



KDIGO Controversies Conference on Symptom-Based Complications in Dialysis - Public Review Comments -

As of September 9, 2021

Industry comments are highlighted in blue

Devika Nair (Vanderbilt University Medical Center):

Looking forward to learning from this conference. Some points of consideration/possible areas for future investigation:

- 1) Symptom burden is also significant in non-dialysis chronic disease
- 2) More research is likely needed to unravel the psychological, physiological, and neurobiological mechanisms of symptom perception in kidney disease
- 3) Unraveling these mechanisms will likely be necessary to develop targeted and/or multimodal approaches to symptom reduction and symptom alleviation.
- 4) If symptoms are routinely addressed in hemodialysis units, nephrologists and care team members must be equipped with scalable strategies to address these symptoms. Importantly, patients must be privy to discernible changes in their care plan that occur as a result of symptom monitoring.

Kirsten Johansen (Hennepin Healthcare):

Although physical activity and exercise are likely considered part of nonpharmacologic treatment of symptoms, I would love to see the role of these explicitly incorporated into the scope. In discussions with patients as part of a Kidney Health Initiative meeting, they had a lot of hope that this could help with fatigue and cramping.

Michelle Richardson (Tufts Medical Center William B Schwartz Division of Nephrology, Pharmacist and PRO Researcher):

Thank you for holding a consensus conference on this incredibly important topic. I think it is important in the scope of work and throughout the conference that we refer to both symptoms in number and also in impact. That is an important differentiation to make, especially for patients, who are really the only ones who can assess their symptoms and the impact those symptoms have on their lives. A recent KHI workgroup conducted a focus group on the symptom of muscle cramping in dialysis. Patients clearly told us that experiencing symptoms

and their impact was "part of their reality", "just part of being on dialysis", "something they learned to deal with", "nothing could be done". This perspective MUST be taken into account and I truly hope there are patients on the panel of this conference.

I also advice the conference panel to consistently use the words systematic and reproducible in the conference terminology. Many clinicians believe they ask about symptoms and do so consistently. However, that is not the case. Without a systematic an reproducible approach (obviously using an instrument that has met basic psychometric criteria), it is a waste of time to pursue symptom assessment and treatment.

In addition to the limited evidence and patient reluctance, cost, drug interactions and increased burden are added concerns to identifying and treating symptoms. There should also be some assessment of symptoms that are related to beginning dialysis and those that may occur once the patient has been on dialysis for some time. I suspect they are different and it would be unwise to lump them all together. Just like you wouldn't lump HD and PD symptoms together.

Breakout group 1: For barriers in setting I would include home vs. incenter, private vs. non-profit, and chronic or acute health care settings. Cultural barriers should also address language and education. Health literacy probably plays a large role in symptom reporting and management. I think this whole section needs to be more in depth who/what/when/where/why are important. What are ideal PROM characteristics? Can they be prioritized? There seems to be emphasis on incorporating the symptom assessment into the chart and the overall assessment, but what about the benefit of the assessment to the patient? There are numerous publications about ideal PROMs and also incorporating PROMs into clinical care and the barriers that are faced. I recommend that KDIGO use these publications to flesh out this breakout group's topics.

Breakout group #4: Differences in home vs. incenter need to be addressed. Add pharmacists to the role of staffing. Identify what symptoms, how they present and their impact. For #3 changes in training - nephrologists need to get comfortable discussing difficult topics. I know that most think they do, but...they don't really. Especially topics where there aren't good treatment options (like with many symptoms) or there are tradeoffs (we can address this symptom but you may have ADR from the medication or need to have additional lifestyle modifications that will have their own impact). Consider adding into the discussion the role of the dialysis PCT in symptom identification and management, training, etc.

The entire document seems to assume adults, but what about pediatric dialysis patients and their symptoms? If that isn't going to be addressed in the conference, that needs to be clearly stated.

Thank you for the opportunity to comment on this important Consensus Conference's Scope of Work. Please don't hesitate to reach out with any questions or need for clarification.

Eduardo Lacson (Tufts/DCI):

First and foremost, I commend KDIGO for taking on this very important aspect of patient-centered nephrology care in dialysis. While we all take stewardship as physicians and caregivers, we have not been very good at listening to our patients with regards to what matters the most in their lives - personal goals, symptoms and even annoyances that at times create unnoticed burdens. PROMs become a key component of addressing these issues and the discussion points identified in the scope/appendix are very appropriate.

I was co-chair of a recent ASN-KHI workgroup that worked on cramping in dialysis with Michelle Richardson, PharmD and we had embarked on a journey that took some unexpected twists and turns as we interacted with subject matter experts and patients. I hope to share some insights and thoughts based on our yearlong journey (hampered by COVID). Members also came into the workgroup with very different perspectives that evolved as we worked together. One aspect that we realized was the mindset of the dialysis patient which may change over time, hence the question on 'frequency' of PROM measurement is very relevant. However, perhaps more nuanced, is whether the PROM questionnaire may need to be evolving over time as well - perhaps being more general in the beginning with more specific questions as patient-specific issues are identified, in order to decrease burden. We presented a "wholistic" diagram for a conceptual framework for assessing cramping that we were expecting to resonate after a review of the literature and input from subject matter experts (including patients) but when we initially brought to our patient feedback and focus groups surprised us with feedback that it was too broad and patients thought they were more relevant to the "whole dialysis experience" rather than specific to the cramping experience and life impact. A lesson that our focus on a particular symptom and its ramifications may at times become too narrow and perhaps there needs to be some thought as to how specific symptoms may intertwine and combine to impact larger representation of burden such as social withdrawal or anxiety or unexpected behavior/attitudes.

I personally wonder about the role of misinformation in some of the responses (e.g. some cramping remedies on the internet or role of fluid/dietary intake) particularly in light of how some of the COVID experience reveal the impact of such misinformation on the public's impression on vaccination, masks, or misinformed remedies such as hydroxychloroquine or ivermectin.

Another issue is that many patients' expectations seem to create different levels of burden or tolerance, whereby descriptions of similar experiences prove to be graded differently, for example between home dialysis vs. in-center dialysis patients. This becomes more relevant when we try to measure symptom response to interventions and determining the equivalence (or not) of clinically measurable changes vs. a meaningful perceived reduction in patient burden.

While there are many more nuanced issues, one last item for this general comment would be how to incorporate patient engagement at a systems level so that it becomes part of the entire workflow whereby symptom assessment and management becomes part of the culture of patient empowerment. While the general picture of patient empowerment focuses on taking

charge of their own care, it really includes engagement at all levels including the aspect of introspection, self-evaluation and confidently sharing burden/symptoms during interactions with caregivers and the healthcare system without fear of shaming or retribution.

I believe that other members of our cramping workgroup, particularly my co-Chair Michelle will have even more insights that may be helpful to this mission. Thank you for this opportunity to comment and I am happy to assist the committee in this wonderful project, as able.

Kitty Jager (Amsterdam University Medical Centers (AMC)):

Dear Colleague, I wonder if we should better address the fact that women far more often have (more severe) symptoms than men. This has been described in the literature for non-dialysis patient with eGFR < 20 ml/min (Van de Luijtgarden MWM et al 2019) and for HD patients (Poulsen CG et al 2017). In other words 'does symptom management deserve a sex specific approach? best wishes, Kitty Jager

Thomas Golper (Vanderbilt University):

Very nice scope of work topics. Drs. Brown and Mehrotra are knowledgeable in most of the areas. In Group 2 item 3 addresses relationship of symptoms to the actual dialysis procedure is extremely important and I do worry that there will be more of an emphasis on symptoms and their relive rather than actually on the metabolic, chemical, and physiological effects of the dialysis treatment. This is a very important rabbit-hole. In Group 4 I do not think there is enough emphasis on the PCP, and on the health system's responsibility. Specifically, Medicare Advantage plans have case managers. I mention this in the context that while we discuss psychology and palliative care, the preparation before dialysis begins can go a long way towards a more stable experience after dialysis is started. I would like to be a part of Group 4.

Anatole Besarab (Stanford):

I fully agree with the need for this review. I took care of dialysis patient s for almost 40 years and symptoms were important in making decisions on initiation and prescription of the dialysis treatments. Kt/V is not enough. At one point, while medical director of a dialysis unit, withdrawal from dialysis was the 2nd leading cause of death. We need to do a better job Missing is time that a physician spends with a patient. You can't know what symptoms are present if all one does is make "Hi, bye" rounds. Frankly the Nurse practitioners and PA, when well trained do a better job. In the 1980's we had psycho-nephrology conferences to help patients and staff with depression, anxiety, and "burn out" I agree with the goals of the 4 break-out groups.

Steven Rosansky (Dorn Research VA, Columbia SC):

I attended the 2018 controversies conference and would love to participate in the upcoming meeting. 'Some of the issues that I think are relevant to this meeting.

One of the most important issues regarding dialysis initiation and symptoms is what symptoms justify dialysis initiation. Guidelines for dialysis initiation encourage symptoms as opposed to eGFR level as the basis for starting dialysis. The latest kdoqi guideline suggests a trial of dialysis

to alleviate a given symptom before starting life long dialysis. The literature is very limited regarding the symptoms patients had when they started dialysis. I have one paper from Japan that reported few symptoms at dialysis initiation , even at a GFR around 5. Clearly fluid overload symptoms from CHF has "justified" dialysis initiation in the US . I with colleagues from UK Canada Australia NZ and France reported in KI that early start of dialysis was common for older adults 75 + with CHF - especially in the US and Canada. Aggressive treatment of CHF with the newer SGLT2 drugs , K binders, aldo antagonists and ace arb rx should be discussed. These treatments for the cardiorenal syndromes could help some of folks avoid later in life dialysis starts?

Another thorny issue-How to differentiate comorbidity symptoms from "uremia " symptoms. US guidelines for dialysis in 2007 I think actually suggested start of dialysis if the combination of comorbidity symptoms and uremia symptoms were present -I think that this was a mistake? The IDEAL study had a table at the end of the NEJM article on the study which gave some symptoms as reasons for some of the patients assigned to later start who started early . The accompanying NEJM editorial said the the start of dialysis was 'just in time" for symptoms. This was a total overreach - since IDEAL was not designed to answer the question of which symptoms/situations drove dialysis start. Much of the data in the table did not even make sense.

Good luck with this meeting!

Isaac Teitelbaum (University of Colorado):

This looks excellent; I would be honored to participate if invited. I have but one general comment and a couple of minor comments on specific items.

General: I see no mention of the pediatric population; is it intended to be included? Are there standardized PROMs in pediatrics? I would imagine the focus shifts more to caregivers than it would in adults; is this something we wish to explore?

Area 1b: Whose responsibility...I believe it was the intent to include the PCP but I don't see that person listed.

Area 3: Again, who's responsible for this, nephrologist vs. PCP.

Kam Kalantar-Zadeh (University of California Irvine (UCI) and International Federation of Kidney Foundation (IFKF-WKA)):

Colleagues - I have shared some of these thoughts and more with Drs Brown and Mehrotra in a separate email and believe that under Breakout Group 1 or 4 and/or as a separate Introduction, it could be useful to present the field of symptoms sciences as it pertains to patients on dialysis. Given the concept of symptom clusters and other symptom science intricacies I have been involved with for the past 4 years after I was appointed as a standing member of an NIH study section known as "Nursing Related Clinical Sciences (NRCS); over the 4 years we managed to increase awareness to the field of palliative care based symptom management including in

nephrology, so that with the higher number of grant applications, the NIH has now expanded the NRCS to the ICSC as I have just retired from this after June 2021. As the only nephrologist in these NIH panels, I have been privileged with a unique opportunity to interact with renowned symptom management experts in other disciplines and to better learn and understand the field of symptom science and management of unpleasant symptoms and to identify the gaps as to why the link to nephrology has been behind despite paradoxically having the big elephant of dialysis therapy for over half a century with all related "unpleasant symptoms" and "symptom clusters" along with related suffering of the patients.

As a result of these interactions I started with a number of concept papers on the potential role of symptom management in our field including in NEJM July 2020 and Lancet Aug 2021 with a core message being on symptom management (see main figures of these paper).

Meanwhile the World Kidney Day steering committee agreed with the suggestion that the Year 2021 be dedicated to this important theme so that patients can be "living well with kidney disease" (the paper of which was published in Kidney International and 30 other journals in early to mid 2021), while our additional symptom management focused paper is awaiting its revision and review in a leading nephrology journals.

In-between we have been working on having a "Living Well With Kidney Disease" consensus conference in Honolulu, HI, on Dec 2-3 (most anticipated faculty have not yet been invited, awaiting one more fundraising decision to ascertain the extent of budget and outreach).
Sincerely

Sandip Mitra (Manchester Hospitals UK & Vice Chair of EUDIAL, ERA-EDTA):

Important piece of work, breakout groups are excellent. Need separation of Dialysis and Not on Dialysis as they are 2 distinct groups to address. I would be happy to support the development of Breakout Group 4.

Rümeysa Kazancıoğlu (Bezmialem Vakıf University):

I would like to thank you for the Scope of the controversy meeting. I would suggest to discuss the frequency of symptom questioning. Would it be wise to do that monthly as with blood tests or less frequently? Best Regards

Claudia Fernanda Leiva Gómez (IMSS, Nutritionist):

Most of the patients, independently the type of treatment, DP or HD, their present malnutrition. Then we must to work in issues that involve feeding the patient, what foods wants, what foods doesn't, and work in that way with them. I have success with most of my patients with that.

Maria Fernanda Slon Roblero (Complejo Hospitalario de Navarra):

First, congratulate you for the initiative to address this issue, since the approach to this topic and the conclusions reached at the end of the Conference, may influence health personnel, to

give greater importance and provide solutions to an aspect in the life of renal patients, such as the symptoms associated with this disease.

I have been reviewing the different topics of the Groups with the different approaches and I think, it is very complete. I see that it addresses not only the detection of symptoms, but also the search for solutions through different approaches.

I believe that through this Conference, trying to go deeper into this topic, we could have an impact and directly improve the quality of life of our patients, to make this disease more bearable and improve their lives. I am looking forward to seeing the results and conclusions of this Conference. Thank you again for the initiative, as it will be of great benefit to all.

Baris Afsar (Suleyman Denirel University):

- 1- There may be a comment regarding home hemodialysis
- 2- The dialysis nurse can organise all the team due to very close contact with patients
- 3- Peritonitis related outcomes in PD patients may need special emphasis
- 4- Incremental dialysis may be also discussed

Haruki Kakita (Kaneka Corporation):

We believe Dialysis Related Amyloidosis (DRA) is a very important complication same as or even more than others listed in the draft agenda. We also believe that diagnosis of DRA should be done clinically which can be done throughout the world, not by using special diagnosis equipment or technique. We hope active discussions will be done on the DRA's diagnostic criteria, prognosis and treatment intervention.

Narinder Bhalla (AstraZeneca):

September 16, 2021

FAO: Drs. Edwina Brown (Imperial College London, UK) & Raj Mehrotra (University of Washington, USA)

RE: AstraZeneca's response to KDIGO's call to action for comments on 'KDIGO Controversies Conference on Symptom-Based Complications in Dialysis - Scope of Work'

Dear Dr Brown & Dr Mehrotra,

In response to KDIGO's invitation for feedback on the Scope of Work for the upcoming KDIGO Controversies Conference on Symptom-Based Complications in Dialysis, location TBD in January 2022, we would like to share our comments on behalf of AstraZeneca. The scope of work appears very comprehensive and we look forward to participating in this important conference. We would like to make the following minor suggestions:

Section	Comment
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<p>Breakout Group 1: Strategies to Incorporate Symptom Assessment into Routine Clinical Care</p> <p>Question 3. <i>"PROMs are typically used to assess symptom burden on dialysis. What is the best way to administer them?"</i></p>	<p>We would like to suggest that you consider discussing the administration of PROMs and establishing a baseline patient's QOL during the patient's NDD or Peri-dialysis phase so as to minimize delays in initiation of treatment such as for anemia of CKD and prevent significant declines in QOL.</p>
<p>Breakout Group 2: Reducing Burden of Physical Symptoms</p>	<p>We would like to suggest that delegates consider the delayed evaluation of patients' CKD burden and burden of anemia of CKD. Additionally, we would like to request a consideration of the long term risks associated with episodic vs. chronic treatment of comorbidities such as anemia of CKD.</p>
<p>Breakout Group 2: Reducing Burden of Physical Symptoms</p> <p>Question 3. <i>"Which physical symptoms are amenable to improvement with modification of the dialysis (HD or PD) regimen/ prescription?"</i></p>	<p>We would like to suggest that you consider adding a sub-question to question 3, such as "Would maintaining potassium homeostasis with adjustment of the dialysis prescription and/or use of recently approved potassium binders reduce symptoms of palpitations, shortness of breath or cramping?"</p> <p>Please consider the following references:</p> <ol style="list-style-type: none"> 1. Alvarez L, Brown D, Hu D, et al. Intradialytic symptoms and recovery time in patients on thrice-weekly in-center hemodialysis: a crosssectional online survey. <i>Kidney Med.</i> 2019;2:125-130. http://dx.doi.org/10.1016/j.xkme.2019.10.010 2. Ju A, Unruh, M, Davison S, et al. Establishing a core outcome measure for fatigue in patients on hemodialysis: a standardized outcomes in nephrology-hemodialysis (SONG-HD) Consensus Workshop Report. <i>Am J Kidney Dis.</i> 2018;72:104-112. http://dx.doi.org/10.1053/j.ajkd.2017.12.018
<p>Breakout Group 2: Reducing Burden of Physical Symptoms</p>	<p>We would like the delegates to consider the impact for patients on hemodialysis when access to dialysis was impacted or when dialysis was</p>

<p>Question 9. <i>“How can we manage the physical impact of COVID-19 pandemic (or other disasters) on patients on hemodialysis?”</i></p>	<p>temporarily converted to twice weekly due to the COVID-19 pandemic and how the risk of hyperkalemia was successfully mitigated with recently approved potassium binders.</p> <p>Please consider the following references:</p> <p>1. Dattani R, Hill P, Medjeral-Thomas N, et al. Oral potassium binders: increasing flexibility in times of crisis. Nephrol Dial Transplant. 2020;35:1446-1448. http://dx.doi.org/10.1093/ndt/gfaa202</p> <p>2. Lodge M, Abeygunaratne T, Alderson H, et al. Safely reducing haemodialysis frequency during the COVID-19 pandemic. BMC Nephrology. 2020;21:532. https://dx.doi.org/10.1186/s12882-020-02172-2</p>
<p>Breakout Group 3: Optimizing Management of Psychological Symptoms</p> <p>Question 4. <i>“Are there psychological symptoms amenable to improvement with modification of the dialysis (HD or PD) regimen/prescription?”</i></p>	<p>We would like to suggest that you consider adding a sub-question to question 4, such as “Would maintaining potassium homeostasis with adjustment of the dialysis prescription and/or use of recently approved potassium binders reduce the psychological burden of ED visits/hospitalizations for arrhythmias/hyperkalemia?”</p>
<p>Breakout Group 4: Systems-Level Opportunities to Optimize Symptom Management</p> <p>Question 4. <i>“What are the unique considerations for low/middle income countries?”</i></p>	<p>We would like to suggest greater emphasis and discussion placed on prevention of transfusions, and other injectable therapy that are associated with higher patient and healthcare burden to be able to administer these treatments in some parts of the world.</p>

If you have any questions regarding the comments, please contact AstraZeneca Medical Information at 1-877-893-1510.

Yours sincerely,
Narinder Bhalla, MD
Executive Director, Medical Biopharmaceuticals AstraZeneca

Rafael Gomez (RTS Columbia):

Breakout Group 1: Strategies to Incorporate Symptom Assessment into Routine Clinical Care

Will cover both physical and psychological symptoms

1a. What are the current barriers in assessing and documenting symptoms routinely in dialysis patients?

In our region, nephrologists usually do not have enough time to interact with the patient either because he/she works in other places or they have too many patients to take care of in the renal units, there is more attention to analytical results and mortality than to look for some physical or emotional symptoms. In some places, the general practitioner is the one that has the greatest contact with the renal patient inside the renal units.

Probably economic factors are influencing some of these behaviors, work overload, lack of tools to identify symptoms (physical and psychological)

1b. How can these barriers be addressed?

The Health systems should define a maximum number of patients for each nephrologist for monthly evaluation with adequate wages (reimbursement). Some dialysis providers try to have as many patients as they could with the same staff (more profit)

In LA the cultural barrier, in general, is not a problem for identifying symptoms, but some native populations may have difficulties because of the language and trust of the occidental medicine. In those cases spend more time understanding the patient's needs is very important.

I think we all are responsible to obtain the information, and together compile the data in one tool, and depending on the main symptoms, one member of the team should lead the decision to make.

I think it is important that every patient at renal units have a primary nephrologist and deal with him most of the time, there must be empathy, is the only way that patients will express openly many symptoms without fear, especially some tabu themes.

2. Given the multitude of symptoms which can be related to dialysis treatment, medications, co-morbidities, social problems, etc., what symptoms should kidney care teams focus on?

Probably some symptoms could be more important for some patients than others, depends on their social context and grade of independence, but pain, fatigue, poor appetite, pruritus, sleep disorders are the most common. Sexual dysfunction is also very common, but the patients sometimes are reluctant to speak about it.

In our region, almost all patients have social problems, which ends in psychological symptoms.

o Should symptoms be classified or categorized into core and non-core?

I think so.

o People undergoing hemodialysis (HD) or peritoneal dialysis (PD) may have different symptom predominance; should symptoms be categorized differently based on the dialysis modality?

Yes, agree, HD patients usually have particular symptoms associated with therapy, especially fatigue, pain, and rapid changes in volume.

3. PROMs are typically used to assess symptom burden on dialysis. What is the best way to administer them?

I think patients themselves with staff advise. (Nurse, social worker, psychologist)

o What is the ideal frequency of assessment to prevent fatigue and perceived intrusion of privacy, and the optimal time limit for form filling?

I think every 6 months.

o Who should complete assessments: patients or the healthcare team?

I think patients

o What is the best format for administering? Pen/paper, telephone, digitally?

For many of our patients in our countries, we prefer Pen/paper

o Should PROMs forms be validated to individual populations?

Will be great if we could validate the PROMs in our country, in Spanish

o How do we incorporate this symptom assessment into the patient chart and the overall clinical assessment? § Consider feedback to the nephrologist, other members of the healthcare team, and to the patient/family/caregiver. § Consider systems where information technology options remain limited.

Insert the PROM in the medical records of the renal unit, so every one of the team may look at it.

4. What are barriers to symptom detection for in-center dialysis versus home-based dialysis modalities?

In HD could be routinized the symptoms and not pay attention anymore. Excess of work that precludes its identification appropriately. Not enough time to listen to the patients' needs.

In PD only a monthly visit, if the symptoms are not severe could be missed. Need an active search for those symptoms.

5. What are barriers to symptom reporting from a patient's perspective (e.g., cultural, social factors) or symptom detection by healthcare providers (e.g., bias in pain treatment during an opioid crisis)?

The patient is not receiving enough attention in their visits.

The patient could express some symptoms but does not get attention for those symptoms, with no real interest.

The patient could be referred to another specialist and not receive the attention they need.

Breakout Group 2: Reducing Burden of Physical Symptoms

These symptoms include but are not limited to fatigue, pain, pruritus, insomnia/sleep disorders, restless legs, sexual dysfunction, loss of appetite, anorexia, nausea, cramps, physical function/mobility, cognitive impairment, shortness of breath, dialysis-related amyloidosis, among others

1. Should nephrologists and other nephrology clinical care providers differentiate between symptoms related to comorbidities, aging, and kidney failure? If so, how should this be done and applied to care delivery?

I think the nephrologist should identify all symptoms, and try to give the best treatment independent if are from aging, CKD, DM, other pathologies. Give importance to symptoms as the patient's expectations. The patient is who grades which symptoms are more important to him/her.

2. Is there a threshold of frequency, intensity, or intrusiveness that should be met before considering treatment for commonly experienced physical symptoms? How can we better account for existing comorbidities? Is there a listing of patient mitigating factors (cultural, social) to physical/psychological symptom detection to look out for?

I think some symptoms are sporadic, but we cannot minimize those. We should ask for those symptoms every 1-2 weeks.

Sometimes we need actively search for symptoms, some patients may think are normal because of the CKD and do not pay initially much attention.

3. Which physical symptoms are amenable to improvement with modification of the dialysis (HD or PD) regimen/ prescription?

Fatigue, cramps, nausea, restless feet, anorexia, poor appetite, sexual dysfunction, amyloidosis, dyspnea. But could be more

5. Which physical symptoms are best managed by pharmacologic treatments?

Pain, sleep disorders, cramps?

6. Are there physical symptoms that are best managed by a combination of nonpharmacologic and pharmacologic treatment?

I think nonpharmacologic strategies are very important. Always be together with pharmacological interventions.

7. What are important considerations for developing and evaluating new treatments for physical symptoms?

I think to know the root of the problem, identify the patient's needs, sometimes the treatment is to listen to the patient, pay attention to him/her, make the patient feel that somebody is worried for them.

8. What are important considerations for low/middle-income countries?

Some considerations were exposed before, probably the burden of work for the staff may interfere with a close relationship with patients (it does not mean that there is no relationship), but to have 150-200 patients to care could be high (it is not in all renal units in my country, but it makes difference when we compare with those with a lower number).

Could be that some places do not have enough staff (social workers, nurses, psychologists), who could deal with the patients (economical reasons)

We do not have PROMs

In our culture, if the patient feels empathy with the staff, they will spontaneously express or manifest their symptoms.

9. How can we manage the physical impact of the COVID-19 pandemic (or other disasters) on patients on hemodialysis?

We need to vaccinate the whole population and their families, to restore to previous life

Breakout Group 3: Optimizing Management of Psychological Symptoms

No comments.

Breakout Group 4: Systems-Level Opportunities to Optimize Symptom Management

Will cover both physical and psychological symptoms

1. What are the models of multidisciplinary kidney care for dialysis patients to optimize symptom management?

a. For example, combined nephrology/palliative care; nurse-led; integrated primary care

b. Role of financial incentives and reimbursement

c. Differences with public versus private dialysis clinics

d. Role of staffing—including access to allied health professionals, psychologists, social workers, dieticians, physiotherapists

flow:

- 1- Define relation staff/patients (patients per nephrologist, patients per social worker, etc.) the financial theme is here
- 2- In Colombia, the dialysis clinics are almost 99% private
- 3- Define PROMs, validate PROMs
- 4- Analyze PROMs, is the information accurate? Fulfill the purpose? It is easy to fill by the patient?
- 5- Depending on the results assign the responsibilities for each staff member. Socialize the results with the staff
- 6- PROMs must be in the medical records
- 7- Take actions with the results and discuss with the patient
- 8- Improve the process with the results

2. What are the resource implications and costs associated with symptom assessment and management?

To expend more time with patients could imply an initial higher cost (time patient/nephrologist-nurse-social worker, psychologist), but later if the outcomes get better, the cost will be lower. Maybe fewer hospitalizations, a better quality of life, better mortality??

3. What changes need to be considered for training in nephrology to enable focus of care on well-being and symptoms?

Identify and know about the existence of the symptoms and realize that is important to the patient, and the need of the patient to be heard

The nephrologist/nurse/support team should let know the patients that they can freely express their feelings and there is hope to resolve many of them.

4. What are the unique considerations for low/middle income countries?

In some of our countries, we still have difficulties with adequate dialysis therapy, either HD or PD, the access to therapies is restricted or partially restricted, under-dialyzed patients are usually more symptomatic, lack specialists, access only to basic medicines. Poor reimbursement to nephrologist mean that they have to attend more patients to earn a salary so the time to spend with the patient may be less than required.

5. How do solutions differ for overcoming barriers to symptom detection for in-center dialysis versus home-based dialysis modalities

Home-based therapies (PD for our regions) need an active detection for symptoms, many of them visit only once every month, some every two months, so it makes it difficult to find out problems, now we could use interactive calls to patients (video) between the regular visits to find hidden symptoms and to explore with more detail in their visits. For HD patients, who go regularly to the dialysis center could be easier to abord. But the more important fact is to

dedicate time to talk and listen carefully to our patients, demonstrate an interest in their complaints, and try to offer the best for them.

Nishi Shinichi (Division of Nephrology and Kidney Center, Kobe University Graduate School of Medicine):

We think the conference concerning “Symptom-Based Complications in Dialysis” is an admirable chance for long-term dialysis patients.

As you know Japan has many long-term dialysis patients and they have many dialysis associated complications. Among them Dialysis Related Amyloidosis (DRA) is a problematic complication which induces joint pain, bone fracture, sleeplessness, and waking disturbance, etc.

- 1). These symptoms lead to the lower ADL or QOL of dialysis patients
 - 2). Japan has already stated the diagnosis guideline of DRA
 - 3). Additionally, the Japanese Society Dialysis Treatment (JSDT) have surveyed the clinical setting of the operation on carpal tunnel syndrome in a large cohort. Some original articles have been published until now
 - 4). For DRA, Japan has beta 2 micro-globulin absorption column as a non-pharmacologic treatment. This equipment can restore the decreased ADL because joint pain alleviates and the ranges of joint motion ameliorate after the use of this absorption column
 - 5). We informed the condition of DRA in Japanese dialysis patients.
1. Nishi S, Hoshino J, et al. Multicentre cross-sectional study for bone-articular lesions associated with dialysis related amyloidosis in Japan. *Nephrology (Carlton)*. 2018;23(7):640-645.
 2. Nishi S, et al. The features of bone articular lesions in dialysis-related amyloidosis (DRA) and criteria for the clinical diagnosis of DRA. *Renal Replacement Therapy* 2019 5:10
 3. Hoshino J, et al. Significance of the decreased risk of dialysis-related amyloidosis now proven by results from Japanese nationwide surveys in 1998 and 2010. *Nephrol Dial Transplant*. 2016 ;31(4):595-602
 4. Hoshino J, et al. Carpal tunnel surgery as proxy for dialysis-related amyloidosis: results from the Japanese society for dialysis therapy. *Am J Nephrol*. 2014;39(5):449-58
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Junichi Hoshino (Toranomon Hospital, Tokyo, Japan):

In patients with dialysis-related amyloidosis (DRA), severely decreased physical function and bodily pain are two major complications, significantly worse than non-DRA patients on dialysis (Hoshino J, *Clin Exp Nephrol* 2017). Therefore, treatments for bodily pain and physical function are two essential parts for these DRA patients.

In this point of view, adequate use of NSAIDs, opioids, renal rehabilitation, and/or beta-2 microglobulin absorption column may be important topics that need to be discussed. In addition, use of purified dialysis water and biocompatible membranes may be also important topics, because these technologies are modifiable factors to reduce the risk of onset of the DRA (Cruz DN, Contrib Nephrol 2008; Yamamoto S, Bone 2009). According to the Japanese nationwide study, it was found that new onset of new carpal tunnel syndrome was delayed for approximately 5 years between 1998 and 2010. And it was also found that beta-2 microglobulin clearance over 80% may reduce risk of DRA (Hoshino J, Nephrol Dial Trnsplant 2016; Hoshino J, Am J Nephrol 2014).

Advances of dialysis technologies may also be topics that need to be discussed.

Hannah Beckwith (Imperial College London/NHS):

Fantastic scope , thank you ever so much for all your work putting this together.

My 2 main comments would be regarding cognitive impairment:

Breakout group 3 includes the question 'How much does cognitive dysfunction impact psychological symptoms?' I think this should be included in group 2 too: How much does cognitive dysfunction impact physical symptoms? For both of these, I would also consider adding a second part 'and are we adequately recognising these symptoms in patients with cognitive dysfunction'? Thanks ever so much.

Ana Elizabeth Figueiredo (Pontifícia Universidade Católica do Rio Grande do Sul):

Group 1 better instruments to assess fatigue in both dialysis modalities

Group 2, maybe have a specific access related pain; uremic breath

Group 4 question 1 item d- be more specific about nurses participation; question 3 item include mindfulness; palliative care.

Rachael Walker (Eastern Institute of Technology, NZ):

Might also be interesting to explore the symptom burden /psychological symptoms between modalities (home/satellite/PD/HHD/nocturnal).

Interesting to understand from a patient perspective -the effect of PROMS or symptom burden being collected but no interventions provided or symptoms not then followed up in clinical care.

Interventions to support patients and caregivers and the role of psychological burden in caregivers/ wider family (especially with home dialysis)

Vivek Jha (George Institute):

Thanks, this looks great and comprehensive. Great work by the steering committee.

Just a few additional points for consideration- Are there any differences between dialysis modalities in presentation and/or approach? What are the special needs of management of patients on home dialysis? The role of continuity of care in symptom management, including in pre-dialysis phase. Physician education in symptom management. Inclusion of symptom management as part of value-based healthcare model. Look forward to the Conference!

Masafumi Fukagawa (Tokai University School of Medicine):

The topic of this conference is very important because support for such symptoms is one of the largest parts of daily practice besides dialysis therapy. As for the contents, the topics to be discussed by breakout group2 is too many and seem to be better separated. Still, discussion on symptoms based on autonomic dysfunction, such as hypotension and abnormal sweating need to be included.

Paul Bennett (University of South Australia, Satellite Healthcare):

We have still a lot to learn in how best to approach PROMs so I applaud KDIGO addressing this. The scope is thorough. My only comment is that in all breakout groups care partners/consumers voices will be required. I expect this has been addressed through KDIGO inviting relevant consumers.

Martin Wilkie (Sheffield Teaching Hospitals):

Thanks - important work. I am interested in the following points

- 1) What does the recognised relationship between patient activation and symptoms among dialysis patients tell us - are there approaches that can enable symptom management through patient training. Interestingly in ShareHD we found no relationship between increasing dialysis related tasks that patients undertook in centre and symptoms or quality of life.
- 2) What are the concerns around the polypharmacy of symptom management - careful strategies are required to avoid the addition of medications with cumulative side effects (drowsiness, falls etc).
- 3) How should we differentiate symptoms that relate to co-morbidity from those related to ESKD - and how does that inform palliative approaches?
- 4) Should the term "palliative" be used much more widely to explain the focus on symptom management without being able to effect a cure.
- 5) How does personality type affect symptom reporting - does denial of symptoms adversely affect patient outcome - patients say "im fine" when they are clearly not.
- 6) If we solicit symptoms that we cannot effectively treat will we generate greater discomfort for our patients?

Kelly Lambert (University of Wollongong):

An important and much needed event.

1. Suggest membership to event is extended beyond Drs and nurses to include other health professionals such as pharmacists, dietitians, social workers, psychology etc.
2. Are those with stage 5 not undertaking dialysis part of this discussion ? The scope of work is not clear to me that the specific needs of this group are to be explicitly addressed as well.

Kunitoshi Iseki (Okinawa Heart and Renal Association, Okinawa, Japan):

Selection of dialysis membrane is important for long-term, more than 10 years, HD patients. Tsuruya K, Arima H, Iseki K, Hirakata K, The Kyushu Dialysis-Related Amyloidosis Study Group. Association of dialysis-related amyloidosis with lower quality of life in patients undergoing hemodialysis for more than 10 years: The Kyushu Dialysis-Related Amyloidosis Study. PLoS One 2021;16(8):e0256421

Rita Suri (McGill University):

1) re: the documentation and monitoring of PROMS: repeated questionnaires can be tiresome, and after they are filled out a couple of times for a given patient, have little yield as patients may stop answering accurately due to response fatigue. Optimal methods would minimize repeated questionnaires and use other more creative means to supplement questionnaires which should be given AT MOST, q6 months. 2) Patients should be included in this conference to determine which symptoms, and monitoring methods are most relevant to their needs.

Marlies Ostermann (Guy's & St Thomas' Hospital London):

The scope is very comprehensive. I have no additional suggestions.

Rukshana Shroff (Great Ormond Street Hospital):

Excellent outline and summary points for discussion in the breakout sessions!

Please also consider:

- children and young adults of school / college going age
- the impact of dietary modifications and fluid restrictions on symptomatology. Consider inviting a dietitian to this meeting (perhaps already established?)
- role of caregivers and the burden of care that is shared by the family as this may well impact on the individual's well-being
- consider comparing symptoms between groups who have received a pre-emptive transplant vs those who have been on dialysis before transplantation. Thank you!

Sunita Bavanandan (Ministry of Health Malaysia):

Wonder if an additional area to cover in scope of work might be 1. What is the role/impact of patient support groups in mitigating symptom-based complications?

Wolfgang Pommer (MVZ Windscheidstrasse):

Remarks to the Conference Paper: Controversies on symptom-based complications in dialysis

Ref. Breakout Group I:

Evaluation of patients' symptoms should generally put in a framework of bio-psycho-social model (i.e. ICF classification). This process should start with referral to renal care at least at stage 3/4 CKD. Different assessments are available to estimate current symptoms burden like physically impairment, psychological stress, social - (family, caregivers, helper etc) and financial resources, and patient's expectations. The process of evaluation should be integrated in advance-care planning (APC) to make a final decision how, when, and if to start renal replacement therapy. Home dialysis methods (hemo, PD, assisted PD) should be generally recommended to empower the patients and their families / caregivers to reduce symptom burden of dialysis treatment. Ideally, the renal team (physicians, nurses, social worker) should be responsible to initiate the process with regularly follow-up (every 12 months). The results of the evaluation should be integrated in prognostic aspects/scores (Obi-index, IVORY, New comorbidity Index [Can WC, 2013], REIN score) to establish a realistic offer to patients along with the APC process. No differences in the assessment process should be made to dialysis modality nor core or non-core symptoms. The health literacy of the individual person (and his or her resources) should be respected and should match to the view of health professionals in the decision making and therapeutic process.

Ref. Breakout Group II:

Recognition and reducing of symptom's burden are the cornerstone of renal treatment. Adequate dialysis modality, time, and delivery should focus on reducing symptoms, improving or stabilizing physical conditions. In general, physical exercise (on dialysis or home-based) should be offered in structured concept along with adequate nutrient intake. Some symptoms like fatigue, pruritus, loss of appetite, and immobility might improve by adequate dialysis management (for instance, extending dialysis time, nocturnal dialysis, daily home-dialysis, hemodiafiltration) while cognitive impairment and sexual dysfunction are almost resistant. Falls induced by inadequate volume depletion or multi-drug treatment (polypharmacy) must be avoided. Psychological distress and depression most likely benefit from behavior intervention managed by psychological experts. Peer-groups / self help or support groups (for instance for PD patients) might be helpful to manage disease-related problems by low-level intervention. Pharmacological treatment for restless legs, pain, and pruritus could be advised if improvement of dialysis procedures or non-pharmacological methods are failing. The best management of disaster scenarios is open to discussion. Advanced planning and a structured process of information, coordinating of support measurements, and precautionary supply management is mandatory in disaster areas.

Ref. Breakout Group III:

Depression, anxiety, frustration, and burn-out are of major impact for dialysis continuation, reducing or stopping treatment and "non"-adherence. Training and education of the renal team to increase mindfulness to these conditions are crucial. These aspects seem to be not regularly integrated into kidney medicine and programs should be designed to overcome this situation (including physicians and nurses). Severe depression should be managed by anti-depressive

medication. Concerns of side-effects derives from over-dosing or promoting renal failure [review by Bezerra de Menezes 2021]. Assessment of cognitive function should be regularly taken by standard testing (MOCA, MMST) to differentiate between dementia and depression. There is lack of evidence of benefits of anti-dementia medication in renal patients. But supporting measures (cognitive training?) and adequate interaction between the renal team and the affected individual (Validation therapy) is strongly recommended.

September 20th, 2021 Wolfgang Pommer, MD

Chandra Mauli Jha (AMMC):

Well detailed scope of work I must say. Comprehensive inclusion of all areas "symptom" as base of complication are covered. I shall be looking upon the outcome of the meeting.

Lillian Pryor (ANNA):

Just a few comments on Breakout Group 1:

- * Some barriers of assessing and documenting symptoms routinely are time and adequate EMR
- * Some are documenting, but not really assessing
- * Documentation is routine
- * No understanding (esp. with PCTs) of some of the changes/symptoms and education is needed
- * Would be hard to classify or categorize symptoms
- * Cultural and social groups need to be better understood, this plays a huge part in disclosure of symptoms
- * PROMs should be completed by the patient and maybe digitally would be better. And not just annually, perhaps quarterly? Hard to complete especially with the SW/Pt. ratio of 1:125
- * Home Dialysis and In-Center are very different when assessing symptoms and home pts. are reluctant to report symptoms.
- * Pain and depression sometimes go hand in hand, and some pts. may be led to believe that this is just a "normal" thing
- * Chronic symptoms become "routine".
- * Perhaps financial incentives could be offered
- * Patients want you to "know who I am before you start telling me what to do"

Manisha Jhamb (University of Pittsburgh):

The scope is very detailed and thoughtful. Some additional considerations. How do we facilitate care coordination with other specialists (pain, psychiatrist, etc.) to provide holistic care? How can we make best use of patients' time in the dialysis unit to address some of these issues (telemedicine with behavioral specialist, exercise during dialysis, etc.)?

Marques Shek Nam Ng (The Chinese University of Hong Kong):

I would like to appreciate the KDIGO for addressing this important aspect of dialysis care in the Controversies Conference on Symptom-Based Complications in Dialysis. I am Marques Ng, the Research Assistant Professor from The Chinese University of Hong Kong who specialises in symptom management in patients with stage 5 chronic kidney disease. I would like to share my comments on the conference' scope of work based on our research findings.

Group 1 / 1b: How can these barriers be addressed? Group 4 / 3: What changes need to be considered for training in nephrology to enable focus of care on well-being and symptoms? We conducted a study to examine the storied experiences of patients about accessing symptom management services. Consistent to our findings (1), healthcare systems and cultural settings are critical factors affecting the access to symptom management services. In addition, the attitudes and communication skills of healthcare professionals play an important role. Patients are more willing to discuss their needs with healthcare professionals who demonstrate professional care caring attitudes. Therefore, training on communication needs to be incorporated in nephrology curriculum. In addition, our findings suggest that a healthcare system that shares the value of person-centred care recognises and addresses patients' needs more effectively compared to that primarily focuses on the disease management. This value warrants wider application in dialysis care.

Group 1 / 2: What symptoms should kidney care teams focus on? Many existing PROMs include a range of common symptoms experienced by patients. In our longitudinal study (2), we found four clusters of symptoms (i.e., uremic, gastrointestinal, skin, and emotional) that demonstrate relatively stable relationships within the clusters. The identification of symptom clusters suggests a cluster-based approach to symptom assessment. Clinicians can extend their assessment by screening other symptoms associated with the core symptoms. This approach can enhance the efficiency of symptom assessment/detection in clinical settings.

Group 1 / 3: What is the best way to administer them? While PROMs may be administered in various formats, there is a limitation for these tools to capture the impact of symptoms in reality. In our qualitative study (3), patients described profound effects of their symptoms on physical and psychosocial function. These effects would influence their preferences and priorities of symptom management. Therefore, instead of using structured questionnaires, we suggest that a PROM that may capture day-to-day experience of symptoms (e.g., a symptom diary) may be used for a comprehensive assessment/detection of symptoms.

Group 2 / 2: Is there a listing of patient mitigating factors (cultural, social) to physical/psychological symptom detection to look out for? Many previous studies have identified factors associated with symptom burden in patients on dialysis (e.g., clinical parameters). However, in our mixed methods study (4), we found that some factors reported by patients are under-studied and warrant attention, such as employment status, lifestyle habits, and weather. Of note, our recent review suggests that financial status is significantly associated with physical and psychological symptoms (5). Clinicians need to consider social and contextual factors while screening patients for symptom management needs.

Group 3 / 1: Is there a threshold of frequency, intensity, or intrusiveness that should be met before considering treatment for commonly experienced psychological symptoms? We conducted an analysis to identify subgroups of patients with distinct symptom experiences and examine the differences in outcomes (6). Our findings show that, compared with patients who reported lower levels of distress associated with psychological symptoms (e.g., feeling sad,

feeling nervous), those with very high levels prone to report the lowest quality of life and more unscheduled clinic visits. Given these negative outcomes, we suggest that psychological symptoms should be treated as early as possible.

I sincerely wish that these comments would contribute to the discussions in the controversies conference. You are welcomed to contact me via email (marquesng@cuhk.edu.hk) for additional information. Thank you very much for your attention.

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Lloyd Vincent (Africa Healthcare Network, Rwanda, Tanzania and Kenya):

Symptom management in CKD populations that will potentially never have access to dialysis: The lack of access, affordability, and availability of dialysis care in the low-income countries (LIC), forces most advanced CKD patients into conservative therapy or palliation. These CKD numbers by far outweigh the gross global dialysis populations and merits consideration. Symptom management in these patients, are left to native medications, local general practitioners or may be the nurses, who are the only available healthcare providers. Often, any care is family driven. Simple, effective, and affordable CKD symptom management considering culture and local realities of the LIC, are a dire need. Research into the effectiveness of potentially generalizable CKD symptom management for particularly common, bothersome, and treatable symptoms, would be useful to the healthcare providers or families of LIC in many ways. This would also involve working with real world issues such as lack of care, affordability, poor compliance, or lack of available therapy. Local evidence and or innovative strategies to meet individual or generalized symptom management along with economics, would be helpful in the context. Studying the barriers to care of symptoms, and to overcome what is possible, would be useful for patients, providers, and the system. This would assist to identify issues within these advanced CKD patients amenable or likely to obtain the needed outcomes to the extent possible. Incorporation of effective research-based symptom management into CKD care within the LIC, to obtain simplified, implementable evidence-based guidelines, could potentially help at least for the start, at the larger regional centers. Research outcomes of the effectiveness of symptom management in these LIC, could potentially be generalizable and

needs research. Tying such a strategy with the implementation of Universal Health Care in some of the LICs, where it is either partial or in the process of total implementation, would need more research.

Betty Ann Wasylynuk (Alberta Kidney Care North):

Thank you for giving me the opportunity to review the KDIGO Scope of Work document. By the scope of coverage, it is obvious there was a great deal of consideration given. I find the scope of coverage comprehensive and clear. I do not have anything further to add or suggest. Thank you.

Abeera Mansur (Regional West Medical Center):

Please focus on a comparison of symptoms of patients on incremental dialysis vs conventional TIW HD vs daily dialysis.

Kazuhiko Tsuruya (Department of Nephrology, Nara Medical University):

I suggest the KDIGO Working Group to add the following sentences to the "Take Home Message": It is very important to promote awareness of diagnostic criteria of dialysis-related amyloidosis (DRA) developed by The Japanese Ministry of Health, Labor, and Welfare Research Group, because clinical diagnosis of DRA has been reported to be associated with decreased quality of life in patients with long-term hemodialysis, which might be inhibited by using beta2-microglobulin adsorption columns (Tsuruya K, et al. PLoS One, 2021).

Jeffrey Budden (Vifor Pharma):

To whom it may concern. I would be interested in a discussion surrounding two additional questions in the working group on physical symptoms (Group 2).

Potential Additional Question 1: What is impact of physical symptoms (e.g., pruritus/pain/fatigue, sleep etc) on psychological symptoms / social interactions (depression, anxiety/frustration) and clinical outcomes (missed/shortened dialysis, mortality, hospitalizations)?

Potential Additional Question 2: is there enough evidence to have consensus document / guidelines for treatment of any of the following physical symptoms: - Pruritus - Pain - Fatigue - Sleep - Restless leg - Other

Matthew Rivara (University of Washington):

This initial Scope of Work/Coverage is impressive and comprehensive. I have a few comments:

1) for Breakout Group 1, I think at least some focus should be on the lack of validated and concise PROMs as a barrier. A question for the group is who should be responsible for developing PROMs? Left to academic researchers via investigator initiated funding? Other routes?

2) For either Breakout Group 1 or 4, there should probably be at least some discussion of how symptom burden may differ by culture/geography, and that much of the literature on symptom burden has been from the US and UK only.

Clara Bohm (University of Manitoba):

Thank you for the opportunity to review the Scope of Work for the Symptom-Based Controversies Conference. I think that all key areas and topics are predominantly covered. One area that is missing is some discussion regarding which symptom-based PROMs should be used in which settings. Specifically, identifying those symptoms and settings for which there are validated or partially validated PROMS and highlighting those symptoms for which there are no validated PROMS is important. This is important for both clinical practice and research. We need to know that the measurement tools we use will be reliable and be able to measure clinically significant change in the clinical setting. In the research setting, we also need to know what work needs to be done in terms of priorities for symptom-based PROM validation.

Sabine van der Veer (University of Manchester, UK):

The scope document looks great and comprehensive. Only some minor comments to add:

- Breakout Group 1, topic 2: add as a 3rd bullet 'What is the current evidence-base on co-occurring symptoms (or, symptom clusters) in people on haemodialysis? How could symptom clusters guide or facilitate feasible and effective symptom assessment/management strategies?'
- Breakout Group 1, topic 3: add as a 5th bullet 'How could symptom self-assessments support patients with self-managing their condition and become more involved in their care? How could it guide agenda setting for clinic consultations and encourage shared decision-making?'
- Breakout Group 4: add a 6th topic on 'Secondary use of routinely collected symptom assessment data', with bullets underneath e.g. 'How could renal centres use their own symptom assessment data to guide local service improvements', and 'Should national audit schemes consider adding symptom burden as an indicator of quality of dialysis care?'