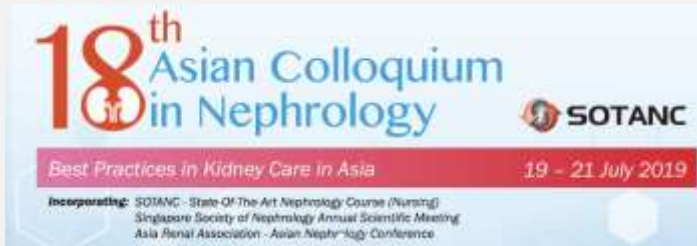


# Debate: Asia Does Not Need Advanced Hemodialysis Technologies

Manish Kaushik  
Singapore General Hospital  
18<sup>th</sup> Asian Colloquium in Nephrology  
21 July 2019, Singapore



# Disclosure

❖ No disclosures relevant to this talk

# Acknowledgement

- ❖ Professor Vivekanand Jha
  - ❖ President, International Society of Nephrology
  - ❖ Executive Director, The George Institute for Global Health India
  - Professor of Nephrology and James Martin Fellow, University of Oxford
- ❖ The George Institute was first founded in Australia in 1999 with the aim of reducing the escalating burden of non-communicable diseases and injury around the world

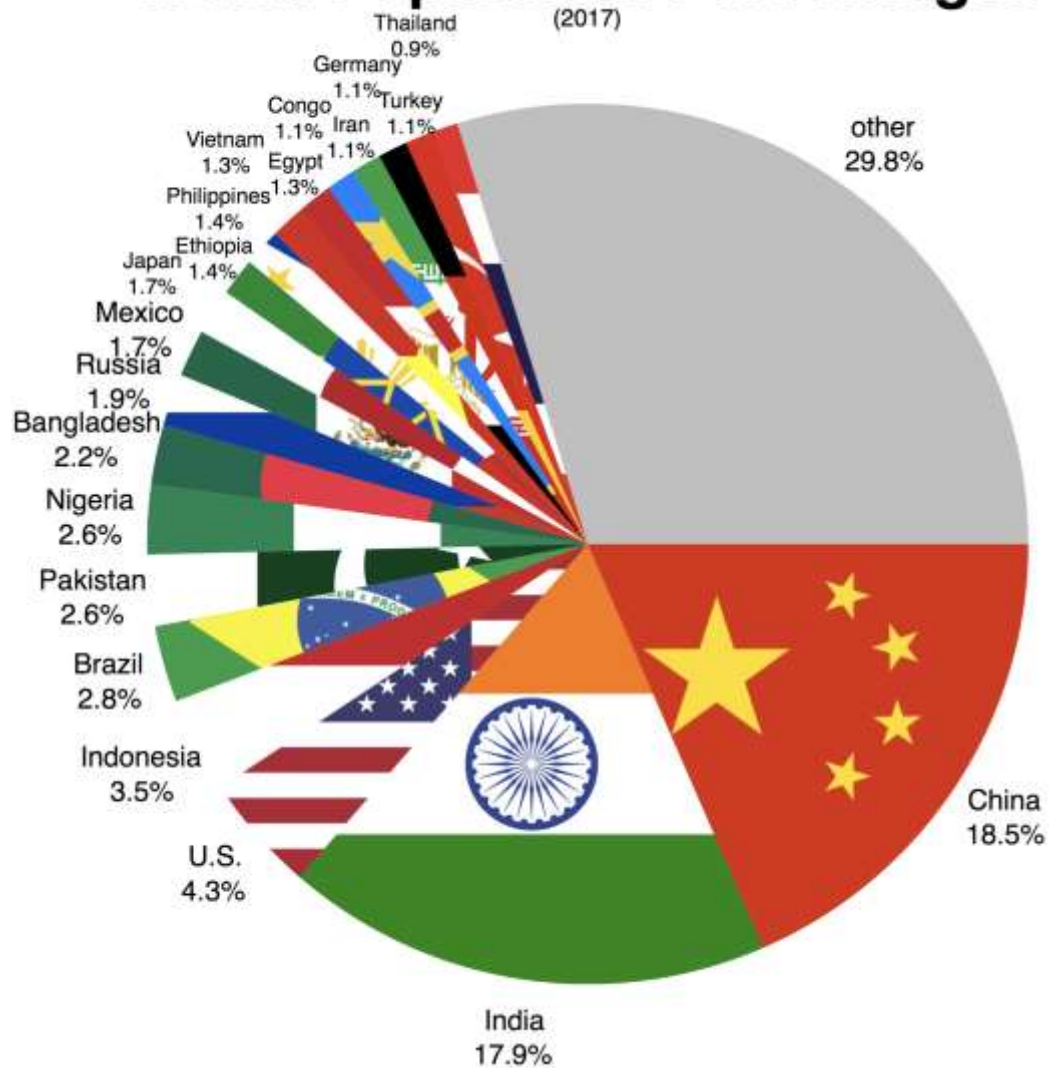
# Agenda

- ❖ Unique challenges for delivery of hemodialysis (HD) in Asia
- ❖ Advanced technologies in HD and their impact on care and outcomes
- ❖ Improvement in care and outcomes is possible by extending use of existing technology to fill the gaps in HD delivery in Asia

# Unique challenges of delivery of hemodialysis (HD) in Asia

# Asia in numbers

## World Population Percentages

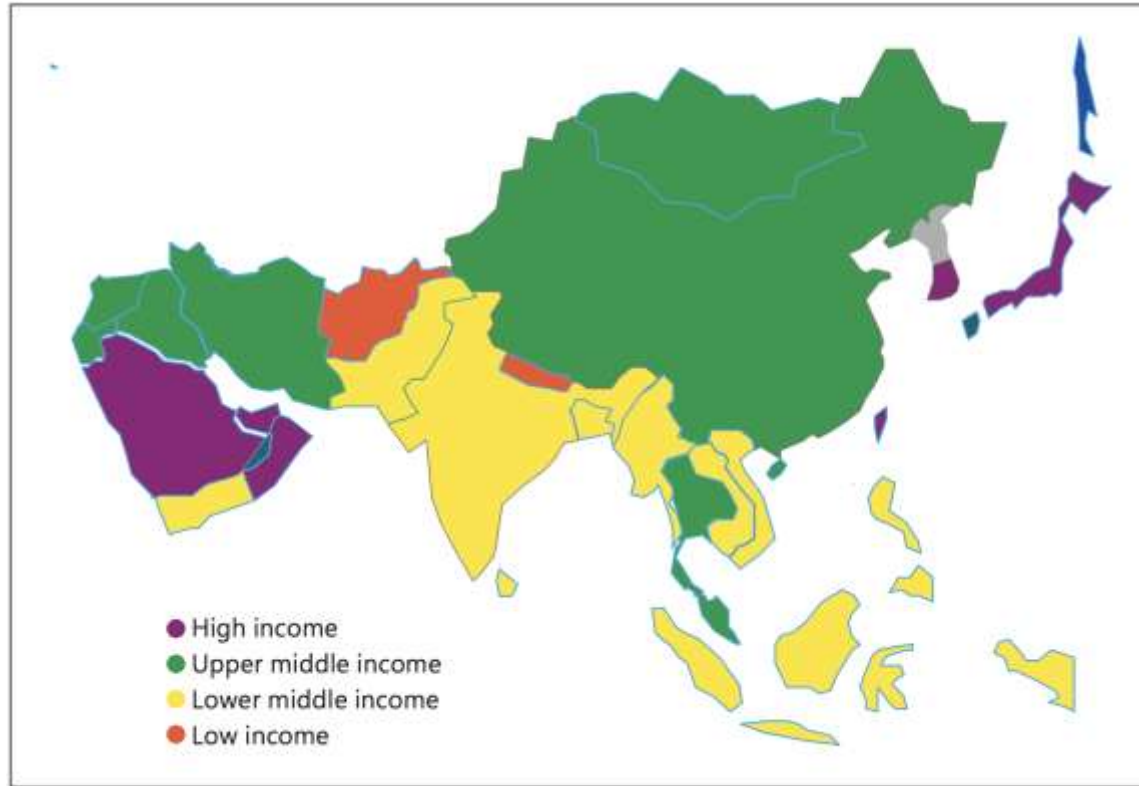


3.3% of world's land mass

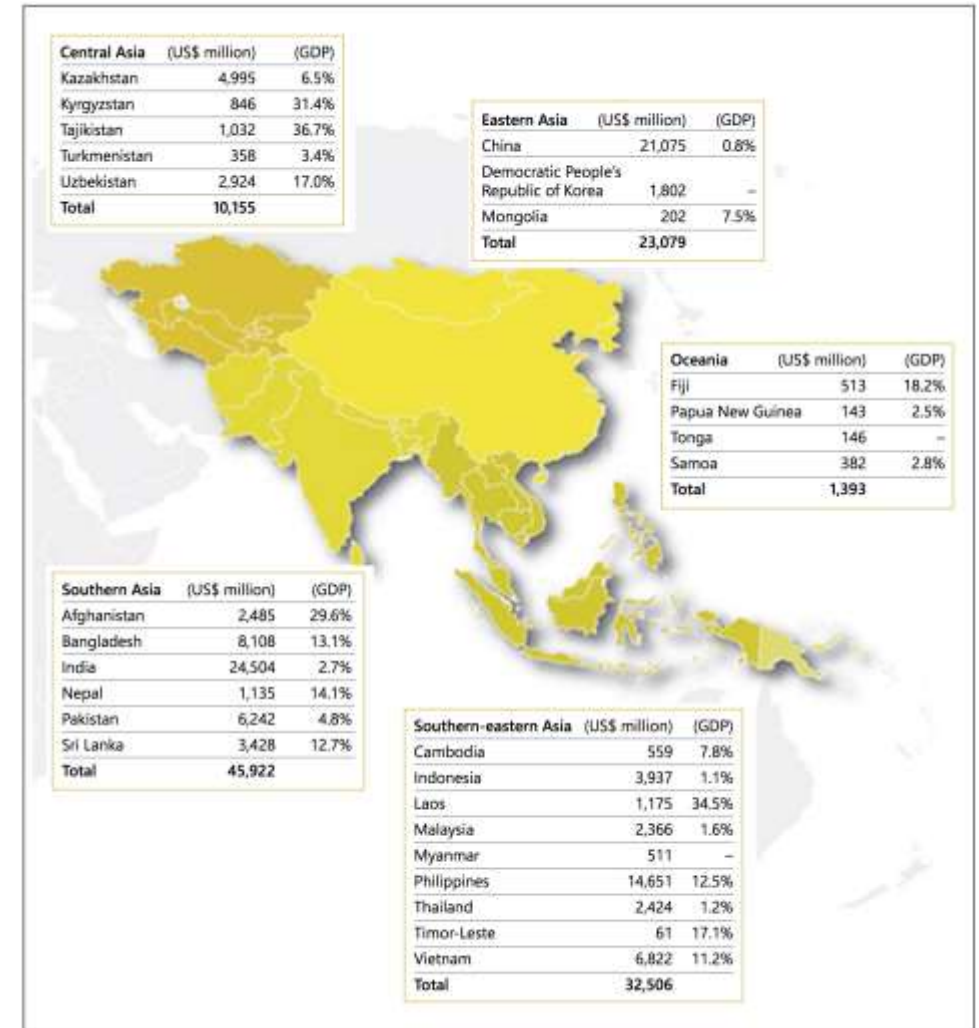
25% of the world's population

Majority below poverty line  
earning <2 USD per day

# Heterogeneity in Asian economies

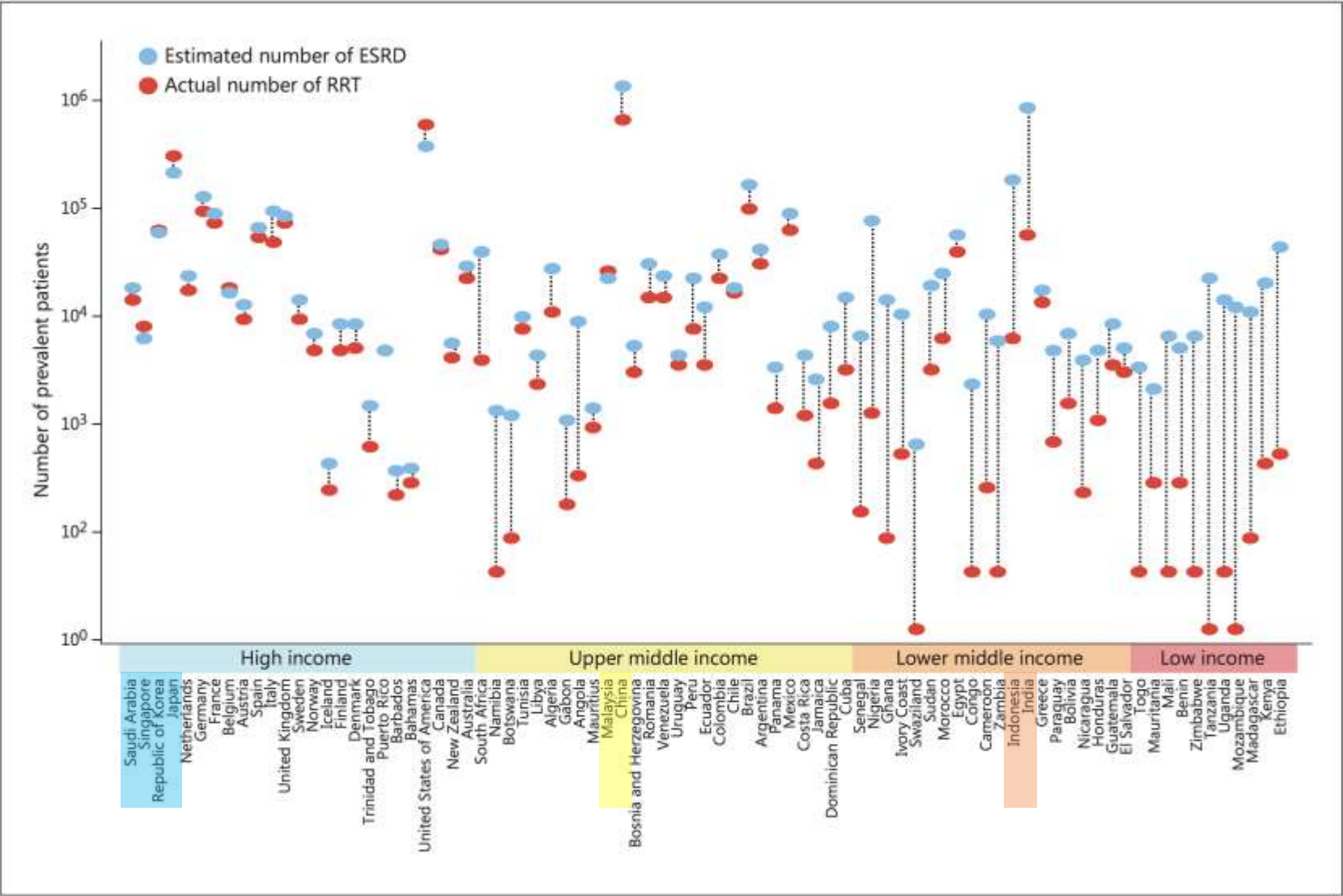


Any review of Asia's dialysis practices or plans for developing or improving care of CKD/ ESKD should take into account these economic contrasts



Navva PKR, Blood Purif 2015; 40:280-287  
Prasad N, Kidney Dis 2015; 1:165-177

# Dialysis Gap: Actual numbers of RRT versus ESKD



Prasad N, Kidney Dis 2015; 1:165-177



# Dialysis in Asian Countries: Challenges

## Pre HD Care

Accessibility to HD  
Affordability of HD: financial models of coverage

Poor patient knowledge  
Screening and early diagnosis  
High % of CKDu  
Late referral to Nephrologist

## HD Care

Shortage of HD facilities and manpower  
Unequal/ preferential delivery of HD  
Quality assurance: vascular access, adequacy, water quality, maintenance etc.  
Dialyzer reuse  
High drop out rates and lost to follow up

No systematic recording, evaluation and reporting of HD in Asia

## Evaluation

# Accessibility to dialysis in Asia

- ❖ 75% referred late for ESKD: associated with worse outcomes
- ❖ Not enough dialysis facilities or over burdened facilities
- ❖ Prefer to dialyze patients who are transplant candidates
- ❖ Dialysis centers available in urban pockets

# State of Nephrology in SEA

Indicator	Afghanistan	Bangladesh	Bhutan	India	Maldives	Nepal	Pakistan	Sri Lanka
Population (millions)	34.7	162.5	0.8	1324.2	0.4	29	193.2	21.2
Percentage of rural population	73	65	61	67	53	81	61	82
Number of physicians (per 1000 people)	0.3	0.5	0.4	0.8	3.6	0.6	1	0.9

Indicator	Afghanistan	Bangladesh	Bhutan	India	Maldives	Nepal	Pakistan	Sri Lanka
Number of nephrologists	<10	123	1	1,639	<5	50	151	30
What proportion of patients who need it are able to get dialysis for ESKD?	<5%	25%	100%	5%–100%	Not known	20%	5%–15%	2%–12%
Number of dialysis units	<10	101	3	1584	<5	53	121	29
Number of dialysis machines	200	1179	8	12,881	<40	410	481	274
Number of transplant centers	1	6	0	233	0	4, all in 1 province	16	7
Funding for dialysis	Private	Mixed	State-funded	Mixed <sup>a</sup>	Private	State-funded	Mixed	State-funded

Jha V, Kidney Int 2019; 95:31-37

# Accessibility to dialysis

Country	No. of patients	Percentage of population	No. of facilities
Cambodia	200	0.001	10
Myanmar	600	0.001	28
Philippines	10,000	0.011	270
Vietnam	14,000	0.015	130
Malaysia	23,500	0.083	600
Thailand	29,500	0.044	500
Korea	45,009	0.093	614
Taiwan	63,655	0.275	552
China	272,000	0.020	3,500
Japan	297,126	0.232	4,152

# Unequal accessibility to dialysis

**Table 1** The number of HD centres in districts is greater than in Yangon (machines numbers are similar), the majority of patients (925/1284 [72%]) are in Yangon

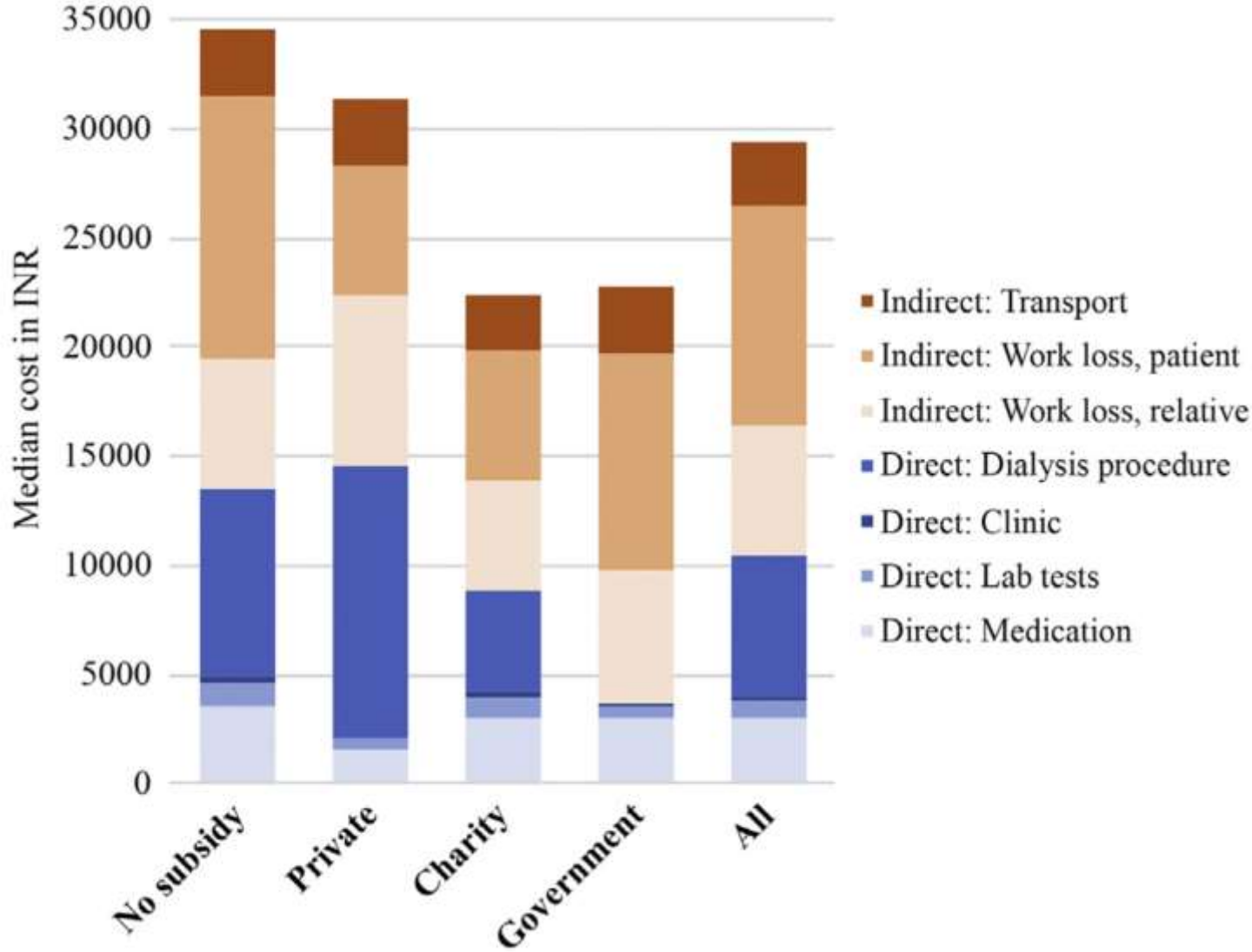
	Yangon			Districts		
	Government	Private	Total	Government	Private	Total
Centres	4	13	(17)	15	16	(31)
HD machines	35	101	(136)	49	60	(109)
Patients	183	742	(925)	179	180	(359)

# Affordability of dialysis

- ❖ Various models of funding
- ❖ Government funding: not inclusive of all
- ❖ Insurance coverage is poor
- ❖ Dialyzer reuse: 98% in Vietnam
- ❖ In a cohort of 463 patients enrolling in to a MHD program 60% left with 3 months

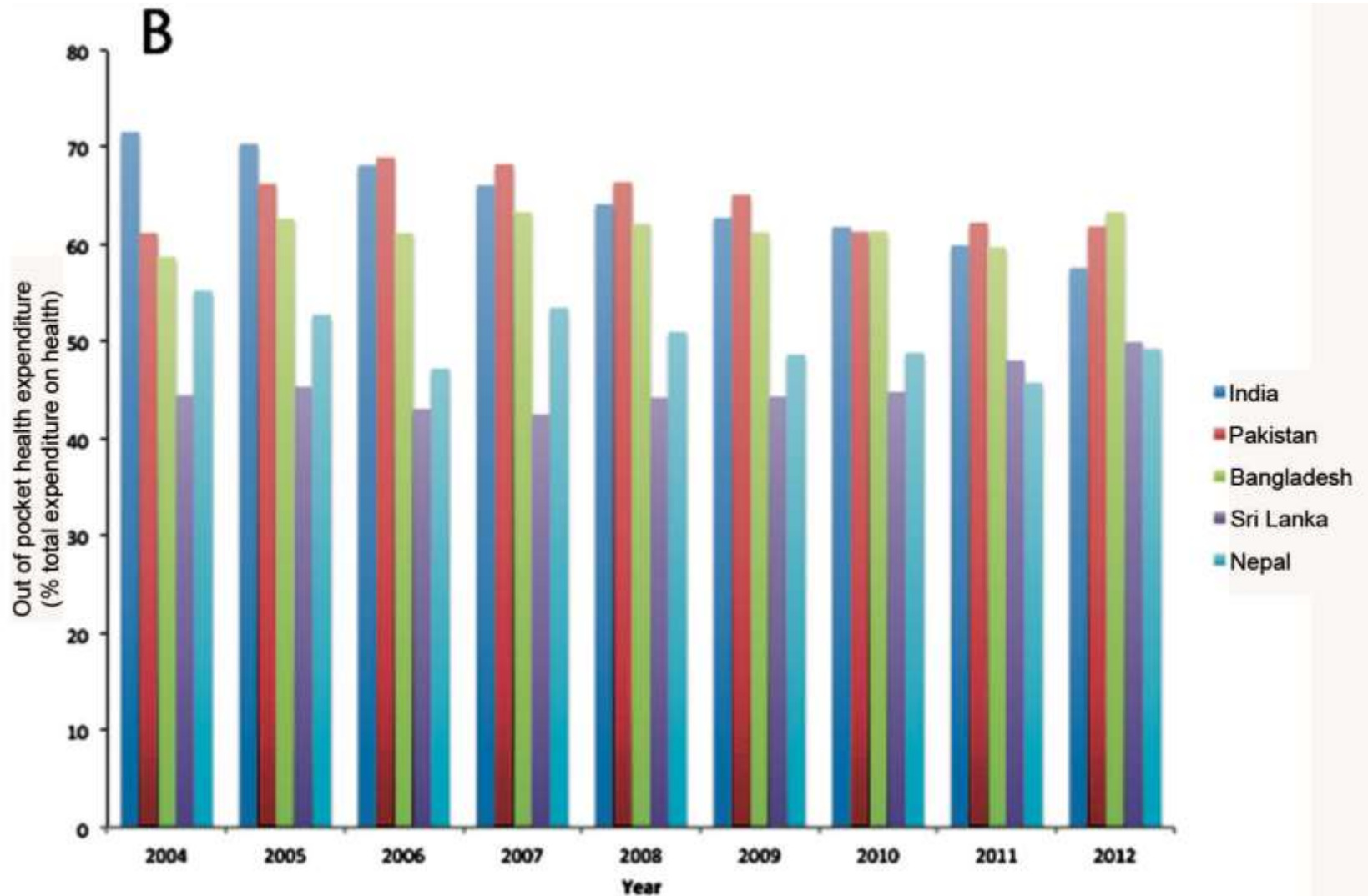
Parameswaran S, Natl Med J India 2011; 24:208-214  
Navva PKR, Blood Purif 2015; 40:280-287  
Hyodo T, Renal Replac Ther 2017; 3:11

# Breakdown of monthly dialysis-related expenses



Bradshaw C, Kidney Int Rep 2019; 4:390-398

# Out of pocket expenditure



Jha V, Clin Nephrol 2015; 83 (Suppl 1):S7-S10



# Delivery of Dialysis

Rates of fulfillment for the target test frequency per year

Rates of fulfillment for the target level of each test

	Hospital A	Hospital B	Hospital C
Hb (6 times/year)	39.85	44.92	32.73
Ferritin (3 times/year)	0.77	33.45	33.91
Ca (6 times/year)	36.25	35.41	27.35
Phosphorus (6 times/year)	35.99	35.39	26.85
iPTH (4 times/year)	18.51	24.84	25.28
Alb (4 times/year)	24.16	25.97	22.14
Kt/V (4 times/y)	24.16	25.97	22.14
Urea reduction rate (4 times/year)	28.53	34.86	19.82

	Hospital A	Hospital B	Hospital C
Target level			
Hb (100–130 g/L)	54.24	66.00	59.51
Ferritin (100–500 ng/dL)	6.66	39.69	34.64
Ca (2.1–2.5 mmol/L)	37.53	55.72	51.33
Phosphorus (1.13–1.78 mmol/L)	28.02	38.95	36.93
iPTH (150–300 ng/mL)	16.20	23.07	21.56
Alb (>35 g/L)	30.08	35.53	35.17
Kt/V (>1.3)	30.08	35.53	35.17
Urea reduction rate (>67.5%)	29.82	38.66	31.10

# Water quality for dialysis

- ❖ Tropical climate: high temperatures, heavy precipitation, floods, water-logging
- ❖ Quality of feed water is variable
- ❖ Treatment systems not optimized to deliver consistent supply and quality of water of acceptable standards
- ❖ Testing frequencies are low and the documentation is poor

# Water quality in SEA

	ET, EU/l	Bacteria, CFU/ml
Facility A		
Tap water	8,076	200
RO water	57	100
Dialysate 1	741	500
Dialysate 2	903	800
Facility B		
Tap water	378	70
RO water	2.9	300
Dialysate 1	38	150
Dialysate 2	49	100
Facility C		
Tap water	1,468	110
RO water	94	22
Dialysate 1	201	600
Dialysate 2	395	1,000
Dialysate 3 <sup>a</sup>	2,295	1,000
Facility D		
Tap water	1,663	110
RO water 1	7.3	120
RO water 2	7.8	100
Dialysate 1	309	800
Dialysate 2	246	800

<sup>a</sup> At a console with an ET-retentive filter.

4 centres in Vietnam and Cambodia

The ET levels in standard dialysates were satisfactory at 2 facilities

The bacterial counts in dialysates were not acceptable at any of the facilities investigated

# Dialysis in Asian Countries: Challenges

## Challenges going forward for Cambodia (2017)



No fund exists to help patients pay for HD treatment.



Dialysis sessions and checkup appointments are often missed.



Time and money needed for transportation, accommodation, and treatment is especially high for patients in the provinces.



There are fewer than 10 nephrologists for a population of over 15 million.



Dialysis centers are available only in Phnom Penh, Battambang, and Siem Reap.

## Challenges going forward for India (2017)



Most dialysis care is provided by the private sector.



There is very little insurance coverage for HD and CAPD.



Nearly 45% of children present with CKD stage 4 or 5, and less than 50% of children presenting with ESRD receive continuous dialysis.



63.4% of CKD stage 5 patients do not receive any form of RRT.

# Dialysis in Asian Countries: Challenges

## Challenges going forward for Lao PDR (2017)



Dialysis treatment is not covered by health insurance, resulting in irregular treatment.



Kidney biopsy is not available in the country yet, so patients must travel to Thailand for biopsy and bear all costs.



No regulatory body or association for kidney disease has been established yet in Lao PDR.



There are no technicians to repair dialysis machines, so representatives are hired from companies, increasing costs and reducing efficiency.



Water systems for dialysis are not regularly inspected.

## Challenges going forward for RRT in Mongolia (2017)



Monitoring and health education is inadequate, resulting in rapid progression to ESRD.



Government financing for treatment, equipment, and infrastructure is insufficient.



Mongolia does not provide training of HD engineers.



Availability of AVF at time of first HD session is rare.



Health insurance does not cover erythropoietin, phosphate-binders, vitamin D, or calcimimetic preparations.



43% of patients receive only 4-8 hours of HD per week due to the limited number of HD machines.

# Dialysis in Asian Countries: Challenges

## Challenges going forward for Myanmar (2017)



Financial allocation to the health sector has increased, but the percentage of out-of-pocket expenditure remains high.



The ratio of nephrologists to patients for the whole population is low.



Patient knowledge of health care needs to be improved.



There is currently no national kidney foundation to monitor or foster advancement of HD centers.



Maintenance checks for dialysis fluid systems and equipment are irregular because there are no clinical engineers.



National guidelines for HD are not yet fully established.

## Challenges going forward in Vietnam (2017)



Only 21,000 of 90,000 patients in need of RRT are receiving treatment, and all HD facilities are overloaded.



Low- rather than high-flux dialyzers are used, and dialyzers are reused many times (because the cost of a dialyzer is reimbursed only after 6 uses).



Most patients are covered by health insurance, but HD is not always affordable due to extra treatment costs at many public and all private hospitals.



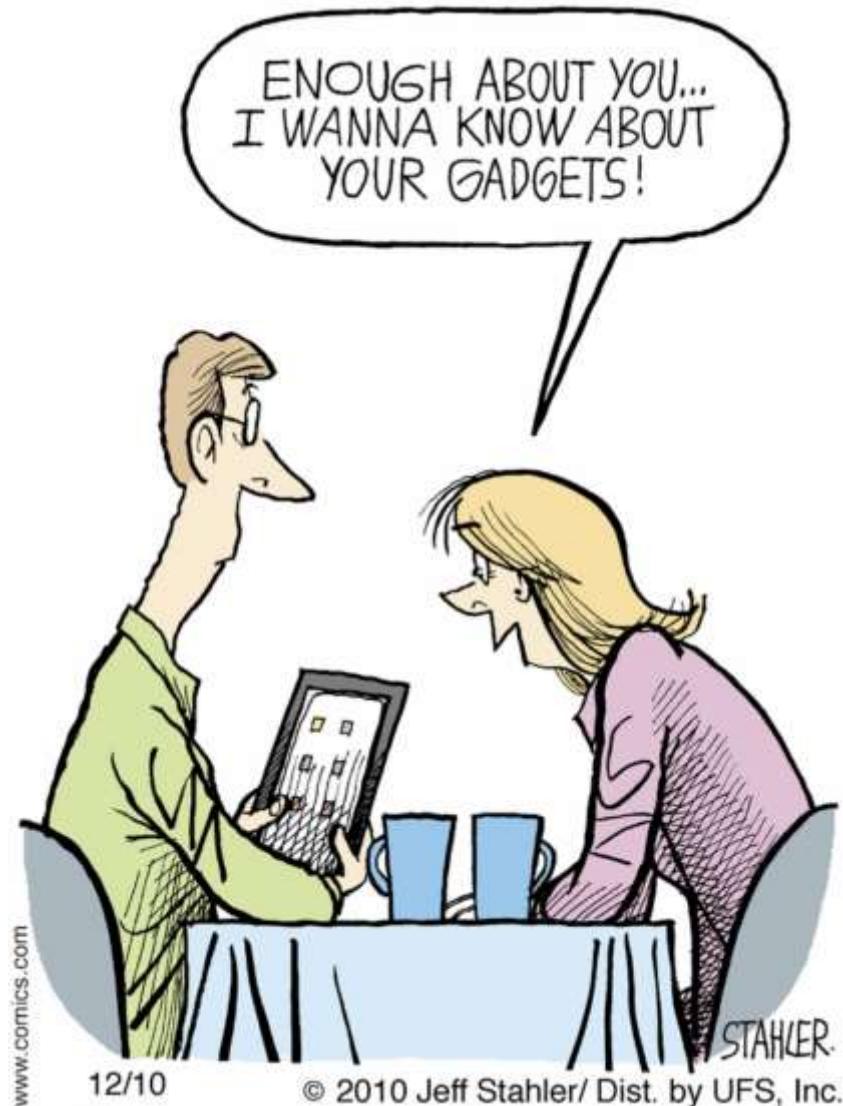
Modern dialysis machines are available, but water quality for dialysis is questionable.



There is also a major shortage of qualified health care providers.

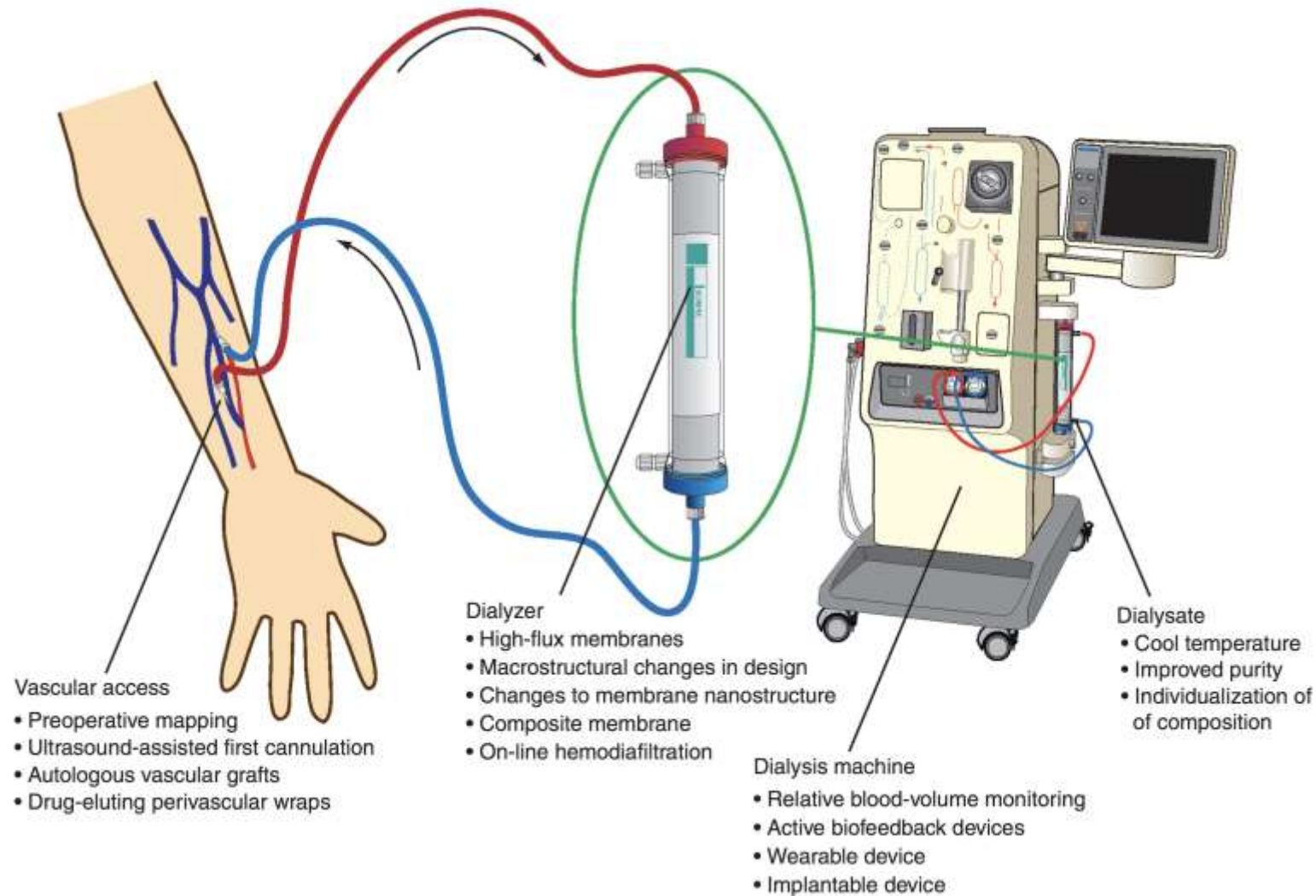
# Advanced technologies in HD and their impact on care and outcomes

# Technology advances and us





# Advanced Hemodialysis Technologies



## Did 20 Years of Technological Innovations in Hemodialysis Contribute to Better Patient Outcomes?

Norbert Lameire, Wim Van Biesen, and Raymond Vanholder

*Renal Division, Department of Medicine, University Hospital, Gent, Belgium*

*Clin J Am Soc Nephrol* 4: S30–S40, 2009. doi: 10.2215/CJN.04000609

# Adequacy of dialysis

- ❖ Current method:  $KT/V$
- ❖ Different ways to express  $KT/V$
- ❖ Reflects the behavior of urea only
- ❖ Presumes changing  $KT/V$  by changing  $K$  or changing  $T$  achieves equal changes in solute removal or outcomes

# Delivery of dialysis

$$KT/V$$

**K: Dialyzer clearance for urea**  
**T: Time of dialysis therapy session**  
**V: Volume of distribution of urea**

# Delivery of dialysis

KT/V

# Delivery of dialysis

KT/V

Bellomo R, The Lancet 2012; 380:756-766

# Delivery of dialysis

**K**T/V

Membrane flux

Online Clearance Monitor (OCM)

On-line HDF

# Membrane Flux and outcomes

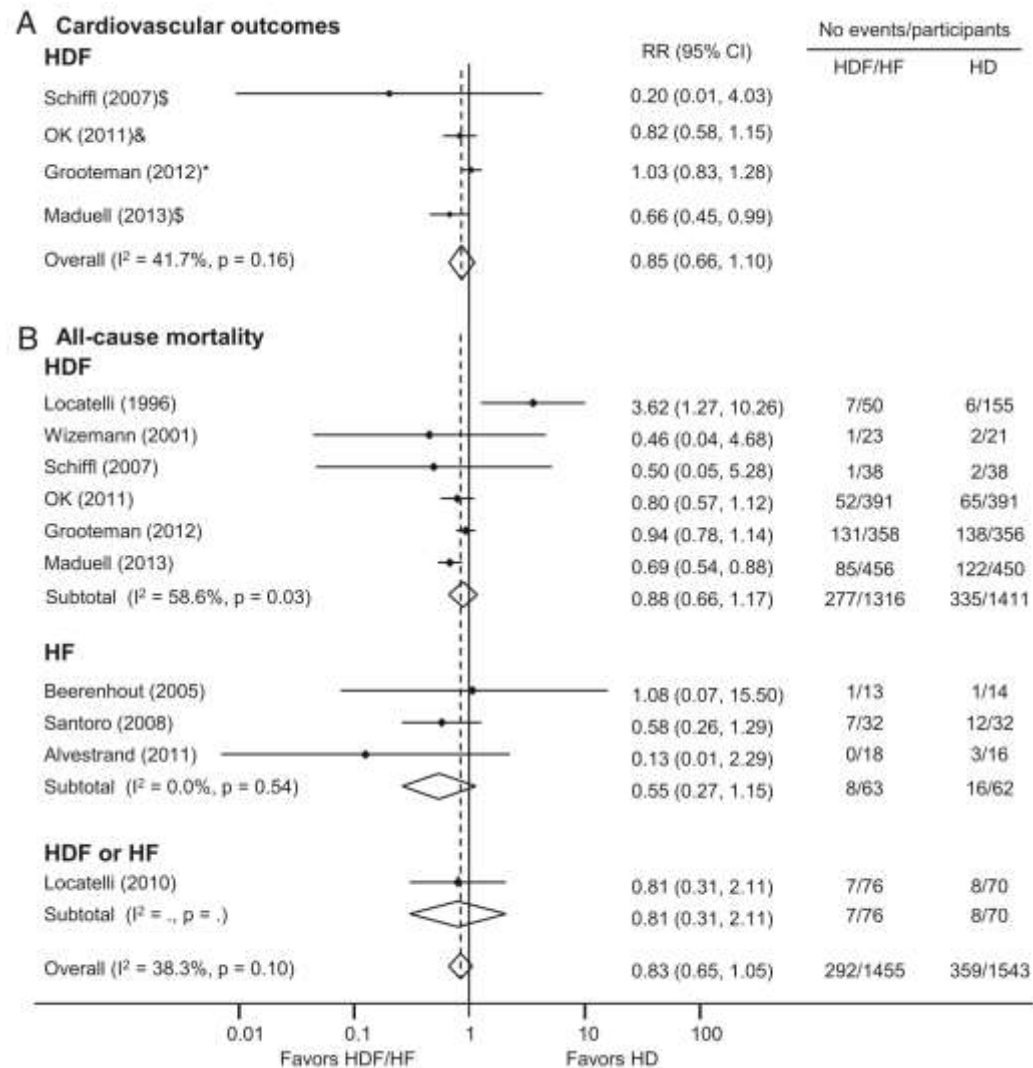
- ❖ HEMO Study: in prevalent HD patients
  - ❖ no significant survival difference between the high-flux and the low-flux membrane types at primary analysis
  - ❖ secondary analyses showed that, compared with the low-flux group, there were significant reductions in the risk for death from cardiac causes and the combined outcome of first hospitalizations or death from a cardiac cause in the high-flux group
  - ❖ *post hoc* analyses showed an outcome benefit for high-flux membranes on the risk for cerebrovascular accidents and on overall mortality risk for patients who were enrolled in the study after 3.7 years of maintenance dialysis (the median time on dialysis for the entire population)



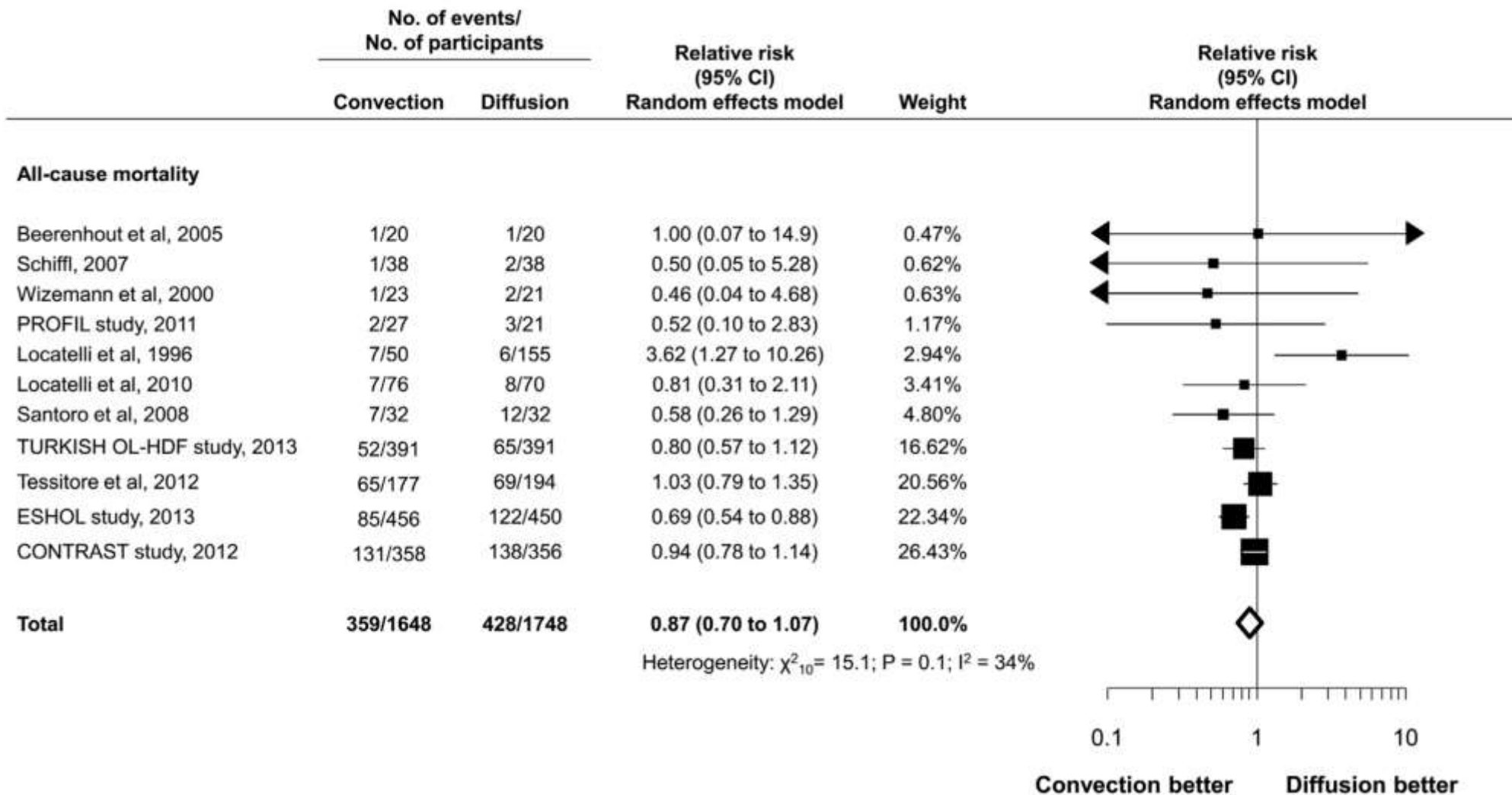
# Membrane Flux and outcomes

- ❖ MPO Study: in incident HD patients
  - ❖ high-flux dialysis showed a significant survival benefit of 37%, after adjustment, of patients with a low serum albumin
  - ❖ in a sub-analysis including patients with diabetes, high-flux dialysis was associated with improved survival
  - ❖ in patients with a serum albumin level 4 g/dl, no survival benefit could be observed with the use of high-flux membranes

# OL-HDF versus HD/ HFHD



# OL-HDF versus HD/ HFHD



Nistor I, AJKD 2014; 63(6):954-967

# Delivery of dialysis

KT/V

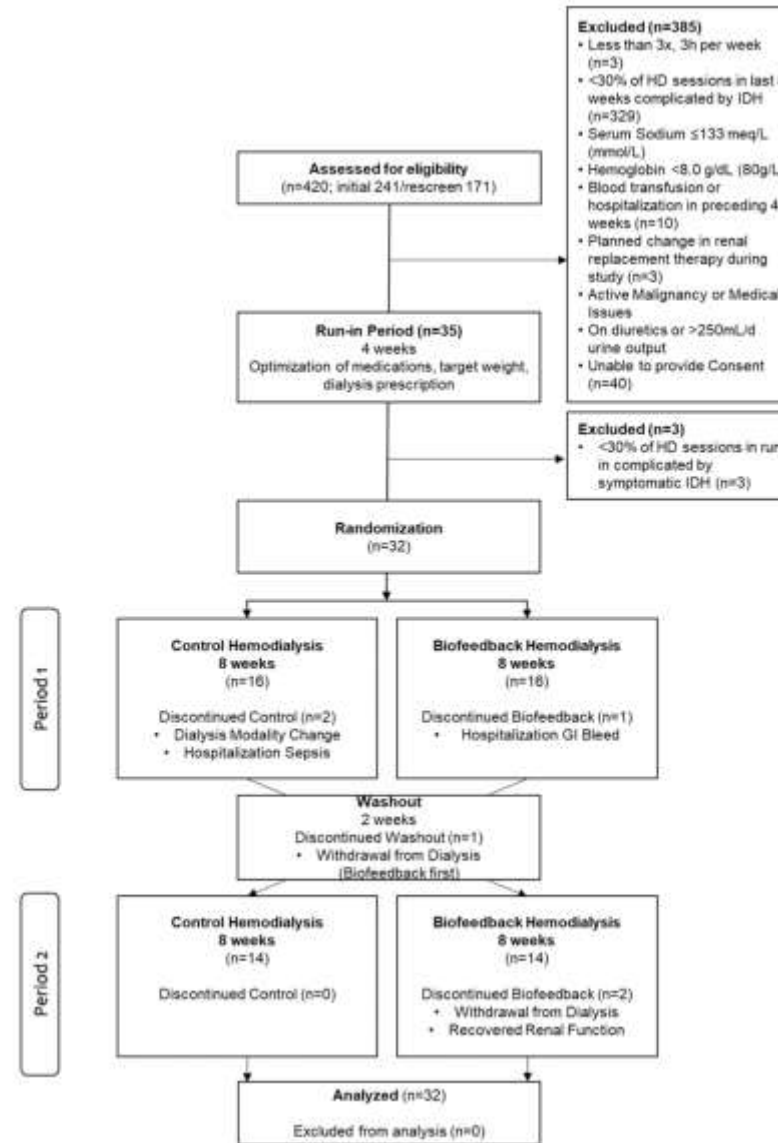
Blood Volume Monitor (BVM)

## Randomized Crossover Trial of Blood Volume Monitoring–Guided Ultrafiltration Biofeedback to Reduce Intradialytic Hypotensive Episodes with Hemodialysis

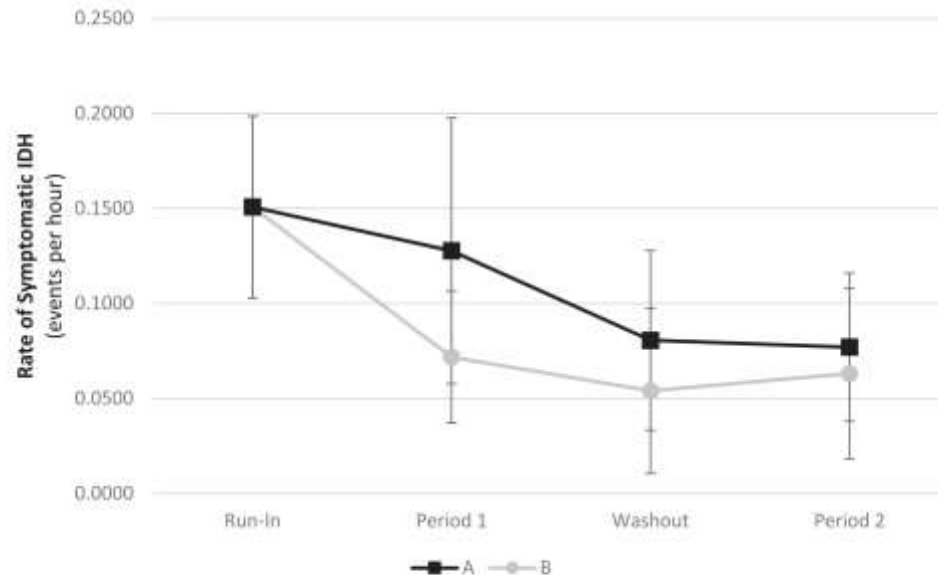
*Kelvin C.W. Leung,\* Robert R. Quinn,\*† Pietro Ravani,\*† Henry Duff,\*‡ and Jennifer M. MacRae\*‡*

*Clin J Am Soc Nephrol* 12: 1831–1840, 2017. doi: <https://doi.org/10.2215/CJN.01030117>

# Biofeedback versus control HD



# Biofeedback versus control HD



**Figure 2.** | The rate of symptomatic IDH did not differ in each period between the two randomization orders. In randomization order A, biofeedback in period 1 followed by control in period 2. In randomization order B, control in period 1 followed by biofeedback in period 2. IDH, intradialytic hypotension.

**Table 3.** Rates of symptomatic IDH, asymptomatic IDH, and symptoms alone by intervention

Variable	Symptomatic IDH Rate, Events/h	Asymptomatic IDH Rate, Events/h	Symptoms Alone Rate, Events/h
Run-in period	0.15 (0.10 to 0.20)	0.31 (0.25 to 0.37)	0.07 (0.04 to 0.10)
<b>Biofeedback period</b>	0.10 (0.06 to 0.14)	0.33 (0.24 to 0.41)	0.05 (0.03 to 0.06)
Start of period	0.15 (0.06 to 0.24)	0.36 (0.25 to 0.47)	
End of period	0.07 (0.03 to 0.10)	0.26 (0.16 to 0.36)	
<b>Control period</b>	0.07 (0.05 to 0.10)	0.30 (0.23 to 0.37)	0.06 (0.04 to 0.08)
Start of period	0.09 (0.04 to 0.13)	0.32 (0.25 to 0.40)	
End of period	0.11 (0.02 to 0.19)	0.33 (0.20 to 0.47)	

Values are expressed as mean (95% confidence interval) unless otherwise indicated. IDH, intradialytic hypotension

## Intradialytic Blood Volume Monitoring in Ambulatory Hemodialysis Patients: A Randomized Trial

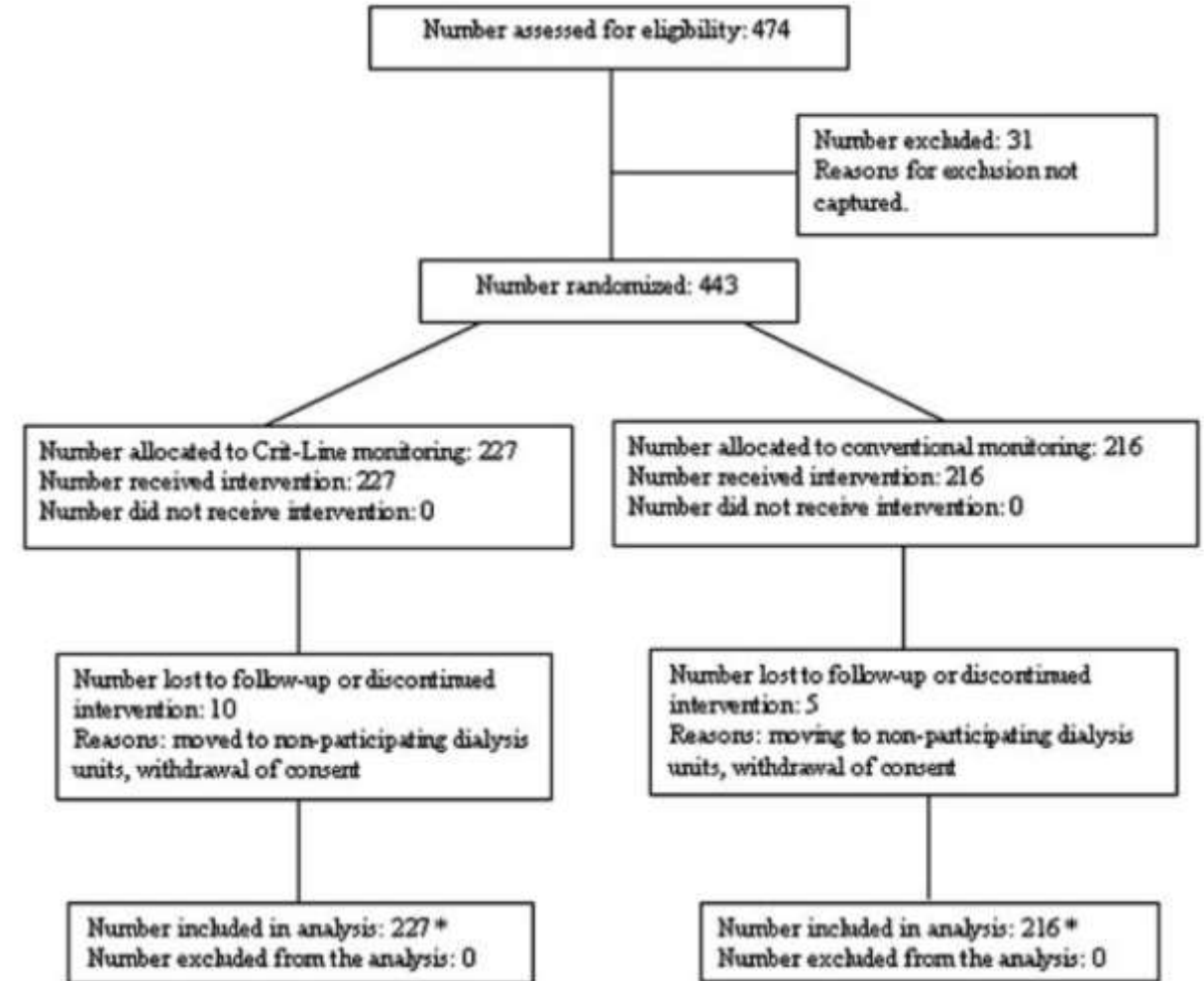
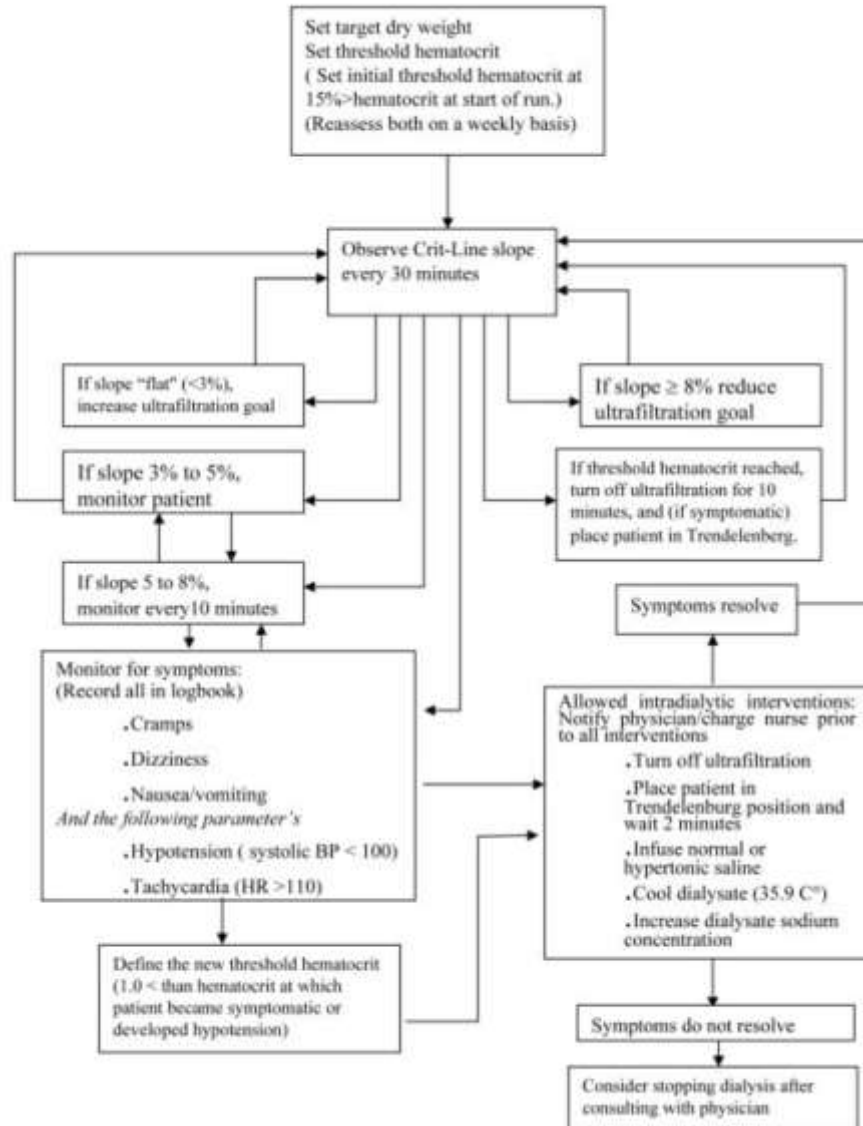
Donal N. Reddan,<sup>\*†‡</sup> Lynda Anne Szczech,<sup>\*‡</sup> Vic Hasselblad,<sup>\*</sup> Edmund G. Lowrie,<sup>§</sup> Robert M. Lindsay,<sup>||</sup> Jonathan Himmelfarb,<sup>¶</sup> Robert D. Toto,<sup>#</sup> John Stivelman,<sup>\*\*</sup> James F. Winchester,<sup>††‡‡</sup> Linda A. Zillman,<sup>\*</sup> Robert M. Califf,<sup>\*‡</sup> and William F. Owen, Jr<sup>‡§§</sup>

*\*Duke Clinical Research Institute, Duke University Medical Center, Durham, North Carolina; †University College Galway, Galway, Ireland; ‡Duke University Medical Center, Department of Medicine, Division of Nephrology, Durham, North Carolina; §Hema Metrics Inc., Kaysville, Utah; ||London Health Sciences Center and University of Western Ontario, London, Ontario, Canada; ¶Maine Medical Center, Portland, Maine; #University of Texas Southwestern Medical Center at Dallas, Dallas, Texas; \*\*Northwest Kidney Centers, Seattle, Washington; ††Beth Israel Medical Center, New York, New York; ‡‡RenalTech International, New York, New York; and; §§University of Tennessee, Memphis, Tennessee*

*J Am Soc Nephrol 16: 2162–2169, 2005. doi: 10.1681/ASN.2004121053*



# CLIMB Study



# CLIMB Study

Rate of fluid removal before and after intervention by treatment group

	Crit-Line Monitoring Group	Conventional Monitoring Group
Preintervention profiles (per hour)		
<3%	54 (24%)	66 (32%)
≥3 and <8%	155 (69%)	125 (60%)
≥8%	17 (8%)	16 (8%)
total patients	226	207
Postintervention profiles		
<3%	41 (23%)	37 (23%)
≥3 and <8%	121 (68%)	103 (65%)
≥8%	16 (9%)	18 (11%)
total patients	178	158

Comparison of mortality by treatment groups with USRDS date

	Crit-Line Group	Usual Care Group
Patients	227	216
Deaths		
observed	19	7
expected	24.7	26.8
Deaths/100 patient-years at risk		
observed	17.4	6.4
expected	22.6	24.6
Standardized mortality ratio	0.77	0.26
$\chi^2$	1.3	14.6
<i>P</i> value	NS	<0.001

# DRIP Study

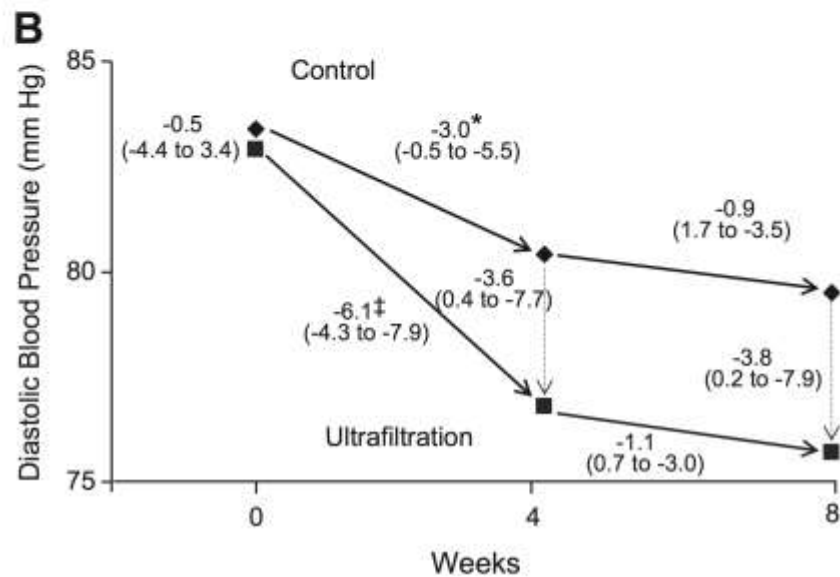
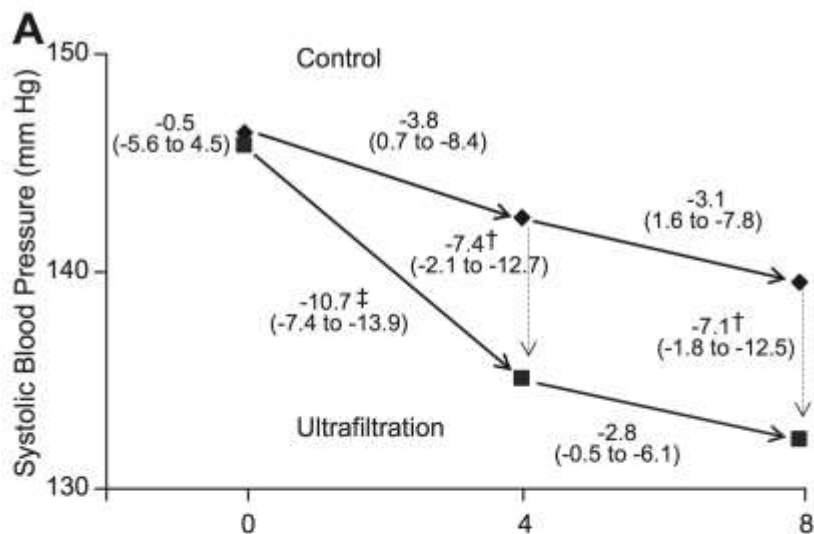
## Clinical Trial

### **Dry-Weight Reduction in Hypertensive Hemodialysis Patients (DRIP)** **A Randomized, Controlled Trial**

Rajiv Agarwal, Pooneh Alborzi, Sangeetha Satyan, Robert P. Light

*Hypertension. 2009;53:500-507.*

# DRIP Study

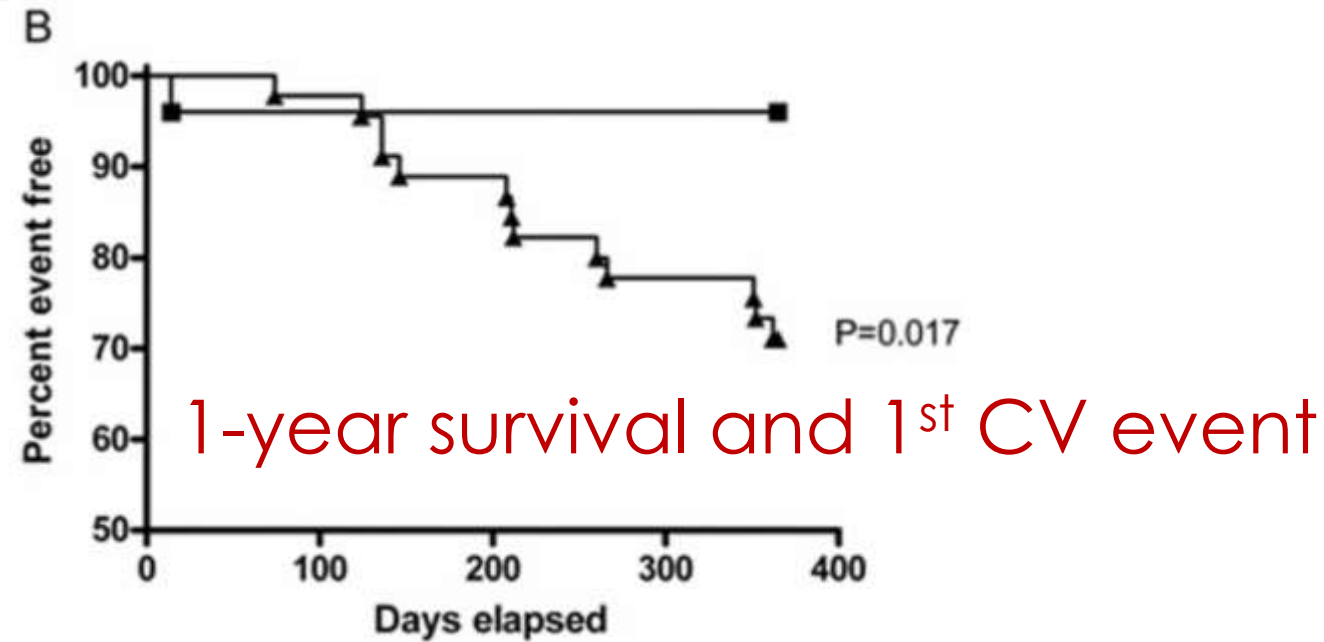
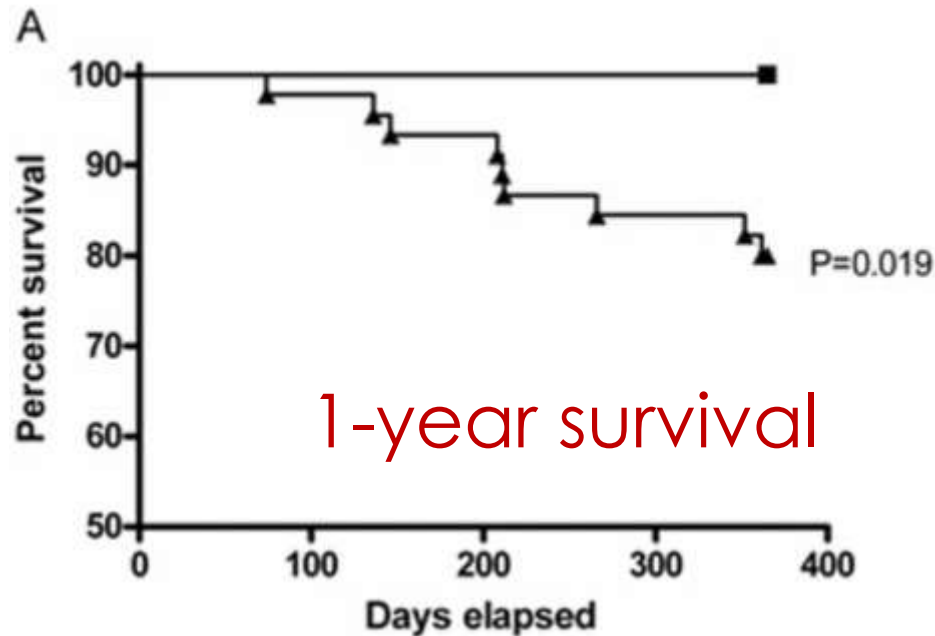


- ❖ In the UF group, an initial additional weight loss of 0.1 kg/10-kg body weight was prescribed per dialysis without increasing the time or frequency of dialysis. This additional weight loss was combined with the ultrafiltration volume required to remove interdialytic weight gain to achieve the desired reduction in dry weight
- ❖ If ultrafiltration was not tolerated based on symptoms and signs, such as muscle cramps, need for excessive saline, or symptomatic hypotension, the additional prescribed weight loss was reduced by 50%
- ❖ If ultrafiltration was still not tolerated, the additional weight loss was further reduced by 50% until even 0.2-kg incremental weight loss per dialysis was not tolerated. At this point, the patient was said to be at his or her dry weight
- ❖ Thus, by this protocol, each patient had to experience symptoms of volume depletion to be at dry weight.

# Hemodialysis and myocardial injury

## Effect on increasing UF and intra-dialysis hemodynamics on development of RWMA

Factor associated with presence of myocardial stunning	Odds Ratio	P value
UF volume during HD of 1L	5.1	0.007
UF volume during HD of 1.5L	11.6	
UF volume during HD of 2L	26.2	
Maximum SBP reduction during HD of 10 mmHg	1.8	0.002
Maximum SBP reduction during HD of 20 mmHg	3.3	
Maximum SBP reduction during HD of 30 mmHg	6.0	



Burton JO, cJASN 2009; 4:914-920

Improvement in care and outcomes is possible by extending the use of existing technology to fill the gaps in HD delivery in Asia

# Improving outcomes on dialysis

## Mortality Decrease Across Disease States in the U.S., 2006-2016\*

Disease	Mortality Decrease (%)
Kidney failure (dialysis)	20
Cancer	13
Diabetes	10
Congestive heart failure	2

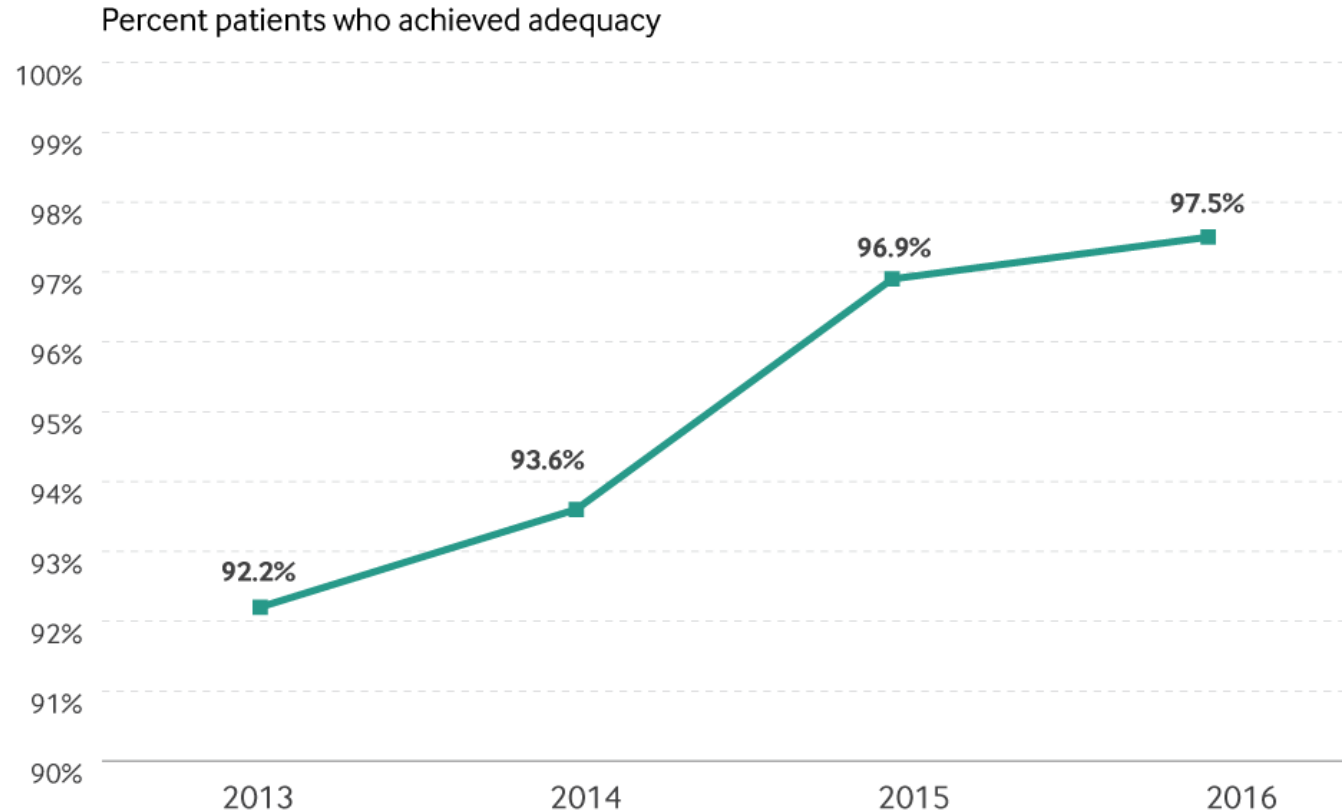
\*Calculated with data for patients  $\geq 65$  years of age.

Source: USRDS 2018 Annual Data Report, Chapter 5, Table F5.5  
NEJM Catalyst (catalyst.nejm.org) © Massachusetts Medical Society

**Mortality of Medicare HD patients decreased from 30.9% in 2006 to 24.7% in 2016**

# Improving outcomes on dialysis

Percentage of U.S. Adult Hemodialysis Patients Achieving Dialysis Adequacy, 2013-2016. 2017 Data will be Released in Early 2019.

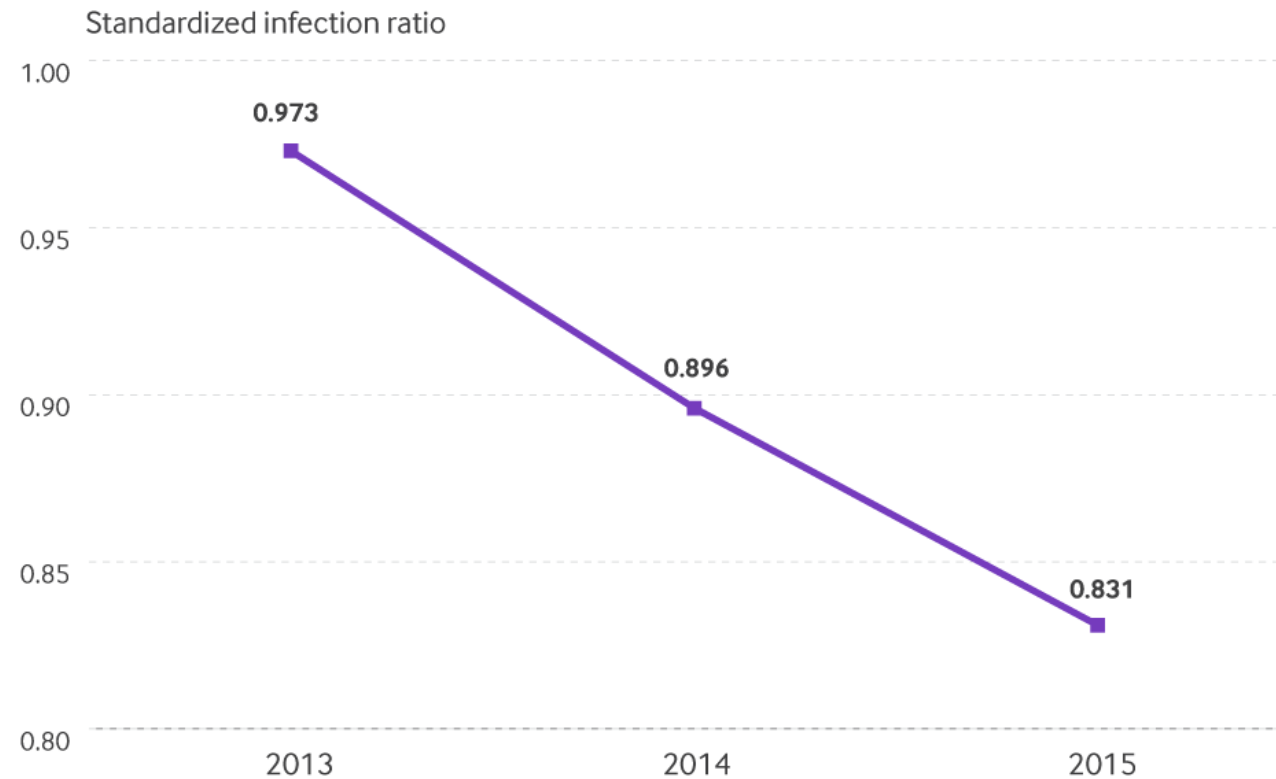


Source: The Authors  
NEJM Catalyst (catalyst.nejm.org) © Massachusetts Medical Society



# Improving outcomes on dialysis

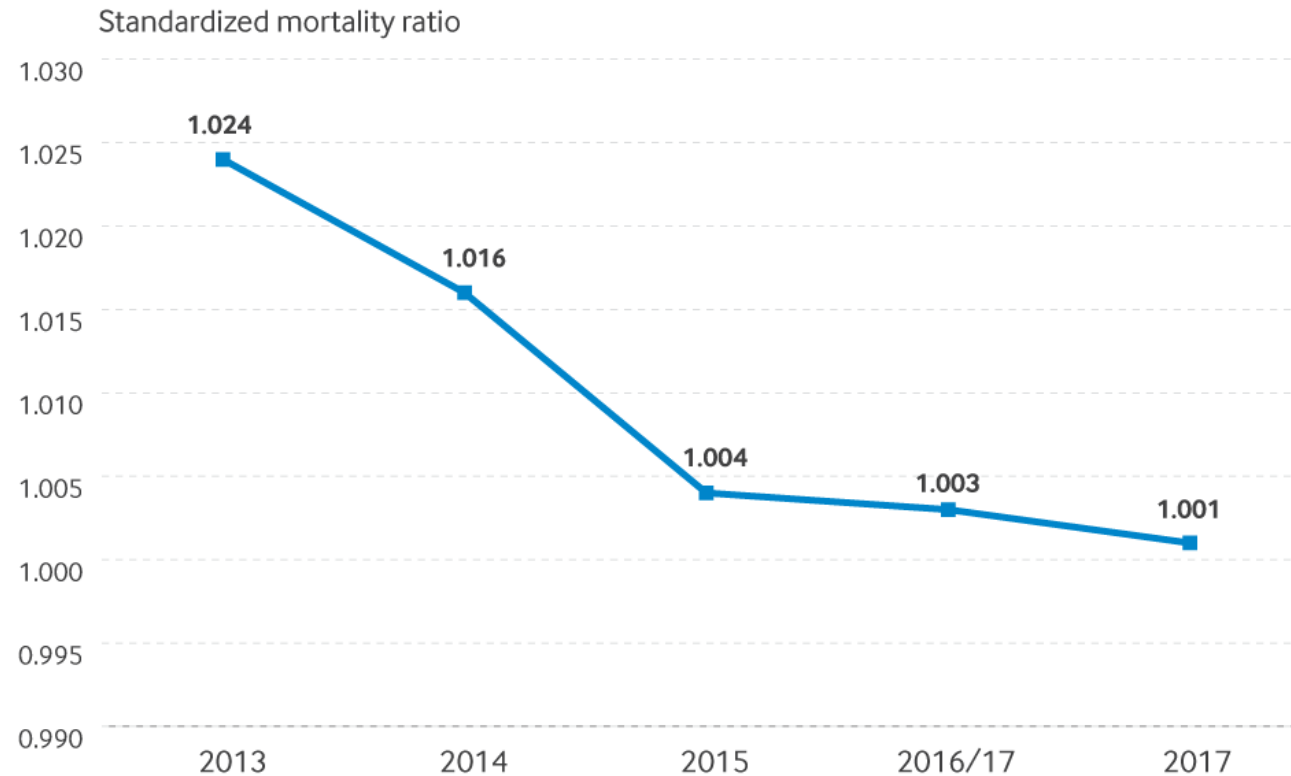
## U.S. Five-Star Dialysis Results: Standardized Infection Ratio Improvements, 2013-2017.



Source: The Authors  
NEJM Catalyst (catalyst.nejm.org) © Massachusetts Medical Society

# Improving outcomes on dialysis

## U.S. Five-Star Dialysis Results: Standardized Mortality Ratio Improvements, 2013-2017.



Source: The Authors  
NEJM Catalyst (catalyst.nejm.org) © Massachusetts Medical Society

# Improving outcomes on dialysis

- ❖ Fistula first effort
- ❖ Performance Excellence and Accountability in Kidney Care (PEAK initiative): collaboration of physicians, patients, dialysis providers, researchers etc. to improve outcomes
- ❖ Specialized integrated pharmacy services to optimize medications and reduce pill burden

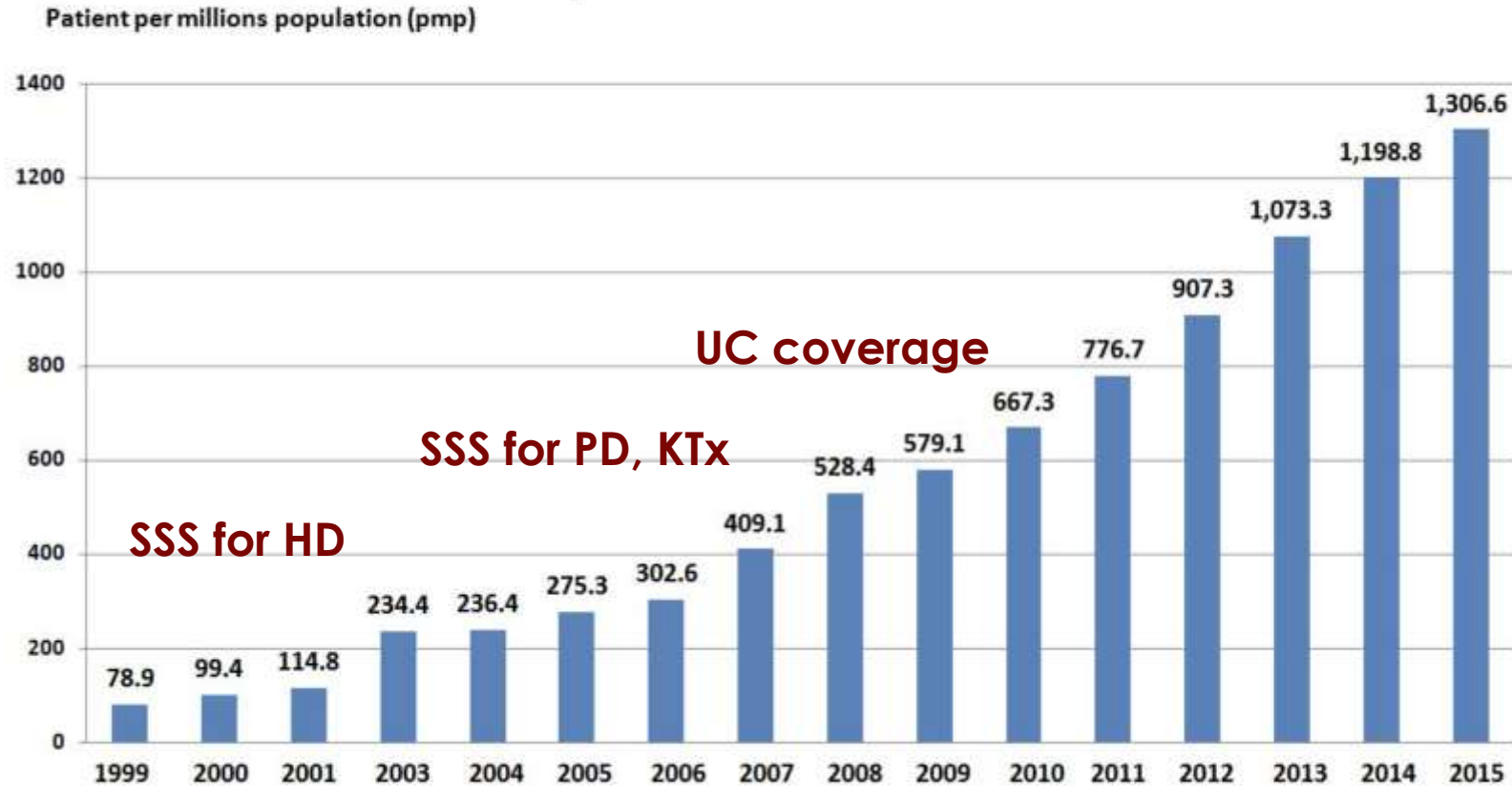
# Improving outcomes on dialysis

Year	Initiative
2006	ESKD Chronic Condition Special Needs Program
2011	Bundled a more complete set of ESKD services
2012	Launched ESKD Quality Initiative Program
2013	Implemented Five-star Quality Rating System
2015	ESKD Seamless Care Organization

# Prevalence of RRT and financial subsidy



## Yearly prevalence trend of renal replacement therapy patients in 1997-2015



\*Missing data in 2002

\*\* Data adjusted for Thai Transplantation Society 2007-2015

# Strategies for CKD and ESKD care in SEA

Need	Strategy
1. Risk factor recognition: need to establish "Unknown" factors	<ul style="list-style-type: none"> <li>• Epidemiological and population-based cohort studies</li> </ul>
2. Screening for kidney disease in population at risk	<ul style="list-style-type: none"> <li>• Increase awareness amongst all types of health-care providers at all levels of health-care delivery</li> <li>• Involve health-care workers starting at the lowest levels of health-care delivery to increase access to community</li> <li>• Regional or national level screening programs, integration with other noncommunicable disease programs</li> </ul>
3. Identification of risk factors for progression of kidney disease	<ul style="list-style-type: none"> <li>• Long-term, prospective CKD cohort studies</li> </ul>
4. Recognition of complications of CKD and their management	<ul style="list-style-type: none"> <li>• Early referral to nephrologist</li> <li>• Sensitization of primary care and specialist physicians</li> </ul>
5. Increase access to dialysis	<ul style="list-style-type: none"> <li>• Establish hemodialysis facilities at secondary and tertiary level healthcare institutions with involvement of both public and private sector health-care setups</li> <li>• Increase awareness about peritoneal dialysis</li> </ul>
6. Increase access to transplantation	<ul style="list-style-type: none"> <li>• Increase awareness about and promote deceased-donor renal transplantation</li> <li>• Develop regional and national level deceased -donor organ sharing programs involving both public and private sector hospitals</li> </ul>

Kumar V, Clin Nephrol 2016; 86 (Suppl 1);S23-S26

# Conclusion

- ❖ The challenges of provision of HD in Asia are unique
- ❖ Establish a robust system of HD delivery in Asia prior to chasing advanced technologies in HD
- ❖ Invest in developing innovative ideas for delivery of HD in Asia
- ❖ Raise awareness of kidney disease in public and in government

# Conclusion

- ❖ Lobby for insurance coverage via public and private means
- ❖ Set up registries at country and regional level
- ❖ Collaborative efforts amongst the stakeholders in the region



# Thank you

# Advanced Hemodialysis Technologies is needed to improve ESKD care in Asia

