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Original Article

ORIGINAL ARTICLE

Sex and gender differences in health-related quality of life in individuals treated with incremental and conventional hemodialysis

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ABSTRACT

Background. Women treated with hemodialysis report lower health-related quality of life (HRQoL) compared with men. Whether this is related to sex-specific (biological) (e.g. under-dialysis due to body composition differences) or gender-specific (sociocultural) factors (e.g. greater domestic/caregiver responsibilities for women) is unknown. We examined the association between sex assigned at birth, gender score and HRQoL in individuals initiating conventional and incremental hemodialysis.

Methods. In this prospective multi-center cohort study, incident adult hemodialysis patients were recruited between 1 June 2020 and 30 April 2022 in Alberta, Canada. Sex assigned at birth and gender identity were self-reported. Gender-related characteristics were assessed by self-administered questionnaire to derive a composite measure of gender. The primary outcome was change in Kidney Disease Quality of Life 36 physical (PCS) and mental (MCS) component scores after 3 months of hemodialysis.

Results. Sixty participants were enrolled (conventional hemodialysis: 14 female, 19 male; incremental hemodialysis: 12 female, 15 male). PCS improved from baseline with conventional ($P = .01$) but not incremental ($P = .52$) hemodialysis in female participants. No difference in MCS was observed by hemodialysis type in female participants. Gender score was not associated with changes in PCS in female participants, irrespective of hemodialysis type. Higher gender score was associated with increased MCS with incremental ($P = .04$), but not conventional ($P = .14$), hemodialysis ($P = .03$ conventional vs incremental) in female participants. No change in PCS or MCS was seen in male participants, irrespective of hemodialysis type or gender score.

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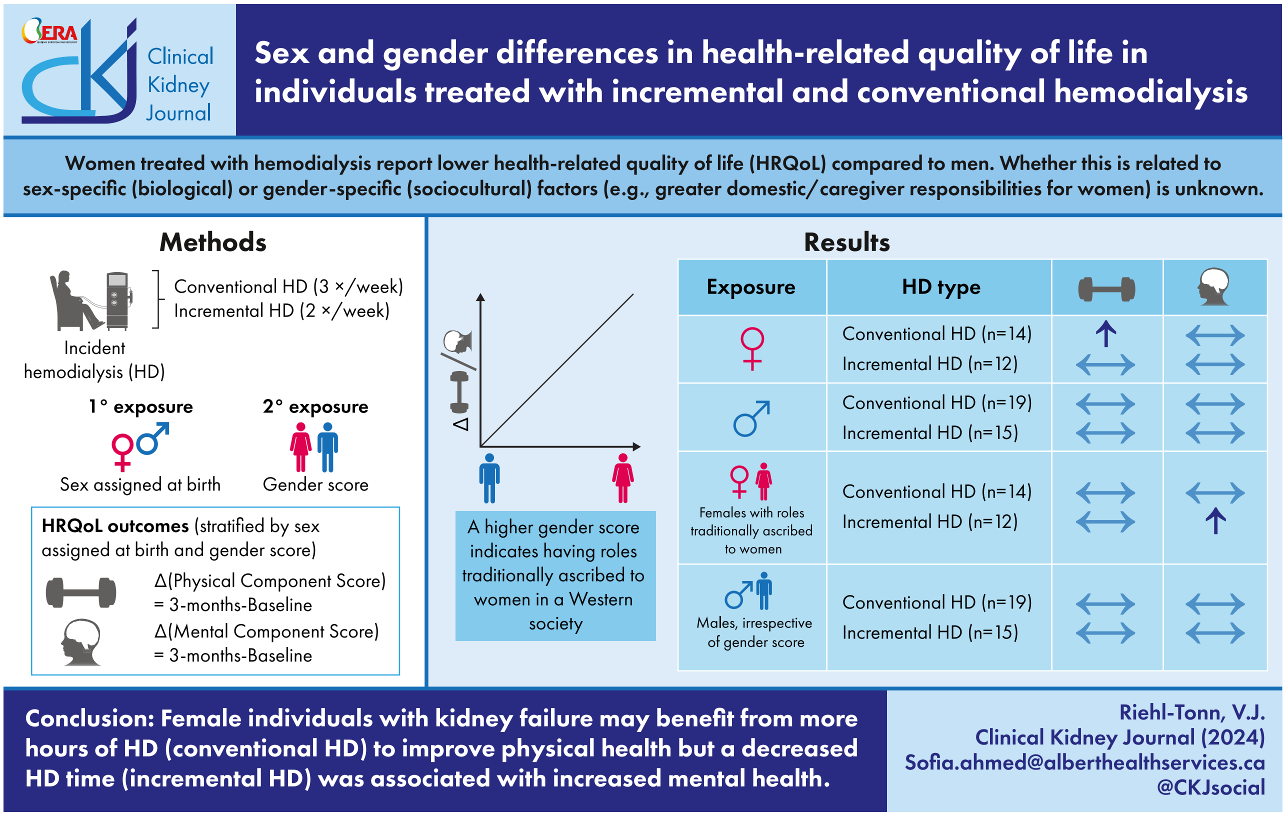
Conclusion. In this exploratory study, conventional hemodialysis was associated with improved PCS in female participants, while incremental hemodialysis was associated with improved MCS in female participants with more roles and responsibilities traditionally ascribed to women. Large prospective studies are required to further investigate these relationships.

GRAPHICAL ABSTRACT



Keywords: conventional hemodialysis, gender, incremental hemodialysis, quality of life, sex

KEY LEARNING POINTS

What was known:

- Women treated with conventional hemodialysis have a reported lower health-related quality of life compared with men.
- Female individuals have a lower volume of distribution, which may result in a lower prescribed dose of hemodialysis to achieve the same target Kt/V as male individuals.
- Incremental, compared with conventional, hemodialysis may allow for improved health-related quality of life.

This study adds:

- Conventional, but not incremental, hemodialysis was associated with improved physical health in female participants with kidney failure.
- Female participants who had more roles typically ascribed to women reported improved mental health with incremental, but not conventional, hemodialysis.
- Male participants reported no change in health-related quality of life, irrespective of hemodialysis type or gender roles.

Potential impact:

- Both sex and gender factors are associated with the impact of hemodialysis on quality of life.
- Identifying and including patient-centered goals through a sex and gender lens is critical to person-centered hemodialysis care.

INTRODUCTION

The impact of hemodialysis on health-related quality of life (HRQoL) is an important patient-identified priority [1]. Women with kidney failure receiving hemodialysis are reported to have a lower HRQoL compared with men [2–4]. The "one size fits all" approach to hemodialysis treatment does not take into account sex (biological) and gender (sociocultural) factors that may influence the effect of hemodialysis dose on HRQoL. Biological differences, such as smaller body size and water distribution, may account for the increased survival rates with a higher dialysis clearance observed in women but not men [5], and thus sex differences in clearance may also negatively affect HRQoL in women. Concomitantly, gender roles including primary earner status [6] and caregiving responsibilities [7] also contribute to HRQoL, and increased frequency of hemodialysis can have a direct negative impact on these important roles [8, 9].

Incremental hemodialysis is a novel personalized approach to the care of individuals living with kidney failure in which the amount of dialysis delivered gradually increases based on the individual's residual kidney function [10–12]. A twice weekly incremental hemodialysis prescription [13] has the potential to improve HRQoL in individuals initiating hemodialysis by reducing the individual's time commitment to hemodialysis treatment, thereby allowing for more time to perform important life roles. However, it also may contribute to relative under-dialysis and poorer HRQoL in female compared with male individuals due to the lower volume of distribution (V_D) in females [14]. As such, we sought to determine the associations between (i) sex assigned at birth and (ii) gender roles and responsibilities and HRQoL in individuals with kidney failure initiating either incremental (twice weekly) or conventional (thrice weekly) in-center hemodialysis. We hypothesized that (i) female, but not male, sex would be associated with lower HRQoL in individuals receiving incremental hemodialysis and (ii) individuals with gender roles and responsibilities commonly attributed to women (e.g. caregiving) would report greater HRQoL with incremental hemodialysis compared with conventional hemodialysis.

MATERIALS AND METHODS

Study design

This was a prospective multicenter cohort study with participants initiating in-center incremental (twice-weekly) or conventional (thrice weekly) 4-h hemodialysis in eight hemodialysis centers located in Calgary and Edmonton, Canada from June 2020 to April 2022 and prospectively followed for 3 months. Ethics approval for the study was obtained from the institutional review boards of all participating centers. The study was conducted according to the Declaration of Helsinki and written informed consent was obtained from all participants.

Study participants

All adults (≥18 years of age) with kidney failure initiating hemodialysis were screened for eligibility to participate in the study. Exclusion criteria were as follows: (i) plan for temporary hemodialysis (e.g. acute kidney injury), (ii) plan to transition onto another form of kidney replacement therapy (KRT), including kidney transplant, within 3 months, (iii) previous experience with any form of KRT or (iv) unable to provide informed consent. Eligibility criteria for initiation of incremental hemodialysis included: (i) 24-h urine output of >600 mL/day, (ii) <2 kg fluid removal between hemodialysis sessions and (iii) medically stable with no uremic symptoms as per nephrologist assessment. The option for initiating incremental hemodialysis was offered to all individuals who met the listed criteria. All other participants initiated conventional hemodialysis.

Data collection

Demographic data including age, etiology of kidney disease, comorbidities and body mass index (BMI) were obtained at enrollment. Sex assigned at birth and gender identity were collected by participant self-report. Estimated glomerular filtration rate (eGFR) and 24-h urine volume were collected at hemodialysis initiation. All participant data were anonymized and entered in REDCap [15].

Measures of exposure: sex assigned at birth and gender roles and responsibilities

The exposures were self-reported sex assigned at birth and gender score at baseline. A gender score was measured at baseline using the GENESIS-PRAXY Gender Questionnaire (Appendix A) to determine a composite gender score encompassing gender identity, roles and relations [16]. The gender score ranges from 0 to 100, in which lower scores are associated with roles traditionally ascribed to men in Western societies and higher scores are associated with roles traditionally ascribed to women in Western societies [16]. Both paper and electronic versions of the GENESIS-PRAXY tool were available for participants.

Measure of outcomes: quality of life

The primary outcome was the change in HRQoL between baseline and 3 months of initiating hemodialysis, measured by physical (PCS) and mental (MCS) component score from the Kidney Disease Quality of Life 36 (KDQOL-36) Item Survey [17, 18], where higher scores indicate better health. After 3 months of hemodialysis initiation, change in PCS is associated with mortality and each 1-point increase in MCS is associated with a 4% decrease in risk of death [19, 20]. The KDQOL-36 was self-administered using paper and electronic versions. HRQoL scores were calculated using the KDQOL-36 Item Summary Measures Manual, which consisted of standardizing the scales and transformation of summary scores [17].

Statistical analysis

To examine associations between sex assigned at birth, gender score and HRQoL scores, we performed descriptive analyses stratified by hemodialysis type. Due to a non-normally distributed sample, values were expressed as median and interquartile range or percentages when appropriate. A last-value carried forward approach was employed with missing data. The proportion of participants that did not fully complete KDQOL-36 are presented in Supplementary data, Table S1. KDQOL-36 item subscales not included in the main analysis are presented by sex and hemodialysis type in Supplementary Data, Table S2. The chi-square test was used to compare categorical variables. After assessing assumptions, multiple linear regression analyses were conducted to determine whether there was an association between the gender score and HRQoL, stratified by hemodialysis type. Linear regression assumptions were tested (Supplementary data, Table S3). Non-parametric tests were used in all other analyses. A P-value <.05 was considered statistically

Table 1: Baseline participant characteristics.

		Female		Male	
Characteristics	Total	Conventional	Incremental	Conventional	Incremental
Participants, *n* (%)	60	14	12	19	15
Gender identity, *n* (%)	60				
Cisgender man	34 (57)			19 (100)	15 (100)
Cisgender woman	26 (43)	14 (100)	12 (100		
Age, years	66 (52–73)	70 (58–73)	64 (38–74)	60 (51–71)	67 (59–77)
Race/ethnicity, *n* (%)					
Racialized	35 (58)	9 (64)	6 (50)[a]	10 (53)	10 (67)
White	15 (25)	1 (7)	5 (42)[a]	6 (32)	3 (20)
Prefer to not say/no response	11 (18)	4 (29)	2 (17)	3 (16)	2 (13)
BMI, kg/m^2	27 (23–30)	26 (24–29)	27 (24–32)	27 (25–31)	26 (21–29)
Etiology of CKD, *n* (%)					
DM	23 (38)	8 (57)	4 (33)	5 (26)	6 (43)
Non-DM	13 (22)	2 (14)	4 (33)	3 (16)	4 (29)
Unknown	6 (10)	1 (7)	0	1 (5)	4 (29)
Not reported	18 (30)	3 (21)	4 (33)	10 (53)	1 (7)
Comorbidities, *n* (%)					
CVD	43 (60)	11 (79)	9 (75)	12 (63)	11 (73)
DM	36 (60)	8 (57)	8 (67)	11 (58)	9 (6)
HTN	15 (25)	2 (14)	4 (33)	5 (26)	4 (27)
eGFR at HD initiation, mL/min/1.73 m^2	7 (6–8)	8 (6–8)	7 (5–8)	6 (5–9)	8 (6–9)
24-h urine volume, mL	800 (700–1100)	530 (300–700)	1125 (900–1200)[b]	1000 (900–1350)	800 (750–880)
Frequency HD, days	3 (2–3)	3 (3–3)	2 (2–2)	3 (3–3)	2 (2–2)
Duration of HD session at initiation, h	4 (3.3–4)	4 (4–4)	4 (3.65–4)	4 (3–4)	4 (3.3–4)
Primary earner, *n* (%)	30 (50)	5 (36)	4 (33)	10 (53)	11 (73)
Personal income, *n* (%)					
<$15 000	9 (15)	1 (7)	3 (25)	2 (11)	3 (20)
$15 000–29 999	14 (23)	5 (36)	2 (17)	5 (26)	2 (13)
$30 000–49 999	9 (15)	1 (7)	2 (17)	3 (16)	3 (20)
$50 000–69 999	8 (13)	2 (14)	1 (8)	2 (11)	3 (20)
$70 000–99 999	5 (8)		3 (25)	1 (5)	1 (7)
>$100 000	1 (2)				1 (7)
Unknown/do not wish to answer	14 (23)	5 (36)	1 (8)	6 (32)	2 (13)
Time spent doing housework, h	7.5 (2.5–14)	8 (4.5–12)	7 (2.5–20)	4 (2–12)	8 (2–10)
Primary person responsible for doing housework, *n* (%)	20 (33)	4 (29)	4 (33)	5 (26)	7 (47)
Stress level at home[c]					
<5	43 (72)	9 (64)	9 (75)	15 (79)	10 (67)
≥5	17 (28)	5 (36)	3 (25)	4 (21)	5 (33)
Gender score	14 (8–35)	17 (5–55)	14 (2–52)	13 (9–23)	17 (8–26)

Data are reported as median (interquartile range) unless otherwise specified.
eGFR was calculated using the 2021 CKD-EPI$_{creatinine}$ equation.
[a]Adds up to >100% due to participants selecting more than one self-reported ethnicity.
[b]$P < .05$ vs conventional HD value in female participants.
[c]Stress was self-evaluated on a scale from 1–10 with 1 being the least stressed and 10 being the most stressed.
CKD, chronic kidney disease; CVD, cardiovascular disease; DM, diabetes mellitus; HD, hemodialysis; HTN, hypertension.

significant. All statistical analyses were conducted using STATA version 17.0 (StataCorp, College Station, TX, USA).

RESULTS

Baseline characteristics

A total of 60 participants enrolled in the study (Table 1), with similar proportions of female and male participants initiated on conventional and incremental hemodialysis. All participants identified as cisgender. Age and BMI values were similar by sex and hemodialysis type. No differences were observed in eGFR level at initiation of hemodialysis by sex or by hemodialysis type. Female participants treated with incremental hemodialysis had higher 24-h urine volume compared with female participants treated with conventional hemodialysis ($P = .005$), while no difference in urine output was observed in male participants treated with incremental hemodialysis compared with those treated with conventional hemodialysis. Participants initiating conventional hemodialysis dialyzed for 3 days a week for 4 h and participants initiating incremental hemodialysis dialyzed 2 days a week for 4 h each session.

Baseline quality of life by sex

Overall, participants had low baseline PCS (32) and MCS (43) with no observed differences by sex (PCS, $P = .53$; MCS, $P = .68$). Female participants treated with conventional hemodialysis reported similar baseline PCS and MCS compared with female participants treated with incremental hemodialysis (PCS, $P = .86$; MCS,

Table 2: Baseline and 3-month PCS and MCS, by sex and hemodialysis type.

	Female		Male	
HRQoL	Conventional	Incremental	Conventional	Incremental
PCS				
Baseline	32 (29–39)	32 (29–39)	32 (27–39)	29 (26–38)
3 months	42 (31–44)[a]	33 (30–37)	32 (27–45)	28 (26–38)
MCS				
Baseline	38 (32–48)	44 (38–53)	44 (38–52)	40 (36–53)
3 months	41 (36–51)	46 (41–51)	49 (38–57)	39 (35–53)

Values are reported as median (interquartile range).
[a]$P < .05$ vs baseline value.

$P = .27$) (Table 2). Similarly, no differences in baseline PCS and MCS were reported by male participants treated with conventional compared with incremental hemodialysis (PCS, $P = .59$; MCS, $P = .82$) (Table 2).

Change in quality of life, by sex assigned at birth

Overall, female participants reported an improvement in physical health (ΔPCS, $P = .02$), but not mental health (ΔMCS, $P = .98$) 3 months after hemodialysis initiation, while male participants reported no difference in physical (ΔPCS, $P = .46$) or mental (ΔMCS, $P = .63$) health. When stratified by hemodialysis type, female participants treated with conventional hemodialysis reported a significant increase in physical health after 3 months (ΔPCS, $P = .01$), whereas female participants treated with incremental hemodialysis reported no change (ΔPCS, $P = .52$) (Fig. 1). No differences in mental health were reported after 3 months in female participants treated with either conventional (ΔMCS, $P = .94$) or incremental hemodialysis (ΔMCS, $P = .94$). Male participants reported no statistically significant change in physical or mental health with conventional (ΔPCS, $P = .21$; ΔMCS, $P = .15$) or incremental hemodialysis (ΔPCS, $P = .80$; ΔMCS, $P = .27$) (Fig. 1). Other KDQOL-36 item subscales are reported in Supplementary data, Table S2.

Baseline gender score

Overall, participants reported lower gender scores consistent with having fewer roles traditionally ascribed to women and more roles ascribed to men in Western societies (Table 1). Gender scores were not normally distributed at baseline (Fig. 2). Gender scores were similar by sex (all female vs all male participants, $P = .72$) or type of hemodialysis (female participants, $P = .81$; male participants, $P = .70$, all values conventional vs incremental hemodialysis).

Gender score and change in quality of life, by sex and hemodialysis type

In female participants overall, the gender score was not significantly associated with change in HRQoL (ΔPCS, $P = .08$; ΔMCS, $P = .59$). However, upon stratification by type of hemodialysis, no association was observed between gender score and change in PCS ($P = .52$) in female participants treated with conventional hemodialysis, although a non-significant association was observed between gender score and change in PCS in female participants treated with incremental hemodialysis ($P = .07$) (Fig. 3A). Similarly, no association was observed between gender score and change in MCS in female participants treated with conventional hemodialysis ($P = .14$), while a positive association was observed between gender score and change in MCS in female participants treated with incremental hemodialysis for 3 months ($P = .04$) ($P = .03$ vs conventional hemodialysis) (Fig. 3B). Adjusting for 24-h urine values did not result in significant changes to the results. In male participants, no association was observed between gender score and change in HRQoL (ΔPCS, $P = .18$; ΔMCS, $P = .70$) for either hemodialysis type (conventional hemodialysis: ΔPCS, $P = .61$; ΔMCS, $P = .69$; incremental hemodialysis: ΔPCS, $P = .14$; ΔMCS, $P = .77$) (Fig. 3C and D). The associations between gender score and change in HRQoL did not differ by hemodialysis type in male participants (ΔPCS, $P = .17$; ΔMCS, $P = .62$, conventional hemodialysis vs incremental hemodialysis).

DISCUSSION

In this exploratory prospective cohort study, we examined the associations between sex assigned at birth, as well as gender roles and responsibilities, and HRQoL in individuals with kidney failure initiating either incremental (twice weekly) or conventional (thrice weekly) in-center hemodialysis. Our key findings were as follows: (i) HRQoL, as measured by composite physical health scores, increased after 3 months of conventional but not incremental hemodialysis in female participants, while no differences were observed in male participants, irrespective of hemodialysis type; (ii) participants with kidney failure treated with in-center hemodialysis, irrespective of sex, report gender scores that may be characterized as more having roles and responsibilities typically ascribed to men; and (iii) female participants reporting more roles and responsibilities typically ascribed to women had a greater increase in mental health with incremental, but not conventional, hemodialysis, while no associations were observed in male individuals treated with either type of hemodialysis. Taken together, our findings suggest that female individuals with kidney failure may benefit from more hours of hemodialysis (e.g. conventional hemodialysis) to improve physical functioning, but that the decreased hemodialysis treatment time associated with incremental hemodialysis is associated with improved mental health in female individuals with more roles and responsibilities typically ascribed to women, such as caregiving. Putting these findings into clinical context, for every 10-point increase on the gender scale towards greater caregiving burden and higher self-reported stress, female individuals treated with incremental, compared with conventional, hemodialysis are predicted to have a 4% greater survival benefit 3 months after hemodialysis initiation [19]. These findings underscore the critical need to consider both sex and gender factors when initiating treatment for kidney failure and highlight the importance of shared-decision making to ensure hemodialysis treatment aligns with the values and preferences of the individual living with kidney disease [21, 22].

The majority of individuals with kidney failure initiate in-center conventional hemodialysis, which is typically prescribed as three sessions/week for 4 h per session. However, in this era of precision health, this approach has recently come under scrutiny as a standardized prescription does not account for a person's needs, values and preferences [23], and guidance on hemodialysis initiation that addresses the individualized needs of those living with kidney failure is being developed [24]. A recent systematic review evaluated the safety, efficacy and cost-effectiveness of incremental compared with conventional hemodialysis and found no differences in mortality, and possibly reduced hospitalizations and lower costs, with incremental hemodialysis [25]. However, data on other treatment-emergent

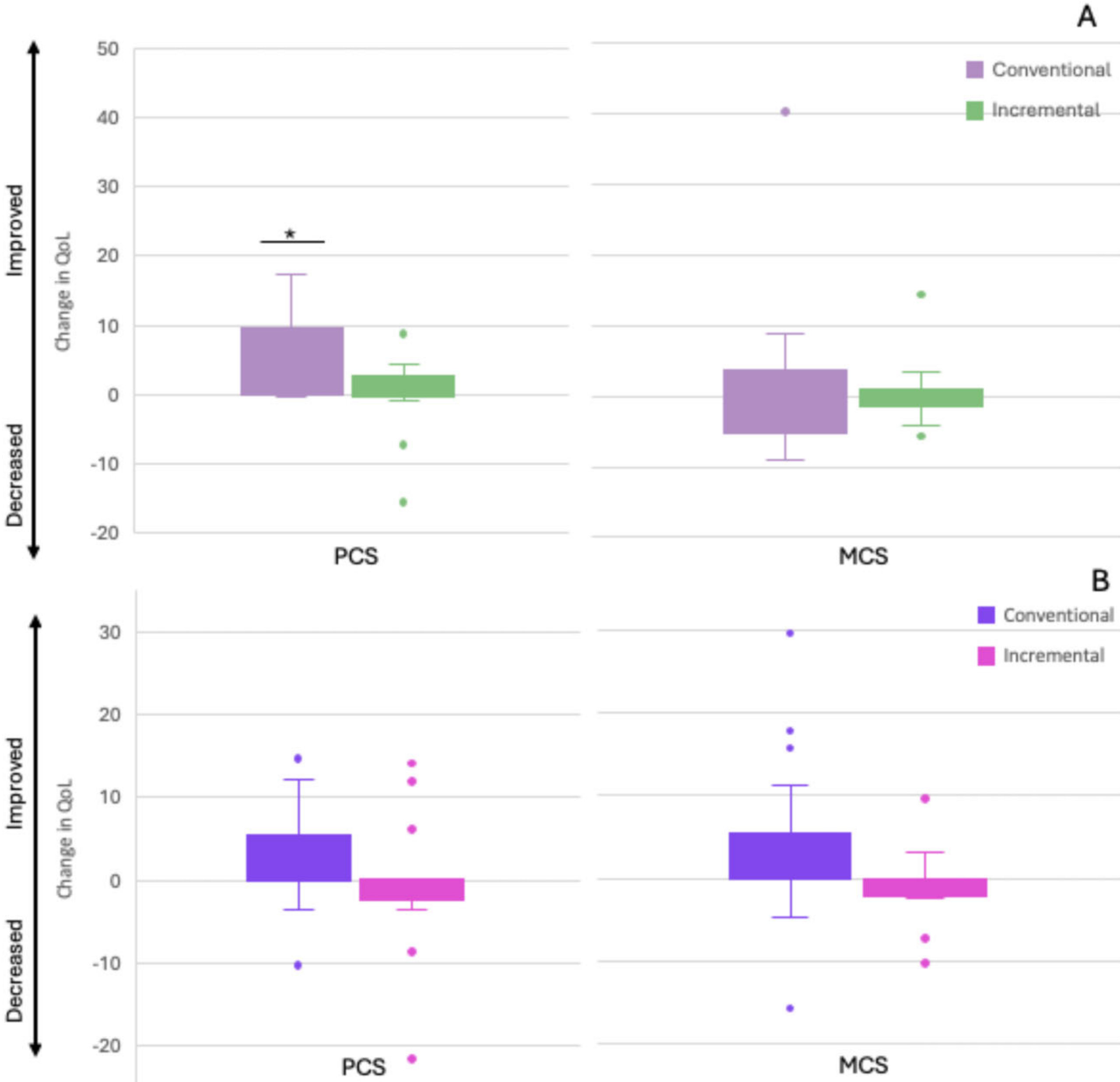


Figure 1: Change in PCS and MCS, by hemodialysis type in (**A**) female and (**B**) male participants.

adverse events and HRQoL were limited, and the authors did not report on sex- or gender-stratified outcomes.

Previous studies have suggested that female individuals with kidney failure may benefit from more intensive hemodialysis compared with male individuals. Although results of the Effect of Dialysis Dose and Membrane Flux in Maintenance Hemodialysis (HEMO) study, a large randomized controlled trial examining the impact of higher compared with lower dialysis dose as measured by Kt/V on survival in persons treated with in-center hemodialysis, were negative [26], a *post hoc* analysis demonstrated greater mortality in women, but not men, randomized to the lower dose [5]. Further, women treated with conventional hemodialysis are increased risk of hospitalization compared with men [27], even after adjusting for Kt/V as a measure of dialysis adequacy. These differences in outcomes have been suggested to be due to sex-based differences in body composition [28], and specifically V_D of urea. Hemodialysis prescriptions target a minimum amount of urea clearance as determined by the dimensionless unit, $Kt/V > 1.2$, which assumes a uniform V_D irrespective of sex. As female individuals have a lower V_D, this may result in a lower prescribed dose of hemodialysis to achieve the same target Kt/V as males and could contribute to sex disparities in outcomes [29].

People living with kidney failure report lower HRQoL compared with the general population [30–32], and women treated with hemodialysis report a lower HRQoL in all domains, including, PCS and MCS, compared with men [2, 3, 33]. While relative underdialysis due to a smaller sex-based V_D in female individuals may be a contributing factor, gender factors, including identity, roles, relations and institutionalized gender [34], may

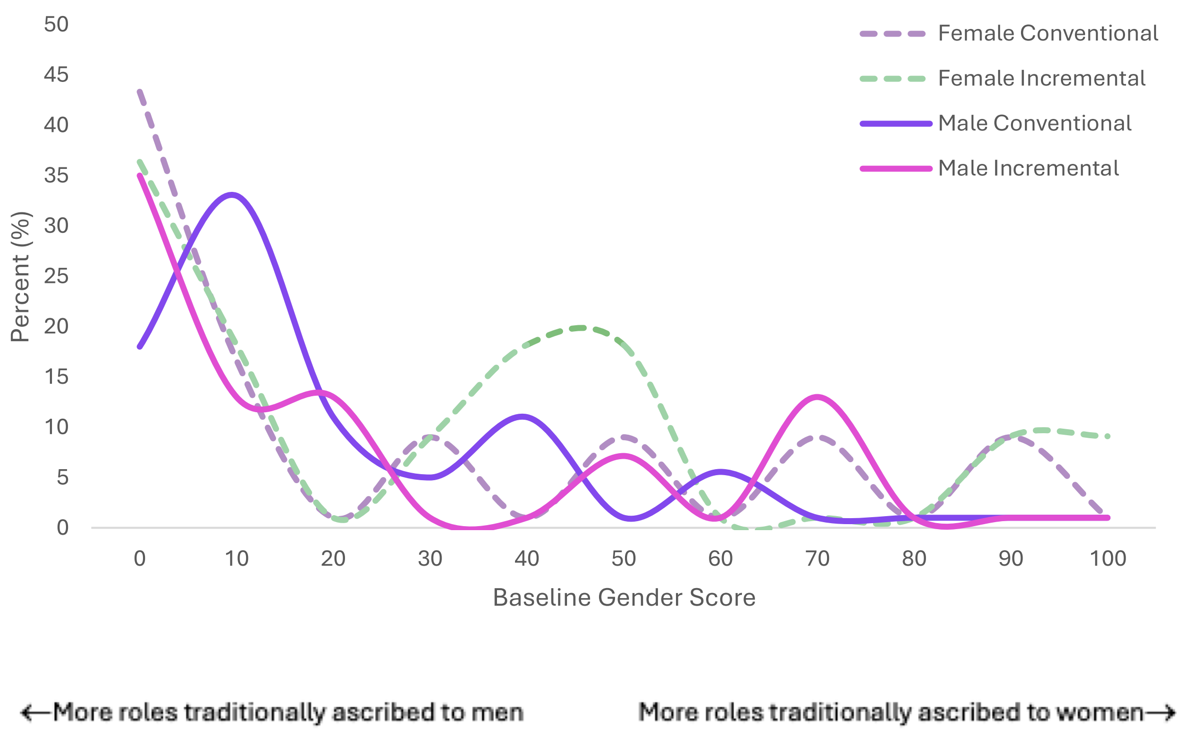


Figure 2: Baseline gender scores, stratified by sex and hemodialysis type.

impact reported HRQoL. Men receiving hemodialysis tend to have a higher level of social support [35] and are more likely to be married [36] compared with women. As social support is positively linked to HRQoL [37, 38], a perceived lack of this by women treated with hemodialysis may explain gender-based differences in HRQoL in individuals with kidney failure. Previous work has shown important associations between gender roles and responsibilities and health outcomes in other populations. For example, younger adults presenting with an acute coronary syndrome (ACS) with more characteristics commonly ascribed to women (e.g. caregiving, greater household domestic responsibilities, lower income, higher stress) are at an increased risk of recurrent ACS over 12 months, independent of sex [39]. In a large prospective cohort study of 90 987 Japanese women and men aged 40–69 years free of prior diagnoses of cancer and cardiovascular disease, women living in multi-generational households (e.g. with spouse-children-parents; or spouse-parents) had a 2- to 3-fold higher risk of coronary heart disease than women living with spouses only [40]; the increased cardiovascular disease risk was hypothesized to be due to stress from multiple family roles. A Finnish population-based register study reported gender differences in how living arrangements in midlife predict myocardial infarction incidence and mortality, where living alone was a greater risk factor in men, but cohabitation was a greater risk in women independent of other sociodemographic factors [41]. However, there is a paucity of research on the association between gender roles and responsibilities and HRQoL in hemodialysis. A common concern with hemodialysis is the time taken away from other important life activities and responsibilities; the improvement in MCS observed in our study in females with roles traditionally ascribed to women treated with incremental, but not conventional, hemodialysis may reflect lower hemodialysis-related interference with daily activities. Interestingly, the majority of study participants, independent of sex or hemodialysis type, reported gender scores consistent with having roles and responsibilities commonly ascribed to men, which may suggest that those with higher gender scores (e.g. greater roles and responsibilities commonly ascribed to women) may have elected to pursue other forms of KRT, including conservative care, although this is speculative. Factors driving lower gender scores include not only spending less time doing housework but also not being the primary person responsible for housework, which may reflect the reality of all persons with kidney failure initiating hemodialysis due to time constraints and symptom burden, irrespective of sex or gender.

This study has limitations. First, the sample size was limited with a relatively short follow-up period. However, previous studies have highlighted that changes in both MCS and PCS within 3 months of initiating hemodialysis are associated with clinically meaningful outcomes [19, 20]. Next, the allocation to hemodialysis initiation with incremental or conventional hemodialysis was not randomized, introducing the potential for confounders. However, randomization to "non-standard" hemodialysis approaches has been previously shown to be challenging and is regarded by some as unethical [42–45]. Our pragmatic approach reflects current practices in nephrology, highlighting the generalizability of the study, although the applicability of the results in other settings remains unclear [46]. Additionally, eligibility criteria for treatment with incremental compared with conventional hemodialysis differ, which limits direct comparisons due to inherent differences in the populations. However, adjusting for 24-h urine values did not modify the observed relationship between gender score and measures of HRQoL, irrespective of sex and hemodialysis type. Our definition of incremental hemodialysis was twice weekly hemodialysis sessions, which may not represent how

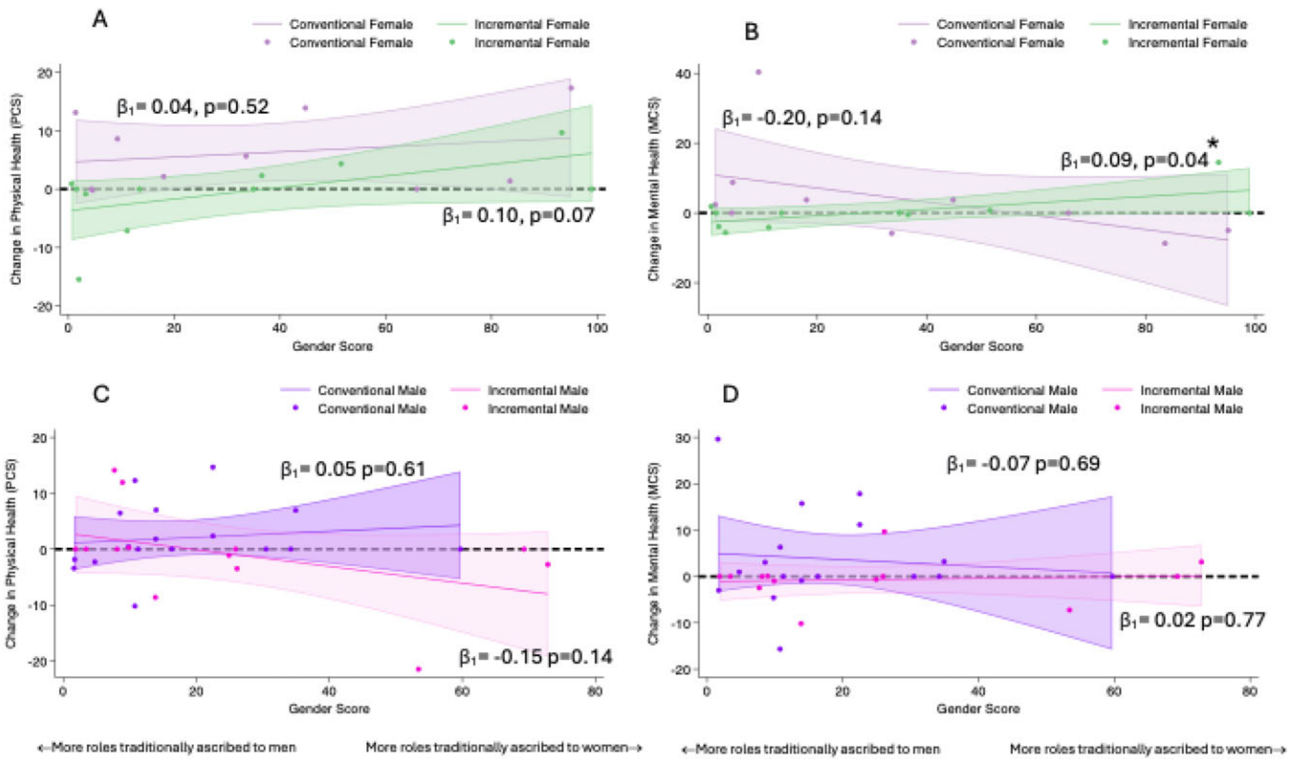


Figure 3: Change in quality of life as a function of gender score, stratified by sex and hemodialysis type: (**A**) PCS and (**B**) MCS in female participants; (**C**) PCS and (**D**) MCS in male participants.

incremental hemodialysis is delivered in other locations. However, there is no standard definition of incremental hemodialysis other than a lower amount of weekly hemodialysis compared with thrice weekly 4-h hemodialysis sessions [47, 48]. We did not measure participants' total body water as a marker of volume of distribution of urea, an important factor in determining dialysis adequacy. Given the important sex differences in body composition between female and male individuals, we only compared HRQoL outcomes by type of hemodialysis within participants of the same sex assigned at birth. Furthermore, participants of the same sex had similar BMI values irrespective of hemodialysis type, suggesting similar measured volumes of distribution of urea. The GENESIS-Praxy Gender Questionnaire has been validated in a population with ACS, but not in the hemodialysis population. However, persons with kidney failure treated with hemodialysis are at high cardiovascular risk [49], suggesting that this tool is appropriate to use in this population. Female participants initiating conventional hemodialysis had lower residual kidney function as measured by 24-h urine output compared with female participants initiating incremental hemodialysis. The difference in 24-h urine may have accounted for the greater increase in physical health with more hemodialysis (e.g. conventional hemodialysis), as literature has shown a higher residual kidney function to be associated with improved HRQoL [50], although inclusion of 24-h urine in our analyses did not change our results. As persons treated with hemodialysis are more likely to report lower physical activity compared with the general population including populations with earlier stages of chronic kidney disease [51], our findings suggesting a higher hemodialysis dose improves physical function in female, but not male, individuals warrant greater exploration. Finally, this was a prospective cohort study designed to explore how sex and gender considerations may impact quality of life in individuals with kidney failure treated with hemodialysis, and any associations observed do not necessarily imply causation. However, sex and gender considerations have been highlighted as important considerations in nephrology research [52], and this study represents a step towards precision care in persons living with kidney disease.

In this incident in-center hemodialysis population, conventional as compared with incremental hemodialysis was associated with greater improvements in reported physical health in female but not male individuals, while incremental as compared with conventional hemodialysis was associated with greater improvements in mental health in female, but not in male, individuals with greater roles and responsibilities commonly ascribed to women. The results of this study highlight the importance of shared decision-making and incorporating both sex and gender factors into hemodialysis practice. However, the sample size was limited, and it remains unclear as to whether the observed changes in HRQoL persist with longer dialysis duration. Before recommendations regarding clinical practice can be made, large-scale prospective studies in a diversity of populations testing associations between sex and gender factors and important patient-identified outcomes are required.

SUPPLEMENTARY DATA

Supplementary data are available at *Clinical Kidney Journal* online.

AUTHORS' CONTRIBUTIONS

V.J.R.-T., S.B.A., J.M.M., M.J.E, S.M.D, N.P., K.D. and K.S.-M. designed the study. Data analysis was completed by V.J.R.-T. and S.B.A., and was interpreted by all authors. L.P. and H.B. provided consent

for use and analysis of GENESIS-Praxy Gender Questionnaire. All authors contributed to and reviewed the manuscript.

DATA AVAILABILITY STATEMENT

Deidentified data is available upon reasonable request to the corresponding author.

CONFLICT OF INTEREST STATEMENT

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