KDIGO Controversies Conference on Supportive / Palliative Care in CKD

December 6-8, 2013

Mexico City, Mexico

Special thanks to

ISN International Society of Nephrology 1960

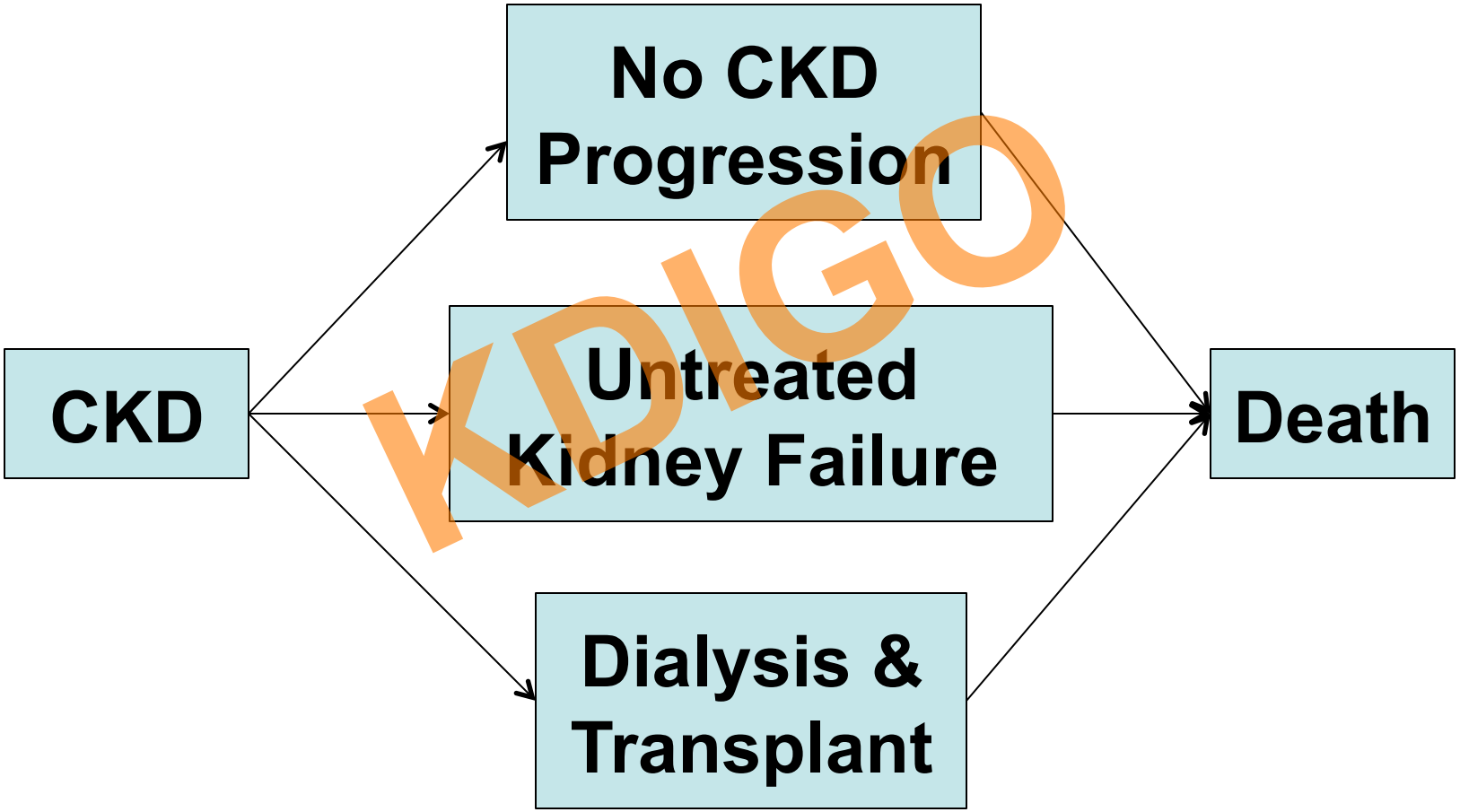
FMR® Fundación Mexicana del Riñón A.C.

Disclosure of Interests

• Litholink/Labcorp	CKD Advisory Board
• Medscape (Novartis)	Sponsored Education
• Rockepoint (Astellas, Novartis)	Sponsored Education
• Merck, Inc.	Speaker honorarium

Chronic Kidney Disease Outcomes

Chronic Kidney Disease Outcomes



Detecting Untreated Kidney Failure

Why should we care?

Detecting Untreated Kidney Failure: *Why Should We Care?*

- Providing access to care
  - Dialysis and transplantation
  - Palliative/supportive care
- Avoiding complications
  - Drug dosing
  - Acute kidney injury
- Preventing morbidity & mortality
  - CVD risk-factor intervention
  - Anemia, MBD, etc.

Detecting Untreated Kidney Failure

What role can registries play?

Prevalence of CKD Stages in the US

CKD Stage[a]	Estimated No. of US Adults in 2000, No. in Millions (95% CI)
1	3.6 (2.7-4.5)
2	6.5 (5.2-7.8)
3	15.5 (14.1-16.8)
4	0.7 (0.5-0.9)

Treated ESRD ~350,000

J Coresh, et al. *JAMA.* 2007;298(17):2038

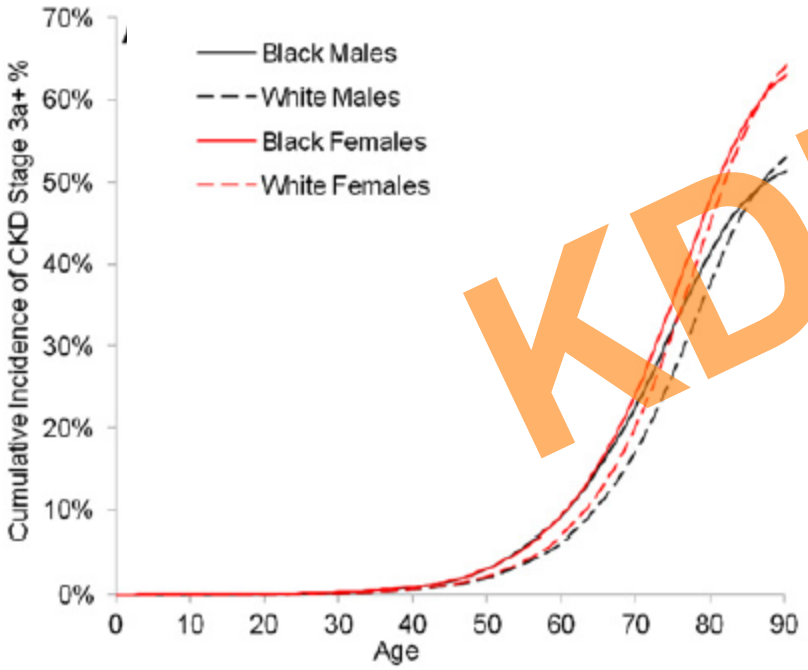
Age and Outcomes in Stage 4 CKD

Age	Death /100 pt-y	ESRD /100 pt-y
18 to 44	2.92 (0.02 to 5.82)	20.29 (13.35 to 27.22)
45 to 54	6.09 (4.72 to 7.47)	17.19 (14.82 to 19.56)
55 to 64	7.58 (6.45 to 8.71)	15.01 (13.40 to 16.61)
65 to 74	11.68 (10.64 to 12.71)	9.31 (8.41 to 10.21)
75 to 84	15.39 (14.43 to 16.36)	6.31 (5.65 to 6.96)
85 to100	25.35 (22.17 to 34.05)	2.65 (1.64 to 3.67)

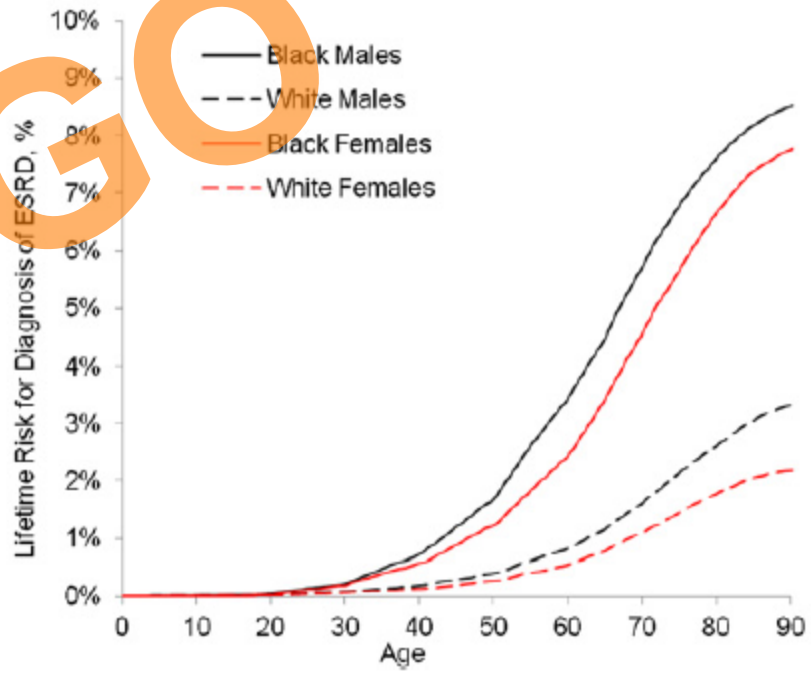
AM O' Hare, et al. *J Am Soc Nephrol 2007;* 18: 2758

Estimated Lifetime Risk of CKD

Stage 3a

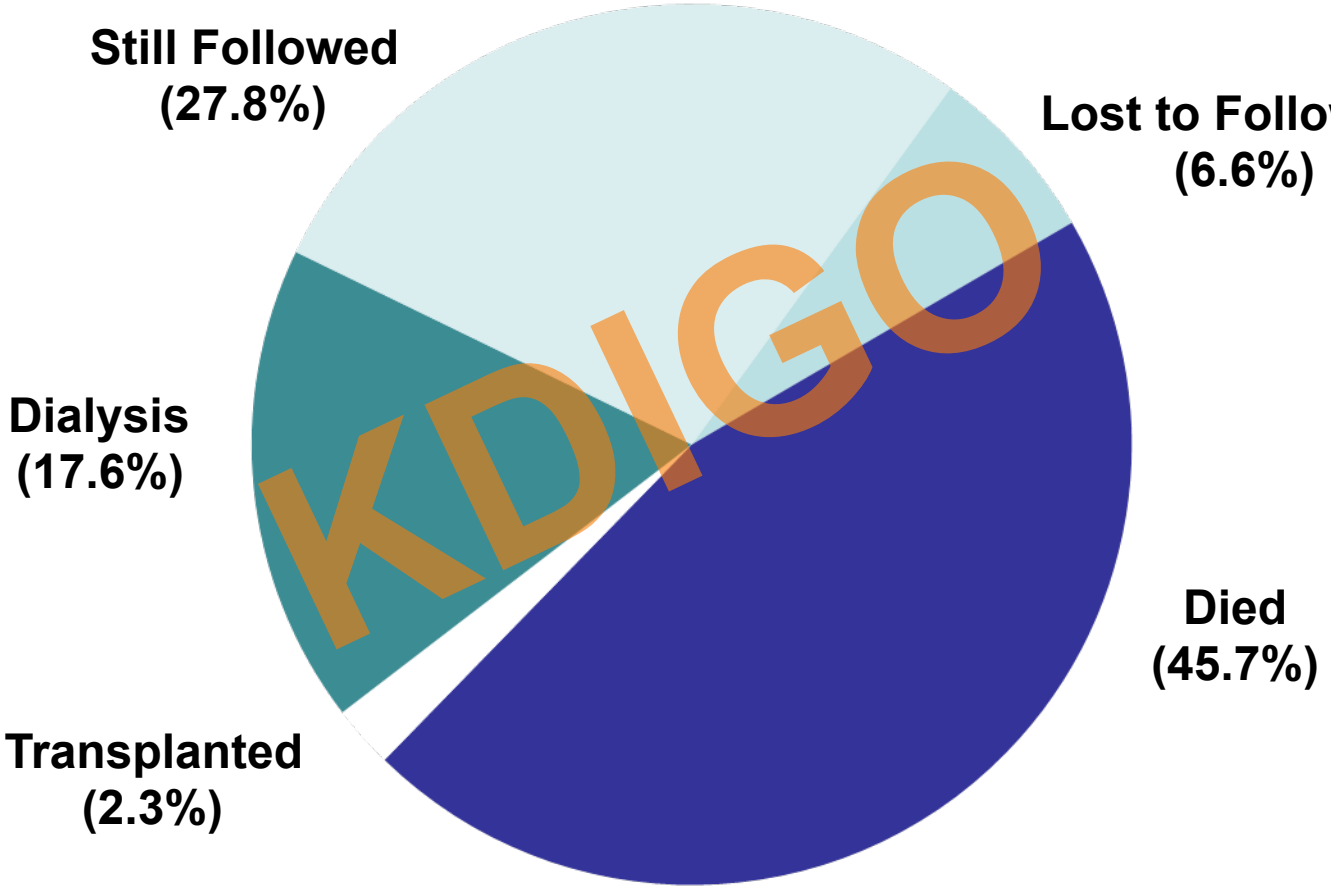


ESRD



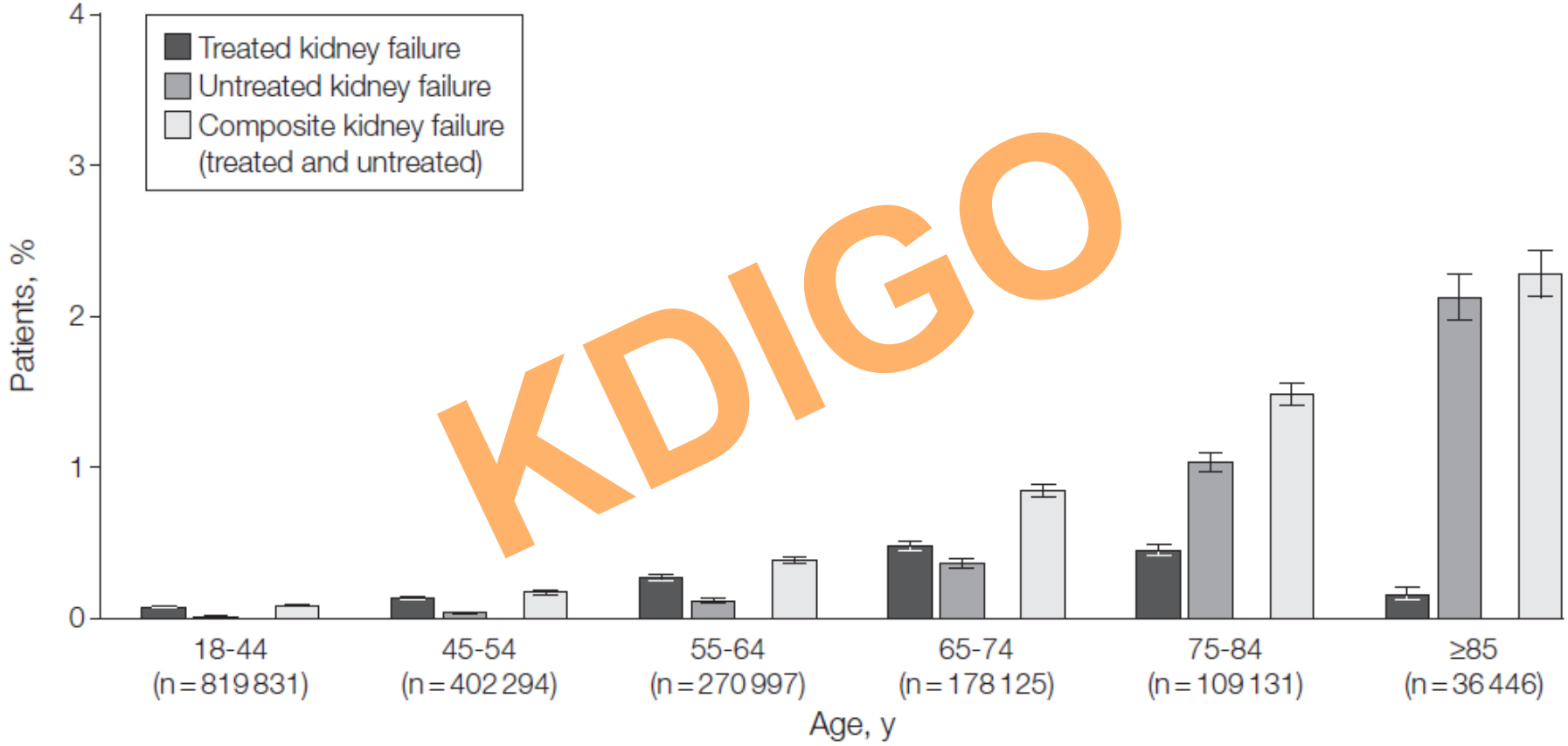
ME Grams, et al. *Am J Kidney Dis.* 2013; 62(2):245

Outcomes for Stage 4 CKD (N=777)



DS Keith el al. *Arch Intern Med*. 2004;164:659

Untreated Kidney Failure in Canada



BR Hemmelgarn et al. *JAMA.* 2012;307(23):2507

International Registry Study?

- International databases
  - General population, and/or
  - High-risk, and/or
  - CKD
- Pool individual patient data
- Goals
  - Incidence of treated & untreated renal failure
  - Provision of care
  - Opportunities for intervention

Minimum Inclusion Criteria

- Cohorts with adequate follow-up
  - Baseline demographics & comorbidity
  - Minimal loss to follow-up
- Estimated GFR
  - Baseline and follow-up
- Provision of care
  - Nephrology visits
- Events
  - Transplant
  - Dialysis
  - Death

Toward a Better Understanding of Untreated Renal Failure …

Thank you!

Data base survey

- Aim:
  - to get a comprehensive understanding of the breadth and width of dialysis databases in particular with respect to variables related to prognosis
- Methodology
  - Literature search
  - Letter to MONDO data base managers
  - Personal communications
  - Web research

Table content prepared by

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- DaVita – Kamyar Kalantar-Zadeh
- DIAVERUM - Giovanni FM Strippoli
- DOPPS – Francesca Tentori & Rajiv Saran
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- FMC North America – Len Usvyat
- Hadassah Hospital – Yosef Haviv
- Imperial College – Albert Powers
- KfH Germany – Claudia Barth & Gero v Gersdorf
- Maastricht University – Jeroen Kooman & Frank van der Sande
- REIN, ERA EDTA, UKRR – Cecile Couchoud
- Renji Hospital Shanghai – Mingli Zhu
- RRI – Peter Kotanko

Data Sources

- RRI, FMC Europe, Asia pacific, Latin America, Kuratorium fuer Heimdialyse (KfH), Haddasah Hospital, Imperial College: Usvyat, *Blood Purification* 2013
- Canada: Canadian Organ Replacement Registry Annual Report: www.cihi.ca
- Australia/New Zealand Dialysis and Transplant Registry Annual Report: www.anzdata.org
- REIN registry : French End-stage renal disease registry. Annual report: http://www.agence-biomedecine.fr/Le-programme-REIN
- ERA EDTA : European End-stage renal disease registry. Annual report : http://www.era-edta-reg.org/
- UKRR : United-Kingdom End-stage renal disease registry. Annual report : http://www.renalreg.com/
- USRDS: United States Renal Data System. Annual Data Report: http://www.usrds.org/2013/
- DOPPS: Dialysis Outcomes and Practice Patterns Study. DOPPS Annual report: http://www.dopps.org/
- Shanghai (single hospital data): Renji Hospital, Dr. Mingli Zhu, personal com.
- DaVita USA: Kalantar-Zadeh et al, *Circulation* 2009; 119:671-9. http://www.ncbi.nlm.nih.gov/pubmed/19171851

LARGE DATABASES (N>10,000 patients) OVERVIEW

DATABASE	COUNTRIES	NUMBER OF PATIENTS	NUMBER OF TREATMENTS
RRI	UNITED STATES	35,000	9,392,000
FMC LATIN AMERICA	BRAZIL / ARGENTINA / CHILE / VENEZUELA / COLOMBIA	40,000	1,000,000
FMC EUROPE	BOSNIA CZECH REPUBLIC/ FRANCE / ITALY / HUNGARY / IRELAND POLAND / PORTUGAL / ROMANIA / RUSSIA / UKRAINE / SERBIA / SLOVAKIA SLOVENIA / SPAIN / UK / SWEDEN / TURKEY / SOUTH AFRICA	59,000	21,770,000
KfH Germany	GERMANY	56,000	26,545,000
DOPPS	AUSTRALIA / BAHRAIN / BELGIUM / CANADA / CHINA / FRANCE GERMANY / ITALY / JAPAN / KUWAIT / NEW ZEALAND / OMAN QATAR / RUSSIA / SAUDI ARABIA / SPAIN / SWEDEN / TURKEY THE UNITED ARAB EMIRATES / UNITED KINGDOM / UNITED STATES	72,,000 +	
USRDS	UNITED STATES	390K(HD) and 31K(PD)	N/A
AUSTRALIAN	AUSTRALIA	25,000	N/A
CANADIAN	CANADA	46,000	N/A
REIN	FRANCE	122,000	464,000
UKRR	ENGLAND / SCOTLAND NORTHERN IRELAND / WALES	53,000	92,000
ERA-EDTA	AUSTRIA / BELGIUM / BOSNIA / HERZEGOVINA / DENMARK / FINLAND FRANCE / GREECE / ICELAND / NORWAY / ROMANIA / SERBIA / SPAIN / SWEDEN / THE NETHERLANDS / UNITED KINGDOM	580,000	1,900,000
DIAVERUM	FRANCE / GERMANY / HUNGARY / ITALY / LITHUANIA / POLAND / SPAIN PORTUGAL / ROMANIA / SWEDEN / TURKEY / UK / SAUDI ARABIA AUSTRALIA / ARGENTINA / CHILE / URUGUAY	23,000	3,400,000/YR
DaVita USA	UNITED STATES	150K(HD) and 15K(PD)	>5mil/yr
FMC NORTH AMERICA	UNITED STATES	>980,000	>227,000,000

DATABASE	BACKGROUND AND DEMOGRAPHICS AGE / GENDER / RACE	ADMIN/DISCHRGE DATA DATES, FIRST-EVER DATE OR RRT, REASONS FR DISCHARGE	MEDICAL HISTORY PRIMARY RENAL DISEASE COMBRIDTIES, CUSTOM GR
RRI	X	X	ICD-9
FMC LATIN AMERICA	EXCEPT RACE	X	ICD-10
FMC EUROPE	EXCEPT RACE	X	ICD-10
KfH Germany	EXCEPT RACE	X	ICD-10 AND CUSTOM GROUPS
DOPPS	X	X	ICD-9
USRDS	X	X	ICD-9
AUSTRALIAN	X	?	X
CANADIAN	X	X	X
REIN	EXCEPT RACE	X	PRD CMC (ICD-10) CAUSE OF DEATH (ICD-10)
UKRR	X	X	PRD / CMC CAUSE OF DEATH
ERA-EDTA	X	X	PRD / CMC CAUSE OF DEATH
DIAVERUM	X EXCEPT RACE IN FRANCE	X	PRD / CMC CAUSE OF DEATH
DaVita USA	X	X	ICD-9
FMC NORTH AMERICA	X	X	ICD-9

DATABASE	HOSPITALIZATIONS ADMIN / DISCHRGE DATES	DISCHRGE DIAGNOSIS	LABORATORY TIMING OF BLOOD DRAWS
RRI	X	ICD-9	MID-WEEK
FMC LATIN AMERICA	X	ICD-10	MID-WEEK
FMC EUROPE	X	ICD-10	MID-WEEK
KfH Germany	X	ICD-10	LONG INTERVAL
DOPPS	X	X	
USRDS	X	ICD-9	MID-WEEK
AUSTRALIAN	?	?	?
CANADIAN	X	ICD-9 AND 10	MID-WEEK
REIN	NBE OF DAYS AND FREQUENCY OVER THE YEAR	N/A	N/A
UKRR CAUSE OF DEATH	NO	NO	NO
ERA-EDTA	N/A	N/A	N/A
DIAVERUM	X	CUSTOM GROUPS	MID-WEEK
DaVita USA	X	ICD-9	EARLY to MID-WEEK
FMC NORTH AMERICA	X	ICD-9	MID-WEEK

DATABASE	ANEMIA MANAGEMENT		MINERAL/BONE	
	HGB MONTLY	FERRITIN/TSAT QUARTERLY	CALCIUM/PHOSPHORUS MONTHLY	PTH QUARTERLY
RRI	X	X	X	X
FMC LATIC AMERICA	X	X	X	X
FMC EUROPE	X	X	X	X
KfH Germany	X	X	X	X
DOPPS	X	X	X	X
USRDS	X	X	X	X
AUSTRALIAN	ANNUALLY	ANNUALLY	ANNUALLY	ANNUALLY
CANADIAN	ANNUALLY	ANNUALLY	ANNUALLY	ANNUALLY
REIN	ANNUALLY	N/A	N/A	N/A
UKRR	QUARTERLY	X	QUARTERLY	X
ERA-EDTA	ANNUALLY*	ANNUALLY*	ANNUALLY*	ANNUALLY*
DIAVERUM	X	X	X	X
DaVita USA	X	X	X	X
FMC NORTH AMERICA	X	X	X	X
* NOT FOR ALL COUNTRIES				

DATABASE	NUTRITION INFLAMMATION			DIALYSIS
	CRP	ALBUMIN (at least quarterly)	WBC NEU., LYM. (MONTHLY)	TREATMENT TIME, eKt/V, URR (PER TREATMENT)
RRI	N/A	X	X	X
FMC LATIN AMERICA	BI-ANNUALLY	VARIABLE	X	MONTHLY
FMC EUROPE	VARIABLE	X	X	X
KfH	VARIABLE	X	X	X
DOPPS	per practice	X	X	MONTHLY
USRDS	N/A	X	X	X
AUSTRALIAN	N/A	ANNUALLY	N/A	X
CANADIAN	N/A	ANNUALLY	ANNUALLY	N/A
REIN	N/A	ANNUALLY	N/A	ANNUALLY
UKRR	QUARTERLY	QUARTERLY	QUARTERLY	QUARTERLY
ERA-EDTA	ANNUALLY*	ANNUALLY*	N/A	ANNUALLY*
DIAVERUM	VARIABLE	X	VARIABLE	MONTLY*
DaVita USA	Small Proportion	X	X	MONTHLY
FMC NORTH AMERICA	by indication	X	X	X

* NOT FOR ALL COUNTRIES

DATABASE	VITAL SIGNS e.g.BP (per treatment)	WEIGHT/ VOLUME PRE/POST DIALYSIS (per treatment)	VASCULAR ACCESS, TYPE , DATES (per treatment)
RRI	X	X	X
FMC LATIN AMERICA	MONTHLY	MONTHLY	MONTHLY
FMC EUROPE	X	X	X
KfH	X	X	X
DOPPS	MONTHLY	MONTHLY	MONTHLY
USRDS	X	X	X
AUSTRALIAN	N/A	N/A	ANNUALLY
CANADIAN	N/A	ANNUALLY	ANNUALLY
REIN	N/A	ANNUALLY	ANNUALLY
UKRR	QUARTERLY	QUARTERLY	ANNUALLY
ERA-EDTA	ANNUALLY*	N/A	ANNUALLY*
DIAVERUM	MONTLY*	MONTHLY*	MONTHLY*
DaVita USA	X	X	X
FMC NORTH AMERICA	X	X	X
* NOT FOR ALL COUNTIRES			

DATABASE	WITHDRAWAL CAPTURED	CAUSE OF WITHDRAWAL	SYMPTOMS	QoL
RRI	X	X	MARGINALLY	X
FMC LATIN AMERICA	X	N/A	N/A	N/A
FMC EUROPE	X	N/A	MARGINALLY	N/A
KfH	X	N/A	N/A	X
DOPPS	X	X	X	KDQOL
USRDS	X	X	N/A	N/A
AUSTRALIAN	X	X	N/A	N/A
CANADIAN	X	N/A	N/A	N/A
REIN	X	MEDICAL COMPLICATION OR PATIENT REFUSAL	N/A	EVERY 5 YRS ON SAMPLE
UKRR	X	X	NO	NO
ERA-EDTA	X	N/A	N/A	N/A
DIAVERUM	X	X	NO	NO
DaVita USA	X	X	TBD	X
FMC NORTH AMERICA	X	X	MARGINALLY	KDQOL

DATABASE	FRAILTY SYMPTOMS	KARNOFSKY	CHOOSING CONSERVATIVE MANAGEMENT
RRI	MARGINALLY	N/A	N/A
FMC LATIN AMERICA	N/A	N/A	N/A
FMC EUROPE	N/A	N/A	N/A
KfH	N/A	N/A	N/A
DOPPS	N/A	N/A	N/A
USRDS	N/A	N/A	N/A
AUSTRALIAN	N/A	N/A	N/A
CANADIAN	N/A	N/A	N/A
REIN	N/A	N/A	N/A
UKRR	N/A	N/A	N/A
ERA-EDTA	N/A	N/A	N/A
DIAVERUM	MARGINALLY	X	NO
DaVita USA	MARGINALLY	N/A	N/A
FMC NORTH AMERICA	MARGINALLY	N/A	N/A

SMALL DATABASES (N<10,000 patients) OVERVIEW

DATABASE	COUNTRIES	NUMBER OF PATIENTS	NUMBER OF TREATMENTS
MAASTRICHT	NETHERLANDS	1,978	159,000
IMPERIAL COLLEGE	UNITED KINGDOM	7,407	1,182,000
HADASSAH	ISRAEL	219	8,000
FMC ASIA PACIFIC	AUSTRALIA / CHINA (HONG KONG) / CHINA (TAIWAN) SINGAPORE / SOUTH KOREA / THAILAND / MALAYSIA PHILLIPINES	12,000	250,000
SHANGHAI	CHINA	632	N/A

DATABASE	BACKGROUND AND DEMOGRAPHICS AGE / GENDER / RACE	ADMIN/DISCHRGE DATA DATES, FIRST-EVER DATE OR RRT, REASONS FOR DISCHARGE	MEDICAL HISTORY PRIMARY RENAL DISEASE COMBRID CONDITIONS CUSTOM GROUPS
MAASTRICHT	EXCEPT RACE	X	ICD-10
IMPERIAL COLLEGE	X	X	ICD-10
HADASSAH	X	X	ICD-10
FMC ASIA PACIFIC	EXCEPT RACE	X	CUSTOM GROUPS
SHANGHAI	EXCEPT RACE	X	CUSTOM GROUPS

DATABASE	HOSPITALIZATIONS ADMIN / DISCHRGE DATES	DISCHRGE DIAGNOSIS	LABORATORY TIMING OF BLOOD DRAWS
MAASTRICHT	N/A	N/A	MID-WEEK
IMPERIAL COLLEGE	X	ICD-10	MID-WEEK
HADASSAH	X	ICD-10	MID-WEEK
FMC ASIA PACIFIC	X	CUSTOM GROUPS	MID-WEEK
SHANGHAI	N/A	N/A	LONG INTERVALS

DATABASE	ANEMIA MANAGEMENT		MINERAL/BONE	
	HGB MONTLY	FERRITIN/TSAT QUARTERLY	CALCIUM/PHOSPHORUS MONTHLY	PTH QUARTERLY
MAASTRICHT	X	X	X	X
IMPERIAL COLLEGE	X	X	X	X
HADASSAH	X	X	X	X
FMC ASIA PACIFIC *	X	X	N/A	X
SHANGHAI	QUARTERLY	BI-ANNUALLY	QUARTERLY	BI-ANNUALLY

* Varies by country

DATABASE	NUTRITION INFLAMMATION			DIALYSIS
	CRP	ALBUMIN (at least quarterly)	WBC NEUTROPHILS LYMPHOCYTES (MONTLY)	TREATMENT TIME, eKt/V, URR (PER TREATMENT)
MAASTRICHT	MONTHLY	X	VARIABLE	X
IMPERIAL COLLEGE	N/A	X	X	X
HADASSAH	N/A	X	X	X
FMC ASIA PACIFIC	ANNUALLY	X	N/A	N/A
SHANGHAI	VARIABLE	QUARTERLY	QUARTERLY	QUARTERLY

DATABASE	VITAL SIGNS e.g. BP (per treatment)	WEIGHT/ VOLUME PRE/POST DIALYSIS (per treatment)	VASCULAR ACCESS, TYPE , DATES (per treatment)
MAASTRICHT	X	X	X
IMPERIAL COLLEGE	X	X	X
HADASSAH	X	X	X
FMC ASIA PACIFIC	MONTHLY	MONTHLY	MONTHLY
SHANGHAI	X	X	X

DATABASE	WITHDRAWAL CAPTURED	CAUSE OF WITHDRAWAL	SYMPTOMS	QoL
MAASTRICHT	X	N/A	N/A	X
IMPERIAL COLLEGE	X	N/A	N/A	N/A
HADASSAH	N/A	N/A	N/A	N/A
FMC ASIA PACIFIC				
SHANGHAI	N/A	N/A	N/A	N/A

DATABASE	FRAILTY SYMPTOMS	KARNOFSKY	CHOOSING CONSERVATIVE MANAGEMENT
MAASTRICHT	N/A	N/A	N/A
IMPERIAL COLLEGE	N/A	N/A	N/A
HADASSAH	N/A	N/A	N/A
FMC ASIA PACIFIC			
SHANGHAI	N/A	N/A	N/A

Preliminary summary

- Dialysis providers maintain data bases with frequently sampled treatment data (in most cases per treatment), directly imported lab values, comprehensive demographic data
- Registry data are less frequently sampled
- Data on frailty symptoms, Karnofsky index, and treatment choices are lacking in most data bases

The MONitoring Dialysis Outcomes (MONDO) initiative

KDIGO Controversies Conference

Mexico City

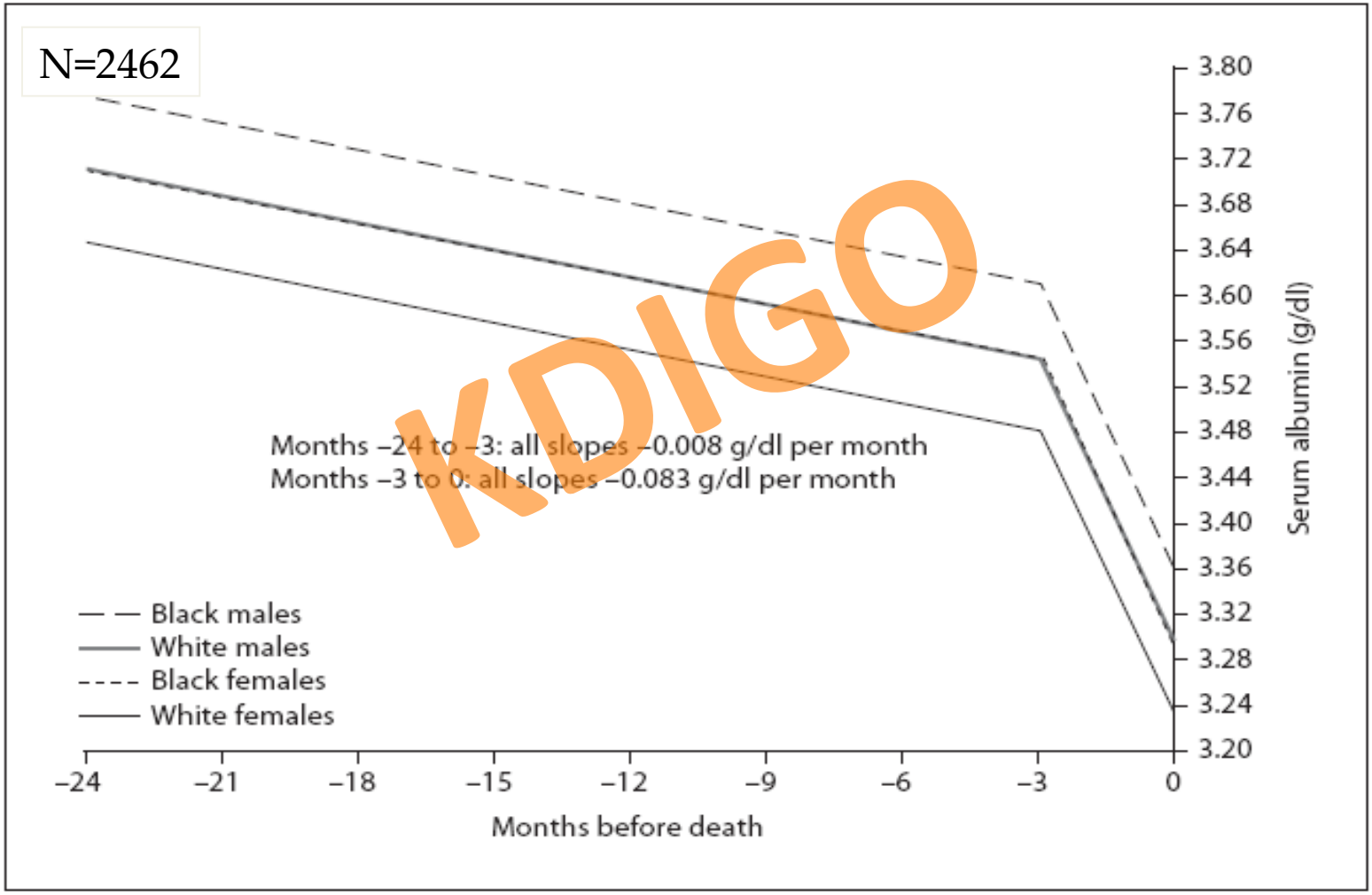
December 6-8, 2013

Peter Kotanko & Len Usvyat

Renal Research Institute, New York

For the MONDO Consortium

Declines in Serum Albumin Levels before Death



Kotanko et al, Blood Purification, 2009; 27: 38-47

Research Question

- *Are we observing phenomena specific to US hemodialysis patients or more general and fundamental biological processes?*
- *What sort of data do we need to address this question?*
  - *Longitudinal and frequently measured data from dialysis populations at a global level*
  - *No readily available data base of that kind 2010*

MONDO Partners (2013)

- Imperial College, UK
- University of Maastricht, The Netherlands
- Hadassah Medical Center, Israel
- Kuratorium für Dialyse und Nierentransplantation (KfH) and University Cologne, Germany
- FMC Europe, Middle East, Latin America
- FMC Asia Pacific
- FMC Canada
- Renal Research Institute, USA
- University Curitiba, Brazil

data

- time range: 2000 to 2012 (data is updated annually)
- number of clinics: ~1,200
- number of patients: ~150,000
- number of treatment and laboratory records: ~30 million
- where:
  - six continents
  - 38 countries

Usvyat, Blood Purification, 2013

countries

- Asia/Australia
  - Australia
  - China (Hong Kong)
  - Malaysia
  - New Zealand
  - Philippines
  - Singapore
  - South Korea
  - China (Taiwan)
  - Thailand
- North America
  - Canada
  - USA
- South America
  - Argentina
  - Brazil
  - Chile
  - Colombia
  - Venezuela
- Africa
  - South Africa
- Europe/Middle East
  - Bosnia
  - Czech Republic
  - France
  - Germany
  - Hungary
  - Ireland
- Europe/Middle East (cont'd)
  - Israel
  - Italy
  - Netherlands
  - Portugal
  - Poland
  - Romania
  - Russia
  - Slovenia
  - Slovakia
  - Spain
  - Serbia
  - Sweden
  - Turkey
  - UAE
  - UK

Usvyat, Blood Purification, 2013

data elements

- *all data is collected from database specific electronic health records (EHR) systems*
- *all data is patient-specific and longitudinal data (per treatment or month)*
- patient and clinic information
  - clinic location
  - age
  - gender
  - race
  - comorbid conditions, smoking status
  - amputations
  - other measures of body size

Usvyat, Blood Purification, 2013

data elements (cont'd)

- morbidity and mortality data
  - hospitalization dates
  - reasons for hospitalizations
  - quality of life surveys
- admission and discharge information
  - admission and discharge dates, exposure time
  - discharge reason

Usvyat, Blood Purification, 2013

data elements (cont'd)

- treatment parameters:
  - pre and post blood pressure
  - pre weight and achieved post weight
  - pre and post temperature (where available)
  - pre and post heart rate (where available)
  - prescribed and effective treatment duration and UF time
  - data on relative blood volume monitoring (where available)
  - vascular access (and related information)
  - all in-center drug administration (type and dose)
  - hemodiafiltration (where available)
  - prescribed target weight (where available)
  - prescribed dialysate composition (where available)

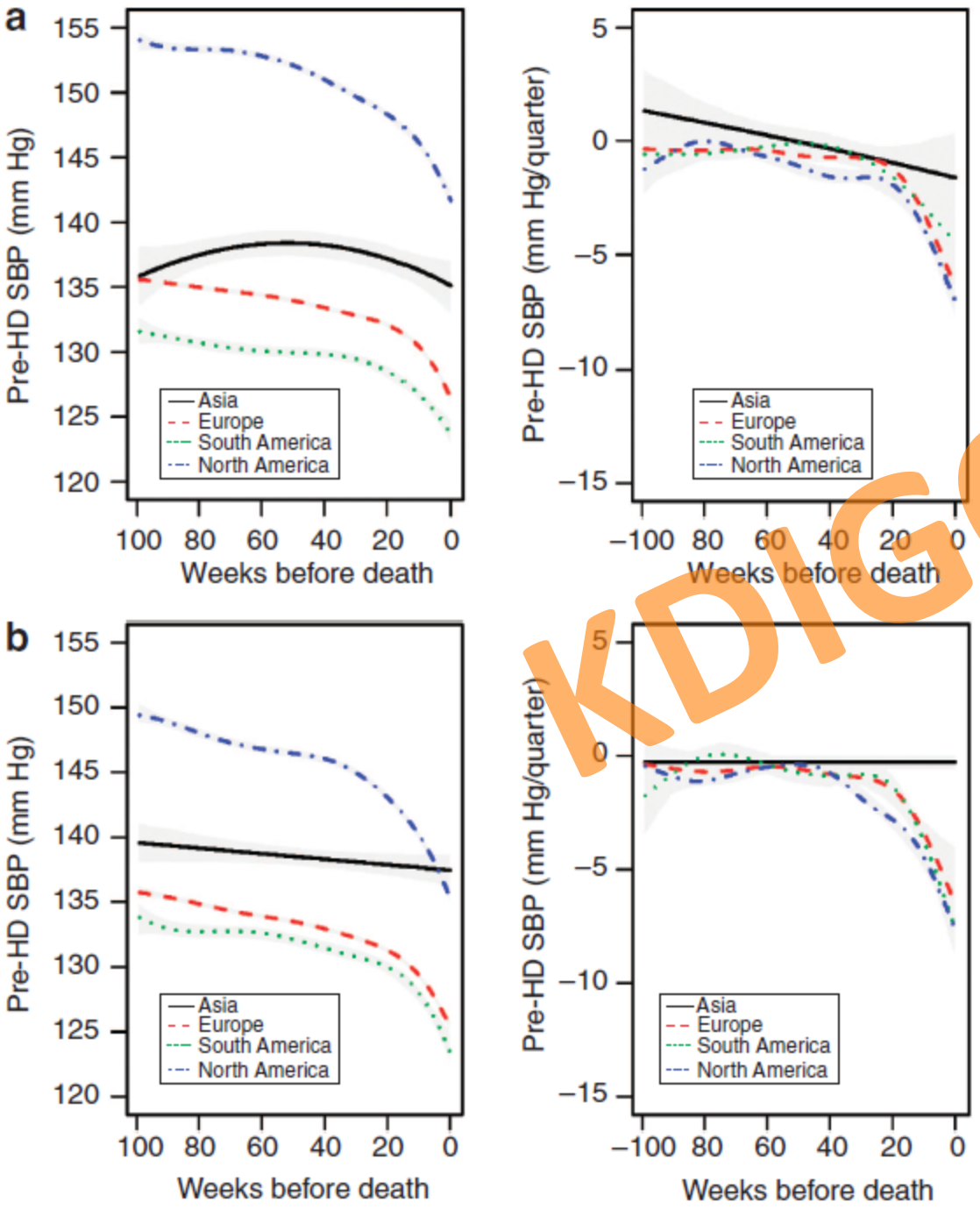
Usvyat, Blood Purification, 2013

data elements (cont.)

- laboratory and adequacy parameters:
  - albumin
  - hgb
  - calcium
  - phosphorus
  - sodium
  - chloride
  - bicarbonate
  - CRP
  - white blood cells
  - TSAT
  - ferritin
  - URR
  - creatinine
  - PCR
  - Kt/V
  - urea distribution volume
  - residual renal function
  - many others
- EKG, bioimpedance (Body Composition Monitor), echocardiography

Usvyat, Blood Purification, 2013

SBP before death



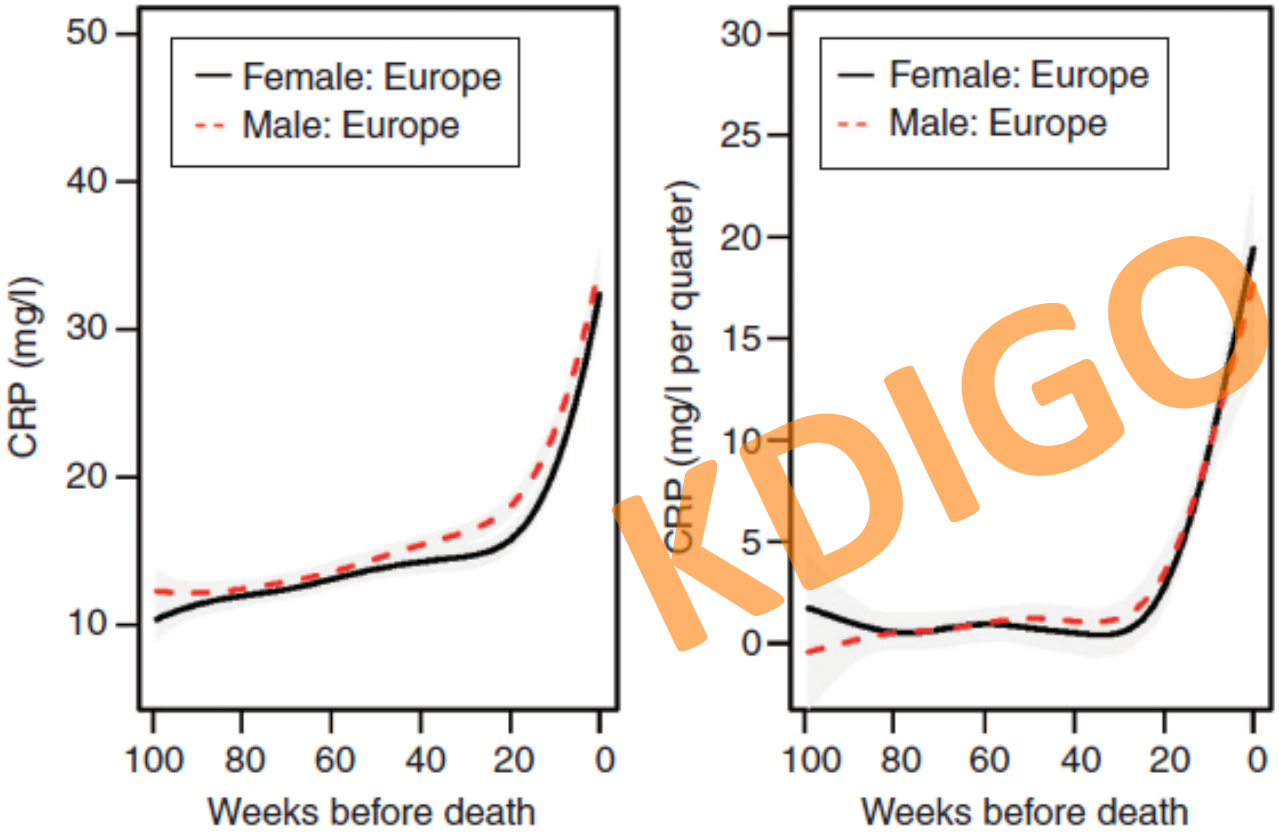
Mean pre-hemodialysis (pre-HD) systolic blood pressure (SBP) and 95% confidence intervals.

(a) Mean pre-dialysis (pre-HD) systolic blood pressure (SBP) and 95% confidence intervals in female patients in he 104 weeks before death. The left panels show estimates of the partially conditional means with 95% confidence intervals, and the right panels show estimates of rate of change trajectories with 95% confidence intervals.

(b) Mean pre-HD SBP and 95% confidence intervals in male patients in the 104 weeks before death.

Usvyat L, Kidney International 2013

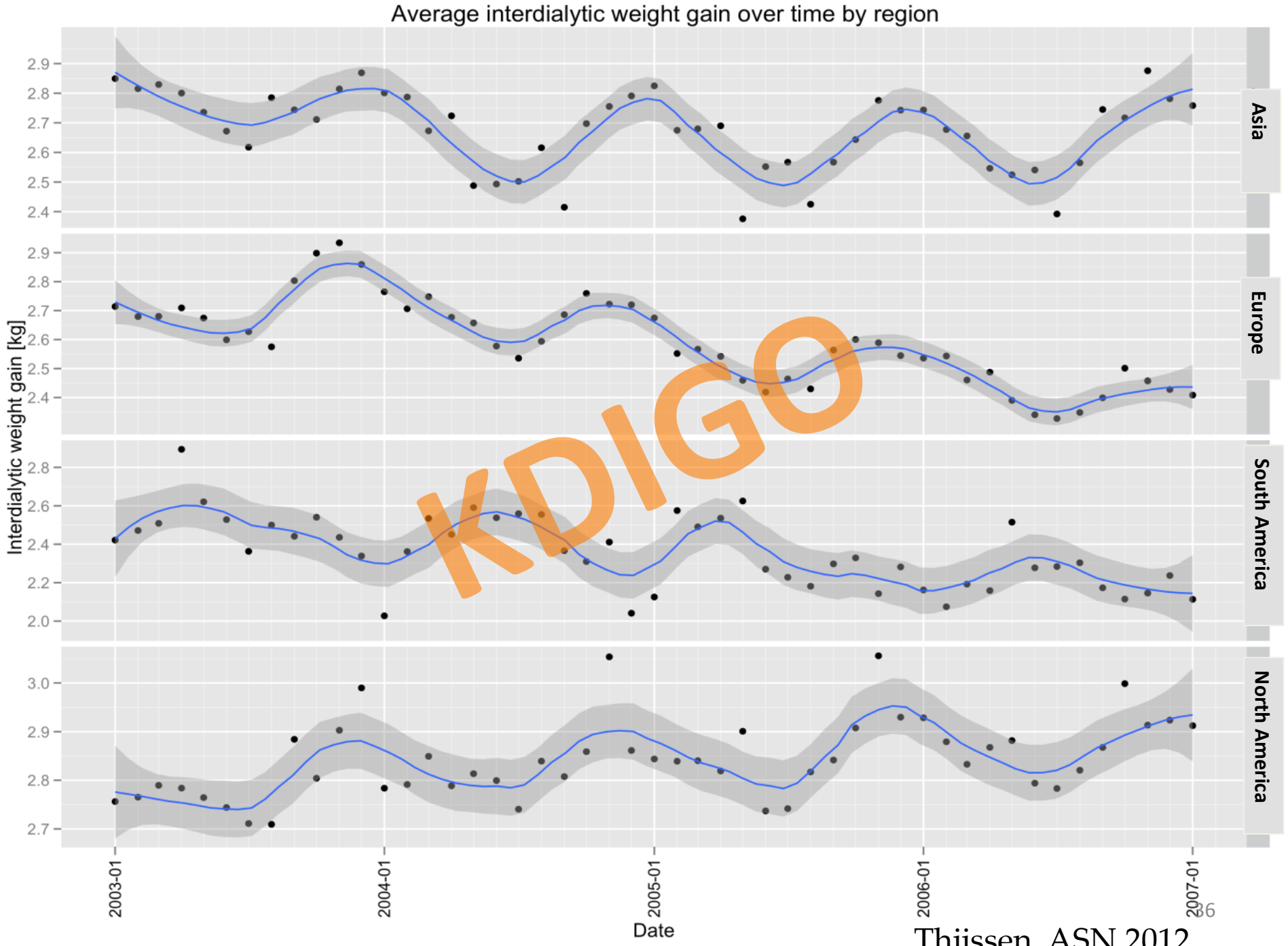
C-reactive protein (CRP) before death



Mean CRP and 95% confidence intervals in the 104 weeks before death.

The left panel shows estimates of the partially conditional means with 95% confidence intervals, and the right panel shows estimates of rate of change trajectories with 95% confidence intervals.

Usvyat L, Kidney International 2013



Thijssen, ASN 2012