Preference for Alternate-Day Versus Conventional In-Center Dialysis: A Health Utility Elicitation

Rafael J. Solimano1, James Lineen2, and David M. J. Naimark1,3

Abstract

Background: Mortality rates for patients on hemodialysis (HD) continue to be high, in particular, following the long interdialytic period, yet thrice-weekly conventional HD (CHD) is still an almost universal regimen. Alternate-day dialysis (ADD) may have advantages over the current schedule because it would eliminate the long interdialytic break. A preliminary, as yet unpublished, patient simulation and cost-utility analysis compared CHD versus ADD and demonstrated that the economic attractiveness of ADD was sensitive, in particular, to patients’ preference for ADD versus CHD. To date, this preference has not been elicited.

Objective: To elicit utilities for both CHD and ADD using 3 standard elicitation methods among a prevalent cohort of patients on CHD.

Design: This study is a single-center survey of patient preferences (utilities).

Setting: This study took place within the dialysis units of Sunnybrook Health Centre, a university-affiliated teaching hospital in Toronto, Ontario, Canada, which encompasses 174 patients on in-center HD.

Patients: Those older than 18 years of age, on thrice-weekly HD, were included in this study.

Measurements: Descriptive statistics were used to summarize patient characteristics and the utility values generated. A multiple linear regression was performed to determine an association between participant characteristics and the utility ratio.

Methods: Via standardized face-to-face interviews by a single investigator, 3 utility elicitation methods, visual analogue scale (VAS), time trade-off (TTO), and standard gamble (SG), were administered to generate utilities for each patient for their current health state of CHD (thrice-weekly). After completing this task, we provided each patient with a concise summary regarding the current literature on how ADD may impact their health. Finally, patients were asked to envision their health while on an ADD regimen while repeating the VAS, TTO, and SG.

Results: We recruited 65 participants. The mean utilities of CHD versus ADD were similar for all 3 methods. Visual analogue scale, TTO, and SG had utility values of 0.6 ± 0.2, 0.6 ± 0.3, and 0.7 ± 0.3, and 0.6 ± 0.2, 0.7 ± 0.3, and 0.7 ± 0.3 for CHD and ADD, respectively. The ratio for CHD to ADD was 1.1 ± 0.4, 1.1 ± 0.5, and 1.0 ± 0.2 for VAS, TTO, and SG, respectively.

Limitations: Small sample size from a single center, where not all participants agreed to participate, wide variability in participant responses and requiring patients to conceptually imagine life on ADD may have affected our results.

Conclusions: Compared with CHD, there was no difference in the preference toward ADD which demonstrates promise that adopting an alternate-day schedule may be acceptable to patients. Furthermore, with the generation of a utility for ADD, this will allow for more precise estimates in future simulation studies of the economic attractiveness of ADD.

Trial registration: Not required as this article is not a systematic review nor does it report the results of a health care intervention.

Abrégé

Contexte: Le taux de mortalité des patients traités par hémodialyse demeure élevé, particulièrement après la longue période interdialytique. Pourtant, l’hémodialyse conventionnelle (HDC) trois fois par semaine est encore un régime quasi universel. La dialyse un jour sur deux (ADD—Alternate Day Dialysis) peut présenter des avantages par rapport au schéma actuel puisqu’elle éliminerait la longue pause interdialytique. Une analyse préliminaire, non encore publiée, de simulation des patients et d’analyse coût-utilité a comparé l’HDC et l’ADD et démontré que l’attractivité économique de l’ADD était sensible; particulièrement à une préférence des patients pour l’ADD comparativement à l’HDC. À ce jour, cette préférence n’est toujours pas établie.
Objectif: Sonder les avantages de l’HDC et de l’ADD sur l’état de santé par trois méthodes d’interrogation standard dans une cohorte de patients hémodialysés.

Type d’étude: Un sondage mené dans un seul centre qui examinait les préférences (satisfaction quant à l’état de santé—utilité) des patients.

Cadre: L’étude s’est tenue aux unités de dialyse du Sunnybrook Health Centre, un hôpital universitaire situé à Toronto (Ontario) au Canada qui regroupe 174 patients hémodialysés en centre.

Sujets: Ont été inclus les adultes suivant un traitement d’hémodialyse trois fois par semaine.

Mesures: Des statistiques descriptives ont servi à résumer les caractéristiques des patients et les valeurs d’utilité générées. Une régression linéaire multiple a été réalisée pour établir l’association entre les caractéristiques du patient et le rapport d’utilité.

Méthodologie: Par l’entremise d’entretiens uniformisés en personne, trois méthodes de sollicitation ont été employées - une échelle visuelle analogique (EVA), l’arbitrage temporel (AT) et le pari standard (PS) - pour générer des valeurs d’utilité pour chaque patient pour la modalité actuelle (HDC - trois fois par semaine). Chaque patient a par la suite reçu un résumé de la littérature scientifique actuelle sur les possibles effets de l’ADD sur l’état de santé. Puis, nous avons fait de nouveau passer les trois questionnaires aux patients en leur demandant d’imaginer leur état de santé s’ils étaient sous traitement par ADD.

Résultats: Nous avons recruté 65 participants. Les valeurs moyennes d’utilité pour l’HDC compare à l’ADD étaient similaires pour les trois méthodes. Les valeurs d’utilité pour l’HDC et l’ADD étaient respectivement de 0,6 ± 0,2 et 0,6 ± 0,2 (EVA); de 0,6 ± 0,3 et 0,7 ± 0,3 (AT); et de 0,7 ± 0,3 et 0,7 ± 0,3 (PS). Les rapports d’utilité entre l’HDC et l’ADD étaient de 1,1 ± 0,4 (EVA), de 1,1 ± 0,5 (AT) et 1,0 ± 0,2 (PS).

Limites: L’échantillon est faible et provient d’un seul centre où tous les patients n’ont pas accepté de participer à l’étude. Également, les résultats pourraient être affectés par la grande variabilité dans les réponses des participants et par le fait d’avoir exigé des patients qu’ils imaginent leur état de santé sous traitement par ADD.

Conclusion: Aucune différence significative n’a été observée quant à une préférence pour l’ADD comparativement à l’HDC, ce qui montre que l’adoption d’un régime d’hémodialyse tous les deux jours serait probablement acceptable pour les patients. D’autre part, la génération de valeurs d’utilité pour l’ADD permettra des estimations plus précises dans les futures études de simulation et d’attractivité économique pour l’ADD.

Keywords
dialysis, alternate-day dialysis, utility, time trade-off, standard gamble

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What was known before
Mortality rates for patients with end-stage renal disease on thrice-weekly hemodialysis are high with an increase in frequency of complications experienced after the long interdialytic period. A prior preliminary patient simulation and cost utility-analysis comparing conventional hemodialysis to alternate-day dialysis demonstrated that at a threshold of $100 000 per extra quality-adjusted life year, alternate-day dialysis becomes cost-effective relative to conventional hemodialysis, albeit dependent on patient’s preference to alternate-day dialysis versus conventional hemodialysis.

What this adds
The objective of this article was to elicit utility values for both conventional and alternate-day dialysis using 3 standard elicitation methods among a prevalent cohort of patients on thrice-weekly hemodialysis to provide data for further development of the alternate-day dialysis decision analytic models.

Introduction
Mortality rates for patients on hemodialysis (HD) continue to be high.1 In particular, patients on conventional HD (CHD) thrice-weekly experience higher risk of sudden cardiac death following the long interdialytic period (Friday-Monday or Saturday-Tuesday),2-4 yet conventional thrice-weekly HD is still an almost universal regimen. Strategies to eliminate the long interdialytic break have been an area of active research.5

The Frequent Hemodialysis Network (FHN) randomized clinical trials have demonstrated promising results

1Department of Medicine, University of Toronto, ON, Canada
2Sligo University Hospital, Ireland
3Institute of Health Policy, Management and Evaluation, University of Toronto, ON, Canada

Corresponding Author:
David M. J. Naimark, Institute of Health Policy, Management and Evaluation, University of Toronto, Rm 386, 1929 Bayview Ave., Toronto, ON, Canada M4G 3E8.
Email: david.naimark@sunnybrook.ca
Methods

Study Setting

We conducted a single-center survey of patient preferences (utilities) between February and November, 2019, within the dialysis units of Sunnybrook Health Centre, a university-affiliated teaching hospital in Toronto, Ontario, Canada, which encompasses 174 patients on in-center HD.

Participants

We approached patients to consider participating who were older than 18 years of age, on maintenance in-center HD, on the standard regimen of thrice-weekly treatments, who were proficient in English, and who had the cognitive capacity to participate and consent to the study (the latter 2 criteria were based on the judgment of the primary HD team members).

We excluded HD patients who could not communicate in English, those with severe visual and/or hearing impairment for which obtaining consent or proceeding with the study would not be feasible, and for those who declined to participate or who otherwise could not complete the informed consent form. To restrict the study to patients who would expect to require HD indefinitely, we excluded patients who were both listed for cadaveric transplantation and had been called in for a potential transplant within 6 months (ie, they were called in to the transplant center but the transplant could not proceed for some reason). Moreover, we excluded participants discharged from a hospital admission, those with initiation or dose titration of psychotropic medications, and/or those with a significant life event (ie, death or sickness of a friend or family member) within 1 month of the start of the enrollment window.

Baseline characteristics including age, gender, body mass index (BMI), cause of end-stage renal disease (ESRD; diabetes, hypertension, glomerulonephritis, polycystic kidney disease, other, unknown), and comorbid medical conditions were ascertained from Sunnybrook information systems (SunnyCare and Accuro™).

Procedure

Individuals were screened by the primary staff nephrologist for each HD shift to determine whether participants were appropriate candidates. If deemed appropriate, an investigator approached each candidate to introduce the study and obtain consent among candidates who agreed to participate. Then, via standardized face-to-face interviews by a single investigator (R.J.S.), the visual analogue scale (VAS), time trade-off (TTO), and standard gamble (SG) methods were administered to elicit utilities for each patient (Supplemental Appendix). We first elicited utilities for the current health state of CHD. After completing this task, we provided each patient with a concise summary, employing nontechnical language, regarding the current literature on how ADD may impact their health: (1) improvement in overall health,5,11-17 (2) improvement in QOL,6,7,11,12,18 (3) improvement with dialysis-related symptoms and time to recovery after dialysis,7,11,12,18 and (4) complications.5,9,19

We then asked the participants to envision their health while on an ADD regimen while subsequently repeating the VAS, TTO, and SG.

Description of the Utility Elicitation Instruments

Visual analogue scale. The VAS is a paper-based instrument whereby the participant marked their assessment of their preference for a health state (CHD followed by ADD) on a scale ranging from 0 to 10 where 0 represents the lowest state of health (death), whereas 10 reflects perfect health. Utility was calculated as the point on the scale divided by 10.

Time trade-off. In the TTO method, each participant was asked to reflect on a health state (CHD followed by ADD) and then choose between 2 hypothetical options: remain in that
state for their remaining life expectancy, chosen arbitrarily and hypothetically to be 15 years, or to trade-off a number of years, thus live for a shorter duration, but in perfect health. The time frames were then adjusted with the duration of life in perfect health decreased systematically until the participant’s preference was indifferent regardless of the choice between the 2 options. At the point of indifference, the utility was computed as the proportion of the lifespan occupied by complete health. For example, if a participant’s point of indifference is between 10 years of healthy life and 15 years in a state of conventional dialysis, then the utility would be 0.67.

**Standard gamble.** To determine utilities by the SG, the participant was asked to make a decision between either staying in their current health state on CHD (or their envisioned health state on ADD) versus undergoing a hypothetical therapy. This therapy has 2 possible outcomes. If successful, the participant would be cured and would live in full health. However, if the therapy is not successful, the participant would experience immediate death. The chance of death associated with this hypothetical therapy was varied in an iterative manner until the patient was indifferent between staying in their current health state versus undergoing the hypothetical therapy. The utility was calculated as 1 minus the probability of death at the point of indifference.

**Statistical Analysis**

Descriptive statistics were used to summarize patient characteristics: means and standard deviations or median and interquartile range (IQR) for continuous variables and percentages for categorical characteristics. To calculate the utility of ADD relative to CHD for each elicitation method and for each participant, the ratio of the utility for ADD was divided by the utility for CHD. These values were summarized with both mean and standard distributions and medians and IQR. Histograms of the ratios across participants and the relative magnitude of mean and median values were used to assess distribution features. The association between participant characteristics (age, gender, and number of comorbid conditions) and utility ratio was performed for each elicitation method using multiple linear regression. All analyses were performed using Microsoft Excel version 15.33 or R version 3.2.3.

Written, informed consent was obtained from each participating patient. The Research Ethics Board of Sunnybrook Health Sciences Centre approved the study.

**Results**

**Patient Characteristics**

Between February and November 2019, from a prevalent population of 174 HD patients, 109 patients were excluded as per the inclusion and exclusion criteria, or due to nonconsent.

**Table 1. Baseline Characteristics of Patients.**

| Characteristic                              | Patients on 3×/week in-center HD (N = 65) |
|--------------------------------------------|------------------------------------------|
| Demographic characteristics                |                                          |
| Age, y (mean ± SD)                         | 64.9 ± 15.6                              |
| Male sex, No. (%)                          | 35 (53.9)                                |
| Weight, kg (mean ± SD)                     | 79.4 ± 24.9                              |
| BMI, kg/m²                                 | 28.7 ± 8.1                               |
| Cause of ESRD, No. (%)                     |                                          |
| Diabetes                                   | 24 (37.0)                                |
| Hypertension                               | 5 (7.7)                                  |
| Diabetes and hypertension                  | 3 (4.6)                                  |
| Glomerulonephritis                         | 8 (12.3)                                 |
| Polycystic kidney disease                  | 3 (4.6)                                  |
| Other                                      | 10 (15.4)                                |
| Unknown                                    | 12 (18.5)                                |
| Comorbid conditionsa (mean ± SD)           | 5.3 ± 2.4                                |
| Dialysis vintage, y (mean ± SD)            | 2.6 ± 1.5                                |

Note. Percentages may not total 100 because of rounding. HD = hemodialysis; BMI = body mass index; ESRD = end-stage renal disease. *Number of any medical conditions listed in the clinical electronic medical record.

**Table 2. Results of All the Utility Assessments.**

| Utility | Median (IQR) | Median (IQR) |
|---------|--------------|--------------|
| VAS     | 0.6 (0.5-0.7)| 0.6 (0.4-0.7)|
| ADD     | 0.6 (0.5-0.7)| 0.4 (1.0-1.2)|
| Ratioa  | 1.1 (1.0-1.2)| 1.0 (1.0-1.2)|
| TTO     | 0.6 (0.4-0.9)| 0.7 (1.0-1.0)|
| ADD     | 0.7 (0.5-0.9)| 0.7 (1.0-1.0)|
| Ratioa  | 1.1 (1.0-1.0)| 1.0 (1.0-1.0)|
| SG      | 0.7 (0.5-0.9)| 0.8 (1.0-1.0)|
| ADD     | 0.7 (0.5-1.0)| 0.8 (1.0-1.0)|
| Ratioa  | 1.0 (1.0-1.0)| 1.0 (1.0-1.0)|
| Average ratioa | 1.1 (0.9-1.2)| 1.0 (0.9-1.2)|

Note. IQR = interquartile range; VAS = visual analogue scale; CHD = conventional hemodialysis; ADD = alternate-day dialysis; TTO = time trade-off; SG = standard gamble. aRatio signifies ADD to CHD. bOf all 3 elicitation methods (VAS, TTO, and SG).

A total of 65 participants were recruited. The mean age of patients recruited was 64.9 ± 15.6 years, with 53.9% male predominance, and with most ESRD attributed to diabetes (37%). There was an average of 5.3 ± 2.4 comorbid conditions (Table 1).

**Utilities for CHD and ADD**

The mean utilities of CHD versus ADD were similar for all 3 methods, VAS, TTO, and SG with similar mean and median values (Table 2). Utilities assessed with VAS showed mean
values of 0.6 ± 0.2 and 0.6 ± 0.2 for CHD and ADD, respectively, with a ratio of 1.1 ± 0.4. Time trade-off results showed that patients would trade-off 9 years for CHD and 8 years for ADD with utility values of 0.6 ± 0.3 and 0.7 ± 0.3 for CHD and ADD, respectively, with a ratio of 1.1 ± 0.5. With the SG methodology, patients would take a 30% risk to achieve “perfect” health for either CHD or ADD with utility values of 0.7 ± 0.3 and 0.7 ± 0.3 and a ratio of 1.0 ± 0.2.

Histograms generated (Figures 1-3) showed relatively symmetric distributions of the ADD to CHD utility ratios for all 3 elicitation methods. Symmetry was also suggested by similar means and median values for ratios from all 3 elicitation methods. Correlation coefficients were low, 0.2, 0.1, and 0.1 for VAS versus TTO (Figure 4), VAS versus SG (Figure 5), and TTO versus SG (Figure 6), respectively.

Regression analysis demonstrated no significant associations between age, gender, number of comorbid conditions, or dialysis vintage for any of the ratio results (Table 3). The *P* values for VAS ratio to age, male gender, number of comorbid conditions, and dialysis vintage were .92, .57, .40, and .40, respectively. The *P* values for TTO ratio to age, male gender, number of comorbid conditions, and dialysis vintage were .25, .45, .43, and .16, respectively. The *P* values for SG ratio to age, male gender, number of comorbid conditions, and dialysis vintage were .63, .50, .27, and .26, respectively.

**Discussion**

In this single-center study of patient preference for conventional versus alternate-day dialysis, interestingly, there was no major difference in the preference of ADD versus CHD in this sample of prevalent patients on maintenance in-center HD, on the standard regimen of thrice-weekly treatments. To our knowledge, these results are the first utility scores generated from a dialysis population regarding an ADD schedule. Furthermore, to validate our findings, our elicited mean utility values for CHD of 0.6 ± 0.3 and 0.7 ± 0.3 for TTO and SG, respectively, were similar to previous values described in literature. A prior systematic review and meta-analysis showed that the utility of HD is 0.61 (95% confidence interval [CI] 0.54-0.68) and 0.75 (95% CI 0.57-0.92) using TTO and SG, respectively.

Comparable to the FHN randomized clinical trials of 6-days-per-week of in-center dialysis, a small pilot study comprising 18 patients also demonstrated improved clinical and biochemical parameters with ADD when compared with CHD. This suggests that patients requiring dialysis may experience the benefits of increased number of dialysis treatments, however, in a more attractive ADD schedule. This could lessen the potential roadblock and resistance to the prospect of losing the long interdialytic break; many patients on CHD are highly resistant to the idea of increasing the frequency of their treatment regimens. Yet, our study patients were found to be indifferent to ADD versus CHD, with average utility values for the ratio of ADD to CHD being 1.1 for VAS and TTO and 1.0 for SG. This demonstrates promise that adoption of an alternate-day schedule may be acceptable to patients in our HD unit; however, generalizing this finding to the entire HD population is less clear. The fact that average utility values derived for CHD were similar to prior studies supports the generalizability of our findings. However, there was substantial individual variability in preference, as judged by the variability in utility values, among patients. The source of this heterogeneity remains uncertain as we were unable to determine an association between age, gender, number of comorbid conditions, or dialysis vintage to any of the utility ratio results.

In health economics, programs or strategies are compared in terms of both their expected costs and benefits. The benefit of health care strategies is frequently denominated in terms of quality-adjusted life years (QALYs) which, in simplest terms, is the product of life-expectancy and a preference weight, otherwise known, as a utility, associated with a particular health state or condition. As supported in literature, annual costs for daily HD are substantially less than those for CHD presumably in large part to reducing hospitalizations. A preliminary, as yet unpublished, patient simulation and cost-utility analysis that compared CHD with ADD, performed by our group, demonstrated that at a threshold of $100 000 per QALY, ADD becomes cost-effective relative to CHD but this is dependent, in particular, to patients’ preference for ADD versus CHD. Now that a utility value exists for patient’s preferences for ADD versus CHD, more precise estimates in future simulation studies of the economic attractiveness of ADD may be employed. However, as noted in our study, the results were not strongly correlated among the elicitation methods with low correlation coefficients which may suggest generally that utility elicitation should not rely on a single method.

This study has several important limitations which could explain why there was no difference in the utility values between the 2 HD schedules. This includes a small sample size from a single center. Unfortunately, not all potential participants agreed to participate, which may have induced a selection bias and reduced the ability to generalize the results to the entire HD population. A formal sample size calculation was not performed; thus, it is difficult to ascertain whether this study was sufficiently powered to determine an effect between CHD versus ADD. Furthermore, the patients who would benefit the most from ADD (ie, those with difficulties in fluid balance or blood pressure control) may already be on an increased dialysis regimen and thus would have been excluded from this study and not captured in the results. Similarly, those who experience problems with their vascular access tend to be sicker and thus also excluded from the study. The wide variability seen in this study could also account for the indifference seen purely due to participant’s responses canceling each other out. Specific comorbidities were not collected, and there was not a specific set of comorbidities that were counted for each individual patient.
Figure 1. Histogram illustrating the alternate-day dialysis (ADD) to conventional hemodialysis (CHD) utility ratios generated with the visual analogue scale.

Figure 2. Histogram illustrating the alternate-day dialysis (ADD) to conventional hemodialysis (CHD) utility ratios generated with the time trade-off.
Figure 3. Histogram illustrating the alternate-day dialysis (ADD) to conventional hemodialysis (CHD) utility ratios generated with the standard gamble.

Figure 4. Utility value ratios—alternate-day dialysis (ADD) to conventional hemodialysis (CHD)—between the visual analogue scale and the time trade-off elicitation methods. Correlation coefficient was low at 0.2.
Figure 5. Utility value ratios—alternate-day dialysis (ADD) to conventional hemodialysis (CHD)—between the visual analogue scale and the standard gamble elicitation methods. Correlation coefficient was low at 0.1.

Figure 6. Utility value ratios—alternate-day dialysis (ADD) to conventional hemodialysis (CHD)—between the time trade-off and the standard gamble elicitation methods. Correlation coefficient was low at 0.1.
Table 3. Summary of the Regression Analysis Between Age, Gender, Number of Comorbid Conditions and Dialysis Vintage to Utility Ratio results.

|       | Coefficient | SE   | P value |
|-------|-------------|------|---------|
|       | VAS         |      |         |
| Intercept | 1.00        | 0.23 | <.001   |
| Age  | 0.00        | 0.00 | .92     |
| Male gender | −0.06      | 0.10 | .57     |
| Comorbid conditions  | 0.02        | 0.02 | .40     |
| Dialysis Vintage  | −0.03       | 0.03 | .40     |
|       | TTO         |      |         |
| Intercept | 0.87        | 0.28 | <.01    |
| Age  | 0.01        | 0.00 | .25     |
| Male gender | 0.10        | 0.13 | .45     |
| Comorbid conditions  | −0.02       | 0.03 | .43     |
| Dialysis Vintage  | −0.06       | 0.04 | .16     |
|       | SG          |      |         |
| Intercept | 1.03        | 0.14 | <.001   |
| Age  | 0.00        | 0.00 | .63     |
| Male gender | 0.04        | 0.06 | .50     |
| Comorbid conditions  | −0.02       | 0.01 | .27     |
| Dialysis Vintage  | −0.02       | 0.02 | .26     |
| Average  | 0.97        | 0.41 | <.001   |
| Age  | 0.00        | 0.00 | .39     |
| Male gender | 0.03        | 0.06 | .69     |
| Comorbid conditions  | −0.01       | 0.01 | .68     |
| Dialysis Vintage  | −0.04       | 0.02 | .08     |

Note. VAS = visual analogue scale; TTO = time trade-off; SG = standard gamble.

Therefore, there may have been a wide variation in the type or number of comorbid conditions depending on the accuracy of the electronic medical record documentation. Finally, we required patients to imagine life on ADD which may have been conceptually too demanding to generate accurate utility values, but currently, ADD is not a common dialysis schedule; therefore, elicitation of utilities from patients who have direct experience with ADD is not feasible.

Strengths of our study include use of well-established methods for eliciting utilities including VAS, TTO, and SG. Furthermore, consistent application of these methods in the sequential order was performed by a single investigator to minimize measurement and question-order bias, respectively, and were elicited from the correct target population (ie, excluded those who expect to be transplanted imminently). Furthermore, because the key question is the preference patients would have for switching from current CHD to a new ADD schedule, we believe that the prevalent CHD population is the most appropriate for this particular utility elicitation.

Conclusion
As compared with CHD, there was no major difference in the preference toward ADD in our HD unit which demonstrates promise that adoption to an alternate-day schedule may be acceptable to our patients. Furthermore, now that a utility value exists in literature for patient’s preferences for ADD versus CHD, this will allow for more precise estimates in future simulation studies of the economic attractiveness of ADD, given current information as well as value-of-information analyses to determine the population-level economic gains that potential randomized trials of ADD versus CHD could produce.

Ethics Approval and Consent to Participate
This study was approved by the Research Ethics Board of Sunnybrook Health Sciences Centre and informed, written, consent was obtained from all study participants.

Consent for Publication
We have the author’s consent for publication.

Availability of Data and Materials
De-identified study data is available by request.

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ORCID iD
Rafael J. Solimano https://orcid.org/0000-0002-2690-9883

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