Insuffisance rénale et épuration extra-rénale chez le patient d'onco-hématologie

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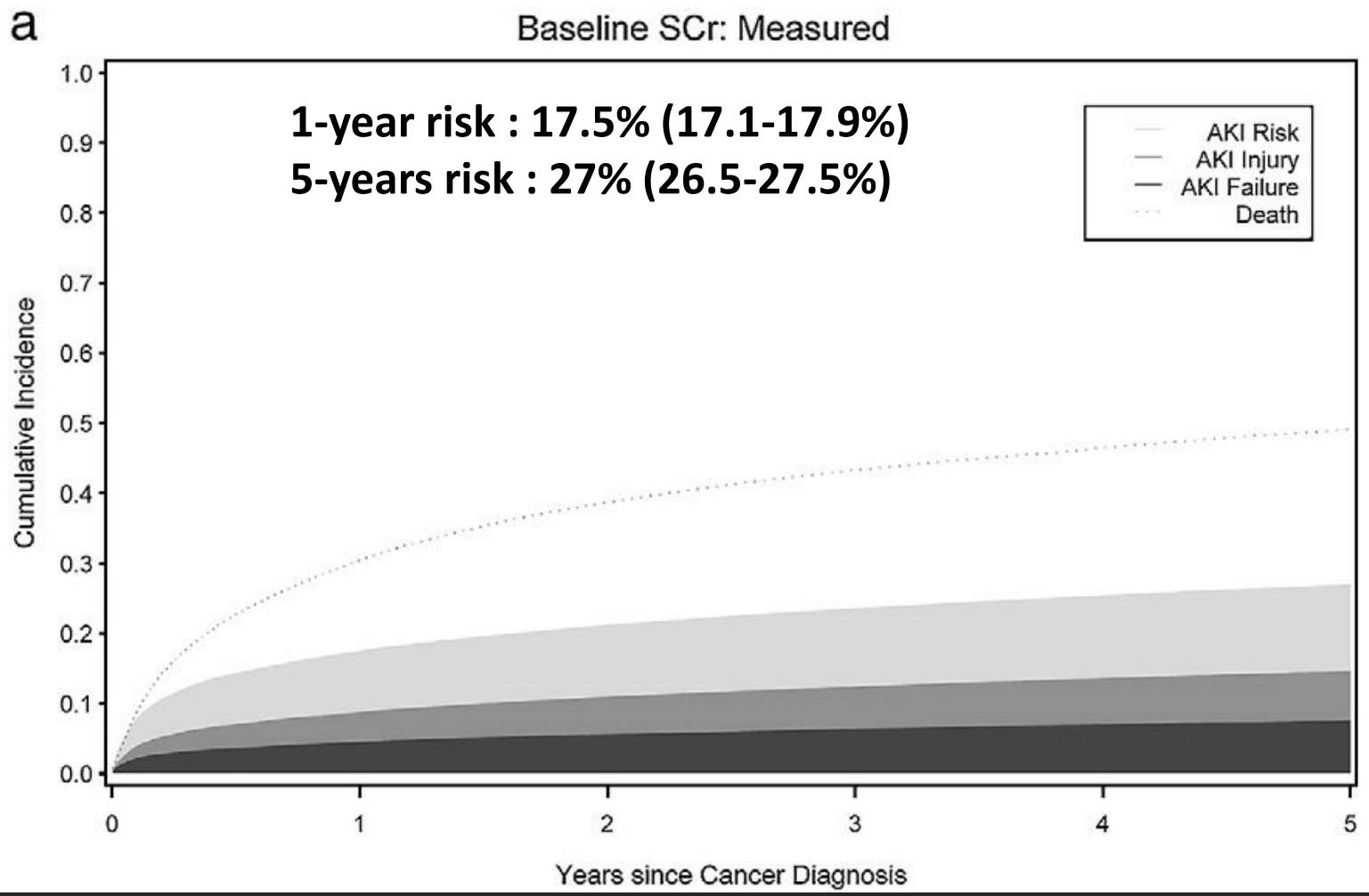
Conflits d’intérêts

- Research grants: MSD, Astute medical
- Speaker fees: MSD, Astellas, Bristol Myers Squibb, Gilead
- Support in organizing educational meetings: MSD, Astellas, JazzPharma
- Advisory board: Sanofi Aventis, Gilead-Kite

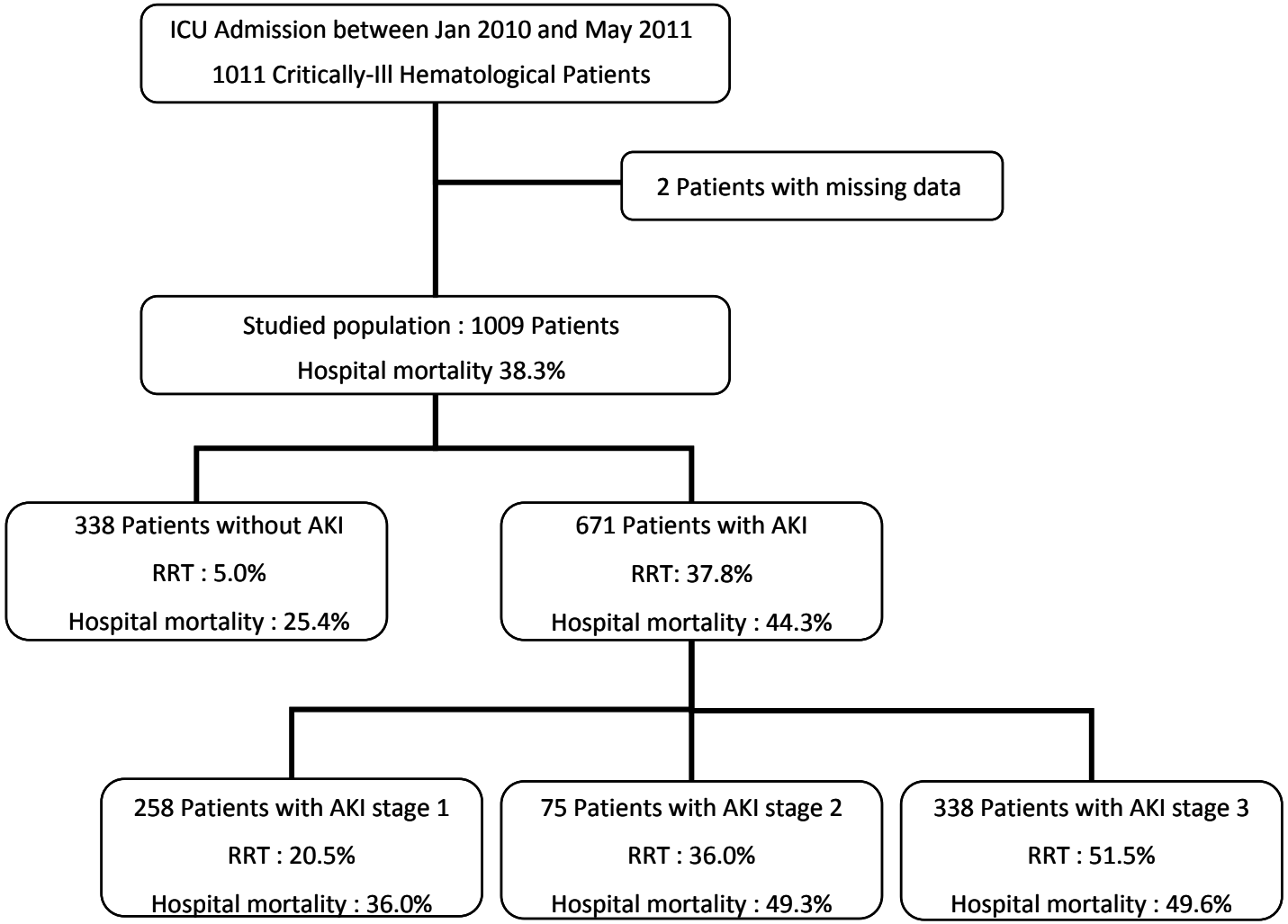
AKI in cancer patients

Prevalence and Consequences



Christiansen et al. Eur J Intern Med 2011

Prevalence and Consequences



Darmon et al. Nephrol Dial Transplant 2015

Risk factors of AKI in ICU cancer patients

	Odds ratio	95% CI	*P* value
Age (/year)	1.02	1.006-1.027	0.001
Chronic Kidney Disease	1.99	0.96-4.16	0.07
History of hypertension	1.65	1.11-2.44	0.02
Tumor lysis syndrome	4.18	2.12-11.2	<0.0001
Nephrotoxic agents	5.25	2.46-11.20	<0.0001
Myeloma	1.89	1.10-2.85	0.02
SOFA score at admission (per	1.15	1.10-1.21	<0.0001

Darmon et al. Nephrol Dial Transplant 2015

AKI and probability to achieve complete remission

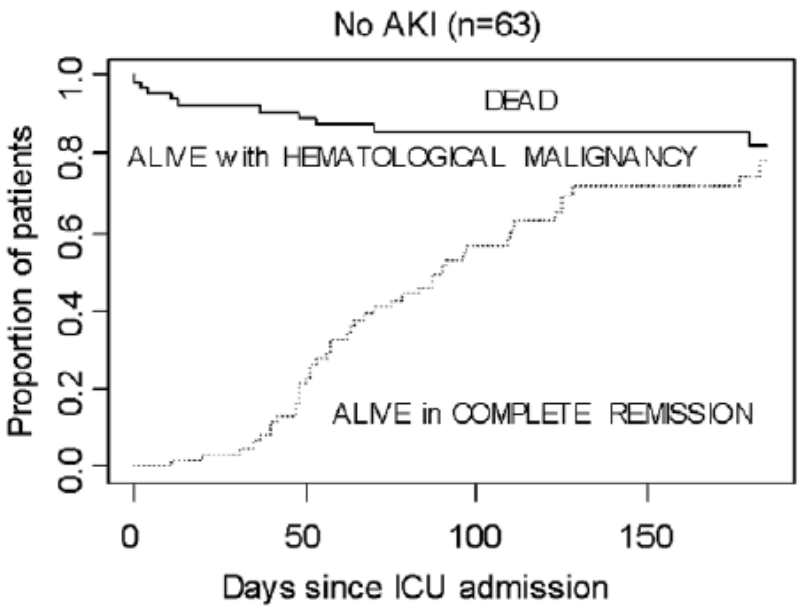
Table 3. Outcome of chemotherapy in patients with and without renal complications at diagnosis.

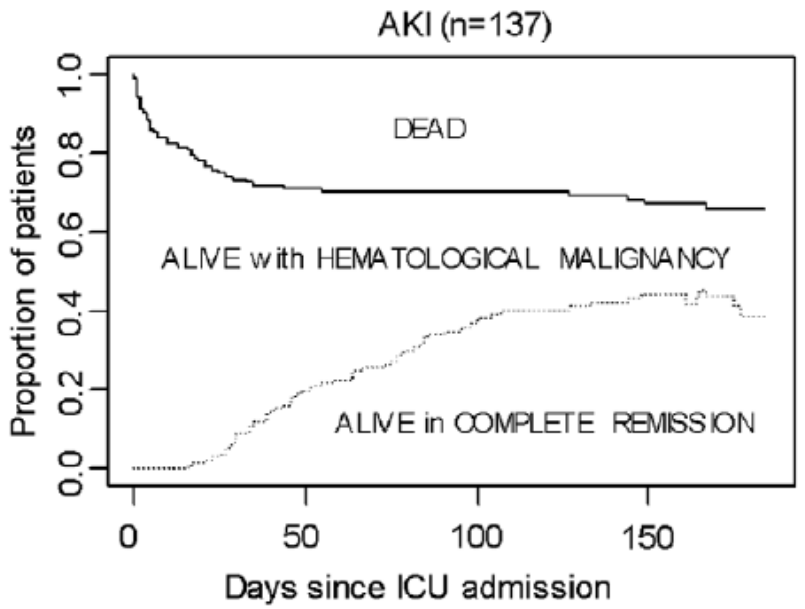
Group of patients	*a. Achieving complete remission*	*b. Failing induction treatment*	*c. Not evaluable*
Renal complications at diagnosis (n=30)	8/23 (34.8%)	15/23 (65.2%)	7/30 (23.3%)
No renal complications at diagnosis (n=136)	88/118 (74.6%)	30/118 (25.4%)	18/136 (13.2)

with patients without a renal complication.

Munker et al. Haematologica 1998

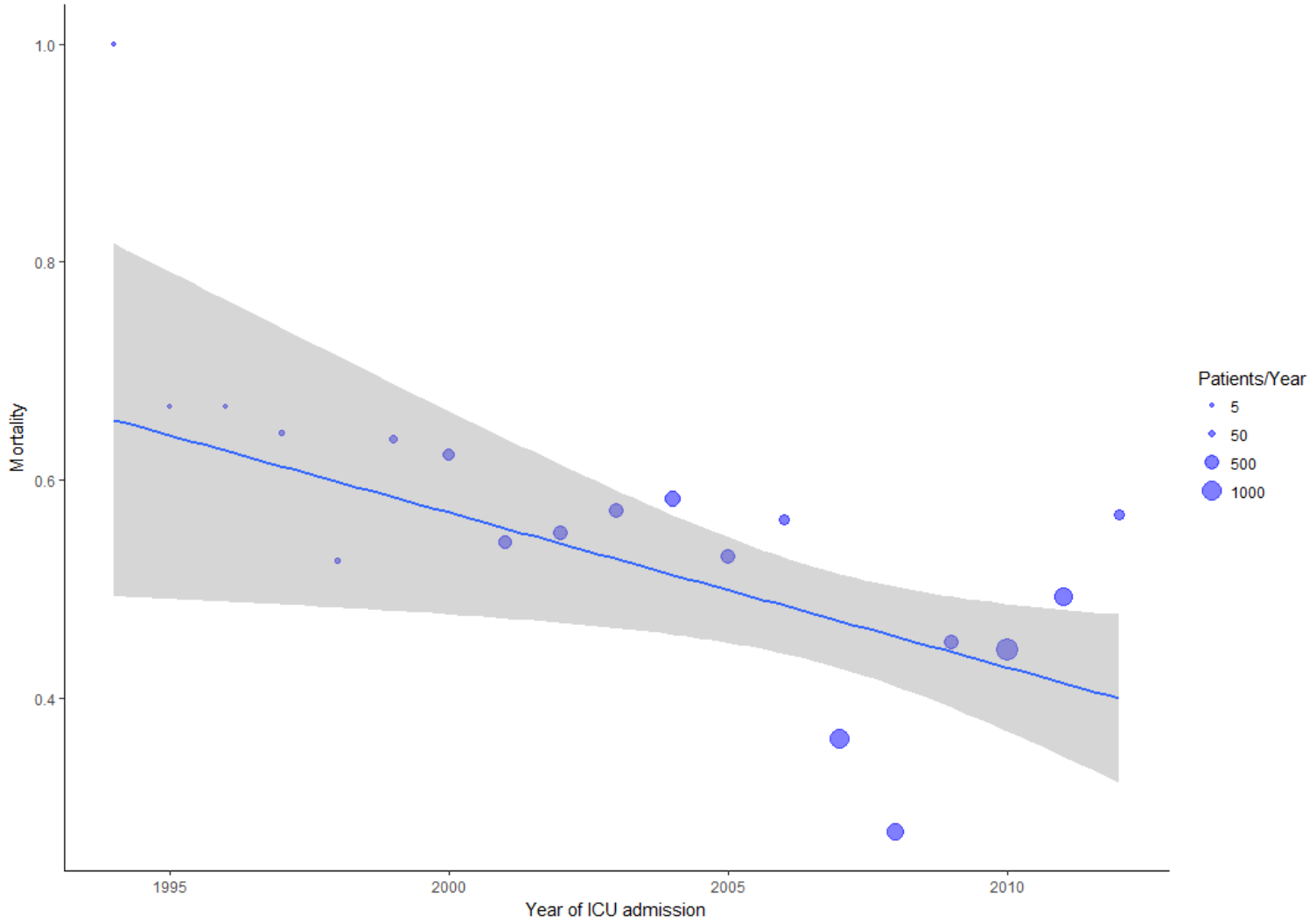
AKI and probability to achieve complete remission





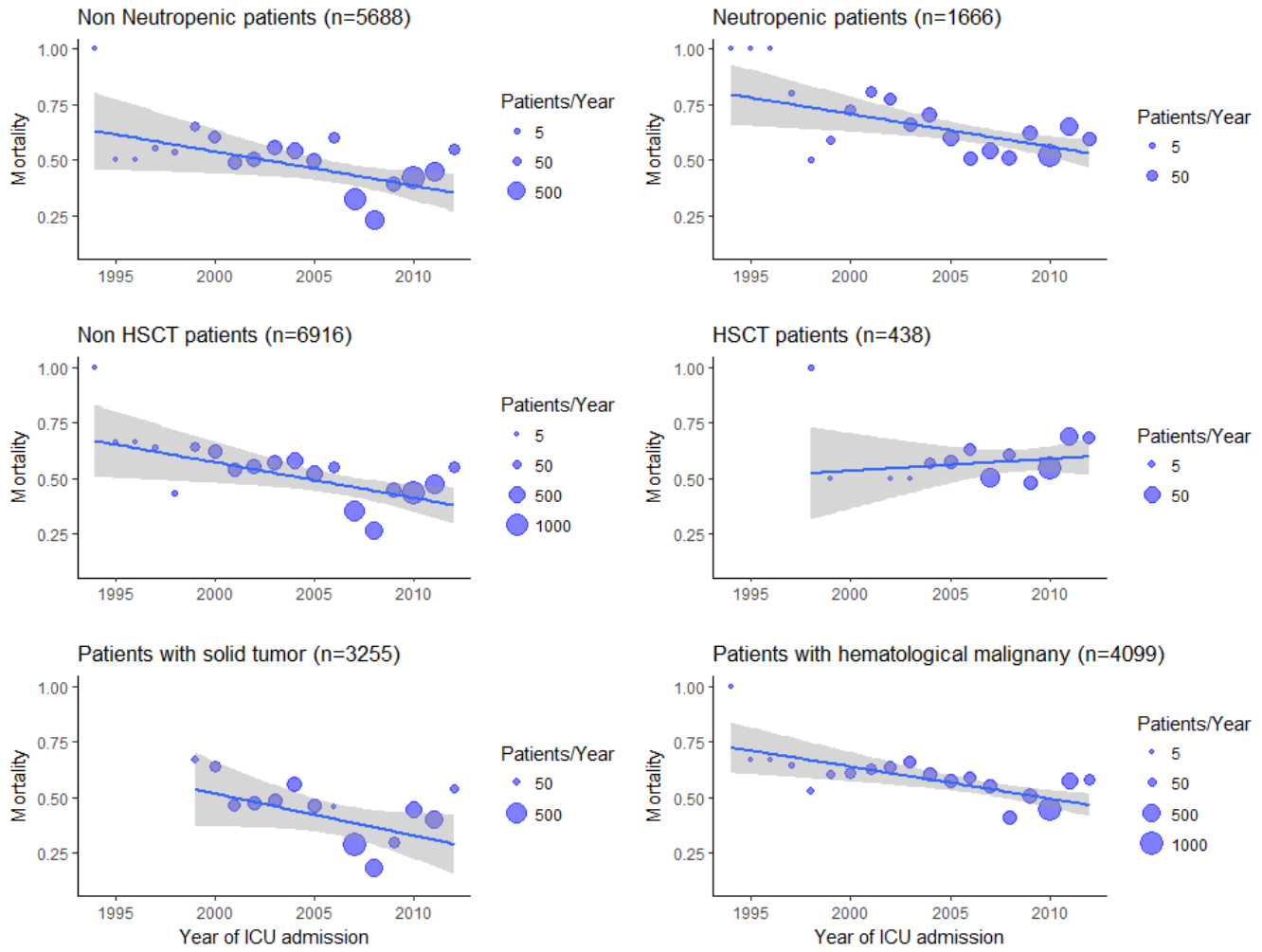
Canet et al. Plos One 2015

Evolution du pronostic des POH



Darmon et al. Intensive Care Med 2019

Evolution du pronostic des POH



Darmon et al. Intensive Care Med 2019

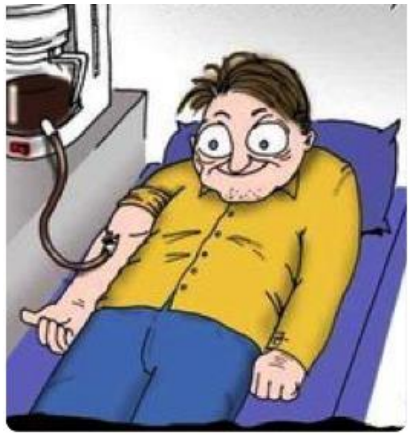
When to start, which technique ?

Which technique ?

Diffusion

Convection

IHD or CRRT



Which technique ?

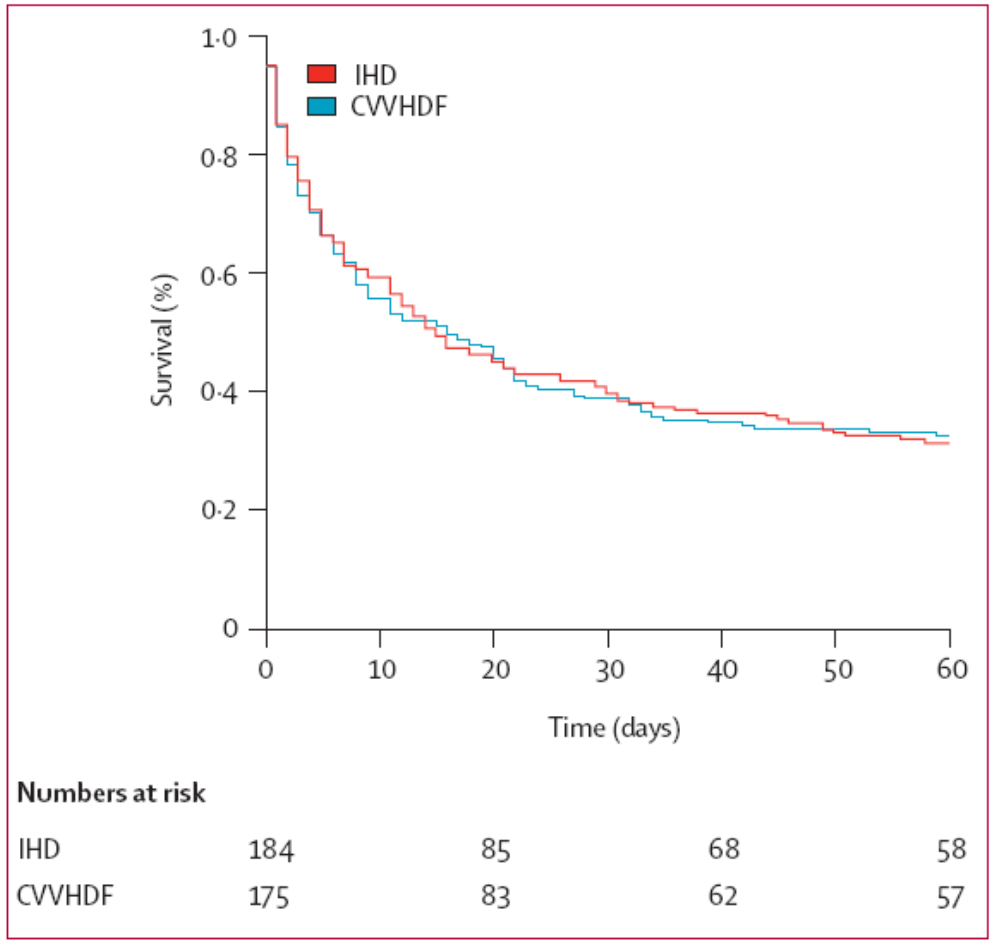


Figure 2: **Estimation of survival rate according to treatment group**
IHD=intermittent haemodialysis, CVVDHF=continuous venovenous haemodiafiltration.

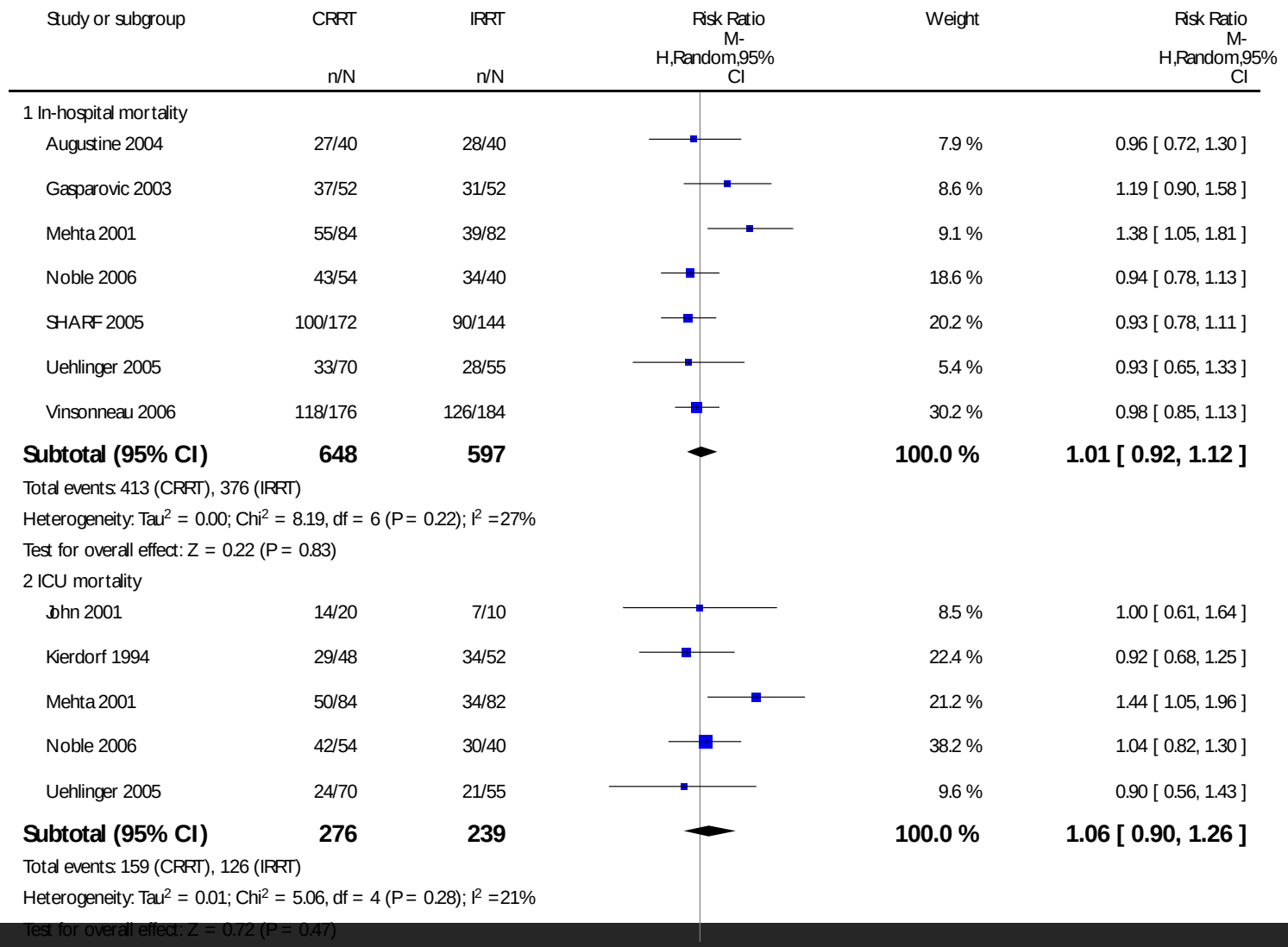
Eligibility
AKI and at least another organ dysf.
- MV: n= 345 (97%)
- Vasopressors: n=313 (87%)

IHD vs. CVVHDF
6 switch from IHD to CVVHDF
31 switch from CVVHDF to IHD

Hypotension (PAS<80 mmHg)
HDI 72 (39%) vs. CVVHDF 61 (35%)

Vinsonneau et al. Lancet 2007

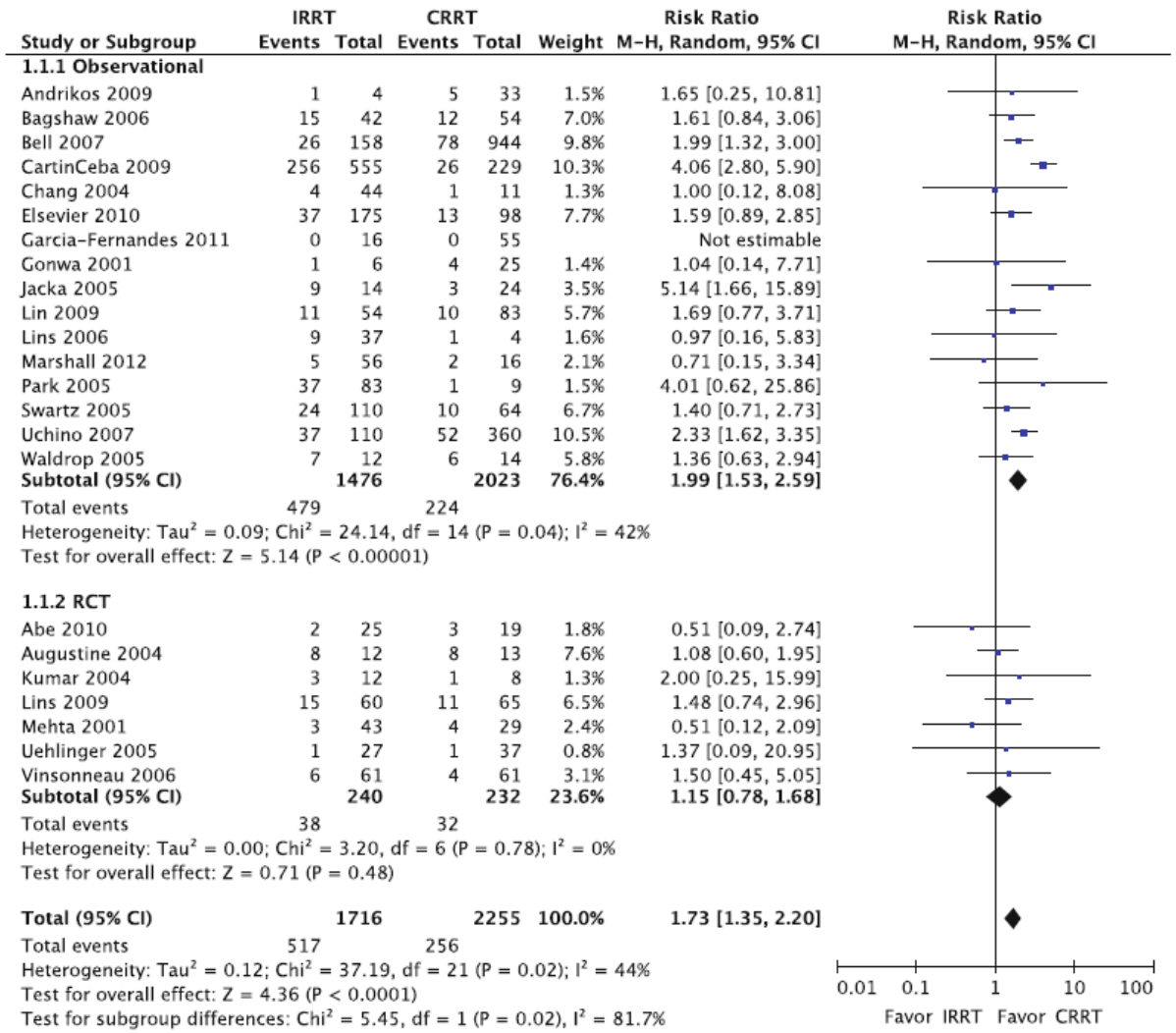
Which technique ?



Study or subgroup	CRRT n/N	IRRT n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 In-hospital mortality					
Augustine 2004	27/40	28/40		7.9 %	0.96 [0.72, 1.30]
Gasparovic 2003	37/52	31/52		8.6 %	1.19 [0.90, 1.58]
Mehta 2001	55/84	39/82		9.1 %	1.38 [1.05, 1.81]
Noble 2006	43/54	34/40		18.6 %	0.94 [0.78, 1.13]
SHARF 2005	100/172	90/144		20.2 %	0.93 [0.78, 1.11]
Uehlinger 2005	33/70	28/55		5.4 %	0.93 [0.65, 1.33]
Vinsonneau 2006	118/176	126/184		30.2 %	0.98 [0.85, 1.13]
Subtotal (95% CI)	**648**	**597**		**100.0 %**	**1.01 [0.92, 1.12]**
Total events: 413 (CRRT), 376 (IRRT)					
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 8.19$, df = 6 (P = 0.22); $I^2 = 27\%$					
Test for overall effect: Z = 0.22 (P = 0.83)					
2 ICU mortality					
John 2001	14/20	7/10		8.5 %	1.00 [0.61, 1.64]
Kierdorf 1994	29/48	34/52		22.4 %	0.92 [0.68, 1.25]
Mehta 2001	50/84	34/82		21.2 %	1.44 [1.05, 1.96]
Noble 2006	42/54	30/40		38.2 %	1.04 [0.82, 1.30]
Uehlinger 2005	24/70	21/55		9.6 %	0.90 [0.56, 1.43]
Subtotal (95% CI)	**276**	**239**		**100.0 %**	**1.06 [0.90, 1.26]**
Total events: 159 (CRRT), 126 (IRRT)					
Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 5.06$, df = 4 (P = 0.28); $I^2 = 21\%$					
Test for overall effect: Z = 0.72 (P = 0.47)					

Rabindranath et al. Cochrane Database of Systematic Reviews 2007

Which technique ?



Study or Subgroup	IRRT Events	IRRT Total	CRRT Events	CRRT Total	Weight	Risk Ratio M-H, Random, 95% CI
1.1.1 Observational						
Andrikos 2009	1	4	5	33	1.5%	1.65 [0.25, 10.81]
Bagshaw 2006	15	42	12	54	7.0%	1.61 [0.84, 3.06]
Bell 2007	26	158	78	944	9.8%	1.99 [1.32, 3.00]
CartinCeba 2009	256	555	26	229	10.3%	4.06 [2.80, 5.90]
Chang 2004	4	44	1	11	1.3%	1.00 [0.12, 8.08]
Elsevier 2010	37	175	13	98	7.7%	1.59 [0.89, 2.85]
Garcia-Fernandes 2011	0	16	0	55		Not estimable
Gonwa 2001	1	6	4	25	1.4%	1.04 [0.14, 7.71]
Jacka 2005	9	14	3	24	3.5%	5.14 [1.66, 15.89]
Lin 2009	11	54	10	83	5.7%	1.69 [0.77, 3.71]
Lins 2006	9	37	1	4	1.6%	0.97 [0.16, 5.83]
Marshall 2012	5	56	2	16	2.1%	0.71 [0.15, 3.34]
Park 2005	37	83	1	9	1.5%	4.01 [0.62, 25.86]
Swartz 2005	24	110	10	64	6.7%	1.40 [0.71, 2.73]
Uchino 2007	37	110	52	360	10.5%	2.33 [1.62, 3.35]
Waldrop 2005	7	12	6	14	5.8%	1.36 [0.63, 2.94]
Subtotal (95% CI)		**1476**		**2023**	**76.4%**	**1.99 [1.53, 2.59]**
Total events	479		224			
Heterogeneity: $Tau^2 = 0.09$; $Chi^2 = 24.14$, df = 14 (P = 0.04); $I^2 = 42\%$						
Test for overall effect: Z = 5.14 (P < 0.00001)						
1.1.2 RCT						
Abe 2010	2	25	3	19	1.8%	0.51 [0.09, 2.74]
Augustine 2004	8	12	8	13	7.6%	1.08 [0.60, 1.95]
Kumar 2004	3	12	1	8	1.3%	2.00 [0.25, 15.99]
Lins 2009	15	60	11	65	6.5%	1.48 [0.74, 2.96]
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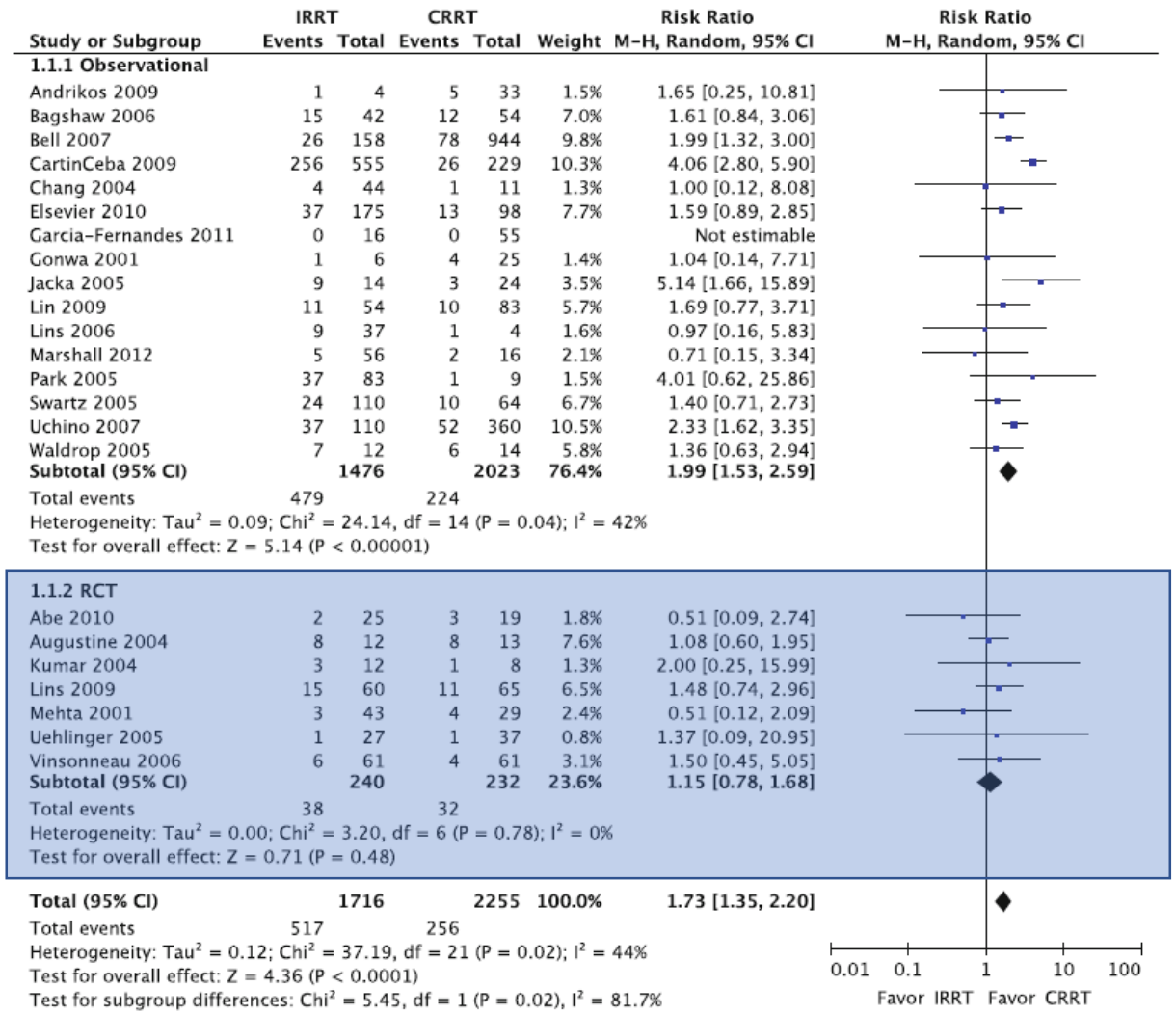
Uehlinger 2005	1	27	1	37	0.8%	1.37 [0.09, 20.95]
Vinsonneau 2006	6	61	4	61	3.1%	1.50 [0.45, 5.05]
Subtotal (95% CI)		**240**		**232**	**23.6%**	**1.15 [0.78, 1.68]**
Total events	38		32			
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 3.20$, df = 6 (P = 0.78); $I^2 = 0\%$						
Test for overall effect: Z = 0.71 (P = 0.48)						
Total (95% CI)		**1716**		**2255**	**100.0%**	**1.73 [1.35, 2.20]**
Total events	517		256			
Heterogeneity: $Tau^2 = 0.12$; $Chi^2 = 37.19$, df = 21 (P = 0.02); $I^2 = 44\%$						
Test for overall effect: Z = 4.36 (P < 0.0001)						
Test for subgroup differences: $Chi^2 = 5.45$, df = 1 (P = 0.02), $I^2 = 81.7\%$						

Schneider et al. Intensive Care Med 2013

Which technique ?



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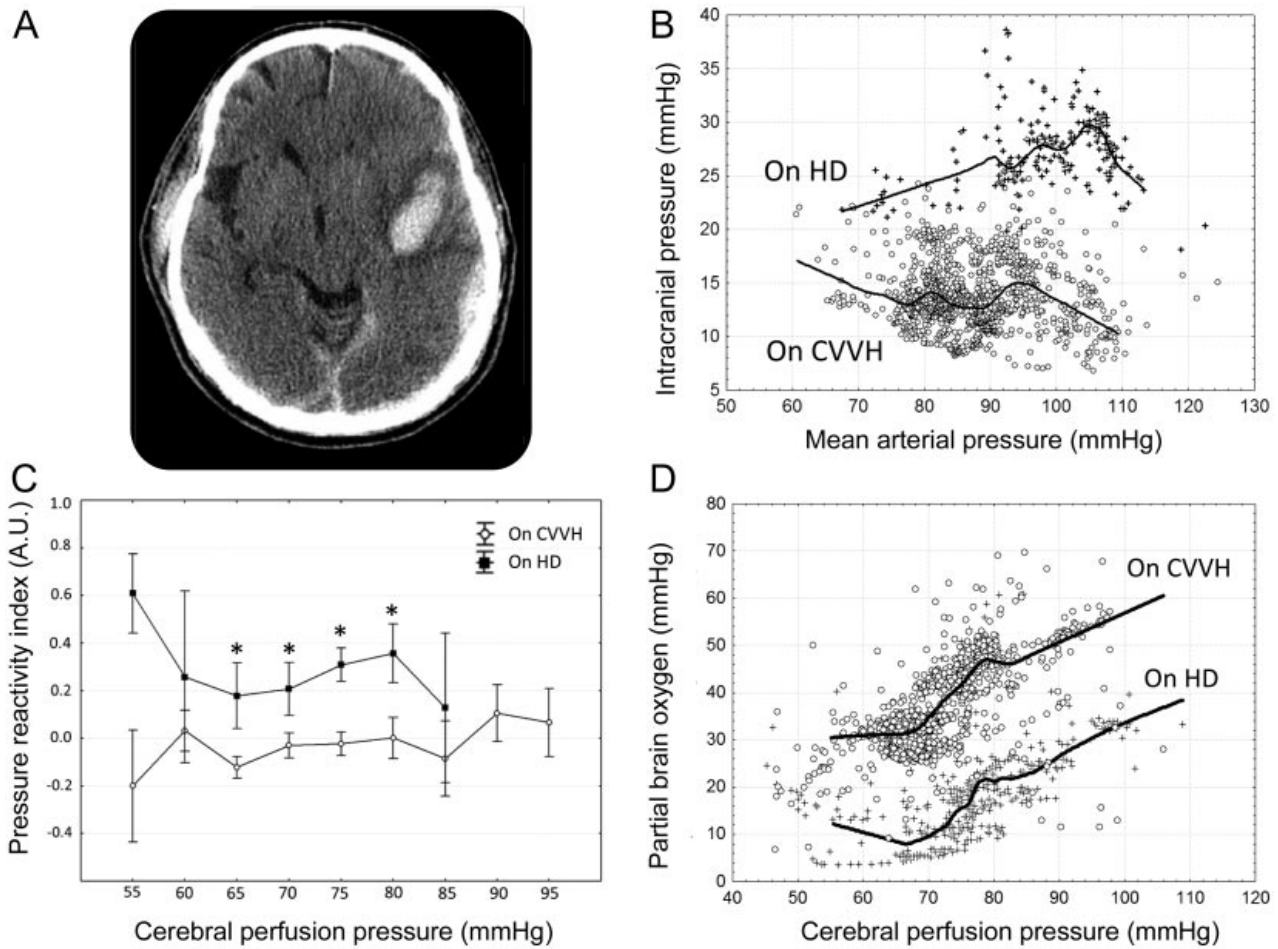
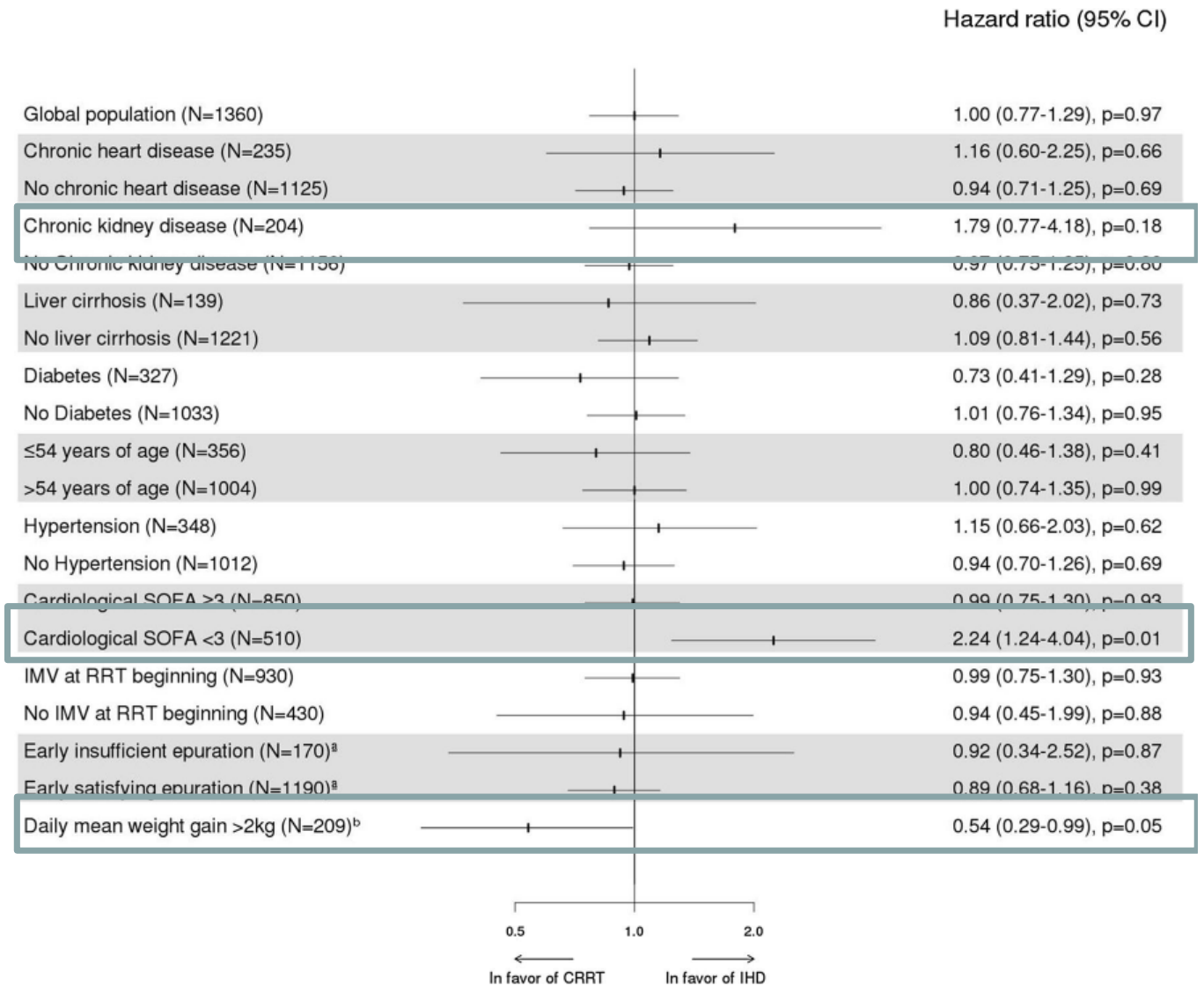
Schneider et al. Intensive Care Med 2013

Two settings in which in do not use IHD



Ko et al. Neurology 2012

Two settings in which in do not use IHD

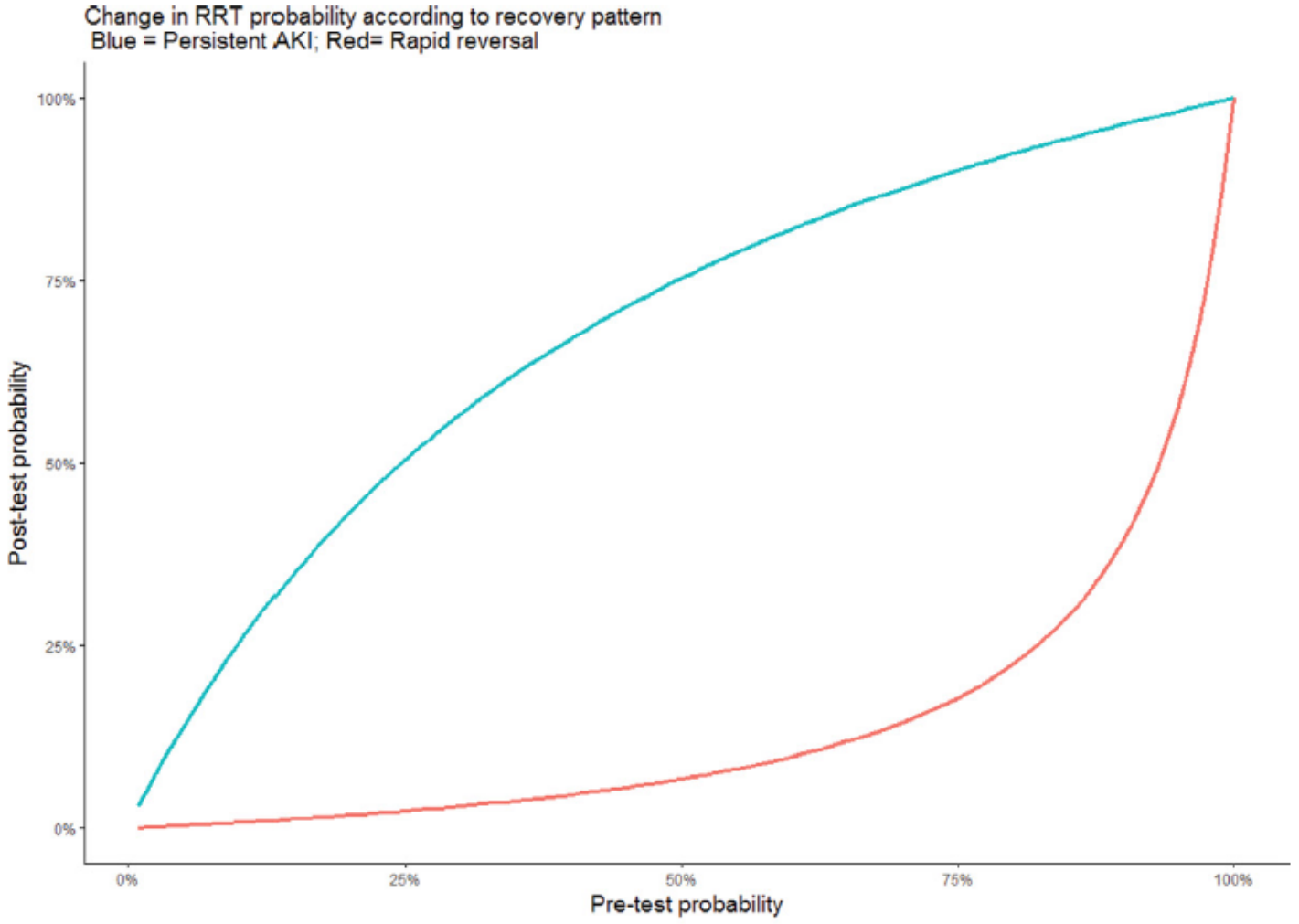


Truche et al. Intensive Care Med 2016

When to start?

Two intricated questions…

When to start RRT
In whom should we start RRT

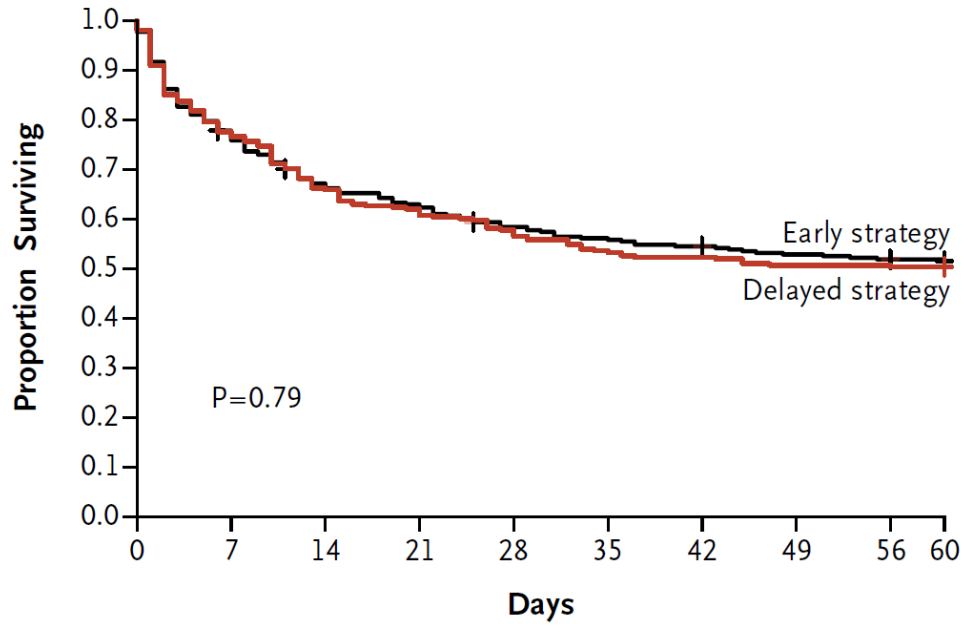


Perinel et al. Crit Care Med 2015

STAART-AKI (feasibility) – AKIKI – IDEAL-ICU

Cumulative survival

A

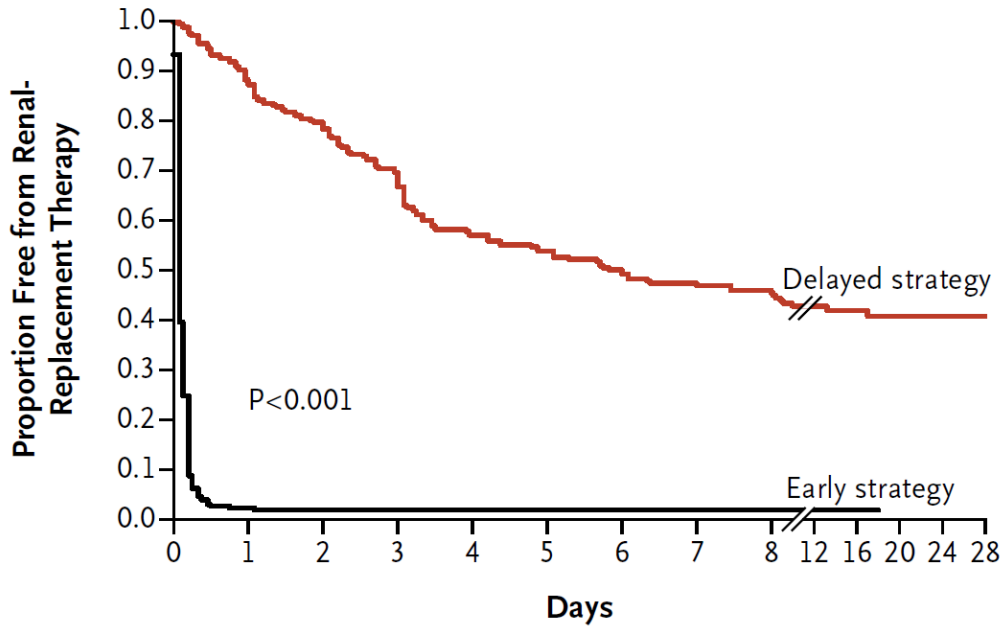


No. at Risk

Early strategy	311	241	207	194	179	172	167	161	158 157
Delayed strategy	308	239	204	191	178	165	161	156	156 155

Proportion of patients free for RRT

B



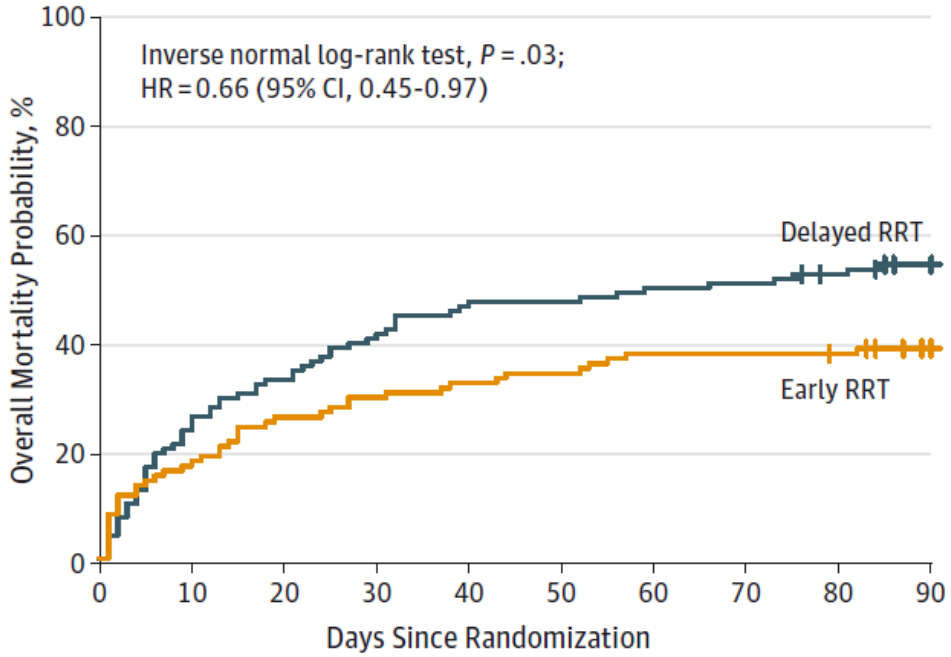
No. at Risk

Early strategy	311	7	4	4	4	4	3	3	3	1	1	0	0	0
Delayed strategy	308	268	229	192	153	135	118	105	92	61	39	28	21	13

Wald et al. Kidney International 2015; Gaudry et al. N Engl J Med 2016; Barbar et al. N Engl J Med 2018

Except in patients with fluid overload

Cumulative mortality



No. at risk

Early RRT	112	92	82	78	75	73	69	69	66	55
Delayed RRT	119	90	79	70	63	62	59	58	54	48

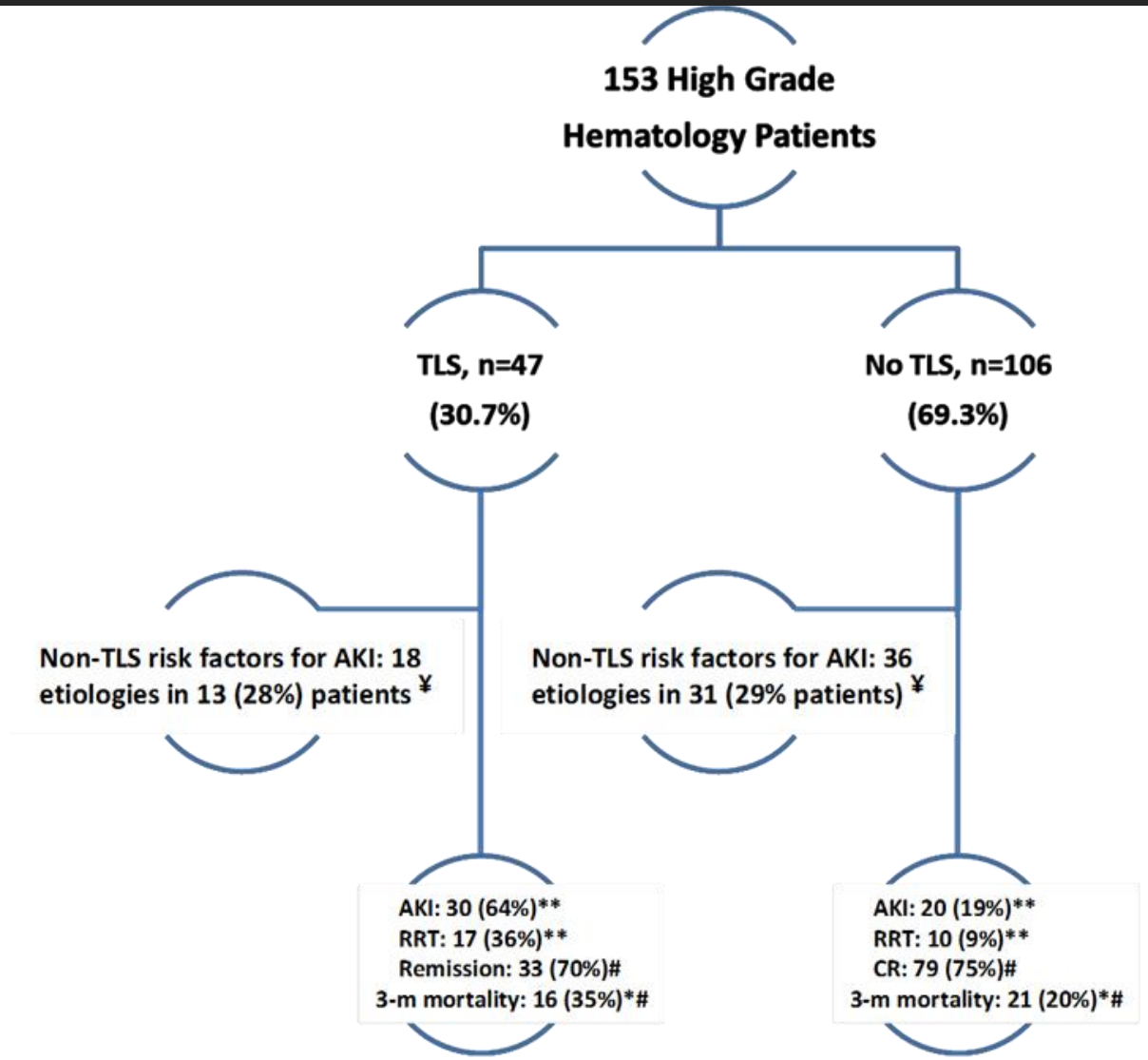
	Late	Early
RRT	91%	100%
HR/OR (95%CI) early vs. delayed		
Day-90 mortality	HR 0.66 (0.45-0.97)	
Coag dysfunction	OR 0.57 (0.33-0.99)	
Free of RRT at day 90	OR 0.55 (0.32-0.93)	
Hospital stay	HR 0.34 (0.22-0.52)	

Fluid overload at study inclusion +7kg [4-10]

Zarbock et al. JAMA 2016

RRT and TLS

Mnemonic to recall risk of TLS : 1/3 ratio



High risk of TLS patients:

1/3 will develop TLS

1/3 of spontaneous TLS

Biological TLS:

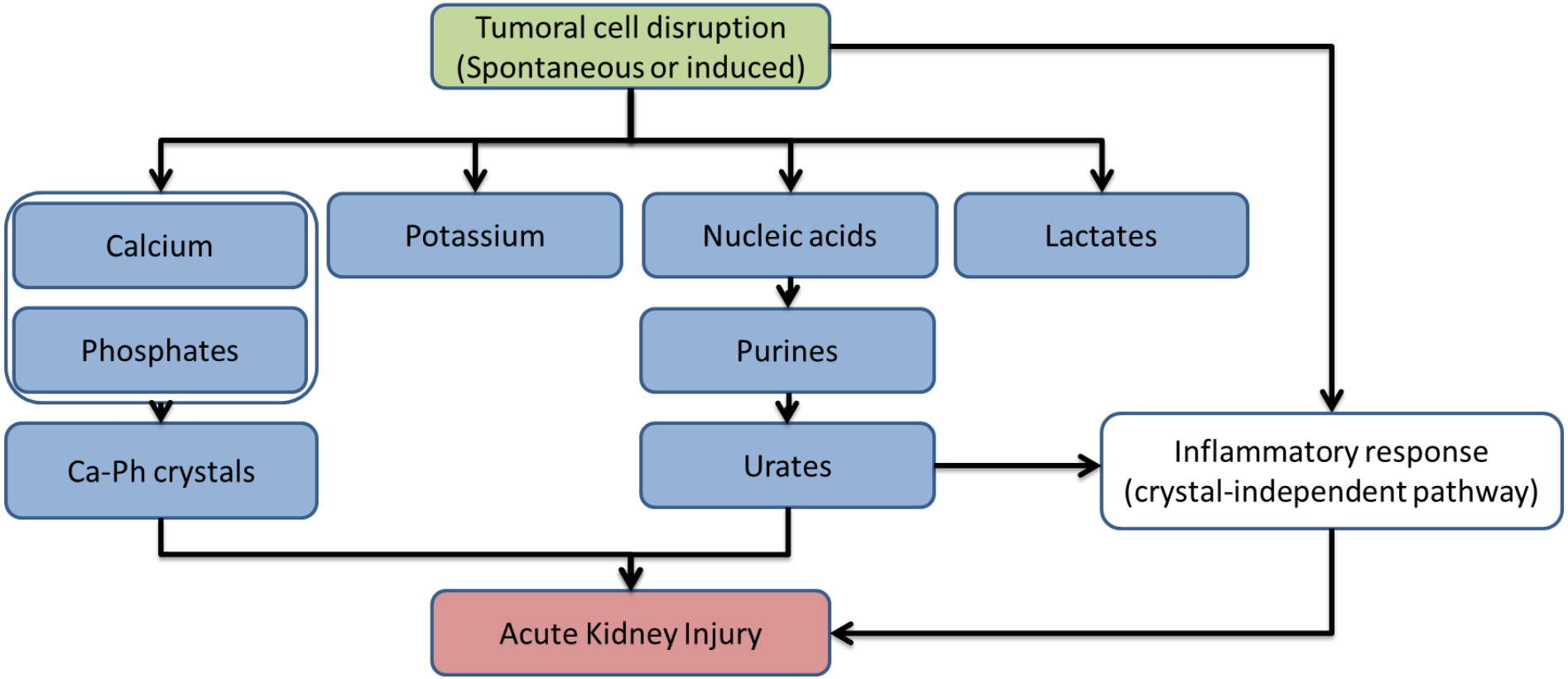
1/3 will remain free from AKI

1/3 will require RRT

1/3 : 3-month mortality

Darmon Brit J Haematol 2013

Tumor Lysis Syndrome



Management and need for RRT

General measures

- Avoid correcting of hypoK or hypoPh before induction
- Avoid urine alkalinisation
- Avoid correcting hypocalcaemia unless symptomatic

Prevention of TLS, and management of biological TLS

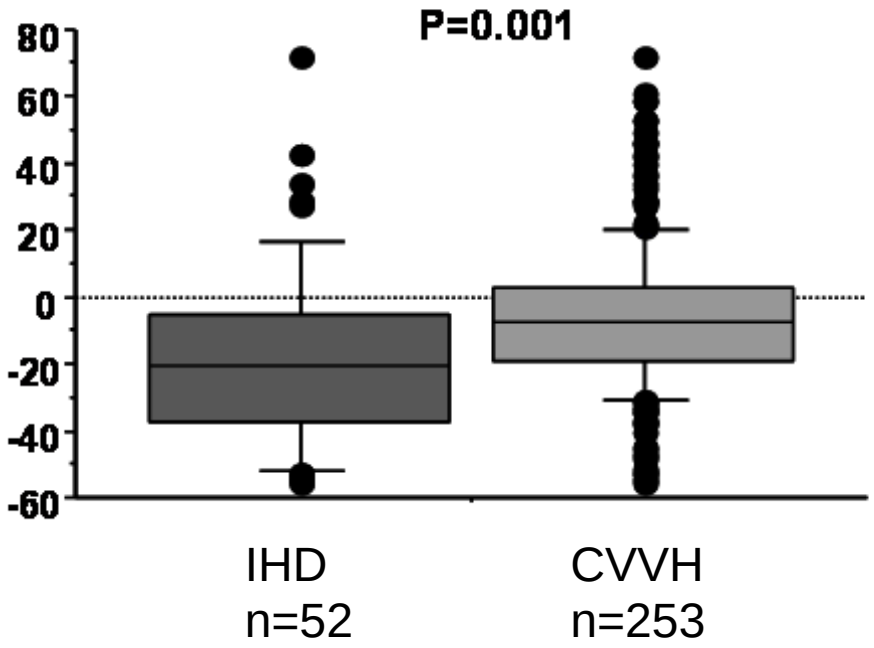
- Volume expansion
- Urate oxidase if high risk for TLS, allopurinol otherwise
- RRT if phosphataemia remains >2mmol/L after 6h of management (?)

Clinical TLS

- Extended intermittent hemodialysis or CVVH
- Immediately if cardiac or neurological manifestations
- AKI despite preventive measures
- Renal dysfunction despite prevention

Optimal RRT modality?

6 hours Phosphate changes
during TLS requiring RRT (%)



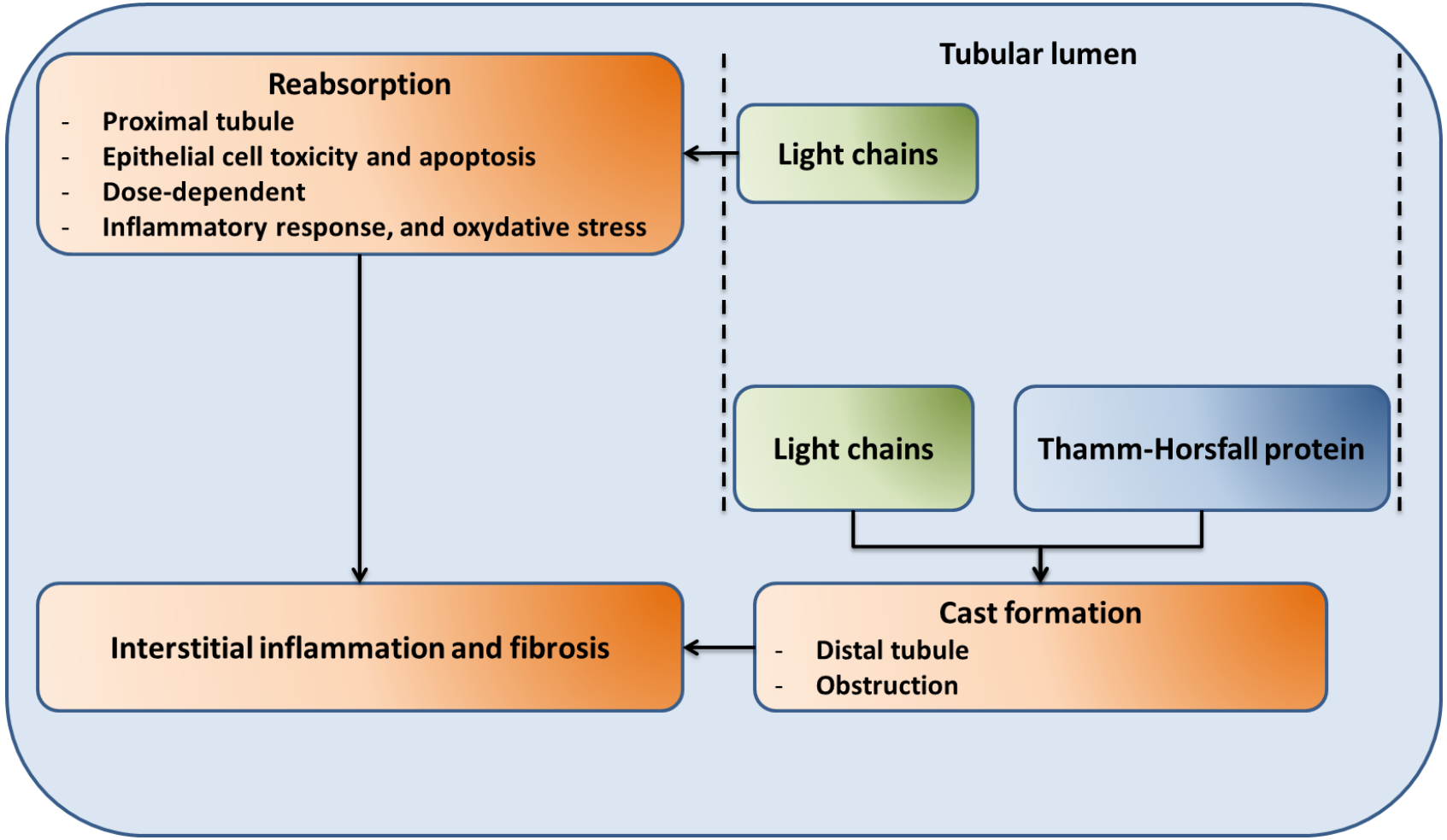
Severe metabolic disturbances

- Hyperkaliemia
- Hyperphosphatemia
- Tumor lysis syndrome

IHD is the modality of choice
Beware to post-IHD rebound

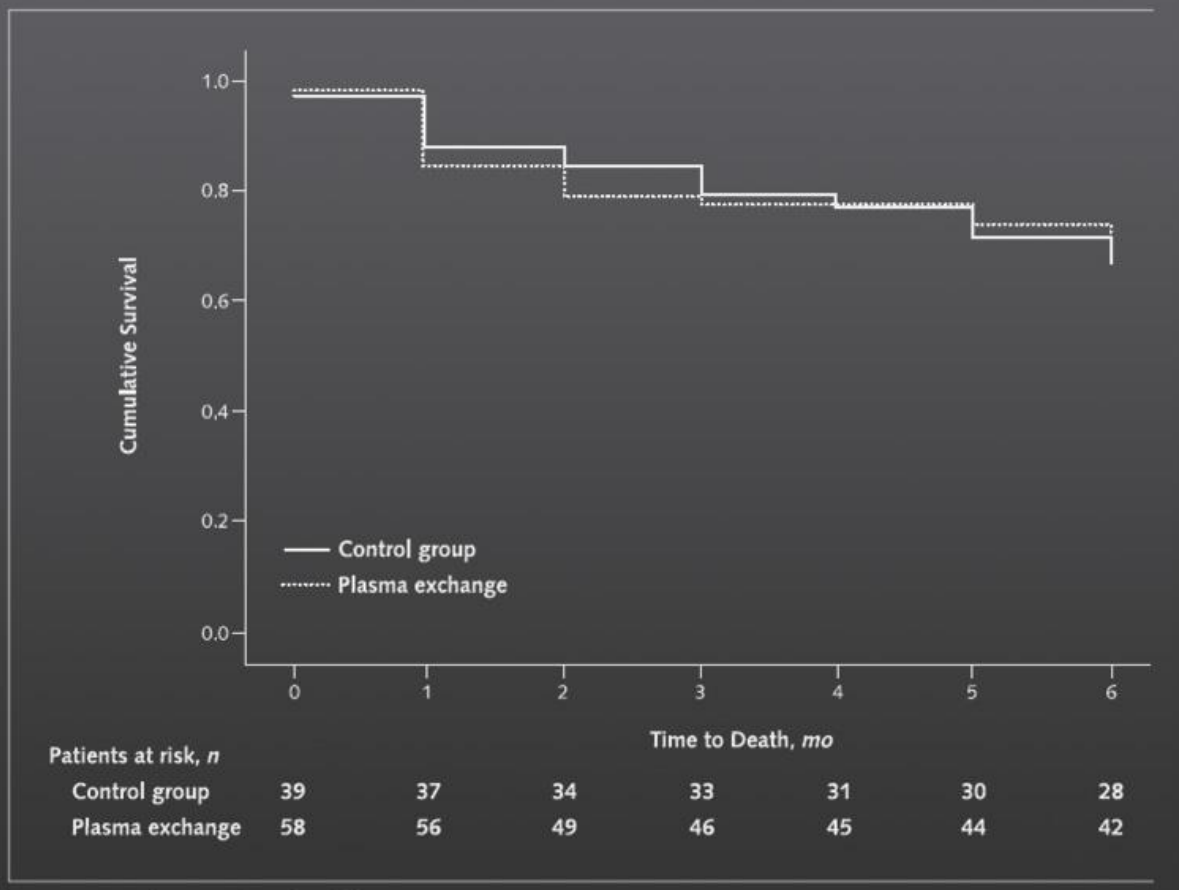
RRT in myeloma patients

Pathophysiology of cast nephropathy



No benefit of plasma exchange

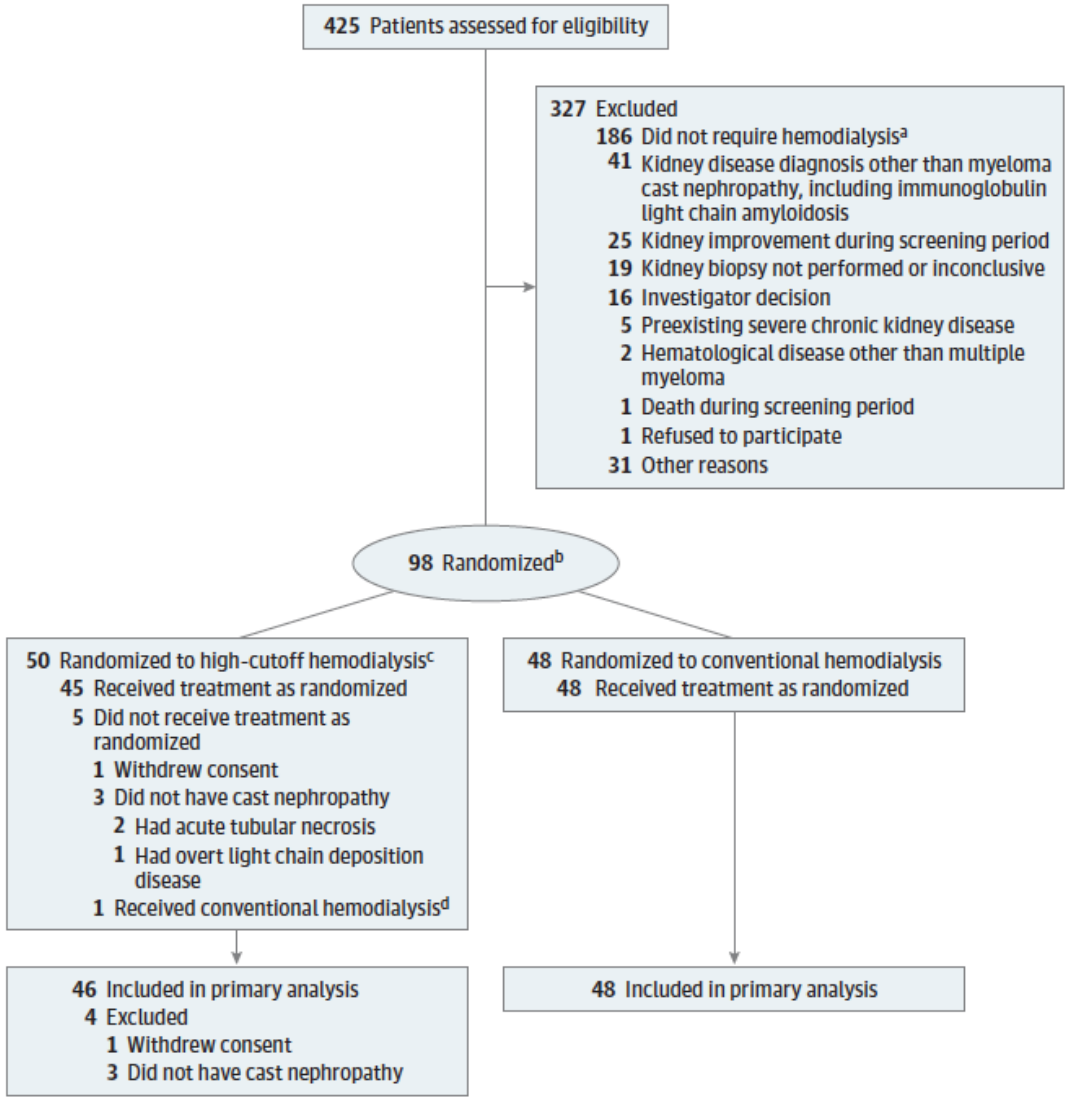
Figure 2. Kaplan–Meier analysis of time to death.



Treatment groups did not statistically significantly differ.

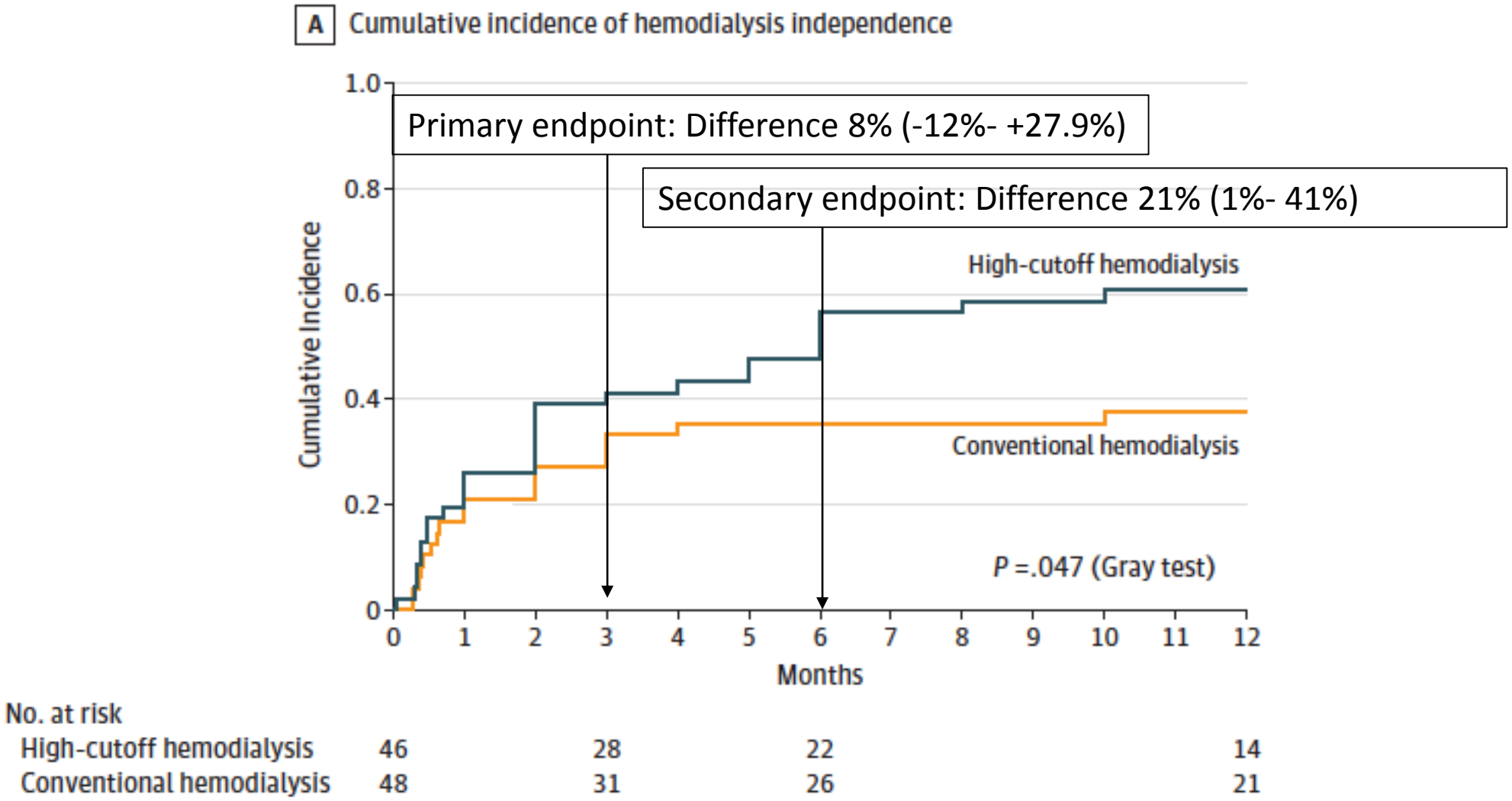
Clark WF, Ann Intern Med 2005

High cut-off membrane RRT in cast nephropathy



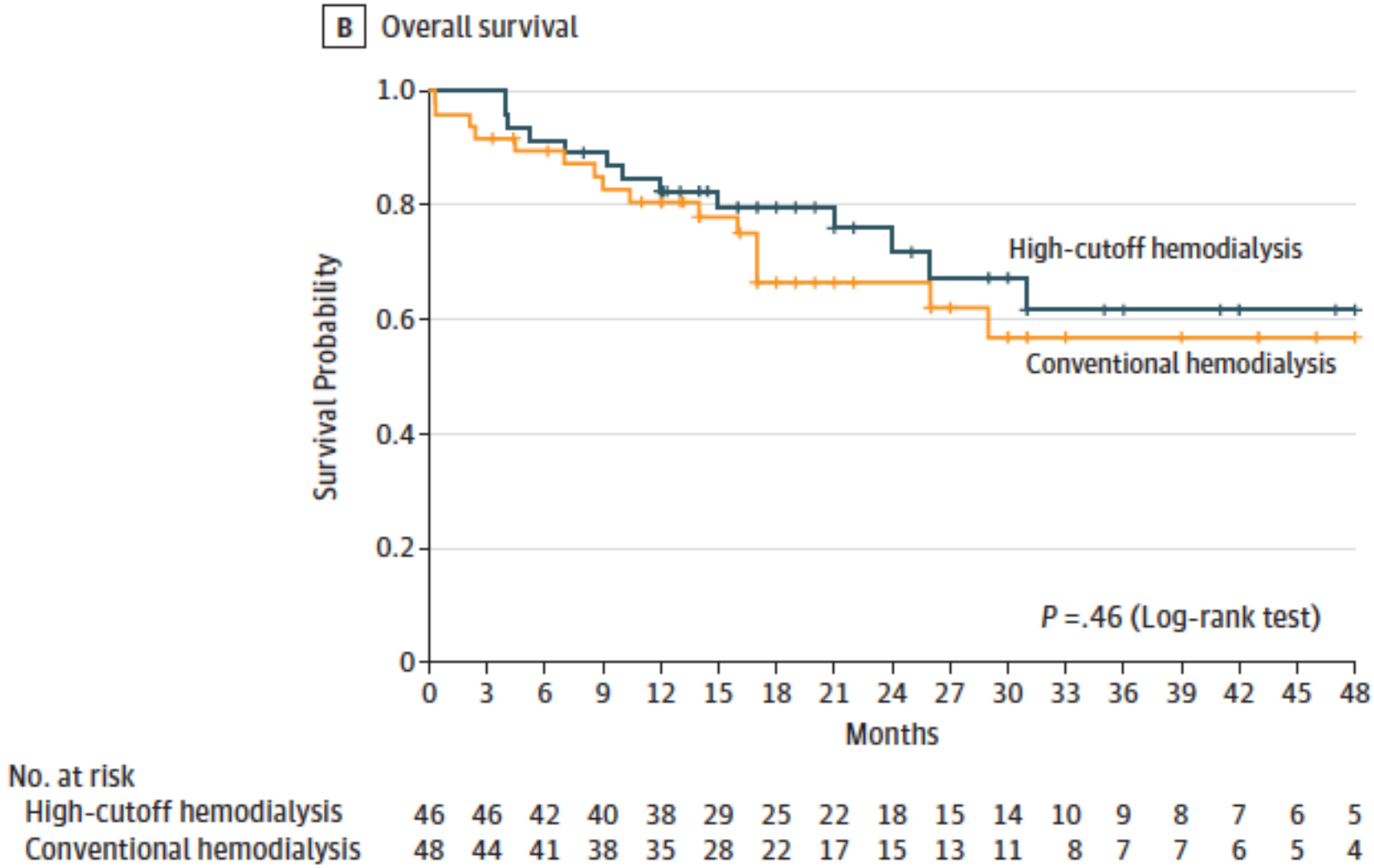
Bridoux et al. JAMA 2017

High cut-off membrane : renal survival



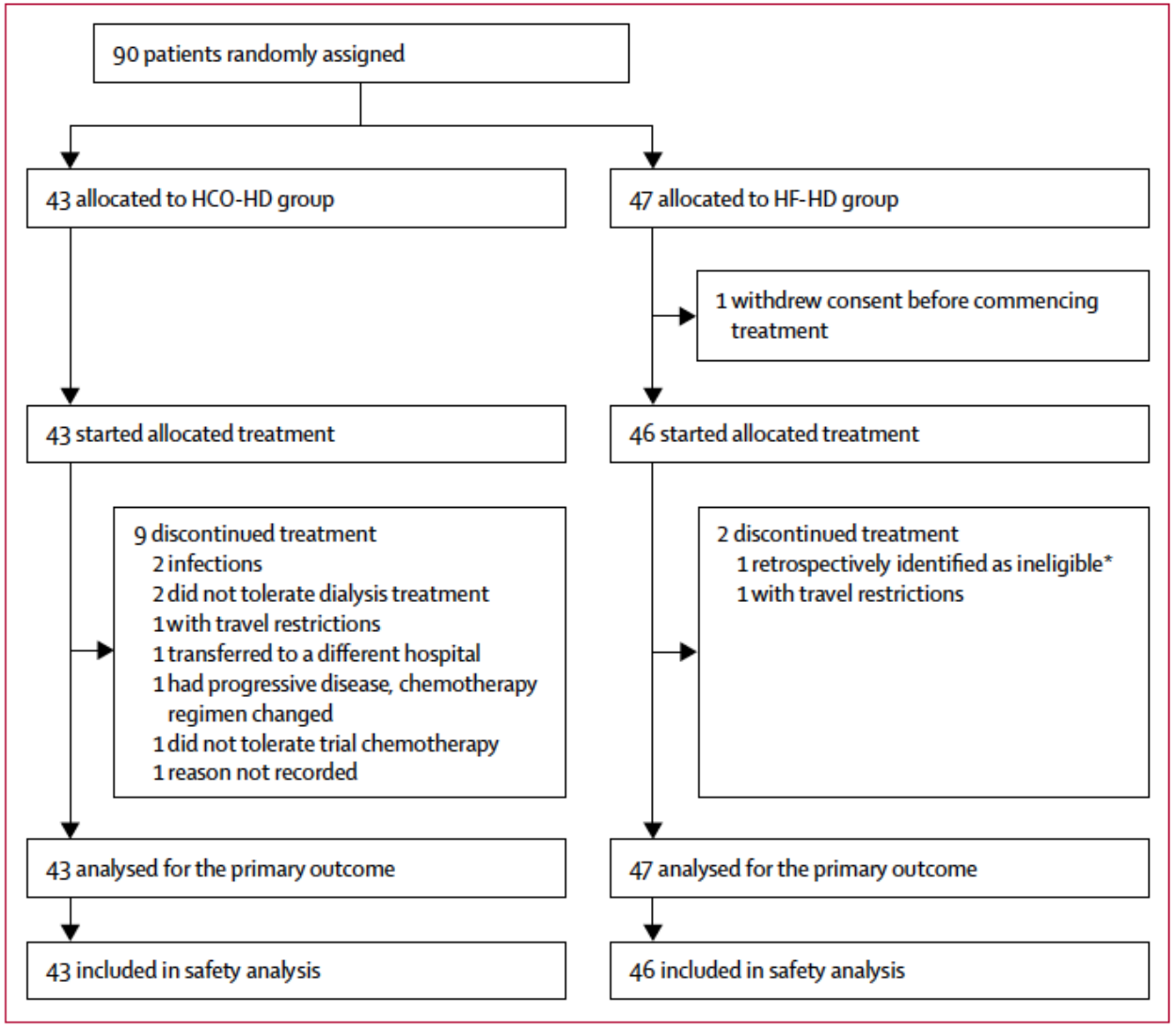
Bridoux et al. JAMA 2017

High cut-off membrane : overall survival



Bridoux et al. JAMA 2017

High cut-off membrane RRT in cast nephropathy



Hutchinson et al. Lancet Hematol 2019

High cut-off membrane : renal survival

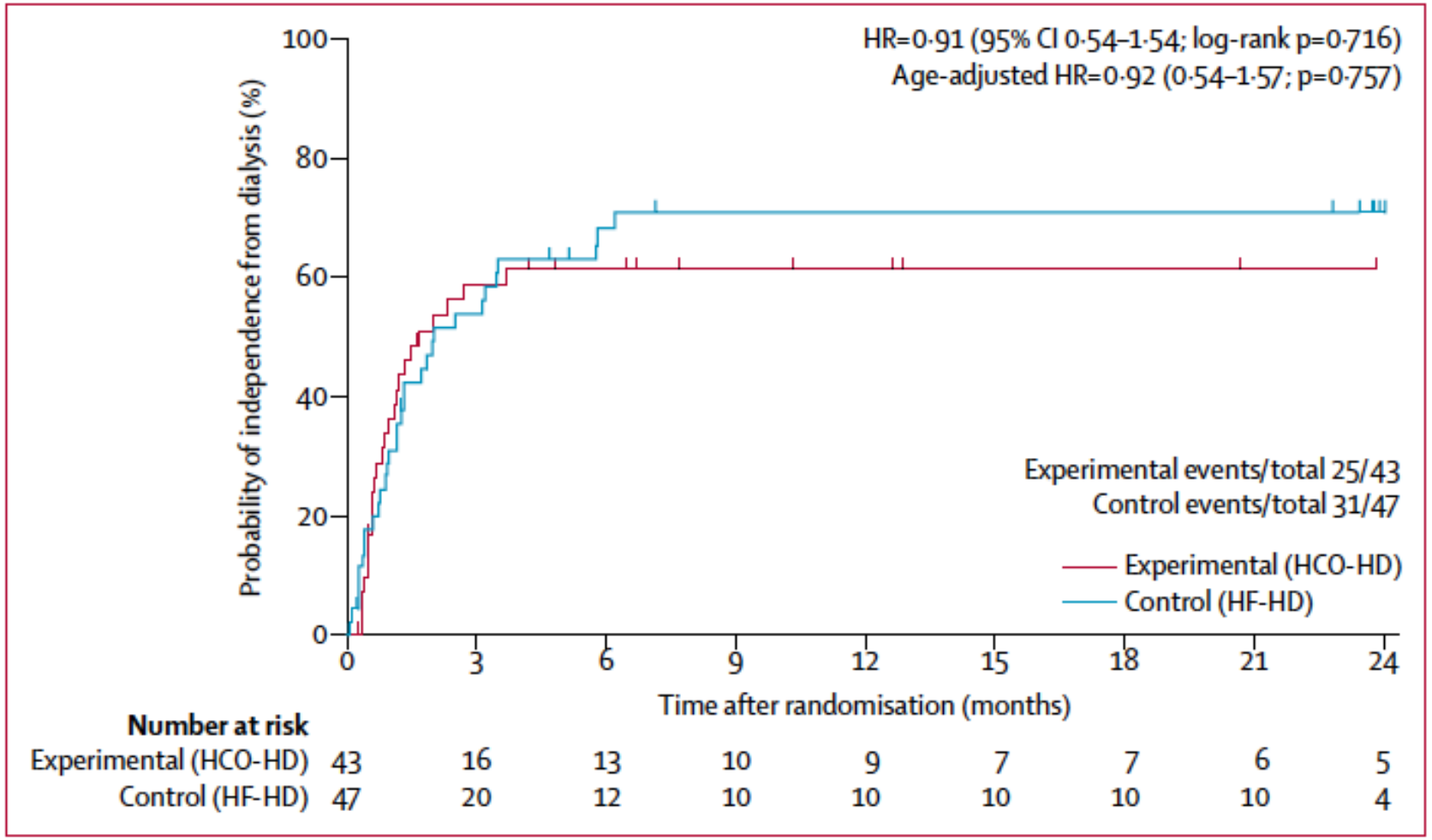
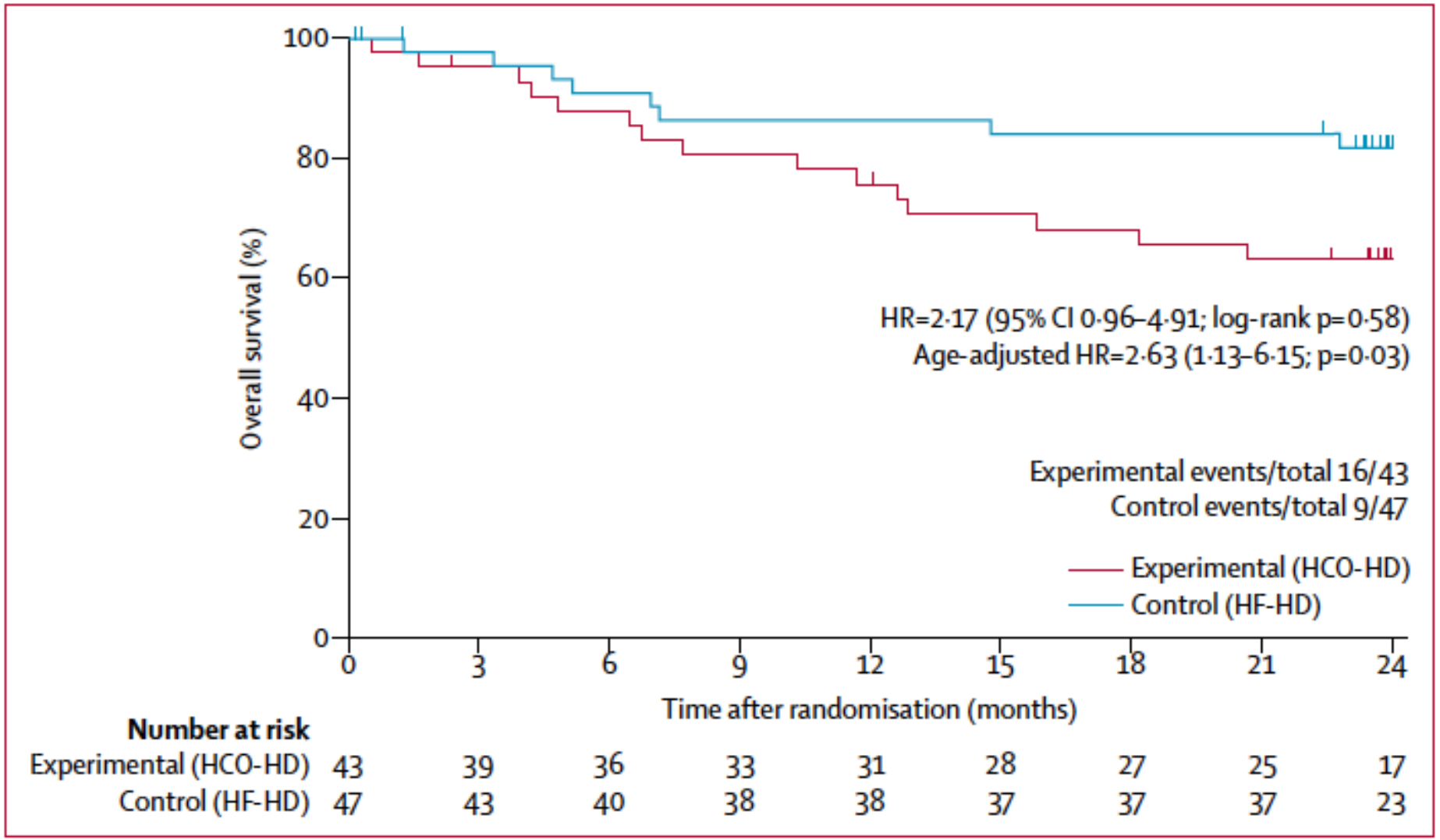


***Figure 3*: Reverse Kaplan-Meier graph of time to independence from dialysis by treatment group**
HCO-HD=high cutoff haemodialysis. HF-HD=high-flux haemodialysis. HR=hazard ratio.

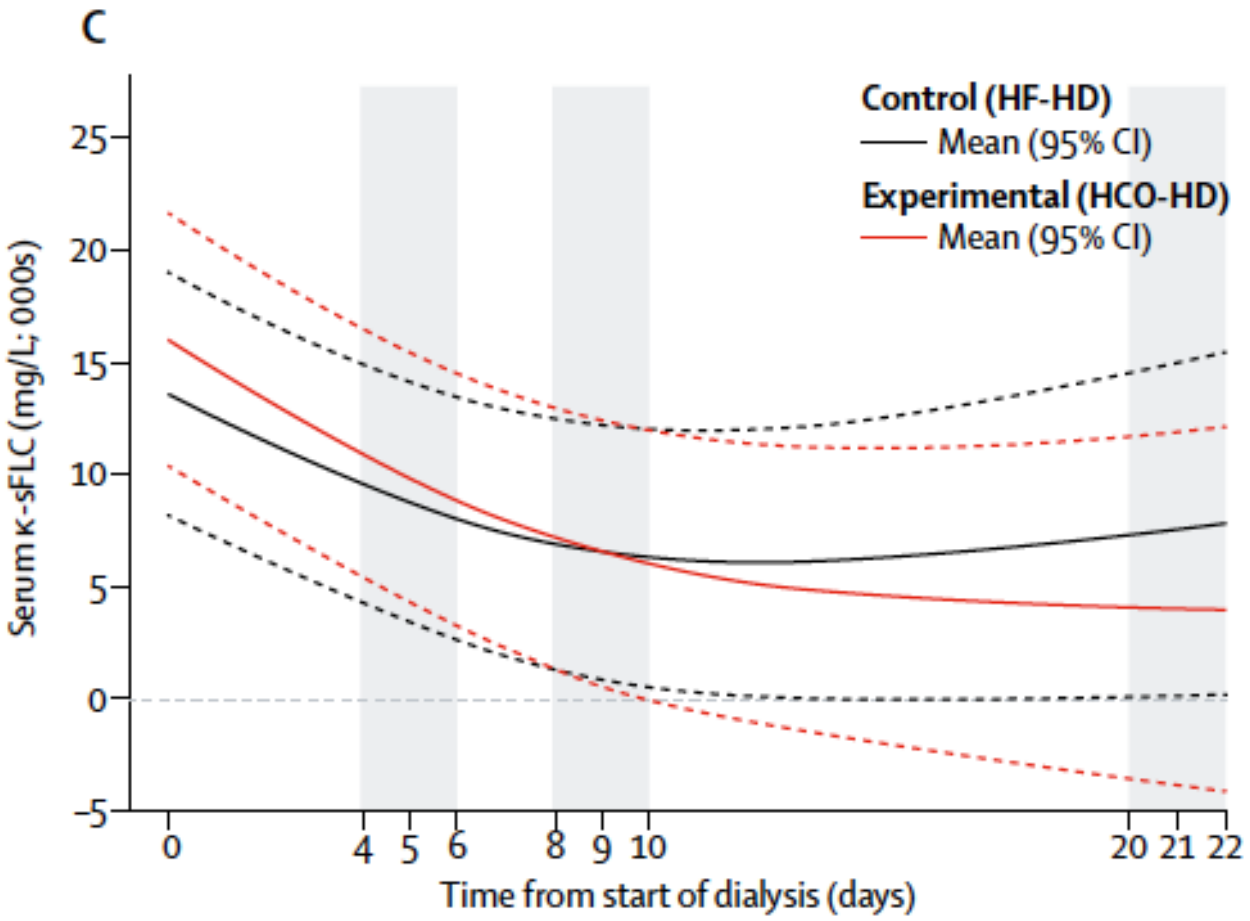
Hutchinson et al. Lancet Hematol 2019

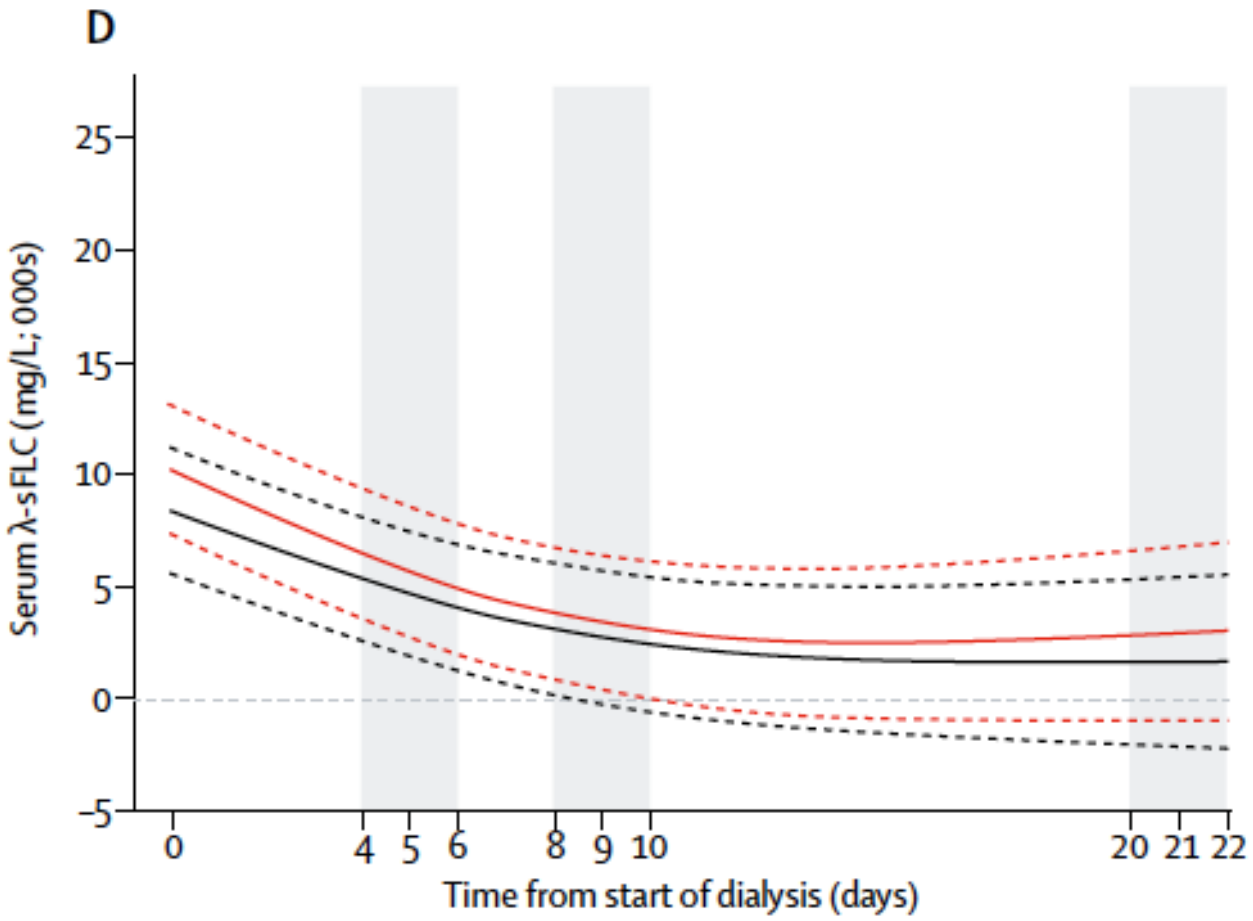
High cut-off membrane : overall survival



Hutchinson et al. Lancet Hematol 2019

High CO membrane : changes in LC concentrations





Hutchinson et al. Lancet Hematol 2019

Conflits d'intérêts

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JOURNAL OF CLINICAL ONCOLOGY

REVIEW ARTICLE

Renal Impairment in Patients With Multiple Myeloma: A Consensus Statement on Behalf of the International Myeloma Working Group

Meletios A. Dimopoulos, Evangelos Terpos, Asher Chanan-Khan, Nelson Leung, Heinz Ludwig, Sundar Jagannath, Ruben Niesvizky, Sergio Giralt, Jean-Paul Fermand, Joan Bladé, Raymond L. Comenzo, Orhan Sezer, Antonio Palumbo, Jean-Luc Harousseau, Paul G. Richardson, Bart Barlogie, Kenneth C. Anderson, Pieter Sonneveld, Patrizia Tosi, Michele Cavo, S. Vincent Rajkumar, Brian G.M. Durie, and Jésus San Miguel

Best available evidence suggest first line treatment of myeloma specific nephropathy should be based upon Bortezomib based chemotherapy

It is recommended to start such therapy whatever the severity of renal dysfunction

Efficacy of Bortezomib based therapy in AKI

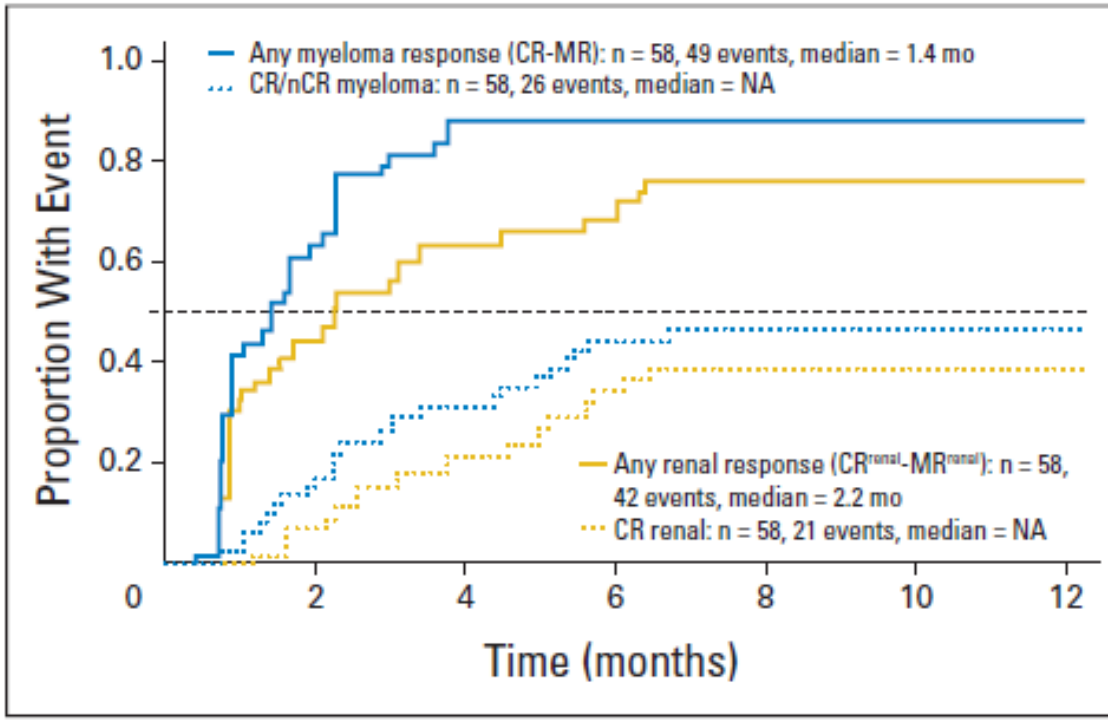


Fig 2. Cumulative incidence of myeloma response (complete response [CR and renal response (CR^{renal} and MR^{renal}) in the evaluable patients. nCR, nea complete response; MR, minor response; NA, not available.

Heinz et al. J Clin Oncol 2010

Some specific complications may require TPE

Protides 160g/L – Myeloma IgG κ

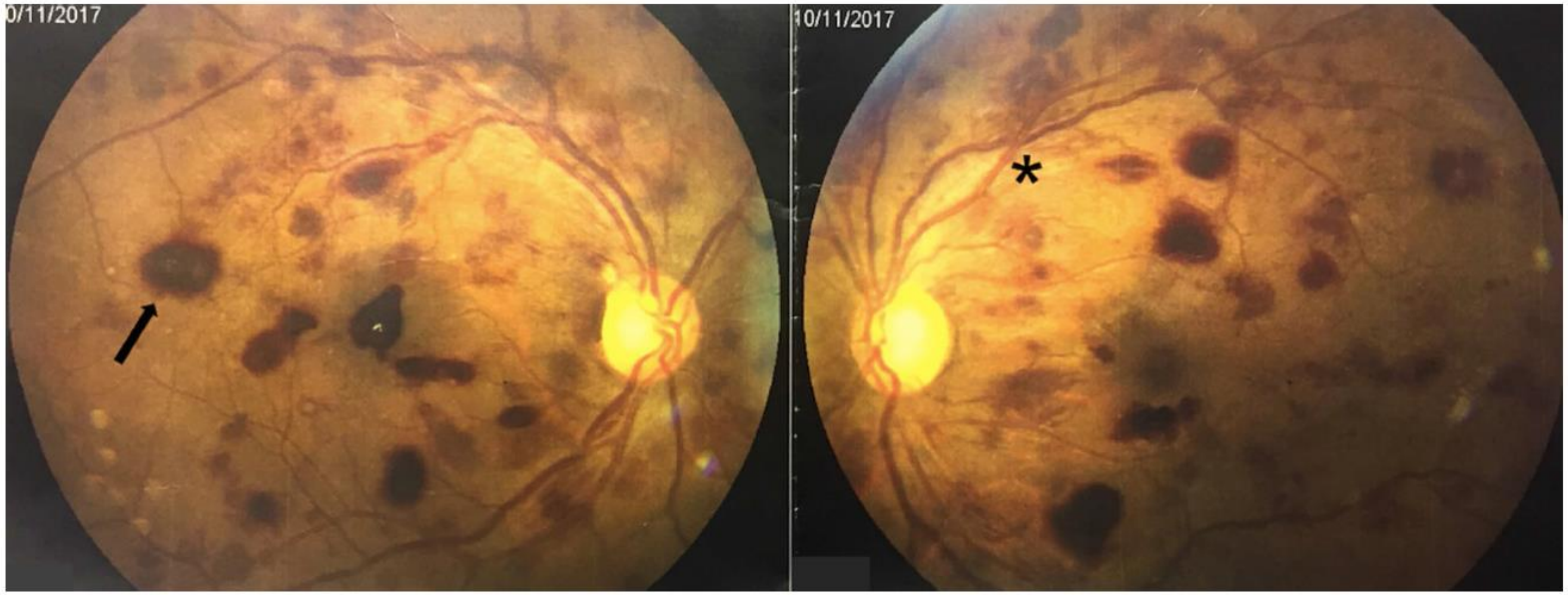


Fig. 1 Fundus image of a 47-year-old man with history of stupor, blurry vision, and nosebleeds. Bilateral retinal vein dilation, tortuosity (star), and voluminous central hemorrhages (arrow)

Dumas et al. Intensive Care 2013

Take home message

RRT in CICP

- Only few specifics in cancer patients

- Use CVVH or IHD according to your expertise and expertise of your team
- Avoid IHD in patients with cerebral injury or massive fluid overload
- Shock probably do not influence RRT tolerance

- Early or late: I would not advocate early except in patients with fluid overload

RRT in CICP

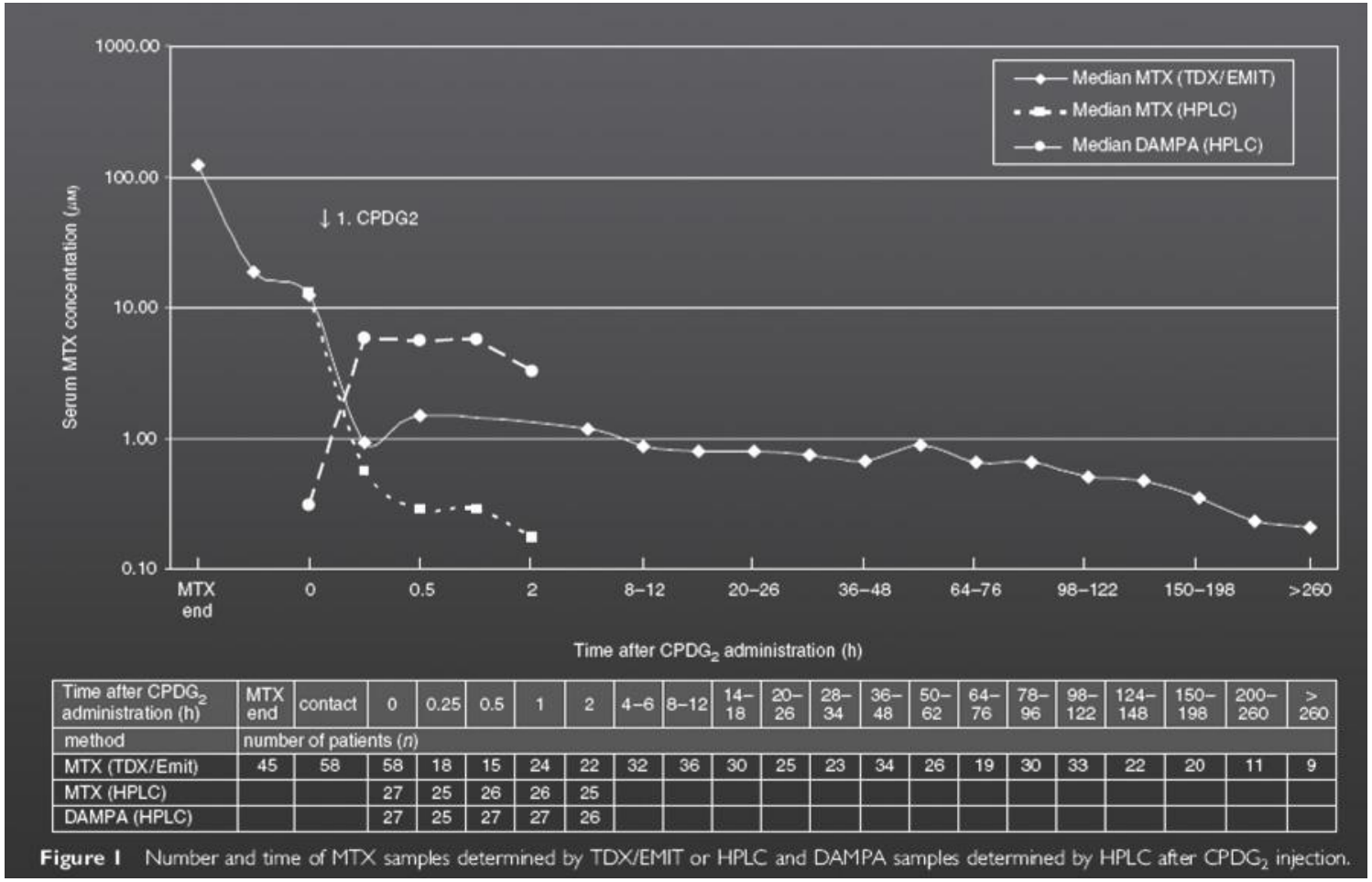
- Two specific context in onco-hematological patients

- TLS: I do start early RRT and am absolutely not sure I am right to do so
- When running RRT during TLS I would advocate HF or multiple daily IHD to avoid phosphate rebound

- Myeloma: RRT is less important than Bortezomib based therapy

Last but not least …

- If you think RRT when discussing MTX toxicity…

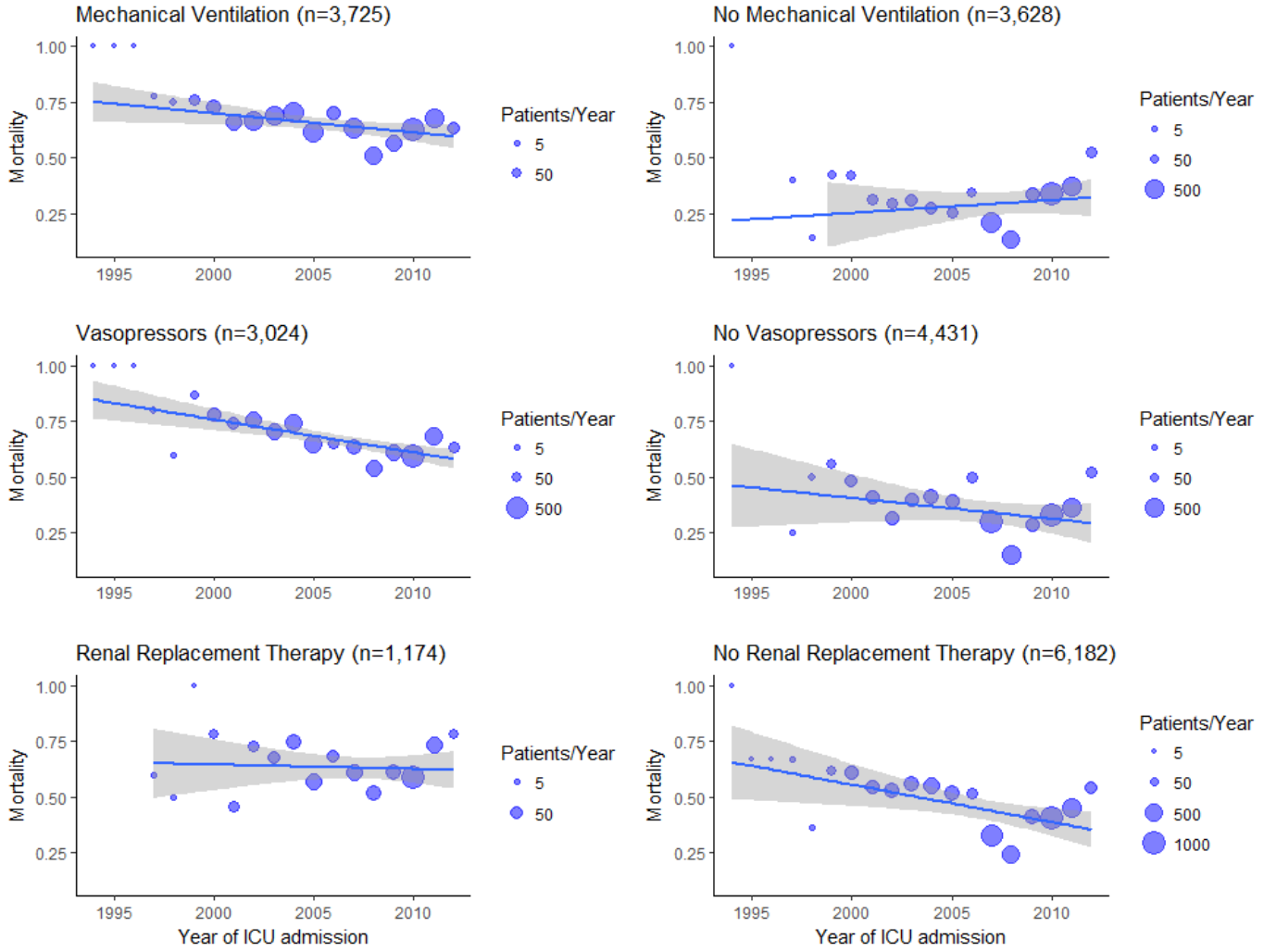


Time after $CPDG_2$ administration (h)	MTX end	contact	0	0.25	0.5	1	2	4–6	8–12	14–18	20–26	28–34	36–48	50–62	64–76	78–96	98–122	124–148	150–198	200–260	> 260
method	number of patients (*n*)																				
MTX (TDX/Emit)	45	58	58	18	15	24	22	32	36	30	25	23	34	26	19	30	33	22	20	11	9
MTX (HPLC)			27	25	26	26	25														
DAMPA (HPLC)			27	25	27	27	26														

Figure 1 Number and time of MTX samples determined by TDX/EMIT or HPLC and DAMPA samples determined by HPLC after $CPDG_2$ injection.

Bruchen et al. Br J Cancer 2005

Evolution du pronostic des POH



Darmon et al. Intensive Care Med 2019

Merci de votre attention