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REVIEW

Socioeconomic Position and Health Among Children and Adolescents With CKD Across the Life-Course

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Children and adolescents in families of lower socioeconomic position (SEP) experience an inequitable burden of reduced access to healthcare and poorer health. For children living with chronic kidney disease (CKD), disadvantaged SEP may exacerbate their considerable disease burden. Across the life-course, CKD may also compromise the SEP of families and young people, leading to accumulating health and socioeconomic disadvantage. This narrative review summarizes the current evidence on relationships of SEP with kidney care and health among children and adolescents with CKD from a life-course approach, including impacts of family SEP on kidney care and health, and bidirectional impacts of CKD on SEP. It highlights relevant conceptual models from social epidemiology, current evidence, clinical and policy implications, and provides directions for future research. Reflecting the balance of available evidence, we focus primarily on high-income countries (HICs), with an overview of key issues in low- and middle-income countries (LMICs). Overall, a growing body of evidence indicates sobering socioeconomic inequities in health and kidney care among children and adolescents with CKD, and adverse socioeconomic impacts of CKD. Dedicated efforts to tackle inequities are critical to ensuring that all young people with CKD have the opportunity to live long and flourishing lives. To prevent accumulating disadvantage, the global nephrology community must advocate for local government action on upstream social determinants of health; and adopt a life-course approach to kidney care that proactively identifies and addresses unmet social needs, targets intervening factors between SEP and health, and minimizes adverse socioeconomic outcomes across financial, educational and vocational domains.

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Children growing up in socioeconomically disadvantaged circumstances experience an inequitable burden of poor health, wellbeing, and reduced access to healthcare.[1,2] Socioeconomic disadvantage is often conceptualized through the construct of SEP, which encompasses a person's status in a social hierarchy, their material, and social resources (and for children, those of their family/caregivers).[3,4] Although socioeconomic status (SES) is also a common term, in this review we use SEP because it encompasses both resource-based and status-based aspects of stratification.[3] SEP is a complex construct comprising overlapping but distinct domains, with the most commonly measured being education, income, and employment or occupation,[3,5] and can be measured at the individual, household, or area-level (Figure 1).

Inequities in child health across family SEP are driven by inequities in the conditions of daily living as well as the structural determinants (including power, money, and resources) that drive these conditions of daily living (i.e., the social determinants of health).[4,6] That is, children in socioeconomically disadvantaged families are more likely to be born, grow, live, learn, play, and work in adverse conditions, which poses risks to their health and wellbeing across the life-course. SEP may also interact with other social factors such as race or ethnicity and gender, with different domains of privilege and disadvantage producing

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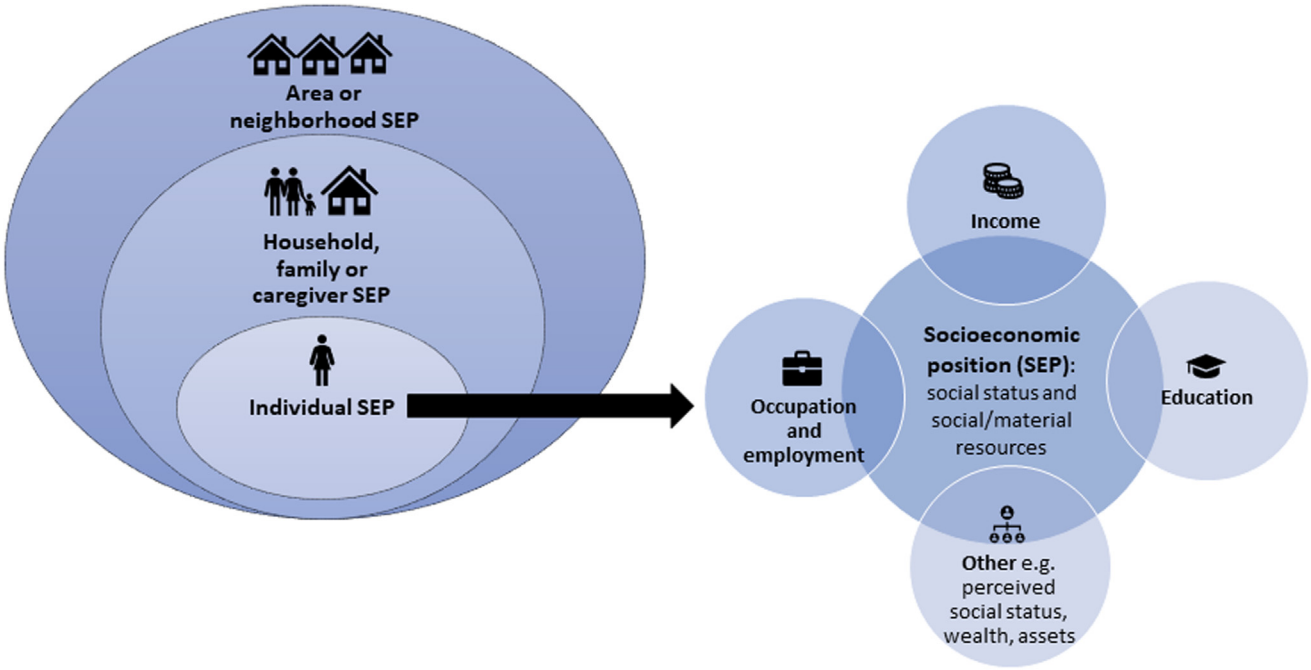

Figure 1. Conceptual illustration of SEP highlighting multiple hierarchical levels (individual, family/household, area/neighborhood) and domains (including income, education, occupation/employment, and others) that make up the construct of SEP. SEP, socioeconomic position.

unique multidimensional social identities that have different impacts on health.[7,8]

In children and adolescents with CKD, lower SEP may exacerbate the burden of poor health and wellbeing outcomes experienced, through greater exposure and vulnerability to adverse material, psychosocial, behavioral, and biological factors that have additive and interactive effects, and fewer protective factors to 'buffer' disease impacts.[9,10] Childhood CKD is often a lifelong illness. While transitioning through life stages, children with CKD may face long-term challenges, including cognitive impairment and academic difficulties, comorbidities; and in adulthood, social and economic challenges in securing employment, building relationships, and finding independence.[11-13] Adopting a life-course approach is essential to understanding impacts of CKD and SEP across development. Although there is an emerging body of studies on relationships between SEP, kidney care, and health in children and adolescents with CKD, there has not been a recent review across SEP and health domains. Understanding these relationships over the life-course is critical to the development of equity-focused interventions that promote health and social flourishing for all young people with CKD.

Aims

In this narrative review, we aim to summarize current evidence on the relationship of SEP with kidney care and health among children and adolescents with CKD, using the life-course approach as an overarching conceptual framework. Given the role of reciprocal relationships between SEP and health in accumulating disadvantage across the life-course, in addition to examining impacts of family SEP on child health and kidney care, we will consider impacts of health and kidney care on the SEP of families and young people with CKD, and whether these are worse for families with existing socioeconomic disadvantage. We also provide clinical and policy implications and directions for future research. We focus primarily on HICs, where much of the previous research has been conducted; however, we also highlight key findings in the emerging evidence from LMICs. Given the importance of an intersectional approach to health inequities, we highlight work on the intersection of SEP with gender and race or ethnicity, and refer to the more detailed literature on these issues. Evidence cited in this review comes from kidney registries, large multicenter cohort and cross-sectional studies, and smaller studies. For ease of reference, key details of some of the most commonly-used large multicenter cohort studies are outlined in Supplementary Table S1.

Socioeconomic Inequities in Health Among Children and Adolescents With CKD: Looking Across the Life-Course

The life-course approach is increasingly recognized as having strong relevance to socioeconomic inequities in child health,[4,14] including in CKD.[15,16] This approach recognizes that health is a dynamic capacity that develops across the life-course, which is shaped by complex interactions between socioeconomic, biological, environmental, and psychological factors over

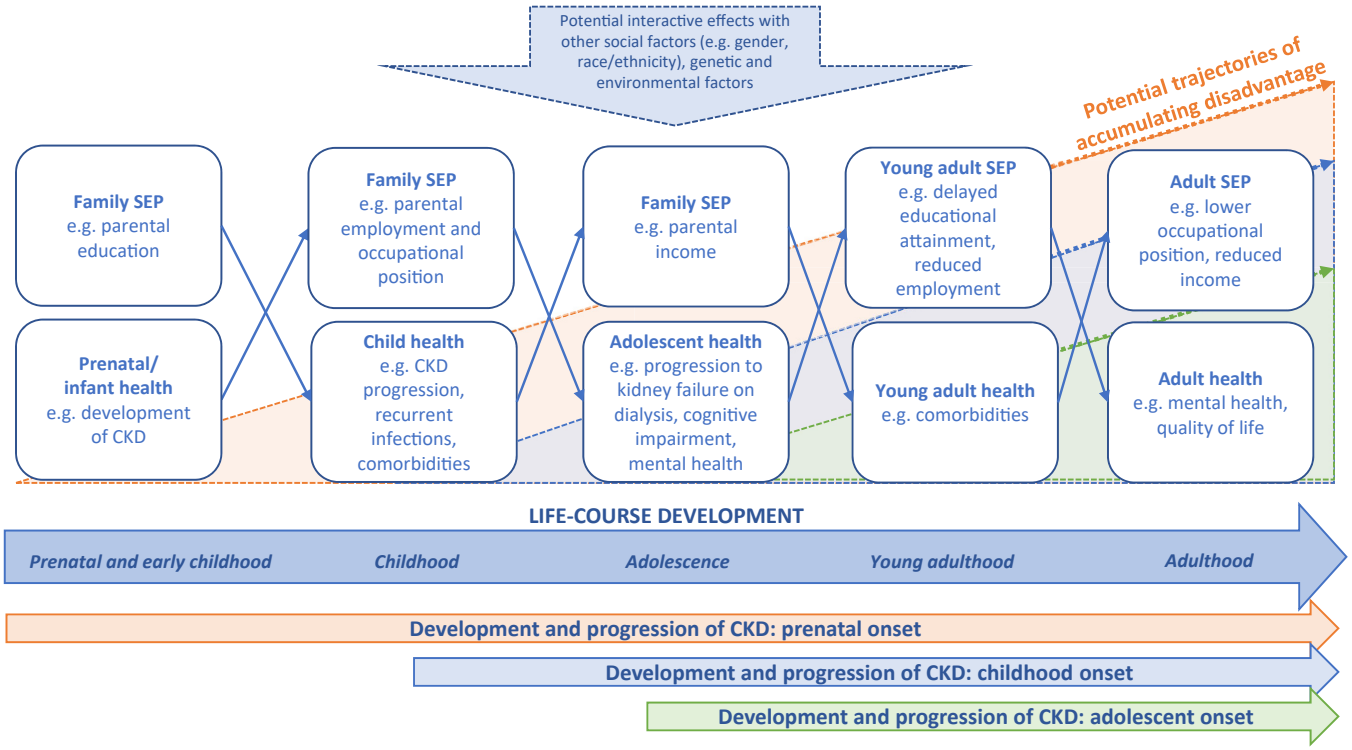

Figure 2. Illustration of potential bidirectional relationships between health and SEP across life-course development and disease stages in pediatric CKD, highlighting the potential for accumulating disadvantage over time. Adapted from Adler and Stewart.[7] The figure illustrates the way that health and socioeconomic disadvantage may accumulate across life stages for children with CKD, because low SEP in one stage may compromise health in the next, and poor health in one life stage may compromise SEP in the next. This is a simplified conceptual model, so does not include all possible associations between SEP and health over time (e.g., SEP at each stage is likely to impact SEP at later stages, and health at each stage is likely to impact health at later stages). The age of onset of CKD may vary across individuals; illustrative trajectories are included to highlight how impacts on health and SEP may vary according to whether CKD develops in the prenatal period, childhood, or adolescence, with compounding disadvantage potentially being greater for children presenting at earlier life stages. Accumulating disadvantage may also be impacted by interactions with other social, genetic, and environmental factors. CKD, chronic kidney disease; SEP, socioeconomic position.

time.[17,18] It highlights the interdependence between life stages, generations, and individuals across society; with health being shaped by factors experienced in previous life stages and generations.[9,19,20] It also emphasizes that effects of exposures may vary depending on their timing, duration, and sequencing. This includes the potential for unique impacts during critical periods (e.g., prenatal and early childhood), heightened impacts during social and biological transition periods (e.g., school entry, adolescence, young adulthood, and pregnancy), and cumulative effects where impacts accumulate with increasing duration.[19-22] It also highlights the potential for age, cohort, and period effects.[17] Further details on life-course theory and methods can be found elsewhere.[9,14,17-19,22]

Importantly, the life-course approach offers a framework for understanding how health inequities emerge and are perpetuated across the life-course.[4,9] A key concept is the potential for bidirectional relationships between health and SEP across life stage; not only does socioeconomic disadvantage pose risks to future health (e.g., children in low SEP families may have more comorbidities), but health problems in one life stage can compromise future SEP, referred to in the Diderichsen model of health inequities as the "social consequences of illness" (e.g., children with CKD may have poorer educational outcomes).[4,7,23] This can lead to an accumulation of health and socioeconomic disadvantage over time,[4,23] as shown in Figure 2 which is adapted from previous work by Adler and Stewart.[7] As highlighted in Figure 2, CKD onset may occur at different developmental stages, and those with earlier onset may experience greater levels of accumulated disadvantage. Although not captured in Figure 2, from a life-course perspective, impacts of CKD and SEP may also differ according to timing (e.g. low SEP in the prenatal period may have "critical period" effects on nephrogenesis and kidney function, CKD onset during secondary school entry may have pronounced impacts on educational outcomes because this is a "sensitive period" of social and biological transition).[16,19,22,24] Impacts of CKD and SEP may also be modified by other social, genetic, and environmental factors.

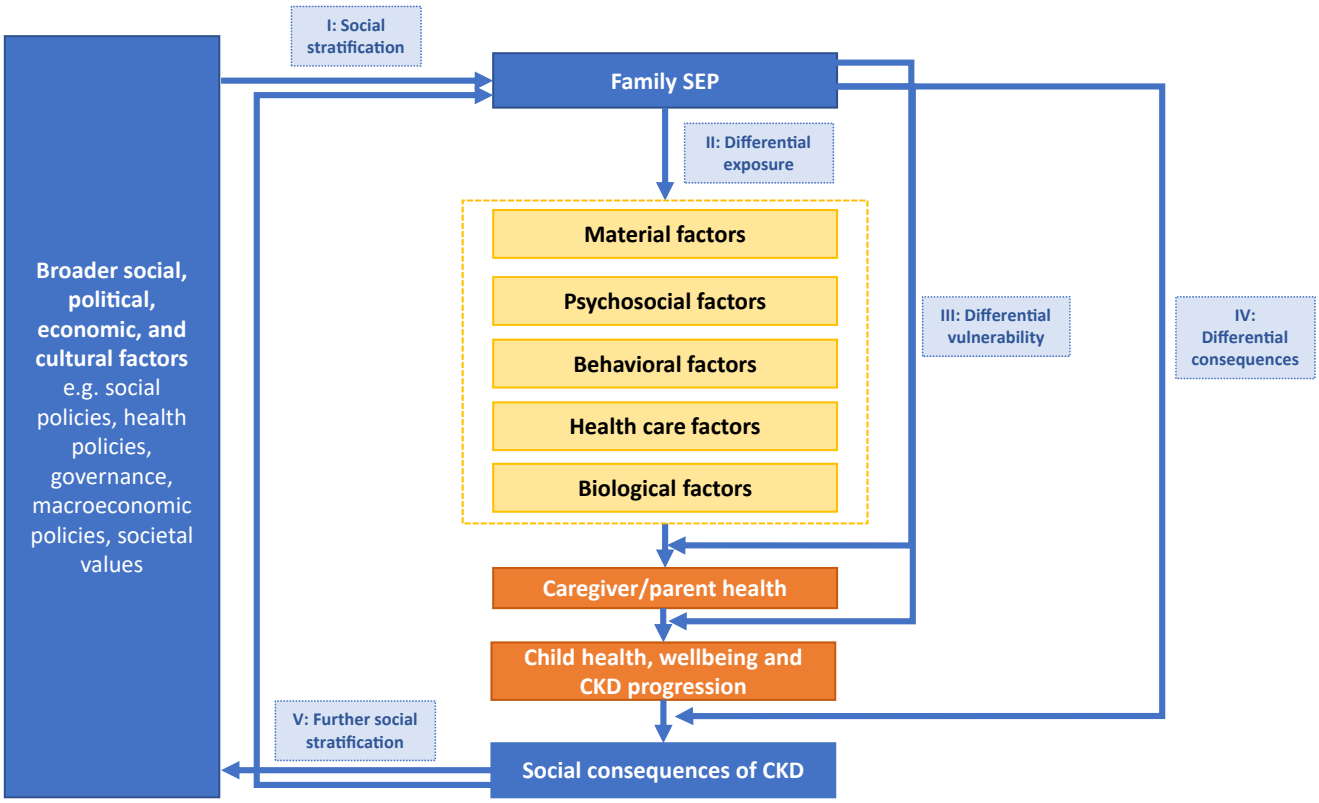

Figure 3. Mechanisms for the generation and perpetuation of health inequities across the life-course among children with CKD, each of which represents a potential policy entry point for interventions, based on the Diderichsen model of health inequities. These include *the following*: *(*i) social stratification, *(*ii) differential exposure to harmful and protective factors, *(*iii) differential vulnerability to exposures, *(*iv) differential social consequences of illness, *(*v) further social stratification. Adapted from the Diderichsen model in Diderichsen et al.[23] and its adaptations in Pearce et al.[4] These mechanisms start at the upstream level with the broad social, economic, and political factors that drive social stratification into different levels of family SEP (mechanism i), moving through to differential exposure (mechanism ii) and vulnerability (mechanism iii) to risk and protective factors (across material, psychosocial, behavioral, healthcare, and biological domains) for children of lower SEP, and on to greater social consequences of CKD (e.g., adverse effects on caregiver employment or income, and child education) for children in lower SEP families. This in turn leads to further social stratification, moderated by broader structural factors. CKD, chronic kidney disease; SEP, socioeconomic position.

Figure 3 is a conceptual model of the mechanisms by which socioeconomic inequities in health are generated and perpetuated across the life-course starting in childhood, adapted from the Diderichsen model[23] and its adaptations in previous work by Pearce et al.,[4,23] for childhood CKD. According to the Diderichsen model, the root cause is social stratification into different SEPs, which is driven by social, economic, and political factors at the structural level (mechanism i). Children in lower SEP families are likely to have greater exposure and vulnerability to health risk factors (mechanisms ii and iii), which results in poorer caregiver and child health. They may also be more vulnerable to adverse social consequences of CKD such as lower education, employment and income (mechanism iv), which can result in further social stratification (mechanism v), and so perpetuate a vicious cycle of disadvantage.[4,23] Each of these mechanisms from the Diderichsen model represents a potential target for health equity interventions, some of which can be addressed through clinician and health system actions (e.g., mechanisms ii, iii, and iv) and others that require broader intersectoral and whole-of-government action (e.g., mechanisms i and v).[4,23] Later in this review, we will consider potential interventions to address these mechanisms among children with CKD.

Issues in Conceptualizing and Measuring SEP

SEP is a contested construct encompassing multiple aspects of social status and resources. Considering multiple SEP domains is important, because each has their own distinct (albeit overlapping) pathways to health and their relevance may vary across life stages, outcomes and populations.[25,26] For example, education may impact health through factors such as health knowledge and behaviors, social support, social status, cognitive or noncognitive skills, and indirect effects via occupation and income because, across the life-course, education tends to drive occupation, which drives income.[5,27] Pathways from occupation to health include perceived control, stress, social status, work conditions, and indirect effects via income.[5,26] Mechanisms for income include material resources, social

status, and stress.[5,26] Importantly, the relevance and interpretation of SEP measures may differ between LMICs and HICs, given the influence of varying economic, social, and political contexts.[28] For example, consumption expenditure measures (goods and services purchased) are primarily used in LMICs, whereas different types of asset-based measures may be relevant in LMICs (e.g., electricity, sanitation, flooring) and HICs (e.g., car ownership).[28]

Although area-level SEP measures are valuable and commonly used, their interpretation is complex; they reflect the aggregate social and/or economic characteristics of individuals in a geographic area (and are often used to proxy individual SEP), and also capture place-based impacts of material deprivation in the living environment.[3,29] Further, they are often composite measures that include diverse social and economic factors associated with socioeconomic disadvantage, and the included domains often vary across measures. Some include measures of health or disability, complicating their use in health inequities studies (e.g., the Index of Relative Socioeconomic Advantage and Disadvantage[30] commonly used in Australia and the Index of Multiple Deprivation[31] commonly used in the UK). Importantly, where they are interpreted as proxies for individual-level SEP, there is a risk of biased estimates, particularly where they use larger areas as units of measurement.[3,29] Detailed discussion of SEP is available elsewhere.[3,5,28,29,32]

Impacts of SEP on Kidney Care and Health Among Children and Adolescents With CKD

Impacts of SEP on CKD Occurrence and CKD Progression

There is some evidence of socioeconomic inequities in the occurrence of kidney failure in children, with descriptive analyses of French REIN registry data showing that children on kidney replacement therapy (KRT) are more likely to reside in socioeconomically disadvantaged areas compared to the general population.[33,34] However, it is not clear whether this reflects a higher rate of CKD and/or greater CKD progression. Although there is extensive evidence that adults of lower SEP are at increased risk of developing CKD[35,36] (aligned with socioeconomic inequities in diabetes and hypertension which are common causes of CKD),[37,38] it is not clear whether there are socioeconomic inequities in CKD occurrence in children, given the role of genetic factors in predominating causes.[12,16] The CKD in Children (CKiD) study of children with mild-to-moderate CKD[39] in North America (Supplementary Table S1) found that lower neighborhood income was associated with faster CKD progression, but this was attenuated after adjustment for child and family characteristics, including race, ethnicity, sex and family income, suggesting that area-level disadvantage may not be driving these inequities. There was no association with a composite measure of area-level disadvantage.[39,40] For caregiver SEP, longitudinal CKiD analyses found similar baseline estimated glomerular filtration rate and estimated glomerular filtration rate decline across family income[41] and no univariable association between family income and CKD progression.[42] However, a small Canadian study[43] found greater unadjusted estimated glomerular filtration rate decline among children with CKD (predialysis) whose caregivers had lower income or education (but not employment or home ownership). Overall, it seems likely that there are socioeconomic inequities in disease progression for children with CKD, but it is not clear whether they are driven primarily at the individual or area-level, and which SEP domains matter most.

Impacts of SEP on KRT Access and Outcomes

Much research has focused on access to and outcomes of KRT,[44] primarily using the area-level SEP measures that are often available in kidney registries, with somewhat conflicting findings. Regarding preemptive transplantation, the optimal treatment for kidney failure, children from socioeconomically disadvantaged areas were less likely to receive a preemptive kidney transplant in analyses from the French REIN registry,[34] UK Renal Registry,[45] a New Zealand national clinical database,[46] and the CKiD study in North America.[39] In CKiD, area-based inequities were attenuated after adjusting for child sex, race, ethnicity, and family income[39]; and another CKiD study identified inequities across family income and education,[47] suggesting further work is needed to distinguish the role of family- versus area-level SEP. In contrast, a registry study did not find inequities in preemptive transplantation across area-level SEP in Australia.[48] In waitlisted children, a registry study in the USA found no area-based SEP inequities in receipt of a transplant or mortality, whereas children living further from the transplant center and in urban areas had increased mortality risks.[49] However, among children initiating KRT on dialysis in France in the REIN registry, those in more disadvantaged areas experienced poorer kidney care, including being more likely to initiate on hemodialysis (HD), initiate urgently with a catheter, and be referred late.[34] In contrast, socioeconomic inequities in late presentation were not found in the UK[45] or New Zealand.[46] For outcomes of kidney transplantation, inequities in graft failure across area-level SEP have been identified in France[33] but not Australia.[48] It is challenging to interpret these results given the complexities of area-based SEP, which may in part explain the

conflicting findings. Nonetheless, current evidence suggests there are area-level SEP inequities in KRT access in multiple HICs, notably for preemptive transplantation.

Impacts of SEP on CKD-Related Complications and Comorbidities

A small number of studies indicate that children in lower SEP families may bear a greater burden of complications and comorbidities. In CKiD, children in lower income families had similar blood pressure and height at baseline but were less likely to improve over time compared to their advantaged peers, likely to result in accumulating inequities across development.[41] In another CKiD study,[39] children in neighborhoods with lower median income had ~1.5 times the odds of hospitalization and emergency department visits, which persisted after adjustment for individual and family characteristics. However, obesity and hypertension did not differ across neighborhood income, and inequities in growth impairment were significant only before adjustment for individual or family characteristics.[39]

Impacts of SEP on Cognitive, Psychosocial, and Quality of Life Outcomes

Consistent with the broader literature on socioeconomic inequities in child development,[50] family SEP appears to impact cognitive and psychosocial functioning for children with CKD. Although there has been limited targeted investigation, a few studies have reported associations with family SEP alongside other predictors. Higher maternal education was associated with higher intelligence quotient and executive functioning in the CKiD cohort.[51] Although the KNOW-Ped CKD study of mild-to-moderate CKD in South Korea[52] (Supplementary Table S1) found no crude association of family SEP with full-scale intelligence quotient, numbers were small, and estimates indicated poorer functioning in the lowest group. Findings for psychosocial functioning and mental health are conflicting, including significant and nonsignificant associations for income[53,54] and education[53,55] across CKiD and KNOW-Ped studies. In the MyKidneyHealth cohort of children and young people with CKD (not on KRT) in North America[56] (Supplementary Table S1), financial hardship was associated with worse depressive symptoms, life satisfaction, and positive affect. Although in the expected direction, associations with other well-being and quality of life measures were not significant.

There is consistent evidence of socioeconomic inequities in health-related quality of life (HRQoL) and overall health among children with CKD, although these may vary by disease stage and SEP domain. In the KCAD study in Australia and New Zealand[57] (Supplementary Table S1), children from families of lower perceived financial status had around 2.5 times the odds of poorer overall health. For income, home ownership, employment status, and composite SEP, children with CKD stage 1 to 5 in more disadvantaged families experienced poorer health, but these inequities were not seen among children on KRT. There were no associations of parental education with overall health. Similarly, the MyKidneyHealth cohort[56] identified inequities in overall health across family financial hardship (measured by ability to pay bills); and whereas supplementary analyses suggested poorer health for children whose parents had lower levels of education, estimates were uncertain. HRQoL studies also highlight financial inequities, with lower family income associated with lower HRQoL in KCAD study analyses in Australia and New Zealand[58]; whereas maternal employment was associated with better HRQoL for children and adolescents with CKD in a Polish study, although there was no association for paternal employment.[59] Results for parental education and child HRQoL are mixed, with no association in 2 European studies (including children with CKD stage 2–5 pre-KRT and on dialysis[59] and children on dialysis or with kidney transplants[60]), whereas considerable inequities were identified for children with mild-to-moderate CKD in North America.[61]

Intersection of SEP With Other Aspects of Social Disadvantage

A growing body of literature documents inequities in kidney care and outcomes across other social factors, including gender[62] (e.g., reduced survival[63] and access to transplantation[64] in girls) and race or ethnicity (e.g., reduced access to transplantation for First Nations children in Australia,[65] Canada,[66] and New Zealand[67]). In relation to gender, interpreting the literature is complex given that many studies do not have sufficient data to differentiate between sex (a biological construct related to chromosomes, gene expression, hormones, and anatomy) and gender (a social construct related to socially-constructed roles and identities of female, male, and gender-diverse people),[68] do not clearly report whether they measured sex or gender, or use the terms interchangeably.[69]

SEP may act as a mediator (an explanatory variable on the causal pathway) or effect modifier (a variable that alters the effect of an exposure) for other aspects of social disadvantage. Although there is not a large body of intersectional research overall, there has been considerable discussion of how family SEP might interact with race or ethnicity in access to and outcomes of KRT for children, notably in the USA.[24,70] Although some work has identified SEP as a key

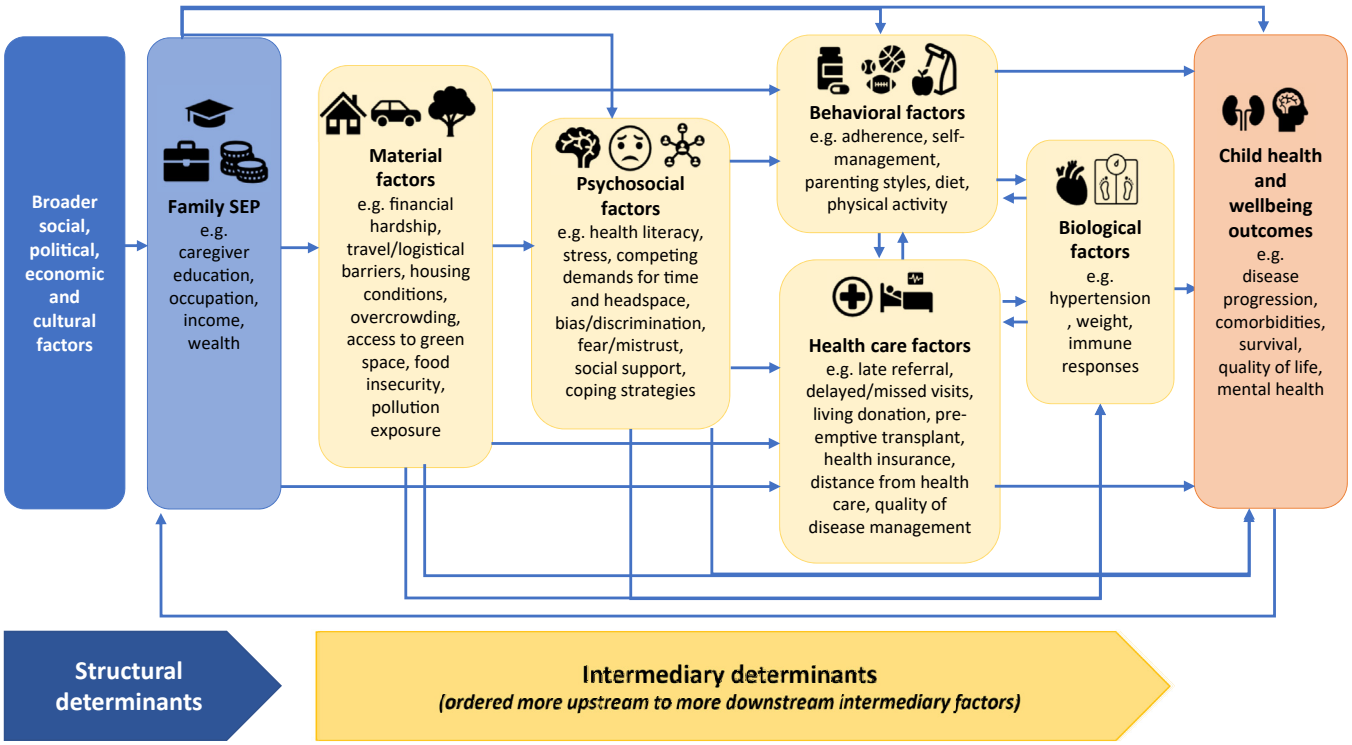

Figure 4. Potential mechanisms and pathways from SEP to health among children and adolescents with CKD, showing structural determinants and intermediary determinants, with intermediary factors ordered from more upstream to more downstream. Adapted from the Commission on Social Determinants of Health conceptual framework in Solar and Irwin[21] and its adaptations in Bell.[77] This figure "zooms in" on the intermediary factors between family SEP and child health across material, psychosocial, behavioral, healthcare, and biological domains, with examples relevant to childhood CKD. Children in more disadvantaged families may have greater exposure and vulnerability to harmful factors (and lower exposure to protective factors) across these domains. Although these intermediary determinants are all considered more downstream than the broader structural determinants on the left of the figure (social, economic and political factors, social stratification, and SEP itself), they can still be ordered from more upstream (material) to more downstream (biological) factors. This figure has been simplified to illustrate the most dominant direction of influence of these factors on each other and does not include all potential arrows between factors; in reality, there may be some influence of more downstream factors on more upstream factors. CKD, chronic kidney disease; SEP, socioeconomic position.

explanatory factor for racial inequities in KRT,[71] others have not.[72-74] Results are also mixed for interactive effects of race or ethnicity with area-level SEP in transplant access and outcomes, with one study showing smaller racial inequities for children in higher income areas,[75] and others finding no interaction.[72-74] Full discussion of these issues is available elsewhere.[24,70,76] There is limited evidence on intersections of SEP with other social factors, such as gender, remoteness, and language.[68] However, several European registry studies have reported no interactive effects between area-level SEP and other social factors in various KRT outcomes (including 2 studies that examined interactions with sex,[33,34] and 1 study that examined interactions with race or ethnicity and distance from treatment center).[45]

Mechanisms and Pathways From SEP to Health

Socioeconomic inequities in health are mediated by complex and multifactorial pathways from disadvantaged SEP to health, including increased exposure and vulnerability to adverse material, psychosocial, behavioral, biological, and healthcare factors (mechanisms ii-iii in Figure 3), often referred to as "intermediary determinants of health."[4,5,21] As illustrated in Figure 4, adapted from the Commission on Social Determinants of Health conceptual framework[21] and its adaptations by Bell,[77] all of these domains may be hypothesized to play a role in socioeconomic inequities in pediatric CKD.[44,78] As discussed earlier, these factors are driven by upstream "structural determinants of health," including SEP, social stratification, and broader social, economic and political factors (Figure 4, mechanism i in Figure 3).[4,21] Importantly, as shown in Figure 4, even the intermediary determinants can be ordered from more upstream (material) to more midstream (psychosocial) and downstream (behavioral, biological, and healthcare) factors that are more proximal to the individual.[77,79,80] This is why upstream actions are critical; due to their potential flow-on effects and the risk of "victim blaming" with solely behavioral interventions because many upstream

causes of behavior are outside individual control.[79,80] There has been very little evaluation of mediators of health inequities for children with CKD, although there are studies related to a few potential mediators, including health literacy,[81] adherence,[82] and kidney care.[33] For preemptive transplantation, a UK registry study[45] indicated that reduced living donation explains some of the area-level SEP inequities among children and adolescents. This may reflect psychosocial factors (e.g., social support, patient activation and knowledge, and clinician bias),[44,45,83,84] which were not available in the data. Lack of data on material, psychosocial, and behavioral mediators (e.g., financial hardship, health literacy, social support, and adherence) is a common challenge.

Effects of CKD on Family, Adolescent, and Young Adult SEP

As in Figures 2 and 3 and highlighted in the Diderichsen model and its adaptations,[4,23] a key mechanism for the perpetuation of health inequities across the life-course is the "social consequences of illness," which can lead to further social stratification and form a cycle of health and socioeconomic disadvantage.[4,16,23] In pediatric CKD, this includes impacts of CKD on caregiver SEP as well as adolescent educational achievement and young adult socioeconomic attainment of the young person themselves.[4,16] This section explores the emerging evidence on this topic, including potential mechanisms.

Impacts of CKD on Family SEP

Families caring for children with CKD often experience a considerable disease and treatment burden, particularly during KRT. An Australian qualitative study explored parental perspectives on the financial impact of caring for a child with CKD (stage 2–5, on dialysis, and with a transplant).[85] Parents reported that the considerable time and energy demands of caring for a child with CKD (e.g., attending appointments and managing medications), and the precarity of their child's health, compromised their capacity to work and their income.[85] Caregivers of children on dialysis had extensive demands associated with attending in-center dialysis or managing home dialysis, which compounded financial hardship.[85] Parents who were living donors had to take time off work for donor evaluation, surgery, and recovery, resulting in income loss.[85] Families often bore high out-of-pocket costs, including medical appointments, travel, accommodation, medications, and equipment.[85] Financial burdens were exacerbated for families in rural and remote areas. Caregivers reported difficulties in accessing support due to lack of information, restrictive eligibility criteria, and systems that were difficult and time-consuming to navigate, leading them to give up on seeking help.[85] Similar themes emerged in a qualitative study of parents' experiences of pediatric kidney transplantation in New Zealand,[86] including financial burdens of donation, costs of travel to transplant centers and care after transplantation, and difficulty accessing support.

There is limited quantitative work on these economic impacts. In a small Polish study,[87] approximately 40% of parents with a child on peritoneal dialysis reported a deterioration in their family's financial situation since their child's CKD diagnosis. This is consistent with descriptive findings of poor employment and income outcomes for caregivers of children on dialysis in Australia and New Zealand[57] and Taiwan.[88] Future studies should define socioeconomic impacts across time and CKD stage, including whether they are worse for families with existing social disadvantage.

Impacts of CKD on Child Educational Outcomes and Young Adult SEP

There is now considerable evidence that children and adolescents with CKD are at risk of reduced academic achievement compared to their peers without CKD.[11] This is likely to reflect disease-related and treatment-related factors, including cognitive impairment secondary to genetic syndromes and factors such as uremia, anemia, proteinuria, and blood pressure; as well as chronic school absences due to medical appointments, dialysis, ill health, fatigue, hospitalization, infection risks, and social challenges, including bullying and feeling self-conscious.[13,89-94] For children with CKD stage 1 to 5, achievement seems to be in the average to low average range, whereas children on dialysis experience larger academic deficits.[11,89,92,95] Children with kidney transplants seem to be at risk of reduced achievement compared to the general population, but the extent relative to other CKD stages is unclear.[11,95] Across all stages, children may be at risk of declining achievement over time.[95]

Current evidence suggests that young people with CKD, notably those on KRT, commonly face barriers to educational attainment and employment.[96-98] International qualitative work[13] has identified barriers, including fatigue, treatment side-effects (e.g., cognitive difficulties), absences and social isolation due to ill health and treatment, delayed independence, and overprotection from caregivers and clinicians.[13] Dialysis seems to pose particularly substantial barriers, including lack of energy, unpredictability of ill health, infections, and rigid treatment schedules.[99] A 2017 meta-analysis estimated that young adults on KRT have 1.9 times the risk of unemployment compared to the

general population controls; whereas encouragingly, there were no differences in higher education attainment.[100] However, most studies focused on transplant recipients,[100] and a later primary study in the UK[101] identified poorer work-related outcomes for young adults on dialysis compared to transplant recipients. Although educational attainment did not differ for young adults on KRT compared to the general population, patients were more likely to have finished school at an older age, suggesting that education may be delayed.[101] Educational delays were also highlighted in another UK study of young adults with kidney failure.[99]

Impacts of childhood CKD on educational and economic outcomes appear to be greater for young people from socioeconomically disadvantaged families, although evidence is limited. CKiD data have shown associations of lower maternal education with increased school absenteeism[91] and reduced academic achievement,[92] and lower income with reduced achievement.[92] In the KCAD study including all CKD stages,[102] children in families of lower global SEP were approximately 60% to 70% less likely to perform well in parent-rated numeracy and literacy. There is also some evidence that young people with pediatric-onset CKD are at increased risk of poorer adult SEP if they have existing social disadvantage; a French cohort study[103] of adults who received a kidney transplant in childhood or adolescence identified lower education, occupation status, and income for adults whose parents had lower education levels.

Relationships Between SEP and Health for Children in LMICs

Globally, there are stark inequities in access to kidney care and outcomes for children and adolescents living in LMICs compared to HICs.[104,105] Resource and infrastructure constraints and lack of access to procedures, medications, and specialist care from pediatric nephrologists often lead to late diagnosis, increased CKD progression, and kidney failure.[106] In many settings, particularly low-income countries, children do not have access to KRT because it is unavailable, geographically inaccessible, or too costly.[105,107-109] It has been estimated that globally, <10% of children with kidney failure receive the KRT they need.[106] In a systematic review of studies in sub-Saharan Africa, only 35% of children remained on dialysis for at least 3 months, with inability to pay being the key driver, and an estimated 95% of children who needed but did not receive dialysis died.[110] Among children who do receive KRT, mortality and height-related outcomes are poorer in countries with lower national income.[111]

Within LMICs, inequitable access to KRT across family SEP is a critical issue given that out-of-pocket funding is common.[44] There is a growing body of evidence on socioeconomic inequities in kidney care and outcomes for children in LMICs. This includes higher mortality rates with lower family education, income, and poorer housing across CKD stages in Nicaragua[112]; lower cognitive functioning with lower caregiver education and income across CKD stages in Thailand[113]; and higher rates of kidney failure treatment discontinuation and death[114] and poorer HRQoL[115] for children with CKD stages 2 to 4 in lower SEP families in India. Economic burdens of treatment, transportation, and missed work can be catastrophic for families.[105] A global survey of 160 countries identified that patient out-of-pocket costs for KRT are greatest in low-income countries and lower-middle income countries, with patients bearing 100% of transplantation costs in 20% of low-income countries.[116] Burdens appear to be particularly extreme for HD,[105,117] with transport costs estimated to be 5.5 times as expensive for families with a child on HD compared to peritoneal dialysis in South Africa (~27% of monthly income for those on HD).[118] High transport costs have also been reported for families receiving free HD in Pakistan.[119] There is also evidence of adverse impacts on child education, with 92% of HD patients in a study in Pakistan receiving no formal education, largely due to poor health (compared to 21% predialysis).[119] Evidence in this field is still relatively limited, with lack of quality registry data and established cohort studies being a key limiting factor.[44,108] Further discussion of inequities for children living in LMICs is available elsewhere.[44,105,106,120]

Clinical and Policy Implications

While the evidence is still emerging, children experiencing socioeconomic disadvantage and CKD seem to be at increased risks of poorer kidney care (particularly reduced preemptive transplantation), greater CKD progression, and poorer HRQoL than their more advantaged peers. Further, they are likely to experience a dual disadvantage in their education, which may compromise their adult SEP; and their families may experience financial hardship, all of which is likely to result in a cycle of accumulating disadvantage. It is critical for the global nephrology community engage in advocacy and action to tackle these inequities and break the cycle of accumulating disadvantage, through multifaceted strategies that address each of the mechanisms in the Diderichsen model[4,23] adapted in Figure 3; reducing inequities and mitigating effects of social stratification, preventing increased exposure and buffering against increased vulnerability to risk factors for children of lower SEP, and preventing adverse

social consequences of CKD and further social stratification.[4,21,23]

Advocacy for whole-of-government and intersectoral action on the social determinants of health is critical, particularly upstream determinants such as SEP and material factors (e.g., income, education, employment, and housing), and action to prevent adverse social consequences for families and young people with CKD.[15,78,121] Ensuring comprehensive income support, flexible work for caregivers, and comprehensive universal healthcare are key priority areas.[44,78,122] Support systems should be easy to navigate for families with low health literacy, and coverage of costs must involve rapid payments or preimbursement and cover the full spectrum of costs (e.g., transport, home modifications, medications, and healthcare).[85,123,124] Addressing structural and financial barriers to living kidney donation for families of lower SEP is critical, including donor income support and coverage of out-of-pocket costs, especially for families in rural and remote areas.[44,86,125] Policies that ensure stable high quality housing and prevent food insecurity are also important.[15,34,121,126] To prevent adverse socioeconomic outcomes for young people, policies and legislation that ensure educational supports, as well as legal protections against work discrimination and the right to work adjustments and flexible work, are critical.[127,128]

In partnership with patients and caregivers, the nephrology community should also take action in clinical practice to prevent adverse health outcomes for children in low SEP families and adverse social consequences for children and families. Nephrology curricula should provide strong knowledge on social determinants of health, with a focus on upstream drivers. Clinical units should assess and address potential biases (e.g., in transplant listing), and promote diversity in leadership, including lived experience of social disadvantage.[44,76] Clinical teams should be alert to unmet social needs and refer to relevant support teams (e.g., social workers and psychologists), who can address risk factors such as transport, health literacy, caregiver distress, housing, financial hardship and food insecurity.[78,85,86] Communication should be tailored to meet health literacy needs (e.g., by reducing information complexity) and enhance health literacy skills.[129] Care should be tailored to minimize adverse impacts on caregiver work and child education (e.g., using telehealth, appointments outside business hours, and scheduling appointments together), particularly for patients in rural and remote areas.[124] Clinical teams should include multidisciplinary support (e.g., occupational therapists, social workers, psychologists, and teachers) to support psychosocial wellbeing, cognitive development, and adaptation to CKD; and equip patients to reach their social, educational, and economic goals.[13,96] Support should be child-centered, flexible, and include a focus on acting early in critical developmental periods (e.g., cognitive development in early childhood) and appropriately during social and biological transition periods such as adolescence and young adulthood (e.g., pathways to work or further study, and transition to adult health services).[20,128,130,131] Academic support should encompass school, home, and hospital; and involve proactive liaison between schools, clinicians, and families.[128,132,133] Young people should be supported to participate in study and training pathways that accommodate the chronicity of their disease and equip them for work. Clinical teams should be equipped to advocate to employers and provide individualized care to manage fatigue and comorbidities that impact work ability.[127,134,135] Discussions about KRT should consider implications for ability to work and study, noting potential benefits of transplantation.[134,135]

Future Research Directions

As much of the existing evidence comes from a limited set of regions (North America, UK, France, Australia, and New Zealand), and inequities are likely to differ across social, political, and economic contexts; a key priority is generating evidence in LMICs and other HICs. Across settings, there is a need to identify explanatory factors for socioeconomic inequities in health through complementary qualitative studies (to identify mediators) and mediation analyses (to quantify their effects). There should be a focus on upstream domains, including material (e.g., financial hardship and housing) and psychosocial factors (e.g., stress, social support, and health literacy). There is also a need for longitudinal examination of bidirectional relationships between health and SEP across disease and developmental stages from childhood to young adulthood, using life-course methods to examine differential impacts of duration, timing, and sequencing of exposures. Further data are also needed on the socioeconomic impacts of CKD on families. Intersectional studies examining the role of SEP as a mediator or effect modifier for other social factors are important to inform intervention targeting and design.[76] There is also a need for qualitative work with families experiencing disadvantage to identify features of effective supports, barriers or enablers to accessing services, and preferences for interventions.

There are also a number of methodological issues to address in future work. Although there has been some targeted investigation of SEP, often it has been considered only in predictive models alongside a

heterogeneous mix of social and clinical variables. This may lead to bias in the estimated total effects of SEP, if there is inadequate adjustment for confounders (leading to residual confounding) or inappropriate adjustment for mediators on the causal pathway from SEP to health (leading to overadjustment bias and potentially collider bias).[136,137] It is critical to conduct research that focuses explicitly on SEP, informed by causal models. Where possible, studies should consider area-level and caregiver-level SEP concurrently, to define the independent and interactive effects of multilevel disadvantage. Another key priority is the collection and analysis of multiple domains of caregiver SEP concurrently, to tease out potential differences across SEP domains. One challenge is the lack of household SEP data in kidney registries.

Finally, intervention-focused research is needed to evaluate the effectiveness and feasibility of strategies to prevent accumulating health and socioeconomic disadvantage for children and families living with CKD. There are several candidate interventions, although qualitative work is needed to identify patient, caregiver, and health professional preferences for these and others. Examples of potential interventions to improve health for children in lower SEP families include the following: integration of routine social determinants screening into clinical practice (alongside referral to effective patient-centered services),[44,78,138,139] patient navigators and peer navigators[78] (e.g., the NAVKIDS[2] trial in pediatric CKD[140]), health literacy training (e.g., the SUCCESS app for adults on dialysis),[129] education and social network activation interventions to increase living donation (e.g., the ASK trial in adult transplant candidates),[141,142] partnerships and colocation with social services to address material needs (e.g., housing, food security),[78,122,138] and psychosocial interventions for child and caregiver stress.[86] Interventions to prevent adverse socioeconomic outcomes for young people with CKD could focus on securing and maintaining employment (e.g., skill development, social support, vocational rehabilitation, and workplace accommodations), peer support, peer navigation, and educational interventions (e.g., tutoring, psychosocial interventions for peer and teacher relationships, and teacher training).[13,94,127,134,135]

Conclusions

A growing body of evidence indicates sobering socioeconomic inequities in health and kidney care among children and adolescents with CKD, alongside adverse socioeconomic impacts of CKD on families and young people. To prevent accumulating disadvantage across the life-course for children and their families, the nephrology community must advocate for government action on upstream social determinants of health; and adopt a life-course approach to kidney care that proactively identifies and addresses unmet social needs, targets intervening factors between SEP and health, and minimizes adverse socioeconomic outcomes across financial, educational, and vocational domains. Acting early in the life-course during critical developmental periods, appropriately during social and biological transition periods, and together with the rest of society, are critical.[20] In partnership with patients, caregivers, and health professionals, future research should identify mediators to serve as intervention targets, explore preferences for interventions, and evaluate complex interventions that target key mechanisms, including social stratification, exposure and vulnerability to risk factors, and social consequences of CKD. Given the unique inequities experienced by children in LMICs, there is a need for high quality registries and cohort studies to inform specialized interventions by local health agencies and governments that are responsive to the population needs in these settings. Globally, dedicated efforts to tackle inequities are critical to ensuring that all young people with CKD have the opportunity to live long and flourishing lives.

DISCLOSURE

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SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Table S1. Key characteristics of commonly-used multicenter cohort studies of children and adolescents with chronic kidney disease.

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