Global capacity for clinical research in nephrology: a survey by the International Society of Nephrology

Ikechi G. Okpechi[1,2], Mona Alrukhaimi[3], Gloria E. Ashuntantang[4], Ezequiel Bellorin-Font[5], Mohammed Benghanem Gharbi[6], Branko Braam[7], John Feehally[8], David C. Harris[9], Vivekanand Jha[10,11], Kailash Jindal[7], David W. Johnson[12,13,14,36], Kamyar Kalantar-Zadeh[15], Rumeyza Kazancioglu[16], Adeera Levin[17], Meaghan Lunney[18], Timothy Olusegun Olanrewaju[19], Vlado Perkovic[20], Jeffrey Perl[21,22], Harun Ur Rashid[23], Eric Rondeau[24,25], Babatunde Lawal Salako[26], Arian Samimi[7], Laura Sola[27], Irma Tchokhonelidze[28], Natasha Wiebe[7], Chih-Wei Yang[29], Feng Ye[7], Alexander Zemchenkov[30,31], Ming-hui Zhao[32,33,34,35] and Aminu K. Bello[7,36]

[1]Division of Nephrology and Hypertension, University of Cape Town, Cape Town, South Africa; [2]Kidney and Hypertension Research Unit, University of Cape Town, Cape Town, South Africa; [3]Department of Medicine, Dubai Medical College, Dubai, United Arab Emirates; [4]Faculty of Medicine and Biomedical Sciences, Yaounde General Hospital, University of Yaounde I, Yaounde, Cameroon; [5]Division of Nephrology and Kidney Transplantation, Hospital Universitario de Caracas, Universidad Central de Venezuela, Caracas, Venezuela; [6]Urinary Tract Diseases Department, Faculty of Medicine and Pharmacy of Casablanca, University Hassan II of Casablanca, Casablanca, Morocco; [7]Department of Medicine, Division of Nephrology, University of Alberta, Edmonton, Alberta, Canada; [8]Department of Infection, Inflammation and Immunity, University Hospitals of Leicester, University of Leicester, Leicester, UK; [9]Centre for Transplantation and Renal Research, Westmead Institute for Medical Research, University of Sydney, Sydney, New South Wales, Australia; [10]George Institute for Global Health India, New Delhi, India; [11]University of Oxford, Oxford, UK; [12]Centre for Kidney Disease Research, University of Queensland at Princess Alexandra Hospital, Brisbane, Australia; [13]Translational Research Institute, Brisbane, Australia; [14]Department of Nephrology, Metro South and Ipswich Nephrology and Transplant Services (MINTS), Princess Alexandra Hospital, Brisbane, Australia; [15]Division of Nephrology and Hypertension, University of California Irvine Medical Center, Orange, California, USA; [16]Division of Nephrology, Bezmialem Vakif University, Istanbul, Turkey; [17]Department of Medicine, Division of Nephrology, University of British Columbia, Vancouver, British Columbia, Canada; [18]Department of Community Health Sciences, University of Calgary, Calgary, Alberta, Canada; [19]Department of Medicine, College of Health Sciences, University of Ilorin, Ilorin, Nigeria; [20]The George Institute for Global Health, University of New South Wales Sydney, Sydney, New South Wales, Australia; [21]Division of Nephrology, St. Michael's Hospital and the Keenan Research Centre in the Li Ka Shing Knowledge Institute, St. Michael's Hospital, Toronto, Ontario, Canada; [22]Department of Medicine, Division of Nephrology, University of Toronto, Toronto, Ontario, Canada; [23]Department of Nephrology, Kidney Foundation Hospital and Research Institute, Dhaka, Bangladesh; [24]Intensive Care Nephrology and Transplantation Department, Hopital Tenon, Assistance Publique-Hopitaux de Paris, Paris, France; [25]Université Paris VI, Paris, France; [26]Department of Medicine, College of Medicine, University of Ibadan, Ibadan, Nigeria; [27]Division Epidemiologia, Direccion General de Salud–Ministerio Salud Publica, Montevideo, Uruguay; [28]Nephrology Development Clinical Center, Tbilisi State Medical University, Tbilisi, Georgia; [29]Kidney Research Center, Department of Nephrology, Chang Gung Memorial Hospital, Chang Gung University College of Medicine, Taoyuan, Taiwan; [30]Department of Internal Disease and Nephrology, North-Western State Medical University named after I.I. Mechnikov, Saint Petersberg, Russia; [31]Department of Nephrology and Dialysis, Pavlov First St. Petersburg State Medical University, St. Petersburg, Russia; [32]Renal Division, Department of Medicine, Peking University First Hospital, Beijing, China; [33]Key Lab of Renal Disease, Ministry of Health of China, Beijing, China; [34]Key Lab of Chronic Kidney Disease Prevention and Treatment, Ministry of Education of China, Beijing, China; and [35]Peking-Tsinghua Center for Life Sciences, Beijing, China

Due to the worldwide rising prevalence of chronic kidney disease (CKD), there is a need to develop strategies through well-designed clinical studies to guide decision making and improve delivery of care to CKD patients. A cross-sectional survey was conducted based on the International Society of Nephrology Global Kidney Health Atlas data. For this study, the survey assessed the capacity of various countries and world regions in participating in and conducting kidney research. Availability of national funding for clinical trials was low (27%, $n = 31$), with the lowest figures obtained from Africa (7%, $n = 2$) and South Asia (0%), whereas high-income countries in North America and Europe had the highest participation in clinical trials. Overall, formal training to conduct clinical trials was inadequate for physicians (46%, $n = 53$) and even lower for nonphysicians, research assistants, and associates in clinical trials (34%, $n = 39$). There was also diminished availability of workforce and funding to conduct observational cohort studies in nephrology, and participation in highly specialized transplant trials was low in many regions. Overall, the availability of infrastructure (bio-banking and facilities for storage of clinical trial medications) was low,

Correspondence: *A.K. Bello, Division of Nephrology and Immunology, Department of Medicine, University of Alberta, 11-107 Clinical Sciences Building, 8440 112 Street NW, Edmonton, Alberta T6B 2B7, Canada. E-mail: aminu1@ualberta.ca*

[36]Co-Chairs, Global Kidney Health Atlas Project.

and it was lowest in low-income and lower-middle–income countries. Ethics approval for study conduct was mandatory in 91% ($n = 106$) of countries and regions, and 62% ($n = 66$) were reported to have institutional committees. Challenges with obtaining timely approval for a study were reported in 53% ($n = 61$) of regions but the challenges were similar across these regions. A potential limitation is the possibility of over-reporting or under-reporting due to social desirability bias. This study highlights some of the major challenges for participating in and conducting kidney research and offers suggestions for improving global kidney research.

Kidney International Supplements (2018) **8,** 82–89; https://doi.org/10.1016/j.kisu.2017.10.012

Copyright © 2017, International Society of Nephrology. Published by Elsevier Inc. All rights reserved.

Chronic kidney disease (CKD) is a global public health problem affecting as many as 10% of all populations. Projections of CKD prevalence show that the problem will continue to increase.[1–3] Among the several detrimental effects of CKD are the risk of progression to end-stage renal disease (ESRD), increased mortality risk due to cardiovascular disease and infections,[4] reduced quality of life,[5] and high cost of care.[6] Additional strategies including screening, diagnostics, and therapies through well-designed clinical research are needed to guide decision making and improve delivery of care.[7] Although the absolute number of publications in nephrology is increasing,[8,9] the number and quality of randomized clinical trials (RCTs) in nephrology are unable to match the needs of a rising disease burden.[10–13] One study assessing nephrology RCT quality and quantity highlighted major differences between nephrology and other specialties.[7] Increasing the output of high-quality studies in nephrology is therefore required to characterize the existing capacity, identify gaps, and provide opportunities for improving the care of CKD patients and bridging the gap between access to CKD care in low- versus high-income countries.[3] Information obtained from such studies could be utilized for policy making and advocacy to improve CKD care, especially in low- and lower-middle–income countries. The aim of this study, a part of the International Society (ISN) Global Kidney Health Atlas (GKHA) survey, was to conduct an on-the-spot assessment of capacity to conduct clinical research focusing on available infrastructure, funding, and workforce for research and the role of regulatory bodies.

Results

In total, 125 of 130 United Nations member states that received an invitation participated in the survey. Of these, 93% ($n = 116$) responded to the questions relevant to participating in and conducting kidney research. The affiliations of survey respondents were nephrologists (85%), non-nephrology physicians (3%), health care administrators or policy makers (6%), and others affiliated with kidney disease patient advocacy (6%).[14]

Capacity for clinical trial participation. Overall, there was low availability of institutionalized granting agencies. For instance, a national agency for funding of clinical trials was present in only (27%, $n = 31$) of countries, with the lowest numbers reported for Africa (7%, $n = 2$). There was a linear increase in capacity to participate in clinical trials by trial category: phase 1 (28%, $n = 33$), phase 2 (40%, $n = 46$), phase 3 (53%, $n = 61$), and phase 4 (53%, $n = 62$). In all the world regions, participation in clinical trials increased with increasing phase of the trial; only Africa had less than 50% participation in all phases of clinical trials. Also, only North America had 100% capacity to participate in all phases (1–4) of clinical trials, while Western Europe had 100% participation in phase 2 to phase 4 clinical trials (Table 1). When participation in clinical trials was assessed by income categories, low-income countries reported 18% ($n = 3$) and 6% ($n = 1$) capacity to participate in phase 1 and 2 trials, respectively, and no capacity to participate in phase 3 to phase 4 trials. By income category, participation in health services trials was found to be highest for low-income countries (76%, $n = 13$), but was observed to be lowest for newly independent states (NIS) and Russia, South Asia, and Eastern and Central European regions (Table 1).

Availability of formal training for physicians and nonphysicians in conducting clinical trials. Only 46% ($n = 53$) of countries had an established formal training program for physicians in conducting clinical trials. Formal training for physicians was unavailable in South Asia (0%) and was very low in Africa (27%, $n = 8$) and the Middle East (15%, $n = 2$). When the availability of formal training for physicians was ranked per income category, availability increased with increasing income level: low income (24%, $n = 4$), lower-middle income (32%, $n = 10$), upper-middle income (47%, $n = 14$), and high income (66%, $n = 25$) (Table 1). Availability of training for non-physicians in conducting clinical trials was slightly but generally lower than that for physicians and was also comparatively lower when countries were ranked by income level.

Availability of bio-banking facilities. Overall, 45% ($n = 52$) of countries indicated that bio-banking facilities were available in their setting, with high-income countries reporting the highest number of countries with bio-banking facilities (79%, $n = 30$). Both countries in the North American region had facilities for bio-banking, and most Western European countries (89%, $n = 8$) reported availability of bio-banking facilities. Only 23% ($n = 7$), 31% ($n = 5$), 33% ($n = 2$), and 38% ($n = 5$) of countries in Africa, Latin America and the Caribbean, NIS and Russia, and the Middle East, respectively, had facilities for bio-banking (Table 1).

Conducting, funding, and participating in observational cohort studies. Table 2 summarizes the responses obtained to questions on availability of trained workforce, resources, and involvement in observational studies in nondialysis, dialysis, and renal transplant patients. Most countries (85%, $n = 99$) had personnel for participating in and conducting

Table 1 | Availability of funding, participation in clinical trials, and formal training of workforce for conducting clinical trials

World region	National agency for funding clinical trials	No. of responding countries	Phase 1	Phase 2	Phase 3	Phase 4	Health service delivery trials	No trial	No. of responding countries	Has formal training for physicians in conducting clinical trial	No. of responding countries	If yes, is it mandatory?	No. of responding countries	Has formal training for nonphysicians/ research assistants and associates in clinical trial	No. of responding countries	If yes, is it mandatory?	No. of responding countries	Has bio-banking facilities	No. of responding countries
Overall	31 (27)	116	33 (28)	46 (40)	61 (53)	62 (53)	67 (58)	17 (15)	116	53 (46)	116	21 (40)	53	39 (34)	116	23 (61)	38	52 (45)	116
ISN region																			
Africa	2 (7)	30	4 (13)	3 (10)	5 (17)	4 (13)	18 (60)	7 (23)	30	8 (27)	30	0 (0)	30	4 (13)	30	1 (25)	30	7 (23)	30
Eastern & Central Europe	3 (19)	16	3 (19)	10 (63)	14 (88)	13 (81)	4 (25)	2 (13)	16	8 (50)	16	5 (63)	16	6 (38)	16	4 (67)	16	11 (69)	16
Latin America & the Caribbean	2 (13)	16	3 (19)	3 (19)	9 (56)	10 (63)	13 (81)	0 (0)	16	11 (69)	16	5 (45)	16	6 (38)	16	5 (83)	16	5 (31)	16
Middle East	4 (31)	13	1 (8)	3 (23)	4 (31)	5 (38)	9 (69)	4 (31)	13	2 (15)	13	1 (50)	13	4 (31)	13	0 (0)	13	5 (38)	13
NIS & Russia	2 (33)	6	1 (17)	2 (33)	4 (67)	4 (67)	0 (0)	0 (0)	6	3 (50)	6	2 (67)	6	2 (33)	6	2 (100)	6	2 (33)	6
North America	2 (100)	2	2 (100)	2 (100)	2 (100)	2 (100)	2 (100)	0 (0)	2	2 (100)	2	0 (0)	2	2 (100)	2	1 (50)	2	2 (100)	2
North & East Asia	3 (50)	6	4 (67)	5 (83)	5 (83)	5 (83)	3 (50)	1 (17)	6	5 (83)	6	2 (40)	6	3 (50)	6	3 (100)	6	5 (83)	6
Oceania & Southeast Asia	8 (62)	13	5 (38)	6 (46)	7 (54)	8 (62)	10 (77)	2 (15)	13	8 (62)	13	2 (25)	13	5 (38)	13	2 (40)	13	7 (54)	13
South Asia	0 (0)	5	3 (60)	3 (60)	2 (40)	2 (40)	0 (0)	1 (20)	5	0 (0)	5	0 (0)	5	1 (20)	5	0 (0)	0	0 (0)	5
Western Europe	5 (56)	9	7 (78)	9 (100)	9 (100)	9 (100)	8 (89)	0 (0)	9	6 (67)	9	4 (67)	9	6 (67)	9	5 (83)	9	8 (89)	9
World Bank income group																			
Low income	2 (12)	17	3 (18)	1 (6)	0 (0)	0 (0)	13 (76)	1 (6)	17	4 (24)	17	0 (0)	4	2 (12)	17	0 (0)	2	1 (6)	17
Lower-middle income	3 (10)	31	5 (16)	7 (23)	9 (29)	9 (29)	12 (39)	10 (32)	31	10 (32)	31	4 (40)	10	7 (23)	31	4 (67)	6	7 (23)	31
Upper-middle income	9 (30)	30	7 (23)	10 (33)	19 (63)	20 (67)	17 (57)	5 (17)	30	14 (47)	30	7 (50)	14	10 (33)	30	6 (60)	10	14 (47)	30
High income	17 (45)	38	18 (47)	28 (74)	33 (87)	33 (87)	25 (66)	1 (3)	38	25 (66)	38	10 (40)	25	20 (53)	38	13 (65)	20	30 (79)	38

NIS, newly independent states.
Numbers in parentheses represent percentages.

Table 2 | Capacity to participate and conduct observational cohort studies

World region	Has capacity (trained workforce) to conduct observational cohort studies	No. of responding countries	Has resources (funding) to conduct observational cohort studies	No. of responding countries	Involved in any observational cohort studies in CKD	No. of responding countries	If yes, where?			
							Non-dialysis CKD	Dialysis populations	Transplant populations	No. of responding countries
Overall	99 (85)	116	56 (48)	116	53 (46)	116	29 (56)	27 (52)	11 (21)	52
ISN region										
Africa	25 (83)	30	11 (37)	30	8 (27)	30	6 (75)	4 (50)	0 (0)	8
Eastern & Central Europe	12 (75)	16	7 (44)	16	8 (50)	16	3 (38)	3 (38)	2 (25)	8
Latin America & the Caribbean	15 (94)	16	3 (19)	16	6 (38)	16	4 (67)	3 (50)	1 (17)	6
Middle East	10 (77)	13	7 (54)	13	5 (38)	13	1 (20)	5 (100)	0 (0)	5
NIS & Russia	4 (67)	6	1 (17)	6	2 (33)	6	0 (0)	1 (50)	1 (50)	2
North America	2 (100)	2	2 (100)	2	2 (100)	2	2 (100)	0 (0)	1 (50)	2
North & East Asia	6 (100)	6	5 (83)	6	6 (100)	6	6 (100)	3 (50)	1 (17)	6
Oceania & Southeast Asia	11 (85)	13	7 (54)	13	7 (54)	13	2 (29)	6 (86)	3 (43)	7
South Asia	5 (100)	5	4 (80)	5	2 (40)	5	1 (50)	0 (0)	1 (50)	2
Western Europe	9 (100)	9	9 (100)	9	7 (78)	9	4 (67)	2 (33)	1 (17)	6
World Bank income group										
Low income	13 (76)	17	4 (24)	17	3 (18)	17	3 (75)	1 (25)	1 (25)	4
Lower-middle income	25 (81)	31	12 (39)	31	10 (31)	31	5 (63)	4 (50)	1 (13)	8
Upper-middle income	25 (83)	30	11 (37)	30	10 (34)	30	7 (64)	7 (64)	1 (9)	11
High income	36 (95)	38	29 (76)	38	30 (79)	38	14 (48)	15 (52)	8 (28)	29

CKD, chronic kidney disease; NIS, newly independent states.
Numbers in parentheses represent percentages.

observational cohort studies, though this was higher in high-income countries than in low-income countries (95%, n = 36 vs. 76%, $n = 13$). Only four regions (North America, North and East Asia, South Asia, and Western Europe) reported 100% availability of trained workforce to conduct observational studies. For all countries and regions, the availability of funding to conduct observational cohort studies did not match workforce availability, as 48% ($n = 56$) of all countries had available funding to conduct observational cohort studies (vs. 85% available workforce). The NIS and Russia and the Latin American and Caribbean regions had the lowest availability of funding for such studies: 17% (n = 1) and 19% (n = 3), respectively, whereas all countries in North America (100%) and Western Europe (100%) reported available funding for observational cohort studies. Involvement in any observational CKD cohort studies closely mirrored availability of funding to participate in such studies. Overall, of those reporting involvement in observational studies, most were involved in nondialysis CKD studies (56%, n = 29) with 21% (n = 11) reporting involvement in transplant-related studies (Table 2). Only 27% (n = 8) of countries from Africa were involved in observational studies, with a slightly higher percentage of countries involved from South Asia (40%, n = 2), NIS and Russia (33%, n = 2), the Middle East (38%, n = 5), and Latin America and the Caribbean (38%, n = 6). No countries in Africa and the Middle East are involved in observational cohort studies in the transplant population.

Capacity for obtaining ethical and/or regulatory approval and storage of clinical trial medications. Table 3 provides a summary of responses obtained for the questions on the availability and type of ethics and drug regulatory authorities (regulatory bodies), challenges with obtaining approval from such committees, and proportion of sites with capacity for storage of clinical trial medications in different countries. It was observed that most countries (91%, $n = 106$) require mandatory ethical clearance before studies can be performed. However, only high-income countries reported a 100% requirement for ethical clearance to carry out studies; the value for this was 82% (n = 14), 84% (n = 26), and 93% (n = 28), respectively, for low-income, lower-middle–income, and upper-middle–income countries. Ethics approval was mostly obtained from institutional review committees, with few countries reporting regional committees. The challenges encountered in getting timely regulatory approval appeared to be similar in most countries. Overall, 20% (n = 23) of countries reported that challenges were often present, and 25% ($n = 29$) reported that challenges were occasionally present.

In 52% (n = 20) of high-income countries, "all sites" or "most sites" had capacity for storing clinical trial medications, compared with only 6% (n = 1) in low-income countries, 23% (n = 7) in lower-middle–income countries, and 30% (n = 9) in upper-middle–income countries (Table 3). In Africa (13%, $n = 4$) and the Middle East (8%, $n = 1$), there was a severe lack of capacity for storing clinical trial medications. Low-income countries also reported a higher percentage of sites (12%, $n = 2$) with zero capacity for

Table 3 | Availability, type of regulatory body, and capacity to store clinical trial medications

World region	Ethics approval is mandatory	No. of responding countries	If yes, the ethics approval is …				No. of responding countries	Challenges in getting timely regulatory approvals			No. of responding countries	Academic centers that coordinate and monitor sites involved in renal clinical trials	No. of responding countries	Proportion of sites with the capacity for storing clinical trial medications					No. of responding countries
			Institutional	Regional	National	Other		Often	Sometimes	Occasionally				All	Most	Some	Few	None	Unknown	
Overall	106 (91)	116	66 (62)	13 (12)	41 (39)	13 (12)	106	23 (20)	38 (33)	29 (25)	116	55 (47)	116	7 (6)	30 (26)	32 (28)	22 (19)	5 (4)	20 (17)	116
ISN region																				
Africa	26 (87)	30	11 (42)	4 (15)	12 (46)	3 (12)	26	5 (17)	9 (30)	7 (23)	30	8 (27)	30	0 (0)	5 (17)	7 (23)	9 (30)	4 (13)	5 (17)	30
Eastern & Central Europe	16 (100)	16	8 (50)	1 (6)	6 (38)	2 (13)	16	2 (13)	7 (44)	1 (6)	16	10 (63)	16	4 (25)	6 (38)	3 (19)	2 (13)	0 (0)	1 (6)	16
Latin America & the Caribbean	15 (94)	16	12 (80)	1 (7)	5 (33)	3 (20)	15	4 (25)	1 (6)	6 (38)	16	6 (38)	16	0 (0)	4 (25)	5 (31)	0 (0)	0 (0)	7 (44)	16
Middle East	10 (77)	13	7 (70)	2 (20)	4 (40)	0 (0)	10	4 (31)	5 (38)	4 (31)	13	5 (38)	13	0 (0)	0 (0)	6 (46)	5 (38)	1 (8)	1 (8)	13
NIS & Russia	6 (100)	6	3 (50)	0 (0)	3 (50)	1 (17)	6	2 (33)	3 (50)	0 (0)	6	2 (33)	6	0 (0)	2 (33)	1 (17)	0 (0)	0 (0)	3 (50)	6
North America	2 (100)	2	2 (100)	1 (50)	0 (0)	0 (0)	2	0 (0)	0 (0)	2 (100)	2	2 (100)	2	0 (0)	2 (100)	0 (0)	0 (0)	0 (0)	0 (0)	2
North & East Asia	6 (100)	6	6 (100)	1 (17)	1 (17)	0 (0)	6	1 (17)	2 (33)	2 (33)	6	6 (100)	6	0 (0)	3 (50)	1 (17)	2 (33)	0 (0)	0 (0)	6
Oceania & Southeast Asia	12 (92)	13	8 (67)	0 (0)	6 (50)	2 (17)	12	1 (8)	6 (46)	4 (31)	13	7 (54)	13	0 (0)	4 (31)	4 (31)	4 (31)	0 (0)	1 (8)	13
South Asia	4 (80)	5	4 (100)	0 (0)	2 (50)	0 (0)	4	2 (40)	3 (60)	0 (0)	5	3 (60)	5	0 (0)	1 (20)	3 (60)	0 (0)	0 (0)	1 (20)	5
Western Europe	9 (100)	9	5 (56)	3 (33)	2 (22)	2 (22)	9	2 (22)	2 (22)	3 (33)	9	6 (67)	9	3 (33)	3 (33)	2 (22)	0 (0)	0 (0)	1 (11)	9
World Bank income group																				
Low income	14 (82)	17	5 (36)	1 (7)	8 (57)	2 (14)	14	2 (12)	5 (29)	3 (18)	17	2 (12)	17	0 (0)	1 (6)	3 (18)	5 (29)	2 (12)	6 (35)	17
Lower-middle income	26 (84)	31	17 (65)	2 (8)	10 (38)	2 (8)	26	7 (23)	11 (35)	6 (19)	31	10 (32)	31	0 (0)	7 (23)	8 (26)	7 (23)	2 (6)	7 (23)	31
Upper-middle income	28 (93)	30	18 (64)	2 (7)	13 (46)	6 (21)	28	7 (23)	12 (40)	6 (20)	30	19 (63)	30	0 (0)	9 (30)	11 (37)	5 (17)	0 (0)	5 (17)	30
High income	38 (100)	38	26 (68)	8 (21)	10 (26)	3 (8)	38	7 (18)	10 (26)	14 (37)	38	24 (63)	38	7 (18)	13 (34)	10 (26)	5 (13)	1 (3)	2 (5)	38

NIS, newly independent states.
The numbers in parentheses represent percentages.

storage of clinical trial medications, compared with 3% (n = 1) for high-income countries.

Discussion

Biomedical research capacity and productivity are known to vary widely; however, high-income countries in North America and Europe are regarded as leaders in biomedical research,[15–17] a reflection of their high gross domestic product, health care and research spending, and access to good quality research infrastructure. This GKHA survey is the first attempt, and the largest effort to date, by the international nephrology community to evaluate the readiness and capacity to conduct kidney research in all parts of the world. The results of this study have documented large gaps and differences across world regions to participate in and/or conduct kidney disease–related research. Specifically, this study highlights weaknesses in funding and a low capacity to take part in clinical trials for low-income and lower-middle–income countries (LMIC) (Supplementary Figure S1).[18] In some ISN regions, there was inadequate or complete absence of formal training of physicians to conduct clinical trials, lack of infrastructure (such as bio-banking facilities and facilities for the storage of trial medications) required to conduct studies, inadequate workforce, and large delays in obtaining regulatory approvals from regulatory authorities for conducting research.

There is evidence that economic indicators such as gross domestic product correlate with scientific productivity.[17,19–21] In India and Southeast Asia, poor funding from public and private sources was identified as a serious limitation to fostering a research culture, reduced interest in research, and a shift of focus to competing challenges such as provision of clinical care.[19] Lack of funding was suggested to have led to impoverished academic and laboratory facilities, worsened by weak institutional interest in encouraging research that meets international standards.[19] The same challenges regarding funding of universities and research institutions could also be responsible for low outputs in Africa and other LMIC regions. Using publication quality and outputs as a metric of research capacity, Winnik *et al.*[17] studied how the dissemination of cardiovascular research may be influenced by the wealth of a nation. After adjusting for markers of research quality and infrastructure, per capita gross domestic product remained a strong predictor for acceptance at congress (adjusted odds ratio [OR] for every 10,000 USD increase in per capita GDP, 1.44; 95% confidence interval [CI], 1.15–1.80), full-text publication within 5 years (adjusted OR, 1.49; 95% CI, 1.17 to 1.90), and high citation frequency (adjusted OR, 2.30; 95% CI 1.31–4.04). They concluded that investigators in less wealthy countries face challenges to disseminate their research, even after accounting for potential differences in the quality of their work and research infrastructure.[17]

Further, this study indirectly gauged workforce availability for kidney research by assessing the availability of training for physicians and nonphysicians in conducting clinical trials. Although clinical trials involve patient care, the roles and responsibilities of members of the study team are unique and

may differ from the usual day-to-day responsibilities in routine patient care. Such duties include awareness of and adherence to good clinical practice, data collection, sample collection and storage, drug storage, and accountability and reporting of events. Thus, in the face of an already low overall workforce for patient care, the workforce available for research may be even lower because adequate training has not been received.

Participation in clinical trials and observational cohort studies of kidney disease was lowest for countries categorized as low-income. This is not surprising given that many of these countries already have challenges with availability of physical infrastructure and organizational structure for health service provision.[22–24] For instance, the availability of bio-banking facilities was found to be lowest in South Asia and Africa, while capacity for storing clinical trial medications was lowest for Africa and the Middle East. Although several countries reported availability of ethics and/or regulatory committees, there were significant hurdles to timely obtainment of regulatory approvals. This can significantly hinder participation in studies. Figure 1 shows data from www.clinicaltrials.gov[18] on participation in CKD trials around the world, with low participation in developing world regions.

There are no generic solutions to the identified challenges and barriers to research. However, concerted effort is required to address these problems. Over the years, the ISN has developed a set of core programs designed to enable nephrologists, especially in low-income countries to access highly valued education and training grants.[25] Understandably, due to the need to improve clinical training and kidney care delivery in developing countries, 5 of the 6 core programs are primarily focused on clinical training (Fellowship Program, Sister Renal Centres Program, Sister Transplant Centre Program, CME Program, and Educational Ambassadors Program); the other program is focused on research support (Clinical Research Program [CRP]) and provides grants for research projects in LMIC settings (http://www.theisn.org/programs). However, it is expected that individual and institutional beneficiaries of the programs that focus on clinical training will also develop their research skills as a byproduct. The ISN has provided significant support to researchers from LMICs for projects in their countries.[25] The ISN-CRP has recently started a training course for manuscript and grant writing in LMICs, and offering other types of research training, especially on study design or clinical trials, would be helpful. To maximize the scale and quality of funded projects, opportunities for partnership funding should be sought. The ISN-CRP also has a broader educational role, for example through webinars and other educational material via the online ISN Academy. Several of these have focused on research capacity and methodology. Other ISN programs such as the ISN-ACT (Advancing Clinical Trials) (http://www.theisn.org/research/isn-act) and iNET-CKD (the International Network of Chronic Kidney Disease cohort studies, https://www.theisn.org/research/inet-ckd) aim to increase the number of international high-quality clinical trials and cohort studies in nephrology, provide networking opportunities, and grow the capacity of the global nephrology community, particularly in countries and regions where clinical trials participation is low or does not take place.

A potential limitation of this study is the possibility of over- or under-reporting due to social desirability bias. However, responses were checked for validity against the response provided by regional leaders to reduce the risk of such biases.

In conclusion, this study, which is the first global effort to assess capacity for kidney research in all countries and world regions, has identified gaps that limit research capacity across the world including inadequate funding, limited workforce, low level of available infrastructure, and issues related to delays

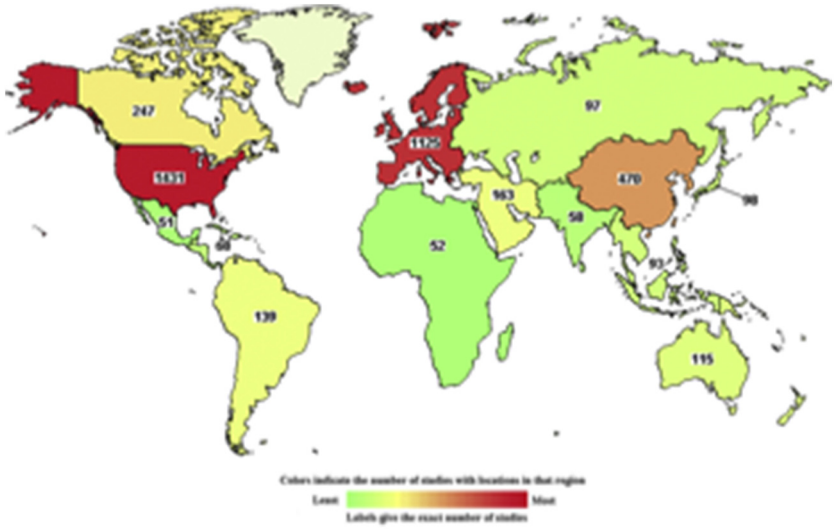

Figure 1 | Worldwide distribution of chronic kidney disease (CKD) studies registered at ClinicalTrials.gov. There is a huge disparity in distribution of studies between high- and low-income countries and regions.[18]

in getting regulatory approval to conduct research. There is a need to coordinate efforts, leveraging already established programs to improve research capacity across the world.

Methods

This study was based on data obtained from all the regions of the world through an online survey carried out by the ISN in 2016. The detailed methodology utilized in the GKHA project has been described in detail elsewhere.[14,26] In brief, the GKHA project was a multinational, cross-sectional survey conducted by the ISN to assess current capacity for kidney care across the world. The survey was conducted in states and territories recognized by the United Nations, focusing on the 130 countries represented by the ISN's 10 regional boards (Africa, East and Central Europe, Latin America, Middle East, North America, North and East Asia, Oceania and Southeast Asia, NIS and Russia, South Asia, and Western Europe). For the purpose of analysis, countries were grouped by 2014 World Bank country classification as low-, lower-middle–, upper-middle–, and high-income nations[27] and ISN region.[28]

The GKHA survey covered 2 broad sections: (i) assessment of capacity and response to CKD and acute kidney injury premised on 6 health system building blocks and (ii) response of the nephrology community to strategies and policy framework formulation as well as capacity for research and development. This study focused specifically on capacity for research and development. The questions were aimed to determine: (i) available funding to conduct clinical trials; (ii) participation in kidney disease clinical trials; (iii) formal training of staff (physicians and nonphysicians) to conduct clinical trials; (iv) availability of facilities for biobanking; (v) availability of workforce and funding for observational cohort studies in kidney disease; (vi) availability, accessibility, and challenges in getting timely regulatory approvals for studies; and (vii) capacity for storing clinical trial medications. The data are presented as frequencies and percentages.

DISCLOSURE

Publication of this article was supported by the International Society of Nephrology. The ISN holds all copyrights on the data obtained through this study.

EB-F declared seeing private patients on a part-time basis. BB declared receiving consulting fees from Otsuka and receives current grant support from Amgen. MBG declared receiving lecture fees from AMGEN, B Braun, Leo Pharma, Novartis, Novo-Nordisk, Promopharm, Roche, Sanofi, Servier, Sophadial, and Sothema. DCH declared receiving lecture fees from Roche Myanmar and Otsuka. VJ declared receiving consulting fees from Baxter and Medtronic and current grant support from the Department of Biotechnology, Government of India, Baxter, and GlaxoSmithKline. DWJ declared receiving consulting fees from AstraZeneca, lecture fees from Baxter Healthcare and Fresenius Medical Care, and support from Baxter Extramural and Clinical Evidence Council grants. KK-Z declared receiving past and future consulting and lecture fees from Abbott, Abbvie, Alexion, Amgen, AstraZeneca, Aveo, Chugai, DaVita, Fresenius, Genentech, Haymarket Media, Hospira, Kabi, Keryx, Novartis, Pfizer, Relypsa, Resverlogix, Sandoz, Sanofi, Shire, Vifor, and UpToDate; future consulting and lecture fees from ZS-Pharma; current grant support from National Institutes of Health; and expert witness engagement for GranuFlo. RK declared receiving lecture fees from Baxter Healthcare. JP declared receiving consulting fees from Fresenius Medical Care, Baxter Healthcare, Otsuka, Boehringer Ingelheim; lecture fees from Baxter Healthcare; and current grant support from Canadian Institutes of Health Research and Baxter Healthcare. All the other authors declared no competing interests.

ACKNOWLEDGMENTS

We thank Drs. Marcello Tonelli and Valerie Luyckx for their contributions to the project and manuscript. We thank Sandrine Damster, research project manager at the International Society of Nephrology (ISN), and Alberta Kidney Disease Network (AKDN) staff (Ghennete Houston, Sue Szigety, and Sophanny Tiv) for their support with the organization and conduct of the survey and project management. We thank the ISN staff (Louise Fox and Luca Segantini) for their support. We thank the executive committee of the ISN, the ISN regional leadership, and the leaders of the ISN Affiliate Societies at regional and country levels for their support toward the success of this initiative.

SUPPLEMENTARY MATERIAL

Figure S1. Worldwide distribution of chronic kidney disease (CKD) studies registered at ClinicalTrials.gov according to study phase. (A) Phase 1. (B) Phase 2. (C) Phase 3. (D) Phase 4.[18]
Supplementary material is linked to the online version of the paper at www.kisupplements.org.

REFERENCES

1. Mills KT, Xu Y, Zhang W, et al. A systematic analysis of worldwide population-based data on the global burden of chronic kidney disease in 2010. *Kidney Int*. 2015;88:950–957.
2. Levin A, Tonelli M, Bonventre J, et al. Global kidney health 2017 and beyond: a roadmap for closing gaps in care, research, and policy. *Lancet*. 2017;390:1888–1917.
3. Liyanage T, Ninomiya T, Jha V, et al. Worldwide access to treatment for end-stage kidney disease: a systematic review. *Lancet*. 2015;385:1975–1982.
4. Matsushita K, van der Velde M, Astor BC, et al. Association of estimated glomerular filtration rate and albuminuria with all-cause and cardiovascular mortality in general population cohorts: a collaborative meta-analysis. *Lancet*. 2010;375:2073–2081.
5. Lee YJ, Kim MS, Cho S, Kim SR. Association of depression and anxiety with reduced quality of life in patients with predialysis chronic kidney disease. *Int J Clin Pract*. 2013;67:363–368.
6. Collins AJ, Foley RN, Herzog C, et al. US Renal Data System 2012 Annual Data Report. *Am J Kidney Dis*. 2013;61:A7. e1–e476.
7. Inrig JK, Califf RM, Tasneem A, et al. The landscape of clinical trials in nephrology: a systematic review of Clinicaltrials.gov. *Am J Kidney Dis*. 2014;63:771–780.
8. Li J, Gao XH, Bian Q, et al. Comparative study of scientific publications in urology and nephrology journals originating from USA, China and Japan (2001-2010). *PLoS One*. 2012;7:e42200.
9. Xu J, Mao ZG, Kong M, et al. Scientific publications in nephrology and urology journals from Chinese authors in East Asia: a 10-year survey of the literature. *PLoS One*. 2011;6:e14781.
10. Samuels JA, Molony DA. Randomized controlled trials in nephrology: state of the evidence and critiquing the evidence. *Adv Chronic Kidney Dis*. 2012;19:40–46.
11. Strippoli GF, Craig JC, Schena FP. The number, quality, and coverage of randomized controlled trials in nephrology. *J Am Soc Nephrol*. 2004;15:411–419.
12. Deo A, Schmid CH, Earley A, et al. Loss to analysis in randomized controlled trials in CKD. *Am J Kidney Dis*. 2011;58:349–355.
13. Palmer SC, Sciancalepore M, Strippoli GF. Trial quality in nephrology: how are we measuring up? *Am J Kidney Dis*. 2011;58:335–337.
14. Bello AK, Levin A, Tonelli M, et al. Assessment of global kidney health care status. *JAMA*. 2017;317:1864–1881.

15. Uthman OA, Uthman MB. Geography of Africa biomedical publications: an analysis of 1996-2005 PubMed papers. *Int J Health Geogr*. 2007;6:46.
16. Benzer A, Pomaroli A, Hauffe H, Schmutzhard E. Geographical analysis of medical publications in 1990. *Lancet*. 1993;341:247.
17. Winnik S, Speer T, Raptis DA, et al. The wealth of nations and the dissemination of cardiovascular research. *Int J Cardiol*. 2013;169:190–195.
18. Clinicaltrials.gov. 2017; Available at: https://www.clinicaltrials.gov/ct2/results/map?term=Chronic+kidney+disease. Accessed January 22, 2017.
19. Horton R. North and South: bridging the information gap. *Lancet*. 2000;355:2231–2236.
20. Meo SA, Usmani AM. Impact of R&D expenditures on research publications, patents and high-tech exports among European countries. *Eur Rev Med Pharmacol Sci*. 2014;18:1–9.
21. Meo SA, Al Masri AA, Usmani AM, et al. Impact of GDP, spending on R&D, number of universities and scientific journals on research publications among Asian countries. *PLoS One*. 2013;8:e66449.
22. Swanepoel CR, Wearne N, Okpechi IG. Nephrology in Africa—not yet uhuru. *Nat Rev Nephrol*. 2013;9:610–622.
23. Kirigia JM, Ota MO, Motari M, et al. National health research systems in the WHO African Region: current status and the way forward. *Health Res Policy Syst*. 2015;13:61.
24. Chugh KS. Five decades of Indian nephrology: a personal journey. *Am J Kidney Dis*. 2009;54:753–763.
25. Feehally J, Couser W, Dupuis S, et al. Nephrology in developing countries: the ISN's story. *Lancet*. 2014;383:1271–1272.
26. Bello AK, Johnson DW, Feehally J, et al. Global Kidney Health Atlas (GKHA): design and methods. *Kidney Int Suppl*. 2017;7:145–153.
27. World Bank Country and Lending Groups – World Bank Data Help Desk. Available at: https://datahelpdesk.worldbank.org/knowledgebase/articles/906519. Accessed August 22, 2017.
28. The International Society of Nephrology (ISN). ISN Regions. Available at: https://www.theisn.org/about-isn/regions. Accessed August 22, 2017.