KDIGO - Controversies Conference

Chronic Kidney Disease as a Global Public Health Problem: Approaches and Initiatives

12-14 October, 2006

Renaissance Amsterdam, Amsterdam

Background:

Kidney Disease: Improving Global Outcomes (KDIGO) is an independently incorporated, non-profit foundation governed by an international Board of Directors with the stated mission to "improve the care and outcomes of kidney disease patients worldwide through promoting coordination, collaboration and integration of initiatives to develop and implement clinical practice guidelines." One of the initiatives undertaken by the Board of Directors of KDIGO is a series if international Controversies Conferences to examine what is known, what can be done with what is known and what needs to be known on controversial topics of clinical relevance in nephrology. The first Controversies Conference on "Definition and Classification of Chronic Kidney Disease was held in Amsterdam in November 2004. At the Controversies Conference in Amsterdam, the definition of CKD proposed by the National Kidney Foundation – Kidney Disease Outcome Quality Initiative (KDOQI) in February 2002 was modified to include transplant patients, and additional clarification provided around other key aspects of the definition and classification system of CKD (see Appendix 1, from Kidney Int 67: 2089-2100, 2005). This conference attended by an international group of laboratory physicians, kidney disease specialists, transplant physicians and other health professionals working on these issues represented an important endorsement of and improvement on the KDOQI definition and classification system by the international community. Since then, the proposed system and changes have been accepted and implemented in several countries and the stages of CKD incorporated in ICD 9 in the U.S. (see Appendix 2, page 14)

Proposal

It is now proposed to convene a new Controversies Conference, "Chronic Kidney Disease as a Global Public Health Problem: Approaches and Initiatives," in order to build on and extend the

recommendations of the initial one that clarified the importance of a simple definition and classification system. Specifically, the conference will address some key aspects of the CKD classification system, to define a framework in which to integrate diagnosis and to explore the associations of CKD with other chronic diseases, including cardiovascular disease, cancer and infectious diseases, on the basis of recent data, and in anticipation of the findings of forthcoming results from on-going studies on these issues.

There is a need to develop a consistent framework in which to evaluate public health initiatives, extend current classification systems, and to ensure that research agendas are coordinated within a uniform framework that would facilitate the comparison, interpretation and clinical applicability of results from reported inter-disciplinary and international studies. The development and adoption of a consistent framework, pertinent to public policy arenas, clinical care and research endeavors, will permit international collaborations and scientific discoveries to be more readily applicable and easily adopted worldwide.

There will be 2 major areas of discussion: 1) Classification, Surveillance and Public Policy for CKD and 2) Associations of CKD with Chronic Diseases. Where there is new knowledge, this will be incorporated into existing paradigms; where there is uncertainty, clear directions for research questions will be developed. The opening plenary session will include brief summaries of the status of KDIGO activities and goals and objectives of the meeting.

1) **Classification, Surveillance and Public Policy for CKD:** The plenary session will include presentation on CKD surveillance, standardization of creatinine measurement, experience in measuring and reporting the estimated glomerular filtration rate (eGFR), implementation of albuminuria testing, revisions to ICD classifications, and public policy initiatives. Breakout sessions will focus on CKD classification (Appendix 2), CKD detection and surveillance (Appendix 3), and public policy (Appendix 4).
2) **Associations of CKD with Chronic Diseases**: The plenary session will include presentations on the World Health Organization perspective on chronic disease, and then the focus will shift to CKD. Two themes will be developed to achieve a more complete

understanding of the associations of CKD with other worldwide chronic health problems: cardiovascular disease, infectious diseases and cancer.

a. **Risk for CKD**: Develop a framework for systematic study of risk factors for CKD (susceptibility, initiation and progression) (see Appendix 1, Table 1), and on risks for CKD in cardiovascular disease (CVD) risk factor conditions (diabetes, hypertension, hyperlipidemia, obesity, etc), as heretofore the best studied model of chronic disease (Appendix 5, Table 5).
b. **CKD as a Risk Factor for Chronic Diseases**: Explore the relationship of CKD as a risk factor for adverse outcomes of the major chronic diseases other than CVD, such as infectious diseases and cancer (Appendix 6. Table 6 and Appendix 7, Table 7), based on the model developed for CVD.

Proposed Participants:

Topic 1:* Clas*sification, Surveillance and Public Policy for CKD

Individuals knowledgeable in public health, laboratory medicine, administrative and regulatory topics: ICD-9, 10, 11, organization of administrative data, regulations, reimbursement and outcomes research. Individuals knowledgeable or involved in governmental and non-governmental initiatives aimed at promoting CKD awareness and raising its profile amongst the public and healthcare professionals. Also those involved in professionals and providers training and education, as well as service delivery and quality of care monitoring and evaluation. Major outcomes of work group would be recommendations and suggestions for implementation, especially public and private CKD awareness initiatives.

Topic 2: Associations of CKD

Individuals knowledgeable in the epidemiology of chronic diseases, including CKD, CVD, infectious disease and cancer. Selected participants from the initial CKD meeting will be invited as well to facilitate the coordination and transition of the outcomes of this conference. Major outcomes of work group would be a consistent framework of reporting and research recommendations for future studies.

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Chronic Kidney Disease as a Global Public Health Problem: Approaches and Initiatives

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CONFERENCE AGENDA

Thursday, 12 October
19:00 – 20:30 hrs

LOCATION

19:00 – 20:30 hrs **Welcoming Reception** **Garden Room**

Day 1 – Friday, 13 October, 2006
07:00 – 19:30 hrs

7:00 – 7:30 hrs **Continental Breakfast**

Koepelkerk

Introduction: Meeting Overview

7:30 – 8:00 hrs **Welcome and Introductions**
Norbert Lameire

8:00 - 8:10 hrs **KDIGO – Past, Present, and Future**
Garabed Eknoyan

8:10 - 8:30 hrs **Goal and Objectives of the Meeting**
Andrew Levey

Plenary Sessions: Classification, Surveillance and Public Policy for CKD

Session Moderators: Andrew Levey, Meguid El Nahas, Allan Collins

8:30 – 8:50 hrs **Global Overview**
Presenter: Meguid El Nahas

8:50 – 9:40 hrs **CKD Surveillance: International Updates**

- **US (NHANES)**– Presenter: Josef Coresh
- **EU (Iceland Data) –** Presenter: Olafur Skuli Indridason
- **Latin America** – Presenter: Emmanuel Burdman
- **China –** Presenter: Jing Chen
- **Okinawa –** Presenter: Kuni Iseki
- **Australia -** Presenter: Robert Atkins

9:40 – 9:55 hrs **Creatinine Standardization: Update**
Presenter: Greg Miller

9:55 – 10:15 hrs **GFR Reporting: Experience**

- **France –** Presenter: Jerome Rossert
- **UK –** Presenter: Donal O'Donaghue

10:15 – 10:30 hrs **Break**

10:30 – 10:45 hrs **Albuminuria Testing: Implementation**
Presenter: David Secombe

10:45 – 11:05 hrs **Revisions to ICD Classifications**
Presenter: Lesley Stevens and Robert Jakob

11:05 – 11:25 hrs **Public Policy Initiatives**
Presenter: Allan Collins

11:25 – 12:00 hrs **Discussion**

12:00 – 13:30 hrs **Working Buffet Lunch**

12:30 - 16:30 hrs **Breakout Sessions**

LOCATION

CKD Classification (See Appendix 1-2) **Spinoza**
Discussion Leaders: Adeera Levin & Jerome Rossert

LOCATION

CKD: Detection and Surveillance (See Appendix 3) **Van Leeuwenhoek**
Discussion Leaders: Neil Powe & Kai-Uwe Eckardt

Public Policy (See Appendix 4) **Erasmus**
Discussion Leaders: Allan Collins and Robert Atkins

16:30 – 17:30 hrs **Meeting of Breakout Group Leaders**
- Summarize and draft recommendations

18:00 – 19:30 hrs **Presentation and Discussion of Recommendations for Classification, Surveillance and Public Policy for CKD** **Koepelkerk**

20:00 – 22:00 hrs **Dinner**

Day Two –Saturday, 14 October
7:30 to 18:30 hrs

7:30 - 8:00 hrs **Continental Breakfast** **LOCATION**

Plenary Sessions: Associations of CKD with Chronic Diseases **Koepelkerk**
Session Moderators: Andrew Levey, Kai-Uwe Eckardt, Adeera Levin

8:00 – 8:20 hrs **Overview**
Presenter: Kai-Uwe Eckardt

8:20 – 8:40 hrs **WHO Chronic Disease Perspective**
Presenter: Robert Jakob

8:40 – 9:10 hrs **Cardiovascular Disease Risk Factors for CKD**
Presenter: Adeera Levin

9:10 – 9:30 hrs **Associations of CKD with Infectious Disease**
Presenter: Bertrand Jaber

9:30 - 10:00 hrs **Break**

10:00 – 10:30 hrs	**Associations of CKD with Cancer** Presenter: Eric Cohen	
10:30 – 11:30 hrs	**Discussion**	
11:30 – 13:00 hrs	**Working Buffet Lunch**	
11:30 – 15:00 hrs	**Breakout Sessions**	**LOCATION**
	Cardiovascular Disease (See Appendix 5) **Discussion Leaders:** Josef Coresh and David Wheeler	**Spinoza**
	Association with Infection (See Appendix 6) **Discussion Leaders:** Bertrand Jaber and Michel Jadoul	**Van Leeuwenhoek**
	Associations with Cancer (See Appendix 7) **Discussion Leaders:** Eric Cohen and Meguid El Nahas	**Erasmus**
15:00 – 16:30 hrs	**Meeting of Breakout Group Leaders** • Summarize and draft recommendations	
16:30 – 18:00 hrs	**Presentation and Discussion of Recommendations For Associations of CKD with Chronic Diseases**	**Koepelkerk**
18:00 – 18:30 hrs	**Closing Remarks**	
19:30 hrs	**Gala Dinner Off-Site**	

Sunday, 15 October

Departures

APPENDIX 1

Figure 1: Stages in the Progression of CKD and Therapeutic Strategies

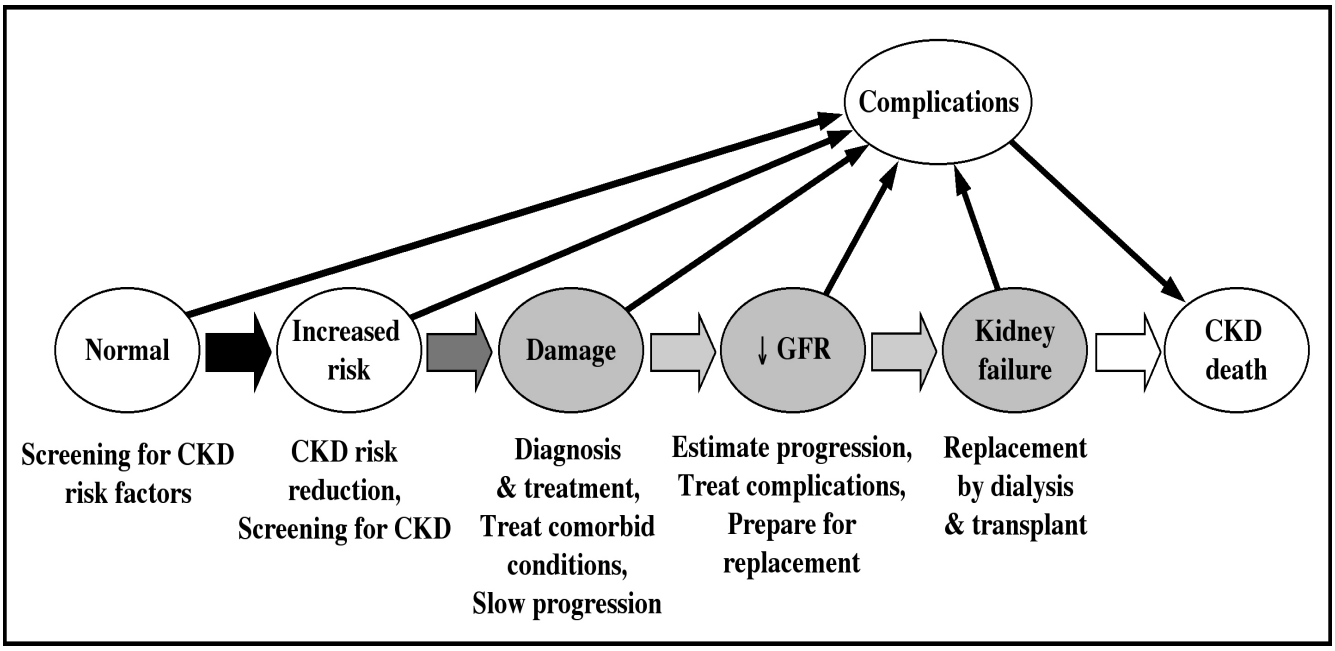

Table 1. Putative Risk Factors for Chronic Kidney Disease and its Outcomes

Risk Factor	Definition	Examples[§]
Susceptibility factors	Increase susceptibility to kidney damage	Older age, family history of chronic kidney disease, congenital or acquired reduction in kidney mass, primary hyperfiltration states (sickle cell disease, glycogen storage diseases, high protein intake), U.S. racial or ethnic minority status, low income or education,
Initiation factors	Directly initiate kidney damage	Diabetes, high blood pressure, obesity, metabolic syndrome, dyslipidemia, hypercalcemia, autoimmune diseases, systemic infections, urinary tract infections, nephrolithiasis, urinary tract obstruction, drug toxicity, endogenous toxins (myeloma), nephrotoxins
Progression factors	Cause worsening kidney damage and faster decline in kidney function after initiation of kidney damage	Higher level of proteinuria, systolic blood pressure, poor glycemic control in diabetes, smoking, high protein intake, nephrotoxins, anemia
End-stage factors	Increase morbidity and mortality in kidney failure	Lower dialysis dose (Kt/V), temporary vascular access, anemia, low serum albumin level, late referral

[§] For many of these hypothesized risk factors, the exact mechanism underlying their association with kidney damage is unclear and many of them may be involved at multiple levels in the pathogenesis of kidney disease. Factors that are implicated at different stages in the development of kidney disease are listed in the initial category in which they could potentially appear.

From: Menon, V., Sarnak MJ., Levey AS. Risk Factors and Kidney Disease in Brenner BM (ed) The Kidney (in press):

Table 2. NKF K/DOQI Definition of Chronic Kidney Disease
Structural or functional abnormalities of the kidneys for ≥3 months, as manifested by either: **1. Kidney damage**, with or without decreased GFR, as defined by • pathologic abnormalities • markers of kidney damage – urinary abnormalities (**proteinuria**) – blood abnormalities (renal tubular syndromes) – imaging abnormalities • kidney transplantation **2. GFR <60 ml/min/1.73 m2**, with or without kidney damage

Table 3. Current CKD Classification Based on Severity and Therapy

Stage	Description	GFR (ml/min/1.73 m^2)
	clinically significant	
1	**Kidney damage with normal or GFR**	**≥ 90**
2	**Kidney damage with mild ↓ GFR**	**60-89**
3 T for transplant	**Moderate ↓ GFR**	**30-59**
4	**Severe ↓ GFR**	**15-29**
5	**Kidney failure** D for dialysis	**< 15 (or dialysis)**

Appendix 2: Breakout Group - CKD Classification

Discussion Leaders: Adeera Levin and Jerome Rossert

The objective of the workgroup is to come up with clear recommendations for modification and implementation of CKD classification to incorporate markers for damage and clinical diagnosis (as recommended by the Amsterdam I conference group, and which can be integrated into existing administrative codes, such as ICD9/10/11) This will permit improved communication and collaboration for the purposes of research and public policy / public awareness due to standardization of coding.

Table 4: Proposed Classification of CKD by Diagnosis

Disease		CKD Classification		
		Stage	Marker of Kidney Damage	Disease (ICD Code list)
Diabetic Kidney Disease	Type 1	Same for all (585.x), V codes for dialysis or transplant	Proteinuria	
	Type 2		Proteinuria	
Non-Diabetic Kidney Disease	Glomerular diseases		Hematuria +Proteinuria	
	Vascular diseases		+Proteinuria	
	Tubulointersitial Diseases		+Pyuria, +Proteinuria, +Imaging studies	
	Cystic Diseases		Cysts	
	Non-diabetic kidney disease not otherwise specified		+Proteinuria	
Transplant			+Proteinuria	

1. **Modification of CKD classification based on diagnosis**
   In response to the various discussions by the nephrology community, it has become clear that a level of detail not necessarily captured by the current staging system (1-5), is required.

   a) Discuss the utility of standardizing approaches to using administrative coding systems to more precisely define CKD, according to markers of kidney damage and disease. Others have suggested including modifiers related to prognosis. While administrative coding systems contain entries related to markers of kidney damage and diagnosis, it is recognized that not all countries use the same standardized administrative coding system, and even within countries or institutions there may be use of different systems. Nonetheless, if the principles of use of coding systems are agreed upon, *i.e.* stage (eGFR) + markers of kidney damage + disease diagnostic markers + prognosis, would the group be able to articulate the pros and cons of such a system? Can the

group foresee any specific issues related to the adoption of a common standardization system internationally?

i. ***Clinical diagnoses (ICD9, ICD10 codes)***
There are a number of codes USRDS uses based on the current ICD9. They are located in the USRDS ADR appendix and should be reviewed and perhaps altered based on the work group recommendations.

ii. ***Histological variations (ICD9, ICD 10 codes)***
We should look at the V codes as well since these codes are also important.

iii. ***Markers of kidney damage.***
Standardization of elements to be used as markers would be important, and if the nephrology community could agree on 'known markers' of CKD, and then test their discriminatory value as above (in different populations etc) that would be of value.

1. Albuminuria/proteinuria (ICD9, ICD 10 codes)
2. Other urinary markers (ICD9, ICD 10 codes)
3. Imaging abnormalities (ICD9, ICD 10 codes)
4. Other markers

b) For epidemiological, clinical and research use, the inclusion of diagnosis, markers and histology is likely important. The group should articulate how this kind of information and standardization would inform the research and public policy agenda of the global kidney community, and give examples where this level of detail may be of value (e.g. see below, re : specific populations).

2. Modification of CKD classification in kidney transplant recipients (brief discussion)

a) GFR estimation in transplantation. What is the current status of validation or development of eGFR equations in KTx patients? What are the benefits and risks of classifying KTx patients according staging system proposed?

b) CKD classification and chronic allograft nephropathy (CAN). There is currently no specific codes for this group only the use of the new 585 codes with the transplant V code; the group should consider making some recommendations based on etiology, diagnoses and histology – as above with native kidneys**.** Would the use of the standardized coding system as per above, in kidney transplant recipients facilitate research and clinical care of this patient group?

c) Issues related to prognosis. Is there evidence for similar or different amounts of co morbidity dependent on the modifiers/markers as per above, native kidney disease? Is there evidence for similar or different rates of progression in kidney transplant recipients patients as compared to CKD in native kidneys?

3. Modification of CKD classification for special populations (if time permits)

There continues to be debate as the applicability of eGFR equations to specific populations; in particular the elderly and the non- Caucasian/ non African American groups. There is accumulating data, which needs to be organized in a framework, especially regarding equations for GFR estimation and prognosis. It would be important for the workgroup to focus on some key issues listed below, and to discuss how the increased precision / use of standardized coding may be very helpful in describing these populations, and then describing differential outcomes.

a) In Asians, Afro-Caribbeans, South Asians, what are the ongoing studies that help to modify the existing GFR estimating equations? Is there sufficient data to support use of different equations in the general populations, different ethnic groups etc yet, or is that something for the future? The groups should discuss the implications of validating and using modified equations in large populations.

b) Given that race or ethnicity cannot be put into diagnostic coding systems, it would be important for the same principles of coding systems to be used so that appropriate comparisons can be made between countries re: burden of illness, rates of progression within different stages etc.

c) In elderly populations, would there be some value in modifications based on stability/ progression over time?

d) In elderly populations, would there be some value in modifications based on risk factors for competing outcomes, such as CVD? i.e. Does a GFR of 50 in an 85 y/o with no risk factors etc, mean the same as 50 in 65 y/o DM or 85 y/o DM with HTN?

Overall output of this workgroup would be seen as identifying the tremendous need for clarity and consensus on improving the classification system for CKD, and recognizing the opportunity for research. It may be premature to propose too rigid of a system without identifying all the current research that is underway in this area. Ideally, an inventory of 'in-press', accepted and ongoing studies should be described at this meeting. The collective knowledge of the workgroup may be very valuable.

Key outputs would include:

1. Developing a consensus on the need for standardization of coding systems to be used by the nephrology community in all countries. If one specific system cannot be adopted, then at least the components that would go into the more detailed coding should be standardized.
2. General recommendation that ICD 10 and 11 be updated to include CKD severity codes from ICD 9.
3. Framing a series of research questions to answer questions regarding
   - ***a)*** the added benefits of a more complex staging system than the current simple 5 stage CKD which has been widely successful in many arenas
   - ***b)*** the priorities in terms of validating equations for special populations
   - ***c)*** the priorities in terms of ensuring that key information, definitions and tools to describe progression of CKD are developed. This would inform the Action plan
   - ***d)*** modeling outcomes, public health implications etc based on different equations/ components of classification system

Current ICD-9 Codes

Diseases of the genitourinary system:

585.1 Chronic kidney disease, Stage 1
585.2 Chronic kidney disease, Stage 2 (mild)
585.3 Chronic kidney disease, Stage 3 (moderate)
585.4 Chronic kidney disease, Stage 4(severe)
585.5 Chronic kidney disease, Stage 5
585.6 End stage renal disease
585.9 Chronic kidney disease, unspecified
599.60 Urinary obstruction, unspecified
599.69 Urinary obstruction, not elsewhere classified

Diseases of the circulatory system:

403.00 Hypertensive kidney disease, malignant, without chronic kidney disease
403.01 Hypertensive kidney disease, malignant, with chronic kidney disease
403.10 Hypertensive kidney disease, benign, without chronic kidney disease
403.11 Hypertensive kidney disease, benign, with chronic kidney disease
403.90 Hypertensive kidney disease, unspecified, without chronic kidney disease
403.91 Hypertensive kidney disease, unspecified, with chronic kidney disease
404.00 Hypertensive heart and kidney disease, malignant, without heart failure or chronic kidney disease
404.01 Hypertensive heart and kidney disease, malignant, with heart failure
404.02 Hypertensive heart and kidney disease, malignant, with chronic kidney disease
404.03 Hypertensive heart and kidney disease, malignant, with heart failure and chronic kidney disease
404.10 Hypertensive heart and kidney disease, benign, without heart failure or chronic kidney disease
404.11 Hypertensive heart and kidney disease, benign, with heart failure
404.12 Hypertensive heart and kidney disease, benign, with chronic kidney disease
404.13 Hypertensive heart and kidney disease, benign, with heart failure and chronic kidney disease
404.90 Hypertensive heart and kidney disease, unspecified, without heart failure or chronic kidney disease
404.91 Hypertensive heart and kidney disease, unspecified, with heart failure
404.92 Hypertensive heart and kidney disease, unspecified, with chronic kidney disease
404.93 Hypertensive heart and kidney disease, unspecified, with heart failure and chronic kidney disease

Frequency of Occurrence of CKD codes in the 5% Medicare sample claims set - CY 2004 (All sources)

ICD9 Code	Description	Count	Percent	
585	Chronic renal failure	862350	49.60%	49.60%
588	Disorders resulting from impaired renal function	190886	10.98%	60.58%
584	Acute renal failure	163562	9.41%	69.99%
403.x1	Hypertensive renal disease with renal failure	126579	7.28%	77.27%
586	Renal failure, unspecified	117539	6.76%	84.03%
250.4	Diabetes with renal manifestations	97707	5.62%	89.65%
591	Hydronephrosis	35654	2.05%	91.70%
189.0	Malignant neoplasm of kidney	30775	1.77%	93.47%
583	Nephritis & nephropathy, not specified as acute or chronic	26856	1.54%	95.02%
440.1	Atherosclerosis of renal artery	23458	1.35%	96.37%
581	Nephrotic syndrome	8717	0.50%	96.87%
582	Chronic glomerulonephritis	8282	0.48%	97.35%
794.4	Abnormal renal function tests	8049	0.46%	97.81%
404.x3	Hypertensive heart & renal disease with heart & renal failure	7425	0.43%	98.24%
404.x2	Hypertensive heart & renal disease with renal failure	5236	0.30%	98.54%
753.12	Polycystic kidney disease, unspecified	4232	0.24%	98.78%
587	Renal sclerosis	3440	0.20%	98.98%
753.13	Polycystic kidney disease, autosomal dominant	2593	0.15%	99.13%
236.91	Neoplasm of uncertain behavior, kidney	2468	0.14%	99.27%
753.2	Obstructive defects of renal pelvis and ureter	1730	0.10%	99.37%
580	Acute glomerulonephritis	1645	0.09%	99.46%
283.11	Hemolytic-uremic syndrome	1598	0.09%	99.56%
274.1	Gouty nephropathy	1532	0.09%	99.64%
223.0	Benign neoplasm of kidney	1350	0.08%	99.72%
753.14	Polycystic kidney disease, autosomal recessive	1257	0.07%	99.79%
189.9	Malignant neoplasm of urinary organ	929	0.05%	99.85%
442.1	Aneurysm of renal artery	780	0.04%	99.89%
572.4	Hepatorenal syndrome	736	0.04%	99.93%
271.4	Renal glycosuria	356	0.02%	99.95%
447.3	Hyperplasia of renal artery	261	0.02%	99.97%
753.16	Medullary cystic kidney	141	0.01%	99.98%
753.19	Other specified cystic kidney disease	107	0.01%	99.98%
753.15	Renal dysplasia	86	0.00%	99.99%
646.2	Unspecified renal disease in pregnancy	70	0.00%	99.99%
753.17	Medullary sponge kidney	48	0.00%	100.00%
016.0	Tuberculosis of kidney	37	0.00%	100.00%
642.1	Hypertension secondary to renal disease complicating childbirth	28	0.00%	100.00%
095.4	Syphilis of kidney	8	0.00%	100.00%

Appendix 3: Breakout Group - CKD: Detection and Surveillance
Discussion Leaders: Neil Powe and Kai-Uwe Eckardt

The objective of the workgroup is to come up with a well-defined strategy for implementation of CKD detection and surveillance applicable to both developed and developing countries along with health economics evaluation of such strategies.

1. **Targeted vs. Universal Implementation of Detection Programs**
    - ***a)*** Traditional public health approaches have been to look for disease in everyone but the financial pressures are making this approach a problem. Therefore targeted screening may be preferable. The screening of children however is easier since they have a large number of public health vaccinations etc before they can enter school. CKD in relationship to other public health initiatives.
        - **i.** CVD
        - **ii.** HTN
        - **iii.** DM
        - **iv.** Hyperlipidemia
        - **v.** Obesity
        - **vi.** Infectious diseases (overlap with Day 2)
        - **vii.** Cancer (overlap with Day 2)
    - ***b)*** Public health objectives of surveillance systems for CKD
        - **i.** Simple testing methods to define the CKD population
    - ***c)*** CKD as an issue for developed versus developing countries

2. **Cost-effectiveness analysis of detection and surveillance CKD programs**
    - *a)* Data is necessary on
        - **i.** Information gathering on surveillance cost
        - **ii.** Information about intervention cost .

3. **Specific issues related to laboratory tests methods**
    - ***a)*** Issues with creatinine assay standardization and eGFR
        - **i.** Issues with ethnic based considerations and modifications; Asians, Chinese, Cubans, etc…
        - **ii.** Relevance to elderly.
    - ***b)*** Issues with albuminuria
    - ***c)*** Relevance to the elderly where the prevalence of albuminuria is likely to be much higher

Key outputs would include:

1. Considerations for targeted screening.
    - **a.** In developed countries, target population for CKD screening to focus on patients with CVD risk factors and those with family history of CKD.
    - **b.** In developing countries, CKD screening should be included as part of screening for CVD risk factors (hypertension, diabetes, dyslipidemia, obesity), and possibly as part of screening for chronic infections.

2. Measurement tools to include a measure of kidney damage (albuminuria) and serum creatinine to estimate GFR (link with previous publication)

Each workgroup should also identify research priorities.

Appendix 4: Breakout Group - Public Policy
Discussion Leaders: Allan Collins and Robert Atkins

The objective of the workgroup is to recommend steps for the public policy implementation of CKD surveillance programs in developed and developing countries.

1. **CKD public policy implementation**
   - ***a) Professional and provider education***
     - **i.** Public detection programs & health care delivery systems to address CKD
     - **ii.** Increase awareness of medical profession
       1. Specialists and primary care
     - **iii.** Increase public awareness and engagement
       1. World Kidney Day
       2. Kidney foundations and professional societies
   - ***b) Explore public-private partnerships***
     - **i.** There needs to be a clear rational set forward for why government and private payers should pay attention. Financial implication of CKD to health care budgets.
     - **ii.** They have many competing public health priorities and a new effort to deal with kidney disease is just not in their interest. However, If CKD is fit into the larger DM and CVD efforts and the issues in children then there has been greater receptiveness. They need to have a clear idea how CKD stages and the treatments would be different. This would be helpful in addressing the chronic disease burden in their countries as well as meeting WHO objectives**.**
     - **iii.** How can professional societies, foundations and patient groups work together to address CKD and prevention? This is a very big public health problem with ageing of the population and CKD is a multiplier disease. In fact the concept of CKD as the multiplier disease should be considered to position it in the public health and clinical world.
   - ***c) Relationship to quality of care***

Key outputs would include:

1) CKD is common in and multiplies risks from CVD and possibly other chronic diseases.
2) Need to coordinate and harmonize efforts for professional and public education.
3) Relationship of CKD detection and intervention to quality of care to change provider behaviors.

Each workgroup should also identify research priorities.

Appendix 5: Breakout Group - Cardiovascular Disease
Discussion Leaders: Josef Coresh and David Wheeler

This section would begin with a review of the proposed classification of risk factors for CKD, and then focus on CVD and CVD risk factors as risk factors for CKD.

Table 5: Proposed Classification for Risk Factors for CKD

Disease		CKD		
		Susceptibility	**Initiation**	**Progression**
Diabetic Kidney Disease	Type 1			
	Type 2			
Non-Diabetic Kidney Disease	Glomerular diseases			
	Vascular diseases			
	Tubulointersitial Diseases			
	Cystic Diseases			
	Non-diabetic kidney disease not otherwise specified			
Transplant				

The evidence that CKD is a risk factor for CVD is quite substantial and has been the topic of previous meetings. In fact, the models used to evaluate and classify CKD as a risk factor for CVD will be the paradigm used at this conference for evaluating the association of CKD with other chronic diseases. Therefore, it will not be the focus of this session. Instead, this breakout session will focus on what is known and not known about presence of CVD (MI, heart failure, etc.) and major CVD risk factors (diabetes, hypertension, dyslipidemia, obesity, and smoking) as CKD risk factors

- Discuss the extent to which susceptibility, initiation and progression can be distinguished.
  - Susceptibility - risk factors for development of kidney disease risk factors, e.g. obesity leading to hypertension
  - Initiation - risk factors for kidney damage (albuminuria) among individuals with normal GFR at baseline, or for decreased GFR among individuals with intact GFR at baseline. Inherently none of the studies guarantee that kidneys are completely free of all pathology at baseline. Studies often use less than microalbuminuria on one occasion and eGFR>60 as the groups free of kidney disease at baseline
  - Progression - risk factors for progression of kidney disease among individuals with established CKD.

- What would be sources of information from which to gain this information?
  - Large cohort studies often lack information on proteinuria which limits the ability to distinguish initiation from progression
  - Cohorts of patients with a specific etiology vs. Population based studies pose different challenges
  - Clinical trial data can be very useful
  - Potentially we could review hypertension/ diabetes / statin trials: to determine benefit and magnitude of benefit for CKD
- Risk factors as markers vs. causes of CKD
  - We can't be certain of causality but can make some distinction as to whether the evidence is strong for: (1) likely causal mechanism, (2) mechanism uncertain, or (3) likely to reflect non-causal association.
- Where data exist we can make summaries; otherwise develop framework and research agenda to help answer questions deemed to be important.

Key Outputs Would Include:

- CKD has a high prevalence among individuals with CVD and several lines of evidence suggest the detection of CKD in this population is important [recommendations for this have been made; we'd focus on the first part of the statement here]
- Research studies should aim to use similar criteria for studying initiation and progression of CKD and strive to incorporate measure of both kidney damage (albuminuria and proteinuria) and kidney function (estimated GFR or relevant markers).
- CKD risk factor associations can be distorted for nutritional risk factors when the CKD definition relies on creatinine suggesting the need for studies which include other markers of decreased kidney function
- Systematic evaluation of the impact of CVD clinical trials on CKD progression is warranted
- Other?

Each workgroup should also identify research priorities.

Appendix 6: Breakout Group Association with Infection
Discussion Leaders: Bertrand Jaber and Michel Jadoul

Goals

The goals of this workgroup are to:

1. Explore the association of CKD with infectious disease, broadly termed, with particular focus on chronic illnesses. Review existing recommendations.

2. Examine whether the natural course of infectious disease is influenced (favorably or unfavorably) by coexisting CKD. Two hypotheses will be explored:
   - **a)** CKD is a marker of greater morbidity in infectious disease
   - **b)** CKD affects the host immune response (favorably or unfavorably) to infectious disease

3. Examine whether treatment of infectious disease is influenced by coexisting CKD. In this setting, two hypotheses will be explored:
   - **a)** Kidney toxicity of drugs hampers effective treatment of infectious disease
   - **b)** CKD is associated with suboptimal effective use of anti-infectious drugs, resulting in over or under exposure to these drugs

4. Examine how CKD is associated with impaired host cellular and humoral immunity, resulting in suboptimal and/or sustained vaccination immune responses. This impaired immunity has potential regional and global implications for vaccination strategies worldwide and possibly, for achieving effective herd immunity. The hepatitis B and pneumococcal vaccines will be highlighted as case-index vaccines where special dose requirement and/or frequency of booster dosing are required to achieve effective and sustained humoral response.

5. Examine how the CKD population is vulnerable to the effects of an infectious disease, and why this population requires a specialized immunization program against a particular infectious disease.

6. Summarize the suboptimal performance of existing methods to estimate kidney function in chronic infectious disease particularly if superimposed on malnutrition due to abnormal muscle mass and/or low body mass index. Human immunodeficiency viral (HIV) infection will be used as the case-index infection to illustrate this problem and emphasis will be placed on the need to develop better tools to estimate GFR. This goal will also explore the value of monitoring anti-infectious drug kidney toxicity using urinary tubular markers of kidney injury, which might precede decreases in GFR.

Table 6. Proposed Framework for CKD as Risk Factor for Infectious Diseases

Infectious Diseases (ID)	CKD prevalence	CKD as a risk factor for ID morbidity	CKD as a risk factor for ID mortality
HCV			
HBV			
HIV			
TB			
Malaria			

Key outputs would include (related to question 1):

1) **Recommendation for CKD detection in chronic infectious diseases (are there enough data for a clinical recommendation ?)**

Research Recommendations (related to questions 2-5):

Appendix 7: Breakout Group - Associations with Cancer
Discussion Leaders: Eric Cohen and Meguid El Nahas

Cancer ↔ CKD

1. CKD that complicates cancer is well-described, especially for renal failure after cancer. Much less well-known is the occurrence of moderate "sub-clinical" reduction in GFR after cancer treatment. This late effect of cancer could affect quality and quantity of life.

a) Determine the extent of this problem, individually and in population number terms.
b) Assess its impact on function and survival.

2. Cancer complicating CKD is well-known for kidney and urothelial cancers, as are the specific cancers related to immunosuppression in kidney transplant patients. It is not known whether people with CKD are more or less at risk for cancer.

a) Determine incidence of cancers in people with CKD, correcting for shared risk factors such as smoking and diabetes.

3. It is likely that in CKD there will be an altered patient response to cancer therapies. This could lead to increased toxicity of cancer chemotherapy or, to lower rates of cure if therapies are under dosed. Azotemia has been an exclusion criterion for participation in cancer drug trials. Thus, data are lacking to guide the care of CKD patients diagnosed with cancer.

a) Assess outcomes of cancer in people with CKD. Databases on mortality of CKD will provide initial information.
b) Identify cancer trials that may include CKD patients.
c) Determine optimal assessment of kidney function in cancer patients to assist in management of CKD complicated by cancer.

Table 7. Proposed Framework for CKD as Risk Factor for Cancers

Cancer	CKD prevalence	CKD as a risk factor for cancer morbidity	CKD as a risk factor cancer mortality
Kidney and urinary tract tumors			
Other solid tumors			
Hematologic malignancies			

Key outputs would include (related to Question 1):

1. **Recommendation for CKD detection in cancer (are there enough data for a clinical recommendation ?)**

Research Recommendations (related to Questions 2-3)