditional biomedical model of multimorbidity by including the evaluation of synergistic elements that contribute to adverse health outcomes within the context of social and economic inequalities.[16 17] In this framework, the clustering of diseases is both a result of and a contributor to social and economic disparities.

Syndemic combines elements from social, ethnographic and medical science to create knowledge that can be used for programme implementation and clinical intervention.[18] This approach has been proposed initially in anthropological and qualitative studies, even if more recently others have employed epidemiological and statistical analysis.[19–21] However, there is currently no consensus on the most effective methodological analysis to use in the field.[22]

In this study, we employed the syndemic framework to analyse the interaction between CKD or ESRD, CVD and SEP (measured as educational level) with the risk of overall mortality and emergency room (ER) access. We used a longitudinal study design, employing the Piedmont Longitudinal Study, which includes a cohort of more than four million people residing in Italy's northwest Piedmont region.

MATERIALS AND METHODS

Study design and data sources

Our study is a longitudinal cohort built upon data from the Piedmont Longitudinal Study (PLS), a vast health-administrative cohort based on the anonymous record linkage of health-administrative data of more than 4 million residents in the Piedmont region of Italy. The PLS uses various data sources which include the Hospital Discharge Registry (HDR), containing information on all individuals discharged from any public and accredited healthcare facility; the archives of drug prescriptions and direct ambulatory drug distribution; the Ticket Exemption registry, containing data on individuals exempt from service payment due to the diagnosis of specific chronic conditions; the archives of ambulatory and outpatient specialist services; demographic information from the Regional Archive of assisted, and the anonymous record linkage to the Piedmont population census of 2011, which contains information on the individual educational level (see online supplemental figure 1).

Study population and study variables

We created two separate cohorts of individuals, one with CKD and another with ESRD. Both cohorts included all individuals with either CKD or ESRD, aged 45–85, who were residents in Piedmont on 1 January 2013 and had available information from the 2011 regional census. The cohorts included all incident cases of CKD and ESRD diagnosed after 1 January 2013 (see online supplemental figure 2). Subsequently, all incident cases of CVD diagnosed after CKD or ESRD were recorded. All prevalent cases before the beginning of the study were excluded using health information from 2011 and 2012, and any CVD cases occurring before a CKD or ESRD diagnosis were also excluded. An adapted version of the validated algorithm from Marino *et al*[23] was used to identify CKD and ESRD incident cases. We used renal dialysis as a proxy for ESRD and excluded subjects with ESRD from the CKD cohort.

CVD included coronary heart disease and cerebrovascular disease, extracted using HDR.[24] Online supplemental table 1 shows the specific algorithms employed.

From the 2011 regional census, we extracted the individual educational level as a proxy for SEP. The educational level was categorised as binary and defined as high (university degree/high school degree) and low (middle school/elementary/no education).[11]

The two cohorts were followed up until 31 December 2018.

Definition of the exposure

To define the exposure status of subjects from CKD or ESRD cohorts, they were classified based on their educational level group and the identification of incident CVD during the follow-up period. The categories were defined as follows:

- Baseline category: individuals with an educational level classified as 'high'.
- Low educational level category: individuals with an educational level classified as 'low'.
- High educational level+incident CVD category: individuals with an educational level classified as 'high' and a diagnosis of incident CVD during the study period.
- Low educational level+incident CVD category: individuals with an educational level classified as 'low'" and a diagnosis of incident CVD during the study period.

Outcomes

The selected outcomes were all-cause mortality and ER acuity. Mortality was assessed using the regional death registry and ER acuity was assessed using the ER registry, which includes all public hospitals in the Piedmont region. We selected the individual first access to the ER with a yellow code (urgency: potential life-threatening situation) or a red code (emergency: imminent life-threatening danger) assigned during the hospital triage. Details on the definition of the ER code system can be found in the online supplemental table 2. We excluded all access to ER related to renal dialysis or kidney transplants.

Covariates

Information regarding age and sex was extracted from the PLS database. Age was categorised into four groups (45–55, 56–65, 66–75 and 76–85). The age range of 45–85 years was selected to minimise variability in CKD management and reduce confounding from age-related differences in treatment approaches, aligning with Kidney Disease Improving Global Outcomes (KDIGO) guidelines that emphasise the differing age-related prognoses and treatment priorities.[6] Direct identification of smoking status and hypertension was not available in the PLS data; hence, we used the drug consumption for chronic obstructive pulmonary disease as a proxy for heavy smokers[24] and the utilisation of antihypertensive medications for hypertension (ATC7: C02*, C03*, C07*, C08* and C09*). Diabetes was defined using a validated algorithm that incorporated data from the HDR, the regional diabetes registry and prescription medications.[25] Additionally, we identified the use of antiplatelet (ATC7: B01AC) and anticoagulant therapies (ATC7: B01AA, B01AB, B01AE, B01AF and B01AX05) through prescription records.

Statistical analysis

We presented the baseline characteristics of the cohorts according to the exposure category, providing percentages for categorical variables. We set the beginning of the follow-up as the day of the individual diagnosis of CKD/ESRD extracted from 1 January

Table 1 Baseline characteristics of the CKD cohort

	Full CKD cohort (N_{tot}=44 420) N (%)	Low educational level (N_{tot}=36 227) N (%)	CVD + high educational level (N_{tot}=1084) N (%)	CVD + low educational level (N_{tot}=6066) N (%)
Sex				
Male	27 227 (61.3)	21 215 (58.6)	930 (85.8)	4086 (67.4)
Female	17 193 (38.7)	15 012 (41.4)	154 (14.2)	1980 (32.6)
Age class				
45–55	3809 (8.6)	2448 (6.8)	56 (5.2)	141 (2.3)
56–65	7858 (17.7)	5699 (15.7)	186 (17.2)	582 (9.6)
66–75	16 192 (36.5)	13 302 (36.7)	425 (39.2)	2071 (34.1)
76–85	16 561 (37.3)	14 778 (40.8)	417 (38.5)	3272 (53.9)
Diabetes	19 520 (43.9)	16 639 (45.9)	527 (48.6)	3336 (55.0)
Antihypertensives	38 904 (87.6)	32 164 (88.8)	1031 (95.1)	5824 (96.0)
Antiplatelet therapy	27 380 (61.6)	22 975 (63.4)	946 (87.3)	5375 (88.6)
Anticoagulant therapy	30 757 (69.2)	25 793 (71.2)	897 (82.7)	5265 (86.8)
Smoking	9649 (21.7)	8419 (23.2)	250 (23.1)	1942 (32.0)

CKD, chronic kidney disease.

2013 until 31 December 2017. Subjects were followed until the end of the follow-up (31 December 2018) or death for all causes/admission to the ER for yellow or red code or were censored if they left the Piedmont region, whichever came first. Because our data did not comply with the proportional hazard assumption, we fit an accelerated failure time (AFT) model with a generalised gamma distribution.[26] The distribution for the AFT model was chosen based on the Akaike Information Criterion (AIC) and the graphical goodness of fit.[27] We calculated time ratios (TR) and 95% CI to investigate the relationship between CKD/ESRD, CVD and educational level with two outcomes: (1) all-cause mortality and (2) ER acuity (yellow/red codes). Separate models were run for each outcome. Both models were adjusted for sex, age, diabetes, heavy smoking, use of antihypertensives, antiplatelet therapy and anticoagulant therapy. Stratification by sex was performed to explore potential sex-specific differences in these associations. All statistical analysis was performed using SAS V.9.4 and STATA V.17.

RESULTS

CKD cohort

The CKD cohort included 44 220 incident cases identified during the follow-up period. 7993 subjects were included in the baseline category (high educational level without incident CVD) and 36 227 in the low educational level category. Subsequently, 1084 subjects with high educational levels and 6066 subjects with low educational levels developed CVD and were moved into the subsequent exposure category accordingly.

The characteristics of the CKD cohort stratified by exposure category are shown in table 1. Overall, subjects with low educational levels and incident CVD had the highest percentages of diabetes and hypertension, as well as the highest use of antiplatelet and antiaggregant therapies, and were more likely heavy smokers.

All-cause mortality and access to the ER

The TR for the association between CKD, CVD and educational level with all-cause mortality and access to ER for yellow/red codes is shown in table 2. Overall, there were 12 341 deaths for all causes and 15 440 access to ER with yellow or red code among patients with CKD with a median follow-up of 3.10 and 2.28 years, respectively.

After adjusting for confounders, subjects with a low educational level who did not have incident CVD during the follow-up period had a 24% (TR 0.76, 95% CI 0.68 to 0.85) reduction in survival time as compared with subjects with a high educational level. Moreover, the reduction in survival times intensified with the addition of incident CVD, with a 92% reduction in survival time as compared with subjects with high educational levels without incident CVD (TR 0.08, 95% CI 0.06 to 0.10). Finally, individuals with both low educational levels and incident CVD had the greatest reduction in survival time, which was reduced by 93% compared with patients with high educational levels without CVD (TR 0.07, 95% CI 0.05 to 0.08). However, the results regarding low educational level and incident CVD and high educational level and incident CVD are not statistically different since the CIs intersect.

Analysis of ER acuity yielded similar findings with the same trend of reduction of survival times for all exposure categories, increasing with the addition of incident CVD. This decrease was

Table 2 Results from accelerated failure time model using generalised gamma distribution for the chronic kidney disease cohort

	All-cause mortality		Emergency room acuity	
	Time ratio	95% CI	Time ratio	95% CI
High educational level	1 (ref)	–	1 (ref)	–
Low educational level	0.76	(0.68 to 0.85)	0.88	(0.81 to 0.94)
High educational level + CVD	0.08	(0.06 to 0.10)	0.18	(0.16 to 0.21)
Low educational level + CVD	0.07	(0.05 to 0.08)	0.16	(0.14 to 0.17)

Adjusted for sex, age, diabetes, antihypertensives, smoking, anticoagulant and antiplatelet therapies.
CVD, cardiovascular disease.

Table 3 Baseline characteristics of the ESRD cohort

	Full ESRD cohort (N_{tot}=4021) N (%)	Low educational level (N_{tot}=3172) N (%)	CVD + high educational level (N_{tot}=141) N (%)	CVD + low educational level (N_{tot}=589) N (%)
Sex				
Male	2473 (61.5)	1870 (58.9)	113 (80.1)	414 (70.3)
Female	1548 (38.5)	1302 (41.1)	28 (19.8)	175 (29.7)
Age class				
45–55	575 (14.3)	374 (11.8)	20 (14.2)	28 (4.7)
56–65	1001 (24.9)	753 (23.7)	40 (28.4)	112 (19.0)
66–75	1451 (36.1)	1196 (37.7)	46 (32.6)	245 (41.6)
76–85	994 (24.7)	849 (26.8)	35 (24.8)	204 (34.6)
Diabetes	1573 (39.1)	1302 (41.1)	59 (41.8)	323 (54.8)
Antihypertensives	3509 (87.3)	2817 (88.8)	136 (96.4)	576 (97.7)
Antiplatelet therapy	2747 (68.3)	2197 (69.3)	132 (93.6)	546 (92.7)
Anticoagulant therapy	2773 (69.0)	2218 (69.9)	115 (81.6)	503 (85.4)
Smoking	741 (18.4)	634 (20.0)	22 (15.6)	144 (24.4)

CVD, cardiovascular disease; ESRD, end-stage renal disease.

most pronounced in the subgroup with low educational levels. Subjects with low educational levels and incident CVD had the highest value, with an 84% reduction in mean survival time for ER acuity (TR 0.16, 95% CI 0.14 to 0.17) as compared with subjects with high educational levels; subjects with high educational levels and CVD had an 82% reduction (TR 0.18, 95% CI 0.16 to 0.21) and subjects with low educational levels only had a 12% reduction (TR 0.88, 95% CI 0.81 to 0.94).

ESRD cohort

Overall, 4021 subjects were included in the ESRD cohort. We assigned 849 subjects in the baseline category (high educational level without incident CVD) and 3172 in the category with low educational level. Of those, 141 subjects with high educational levels and 589 subjects with low educational levels had CVD during the follow-up period and were moved into the subsequent exposure category accordingly.

The characteristics of the ESRD cohort stratified by exposure category are shown in table 3. Individuals with low educational levels and CVD had the highest rates of diabetes and hypertension, the use of antiplatelet and antiaggregant therapies and were more likely heavy smokers.

All-cause mortality and access to the ER

Throughout the study, a total of 1303 deaths from all causes and 1640 access to the ER with yellow or red codes were observed among patients with ESRD, with median follow-up periods of 3.10 and 2.11 years, respectively. The TR for the associations between ESRD, CVD and low educational level with both all-cause mortality and access to the ER for yellow/red codes is presented in table 4.

Patients with ESRD with low educational levels showed a slight reduction in survival time for both all-cause mortality and access to the ER, although this reduction was not statistically significant for either outcome. Subjects with incident CVD and high educational level had the most accelerated survival with 92% (TR 0.08, 95% CI 0.05 to 0.14) for mortality and 80% (TR 0.20, 95% CI 0.14 to 0.30) for ER acuity. ESRD subjects with low educational levels and CVD had a significantly reduced survival time for both outcomes compared with subjects with high educational levels (mortality-TR 0.14, 95% CI 0.09 to 0.21; ER acuity-TR 0.25, 95% CI 0.19 to 0.34). However, unlike the CKD cohort, this reduction was not the greatest within the subgroups. Nonetheless, similar to the CKD cohort, the CIs intersect, indicating no significant differences between the estimates of high educational level and incident CVD and low educational level and incident CVD.

Subgroup analysis

Subgroup analysis by sex for both cohorts and outcomes is shown in figure 1. Stratified analysis showed the same pattern as the full cohort, with no significant differences between males and females for all outcomes and exposure categories.

DISCUSSION

In this large population-based study consisting of all residents aged 45–85 in the Piedmont region with CKD or ESRD, we found that while CVD and low educational level individually

Table 4 Results from accelerated failure time model using generalised gamma distribution for the end-stage renal disease cohort

	All-cause mortality		Emergency room acuity	
	Time ratio	95% CI	Time ratio	95% CI
High educational level	1 (ref)	–	1 (ref)	–
Low educational level	0.78	(0.59 to 1.02)	0.94	(0.78 to 1.14)
High educational level + CVD	0.08	(0.05 to 0.14)	0.20	(0.14 to 0.30)
Low educational level + CVD	0.14	(0.09 to 0.21)	0.25	(0.19 to 0.34)

Adjusted for sex, age, diabetes, antihypertensives, smoking, anticoagulant and antiplatelet therapies.
CVD, cardiovascular disease.

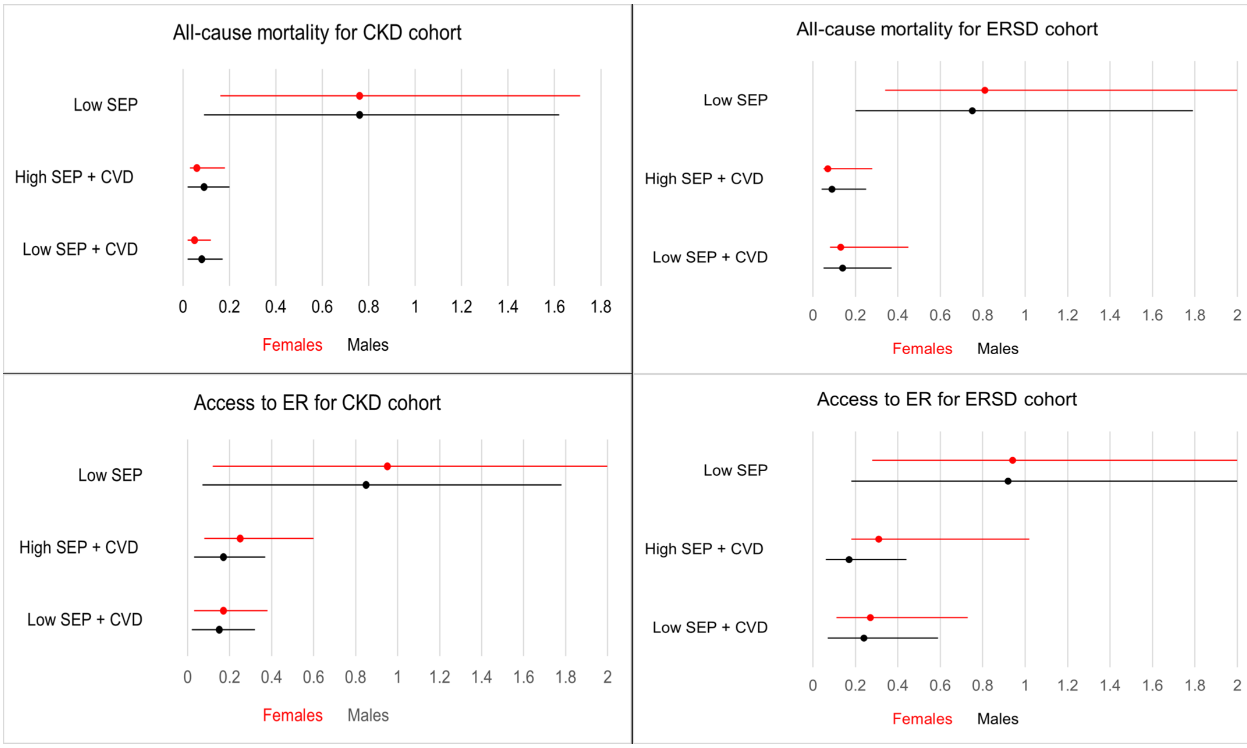

Figure 1 Results from the accelerated failure time model using generalised gamma distribution for the CKD cohort and ESRD cohort stratified by sex. CKD, chronic kidney disease; CVD, cardiovascular disease; ESRD, end-stage renal disease.; ER, emergency room; SEP, socioeconomic position.

reduce CKD survival, their combination magnifies the risk of death and ER acuity in the population of subjects with CKD, independent of known risk factors. ESRD showed a different pattern, with CVD having the most substantial impact on survival time, while the influence of low educational level alone did not reach statistical significance. Using a syndemic approach changed how we analyse health conditions and socioeconomic factors, combining variables to study our integrated impact alongside a standard statistical method.

CVD is known to be one of the main comorbidities in patients with CKD, and, in many cases, patients with CKD die from cardiovascular causes before the disease progresses to kidney failure.[28] Furthermore, even individuals with advanced stages of CKD, such as ESRD, are more likely to die from CVD than from renal failure itself.[7 29 30] The relationship between CKD and CVD has been extensively documented. While age, hypertension, diabetes, obesity and smoking are commonly acknowledged as risk factors, they do not fully account for the relationship.[31 32] CKD independently elevates the risk of CVD and cerebrovascular disease through several mechanisms, including anaemia, vascular stiffness, left ventricular hypertrophy, reduced coronary reserve, dyslipidaemia and a proinflammatory state.[8 33 34] Additionally, the renin-angiotensin system, increased sympathetic nerve activity and endothelial dysfunction are key contributors to this elevated risk.[35] Our study revealed that individuals with CKD or ESRD in the subgroup who experienced incident CVD during the follow-up period, regardless of their educational level, were consistently more likely to access the ER or experience mortality when compared with subjects who did not have incident CVD.

Our study also showed that a low educational level can significantly decrease survival both in subjects with CKD only and in individuals with a combination of CKD and CVD. Individuals with low educational levels faced a higher risk of mortality or ER acuity when combined with CKD and CVD compared with subjects with high educational levels.

In our study, we used the educational level as a proxy measure to define SEP, recognising its significant impact on health outcomes.[9 11 12]

The high proportion of individuals with low educational attainment in our study is likely due to the older age of the population. Many of these individuals grew up before mandatory education became widely available, resulting in limited educational opportunities for older generations. This historical context helps explain the lower educational levels observed in this population.

A lower SEP can contribute to an elevated risk of developing CKD and a worsened prognosis for individuals already affected by this condition. Many of the common risk factors for CKD are closely linked to socioeconomic disparities. Consequently, increasing the burden of these risk factors may lead to a higher incidence of CKD. Indeed, studies have shown that, regardless of the method used to quantify SEP, socioeconomic disparities have an adverse impact on the prevalence of CKD.[13 14]

Moreover, SEP is known to influence CVD, as it does for CKD, by increasing the burden of risk factors and worsening prognosis. SEP independently increased cardiovascular risk and related mortality in a similar manner to traditional risk factors, according to a study by Stringhini *et al*.[15] Furthermore, an elevated risk of CVD has been associated with lower educational status and a lack of awareness of CKD among patients with CKD at stage 3.[36] The management of CKD and ESRD carries a substantial economic burden and varies significantly across countries. This disparity stems from how each healthcare system distributes the cost. Patients may bear the entire burden themselves, rely on private health insurance or benefit from partial or full coverage by their national healthcare system.[37 38] Patients with ESRD have significant financial burdens due to the high cost of renal dialysis and transplantation. This can worsen socioeconomic disparities in countries where these services are not freely available. However, in Italy, the location of our study, the National Health System (NHS) is based on the Beveridge economic model, which is founded on the principle of universality. This implies that these services are provided free of charge to all residents by the Italian NHS.[39]

Furthermore, a low SEP can be associated with reduced health literacy and healthcare access. This results in individuals being less aware of modifiable CVD risk factors and prevention strategies. A low SEP may be associated with unhealthy lifestyle habits, which can contribute to the development of CKD, CVD and other adverse health outcomes.[40]

On the one hand, in our study, we found that low educational level was not significantly associated with an increase in all-cause mortality or access to the ER for subjects with ESRD. Consequently, the combination of low educational level and CVD did not have the worst impact. Instead, incident CVD alone, particularly in those with high educational levels, had the greatest effect, even though the difference compared with subjects of the low educational level category was not significant.

Subjects with ESRD are considered extremely vulnerable patients due to the severity of the condition and the susceptibility to other comorbidities. They are closely monitored at dialysis centres, where they receive all necessary services free of charge. This may be one of the reasons why socioeconomic inequalities do not significantly worsen the health outcomes of these patients. The universal coverage and equitable access to healthcare provided by the Italian NHS could mitigate the impact of SEP on mortality rates among these patients. The relationship between SEP and health outcomes may be influenced by the characteristics of healthcare systems, including the level of access and the quality of care provided. For example, in countries with less comprehensive healthcare coverage, disparities in SEP may have a more pronounced effect on mortality for patients with ESRD.

Furthermore, an additional potential explanation for the observed lack of significant influence of educational level on the survival of patients with ERSD may be related to the fact that, among individuals with a low educational level, only those with a healthier profile survive, while the others die from other causes. Indeed, patients with ESRD are known to be likely affected by other comorbid conditions, which might be more important determinants of survival than educational level.

On the other hand, our results show that the educational level was associated with both outcomes in patients with CKD as well as incident CVD. Even if we could not see a statistically significant difference between educational level groups, the combination of CVD and low educational level resulted in the worst health outcomes, suggesting that a syndemic effect could be present between CKD, CVD and low educational level.

Strengths and limitations

One of the major strengths of our study is its use of a wide and heterogeneous longitudinal cohort analysis to investigate the syndemic framework, which remains relatively underused in syndemic research.

However, our study has some limitations. First, our findings are based on data from a single Italian region and may not be generalisable to other populations or healthcare systems. Due to the nature of the data, we were not able to distinguish between CKD stages and levels of estimated glomerular filtration rate and/or albuminuria. Additionally, we were unable to retrieve direct information on smoking status and hypertension, necessitating proxy measures. Data for body mass index was also not accessible for analysis. Moreover, using educational level as the sole proxy for SEP might reduce the complexity of the association under study, as incorporating other variables such as income and occupational status could provide a more comprehensive measure of SEP. Lastly, the data did not allow us to explore the underlying causes of CKD and ESRD.

In conclusion, our study in the Piedmont region of Italy suggests a potential syndemic interaction between individuals residing in the Piedmont region involving CKD, CVD and educational level. This interaction was present in CKD patients, but not those with ESRD. By acknowledging the interplay between social determinants, health conditions and health outcomes, multidisciplinary public health policies can be designed to address the specific needs of disadvantaged populations. These policies could focus on enhanced monitoring of patients with CKD and CVD, potentially mitigating the influence of educational level and promoting equitable health outcomes. Failure to do so risks perpetuating existing disparities and widening the gap, leaving those already at a disadvantage further behind in terms of access to care and health outcomes.

While our study offers initial evidence of the existence of a syndemic cluster involving CKD, CVD and educational level, further investigation can include diverse settings with varying healthcare systems (both public and private) that would provide a more comprehensive understanding of this complex interplay.

Contributors Conceptualisation: LD, FR and SS; methodology: LD and FR; formal analysis: LD; writing the original draft preparation: LD; writing the review and editing: LD, FR, SS, LM, AM, CD, WG and RG; supervision: FR, SS and RG. FR acted as guarantor. All authors have read and agreed to the published version of the manuscript.

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