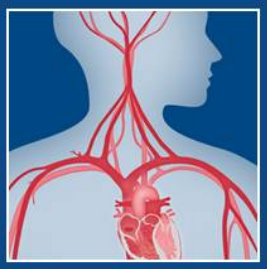
Nephro Update Europe 2019
20 – 21 September, Prague

Cardiovascular Disease



Danilo Fliser, Germany

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Epidemiology of CV disease in CKD

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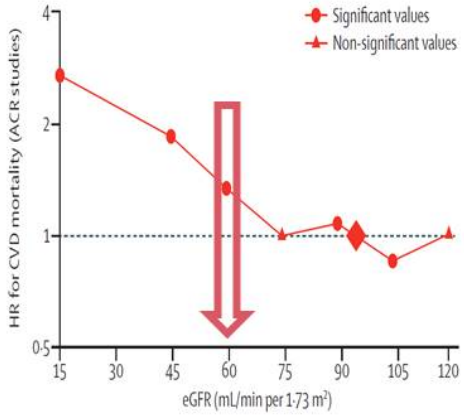
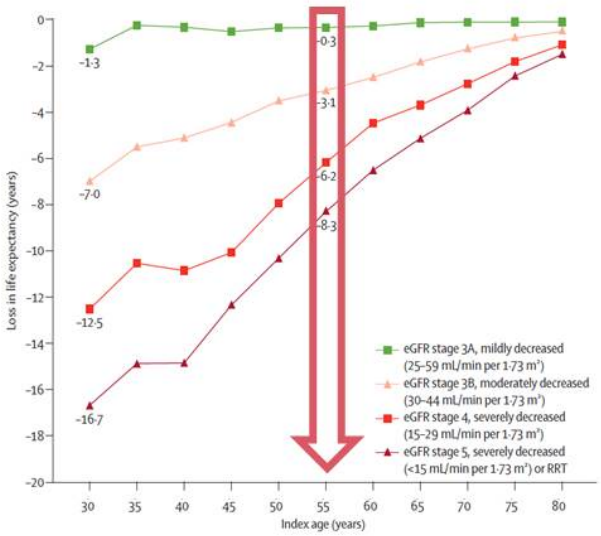
State of the art

CKD patients have a high CV morbidity & mortality



CKD Stage 3



Gansevoort RT et al. ***Lancet*** 2013; 382: 339

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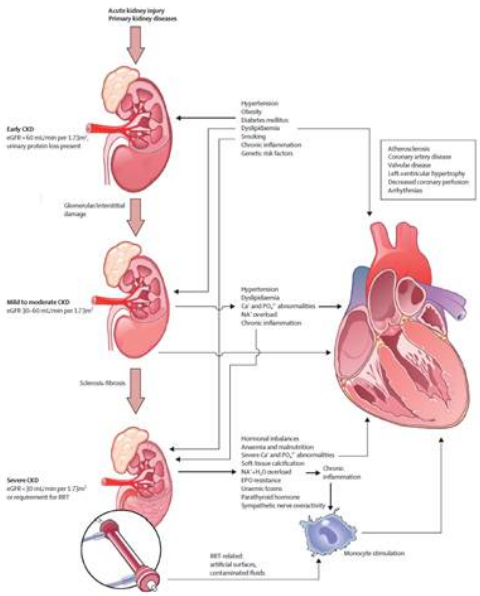
State of the art

- **non-traditional** (uremia-related) CV risk factors play a role
- causes of CV death may differ from those in the general population
- the utility of measures to reduce CV mortality may differ as well



Gansevoort RT et al. ***Lancet*** 2013; 382: 339

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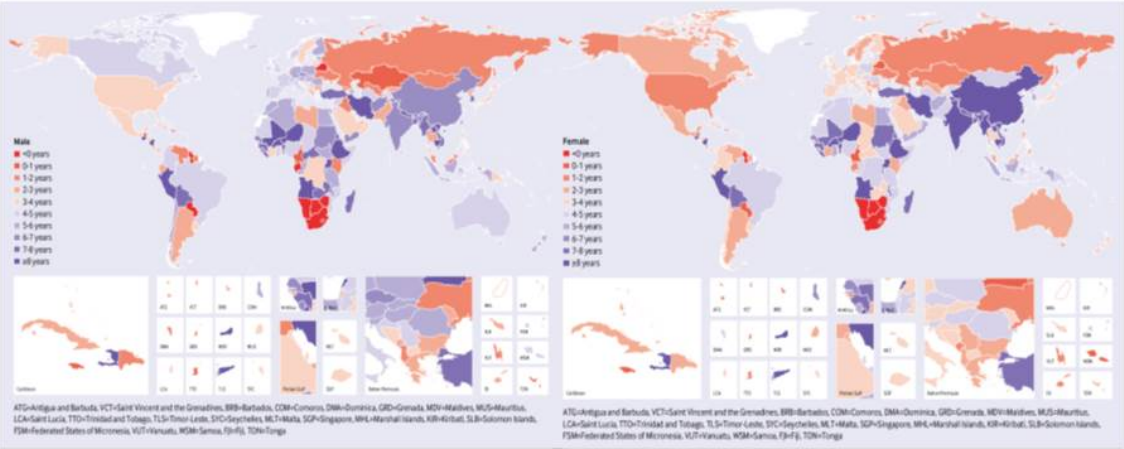
CKD and life expectancy

Contribution of 306 diseases to the changes in health adjusted life expectancy at birth (**$HALE_0$**) between 1990 and 2013



Chen H et al. ***Br Med J*** 2019; 364: l969

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CKD and life expectancy

Regions	Top 10 negative contributors to changes in $HALE_0$ in terms of total effect									
	1	2	3	4	5	6	7	8	9	10
Global	HIV/AIDS	Diabetes	Chr kidney	M headache	Depression	Other MSK	Drugs	ILD	Haemoglo	Alzheimer
Central sub-Saharan Africa	HIV/AIDS	Self harm	Cirr hep C	Diabetes	M headache	IHD	Endocrine	HTN HD	Skin	NN sepsis
Eastern sub-Saharan Africa	HIV/AIDS	M headache	Back & neck	Other MSK	Diabetes	Depression	Alzheimer	Prostate C	Intel dis	Drugs
Western sub-Saharan Africa	HIV/AIDS	Diabetes	Road injuries	Stroke	IHD	HTN HD	CMP	Drugs	M headache	Endocrine
South Asia	Self harm	Diabetes	Chr kidney	IHD	HTN HD	M headache	Depression	Road injuries	Other cardio	Other MSK
Oceania	Diabetes	HIV/AIDS	Chr kidney	Violence	Liver C	Medical	Animal	Breast C	CMP	Congenital
Southern sub-Saharan Africa	HIV/AIDS	Violence	Diabetes	Self harm	Alcohol	Mechanic	Road injuries	Endocrine	Other MSK	M headache
Andean Latin America	Other MSK	HIV/AIDS	Diabetes	Cirr hep C	Chr kidney	Alcohol	Congenital	Liver C	Pancreatic C	Prostate C
Southeast Asia	Diabetes	HIV/AIDS	Alzheimer	COPD	Migraine	Other MSK	Drugs	M headache	Urinary	Liver C
North Africa and Middle East	Diabetes	M headache	Drugs	Liver C	HIV/AIDS	Other MSK	Depression	Self harm	Medical	Endocrine
Central Asia	Diabetes	Cirr hep B	HIV/AIDS	Cirr alcohol	M headache	War	Other cardio	Cirr hep C	Other cirr	Pancreatic C
Caribbean	Diabetes	Nature	Prostate C	Chr kidney	Liver C	Other MSK	Pancreatic C	HTN HD	Medical	M headache
Tropical Latin America	Diabetes	Other MSK	Depression	Prostate C	Alzheimer	Anxiety	Brain C	Endocrine	Colorect C	M headache
East Asia	Diabetes	Back & neck	Chr kidney	ILD	M headache	HIV/AIDS	Lung C	CMP	Other respira	Prostate C
Eastern Europe	CMP	HIV/AIDS	M headache	Cirr hep C	Other MSK	Cirr alcohol	Diabetes	Tuberculosis	HTN HD	Cirr hep B
Central Latin America	Chr kidney	Diabetes	Other MSK	HIV/AIDS	Prostate C	Alzheimer	M headache	Colorect C	Atrial FF	Brain C
Central Europe	M headache	Diabetes	Atrial FF	Back & neck	Alzheimer	Kidney C	Prostate C	War	Drugs	Inflam bowel
Southern Latin America	Other MSK	Pancreatic C	Drugs	COPD	Other inj	HIV/AIDS	Diabetes	M headache	HTN HD	Urinary
High income North America	Diabetes	Drugs	Chr kidney	Alzheimer	Back & neck	M headache	Parkinson	Other MSK	Depression	Cirr hep C
Western Europe	Alzheimer	Diabetes	M headache	Other MSK	Atrial FF	Urinary	Multiple sclerosis	Prostate C	Other NN	Diarrhoea
Australasia	Diabetes	Other cardio	Atrial FF	Inflam bowel	M headache	Other NN	Other MSK	Chr kidney	Drugs	Liver C
High income Asia-Pacific	Diabetes	Back & neck	Self harm	Other cardio	M headache	Parkinson	Colorect C	Prostate C	Breast C	Other MSK

HIV/AIDS	HIV/AIDS	Diabetes	Diabetes mellitus	Chr kidney	Chronic kidney disease
M headache	Primary headache with medication overuse	Depression	Depressive disorders	Other MSK	Other musculoskeletal disorders
Drugs	Drug use disorders	ILD	Interstitial lung disease and pulmonary sarcoidosis	Haemoglo	Haemoglobinopathies and haemolytic anaemias
Alzheimer	Alzheimer's disease and other dementias	Prostate C	Prostate cancer		

Chen H et al. ***Br Med J*** 2019; 364: l969

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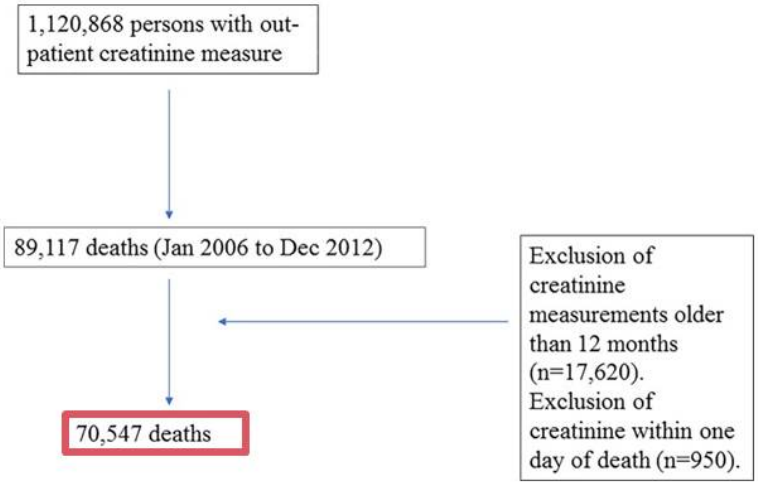
CKD and causes of death

Stockholm CREAtinine Measurements cohort
(eGFR by CKD-EPI formula)



Runesson B et al. ***PloS One*** 2019; 14: e0209440

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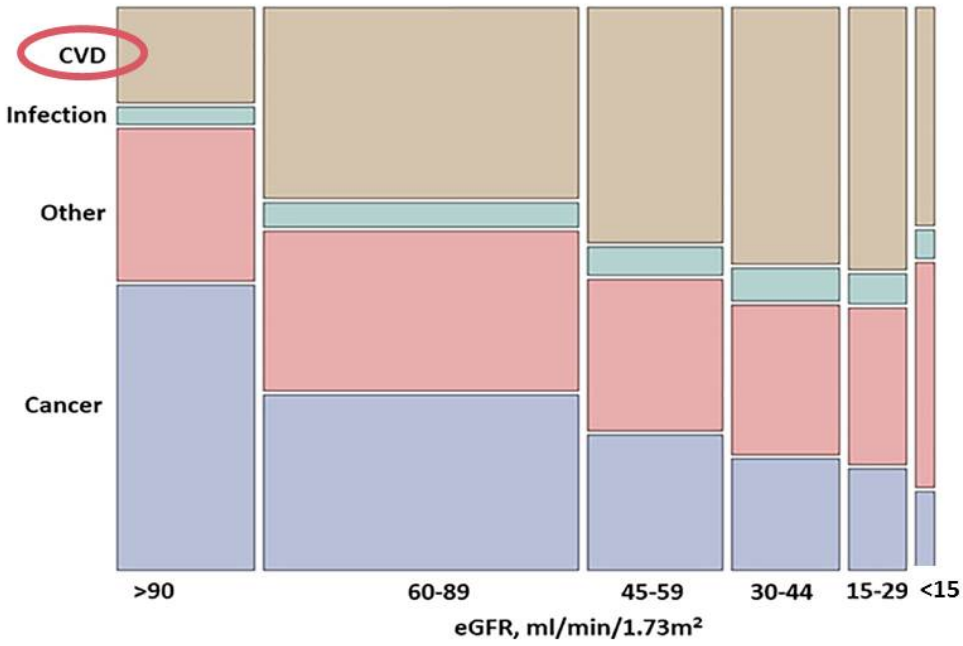
CKD and causes of death



Runesson B et al. ***PloS One*** 2019; 14: e0209440

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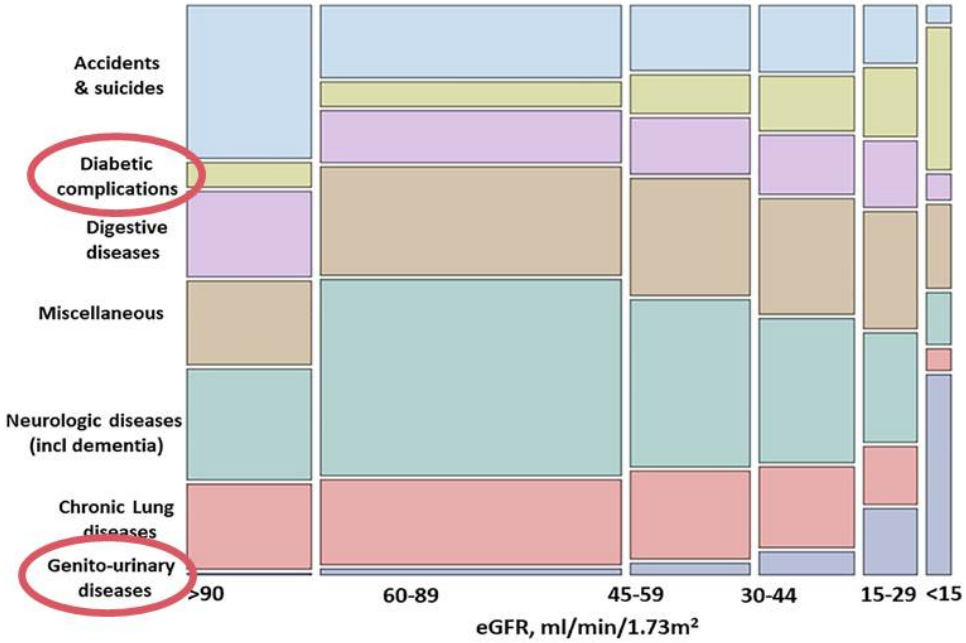
CKD and causes of death



Runesson B et al. ***PloS One*** 2019; 14: e0209440

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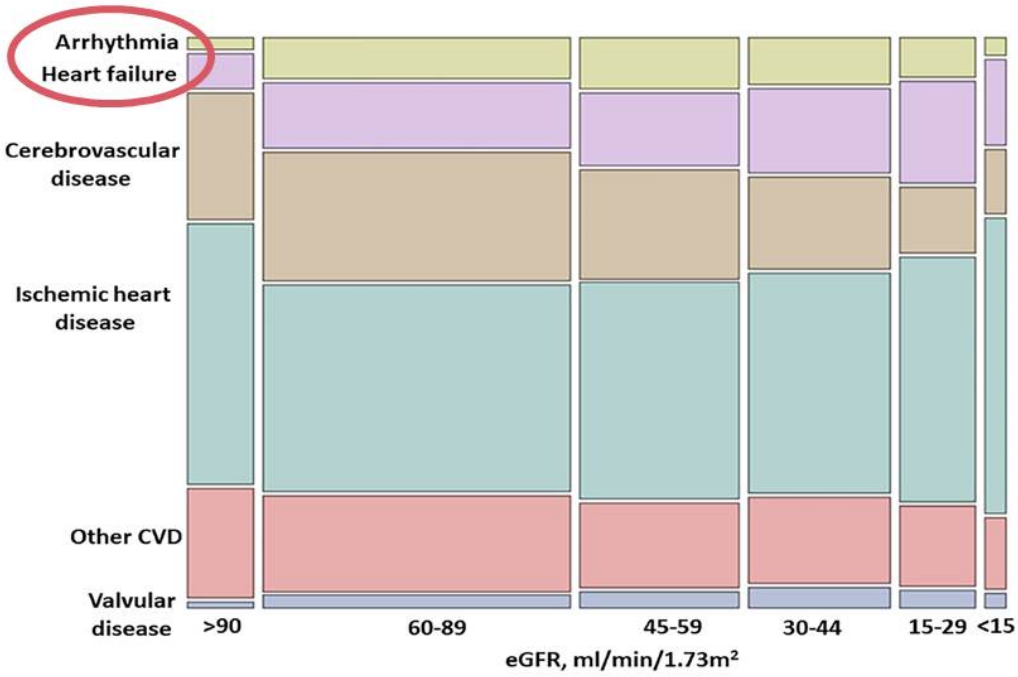
Causes of CV death in CKD



Runesson B et al. ***PloS One*** 2019; 14: e0209440

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Atrial fibrillation and CVD in CKD

- Association of new-onset AF with subsequent risks of CV events and death in the Chronic Renal Insufficiency Cohort Study (**CKD stage 2-4**)
- Among 3.080 participants 323 (**10.5%**) developed incident AF during a mean **6.1 years** of follow-up
- Participants who developed AF had higher adjusted rates of **heart failure** (HR **5.17**; 95% CI 3.89 to 6.87), myocardial infarction (HR **3.64**; 95% CI 2.50 to 5.31), stroke (HR **2.66**; 95% CI 1.50 to 4.74), and death (HR **3.30**; 95% CI 2.65 to 4.12)

Bansal N et al. ***J Am Soc Nephrol*** 2018; 12: 2859

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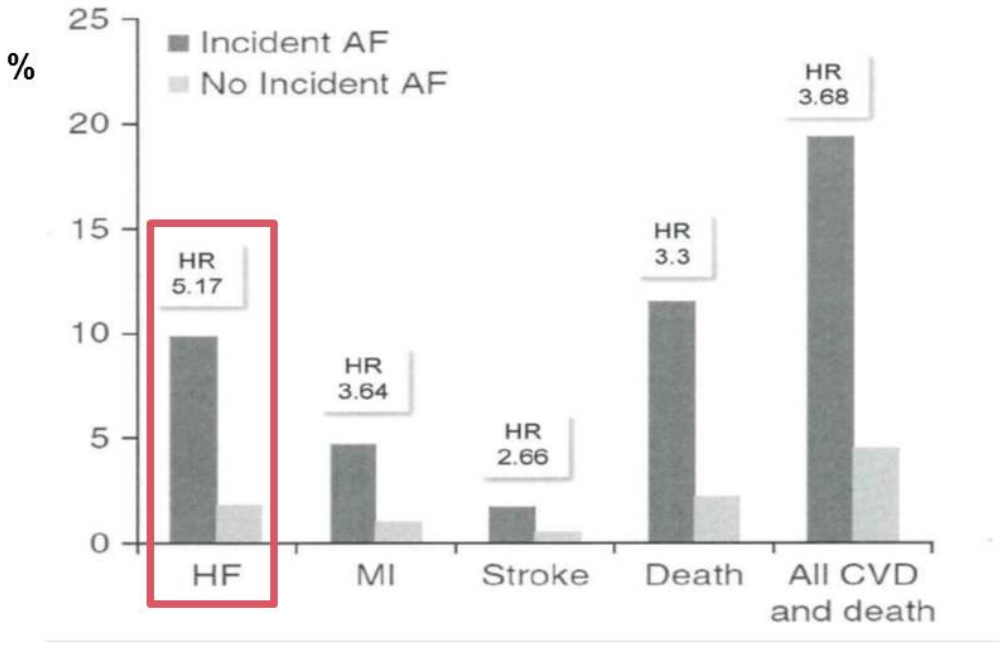
Atrial fibrillation and CVD in CKD



Bansal N et al. ***J Am Soc Nephrol*** 2018; 12: 2859

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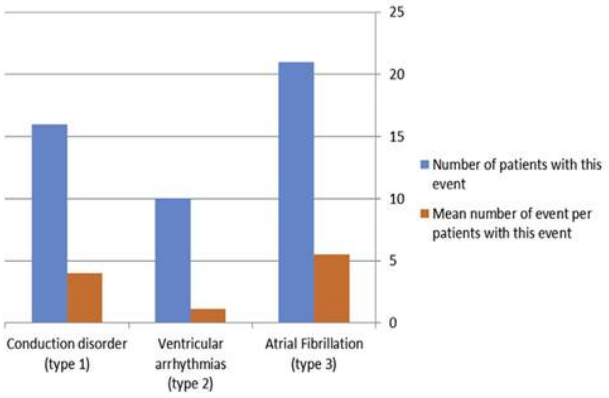
Arrhythmias and CV death in CKD

- Continuous rhythm monitoring was performed using the remote monitoring capability of the **implantable loop recorder device** in 71 patients on regular hemodialysis
- During the follow-up of 21.3 ± 6.9 months **16** patients died:
  - **7** of CV causes
  - **4** sudden deaths (with progressive **bradycardia** followed by **asystole**)



Sacher F et al. ***JACC Clin Electrophysiol*** 2018; 4: 397

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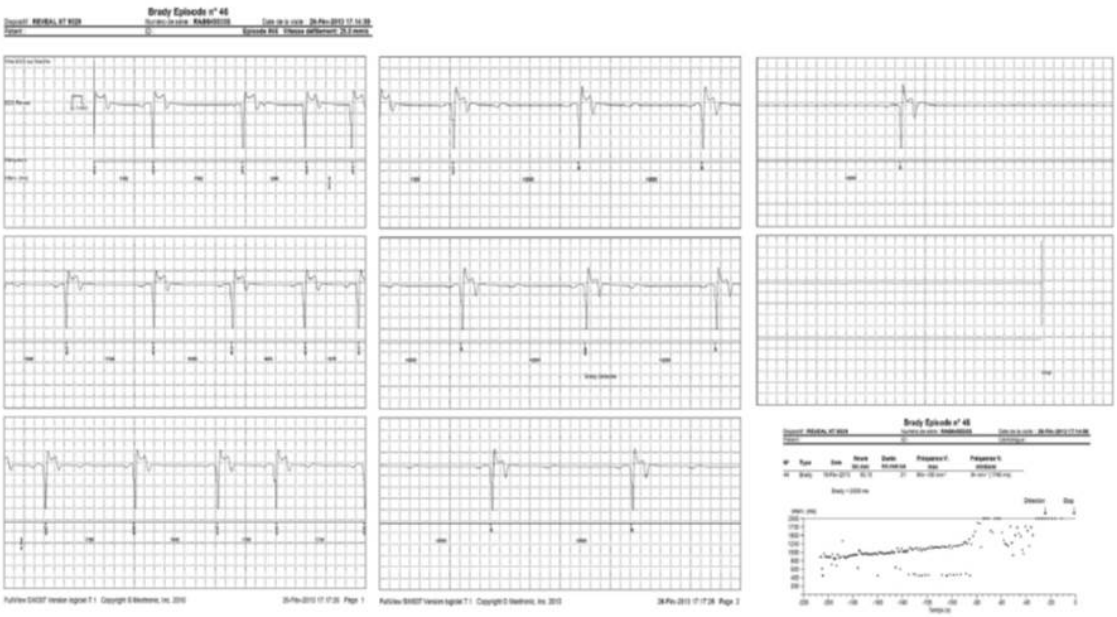
Arrhythmias and CV death in CKD



Sacher F et al. ***JACC Clin Electrophysiol*** 2018; 4: 397

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Arrhythmias and CV death in CKD

- **Implantable loop recorder** may be considered in patients on hemodialysis prone to significant conduction disorders such as ventricular arrhythmia, or atrial fibrillation/flutter to allow identification and initiation of adequate treatment
- Therapeutic strategies **reducing serum potassium variability** could decrease the rate of sudden death in these patients

Sacher F et al. ***JACC Clin Electrophysiol*** 2018; 4: 397

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Hemodialysis and arrhythmias

- Prospective observation of 66 patients on hemodialysis who underwent loop recorder implantation with **continuous electrocardiographic monitoring**
- Weekly to bi-weekly testing of pre- and post-dialysis electrolytes, and detailed capture of hemodialysis prescription and flow sheet data for **6 months**

Tumlin JA et al. ***BMC Nephrology*** 2019; 20: 80

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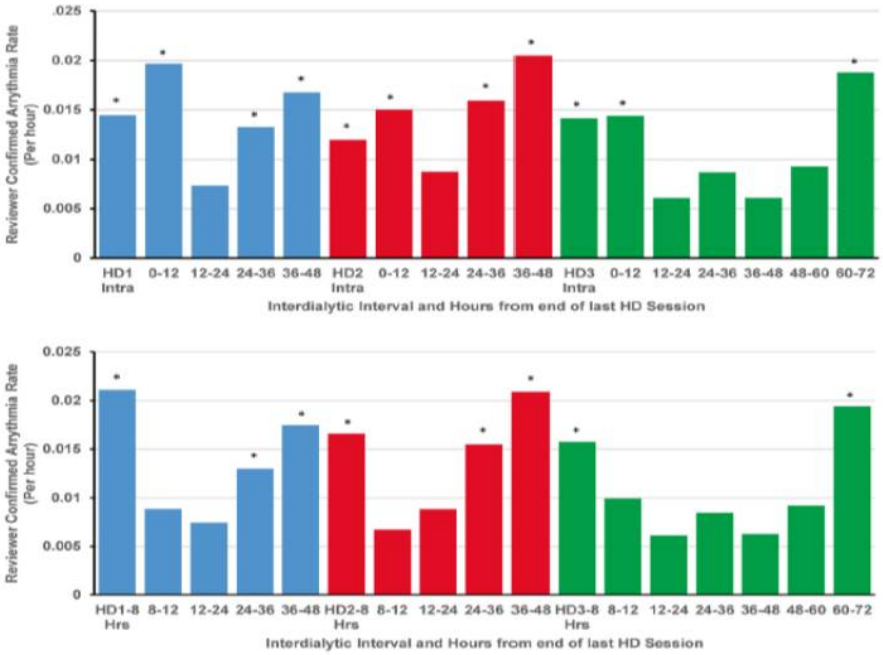
Hemodialysis and arrhythmias



Tumlin JA et al. ***BMC Nephrology*** 2019; 20: 80

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Hemodialysis and arrhythmias

- 12,480 events were detected in 64 (**97%**) patients; nadir of reviewer confirmed arrhythmias was 12-24 hours after dialysis and increased during the final 12 hours of the inter-dialytic interval through the first 8 hours after dialysis
- Higher pre-dialysis serum magnesium was associated with lower incidence rate ratio for arrythmia as was dialysate calcium concentration > 2.5 mEq/L
- **Arrhythmia rate was maximal with concurrently high intra-dialytic volume and potassium removal**

Tumlin JA et al. ***BMC Nephrology*** 2019; 20: 80

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Take-Home Message

- Progressive CKD is associated with an increase in **heart failure**, **arrhythmia** and **sudden death**
- CKD patients with new-onset atrial fibrillation have a relatively higher risk for myocardial infarction and **heart failure** than for stroke
- **Implantable loop recorder** may be considered in patients prone to significant conduction disorders to allow identification and adequate treatment

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Anticoagulation and antiplatelet therapy

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State of the Art

- Atrial fibrillation is common in CKD, but the benefit of vitamin K antagonists (e.g. **phenprocoumon**, **warfarin**) for prevention of stroke is unclear
- Large studies with **N**onvitamin K-dependent **O**ral **A**nti**C**oagulant agents in CKD are lacking
- Benefit of **aspirin** in primary prevention is unclear, particularly in CKD patients, who are at high risk for bleeding complications

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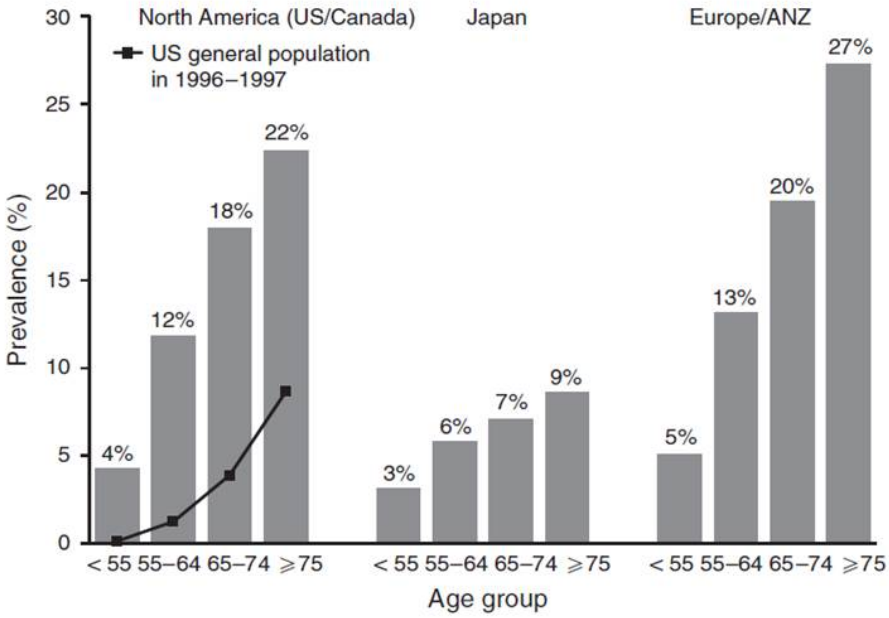
Atrial fibrillation in CKD

DOPPS



Wizemann V et al. ***Kidney Int*** 2010; 77: 1098

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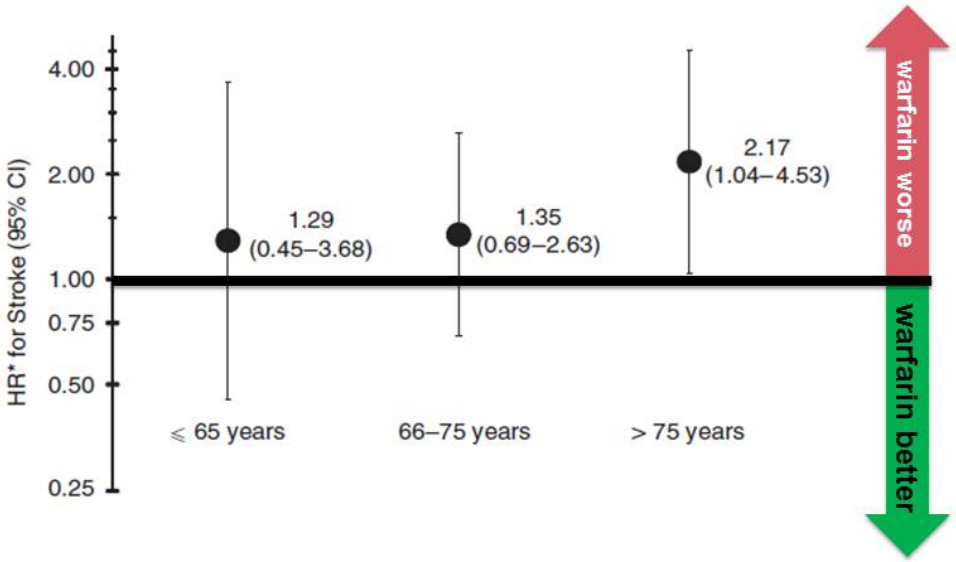
Anticoagulation in CKD

DOPPS



Wizemann V et al. ***Kidney Int*** 2010; 77: 1098

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Anticoagulation in CKD

Outcomes **R**egistry for **B**etter **I**nformed **T**reatment of **A**trial**F**ibrillation

9.019 patients with AF	No CKD (n=5529)	Stage III CKD (n=2930)	Stage IV or V CKD (n=560)	*P* Value
Antiplatelet therapy				
Any antiplatelet therapy	48.5%	46.2%	49.1%	0.1085
Aspirin	45.7%	42.6%	43.9%	0.0231
Dose ≥100 mg/day (among aspirin patients)	24.6%	16.3%	16.3%	<0.0001
Clopidogrel	6.3%	8.5%	12.0%	<0.0001
Prasugrel	0.1%	0.1%	0.0%	0.6034
Dipyridamole/aspirin	0.1%	0.2%	0.4%	0.2573
Oral anticoagulation				
Any OAC (Dabigatran or Warfarin)	76.6%	77.7%	68.0%	<0.0001
Dabigatran	5.9%	3.9%	1.4%	<0.0001
Warfarin	70.8%	73.9%	66.6%	0.0003
Combination therapy				
Any anticoagulant and antiplatelet	30.3%	28.9%	23.6%	0.0031
Dabigatran and antiplatelet	2.0%	1.4%	0.4%	0.0028
Warfarin and antiplatelet	28.3%	27.6%	23.2%	0.0381

Washam JB et al. ***J Am Heart Assoc*** 2018; 7: e008928

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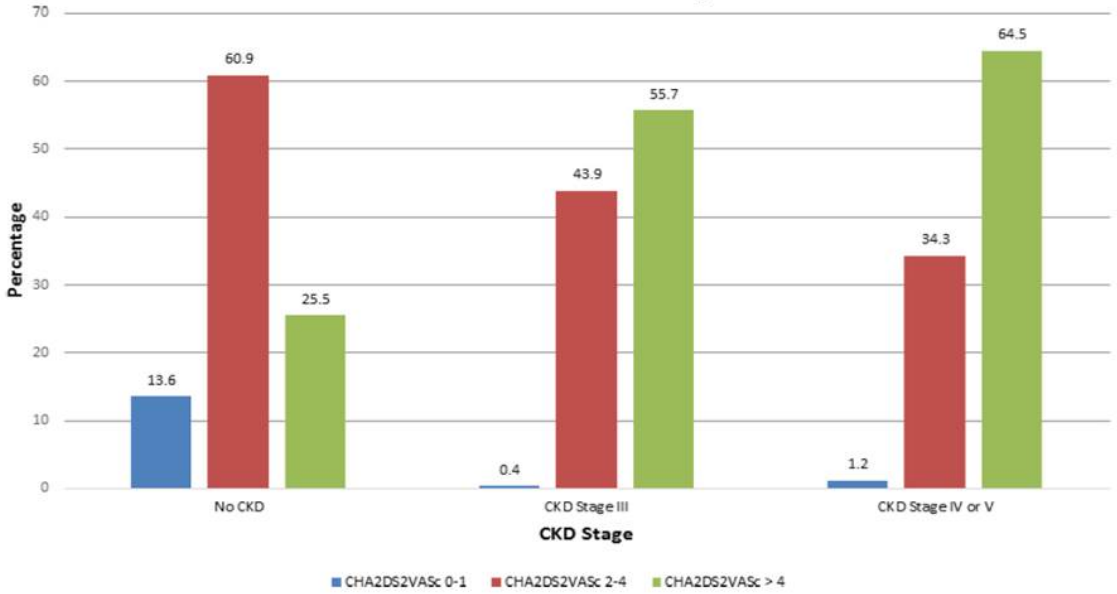
Anticoagulation in CKD

CHA2DS2VASc scores according to CKD Status



Washam JB et al. ***J Am Heart Assoc*** 2018 Sep 18;7(18):e008928

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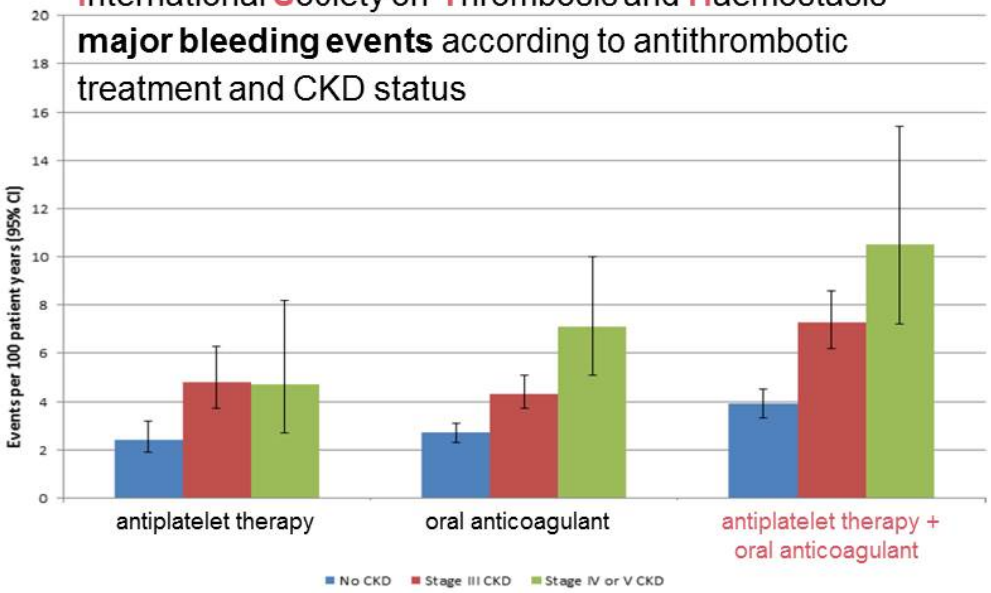
Anticoagulation in CKD

International Society on Thrombosis and Haemostasis

major bleeding events according to antithrombotic treatment and CKD status



Washam JB et al. ***J Am Heart Assoc*** 2018 Sep 18;7(18):e008928

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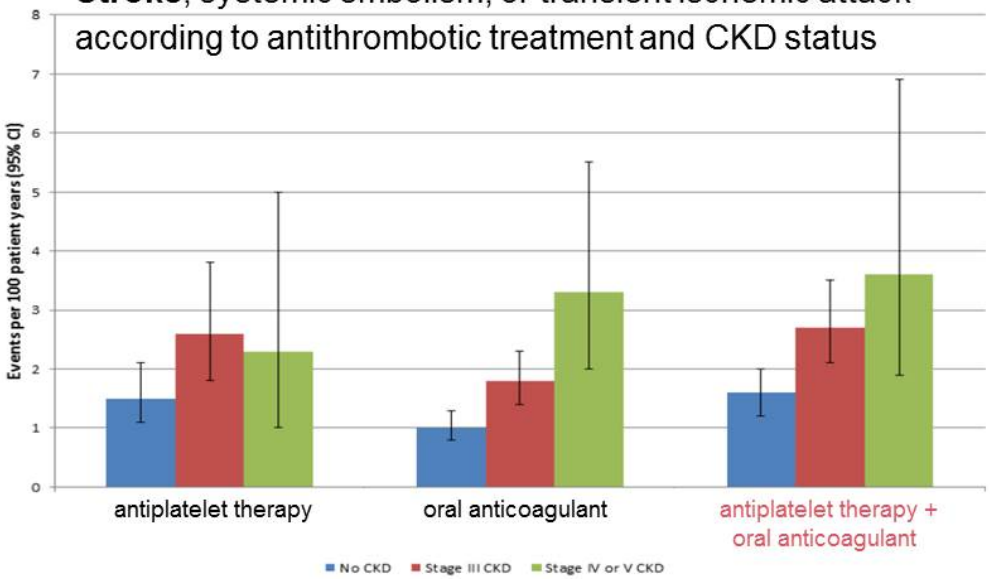
Anticoagulation in CKD

Stroke, systemic embolism, or transient ischemic attack according to antithrombotic treatment and CKD status



Washam JB et al. ***J Am Heart Assoc*** 2018 Sep 18;7(18):e008928

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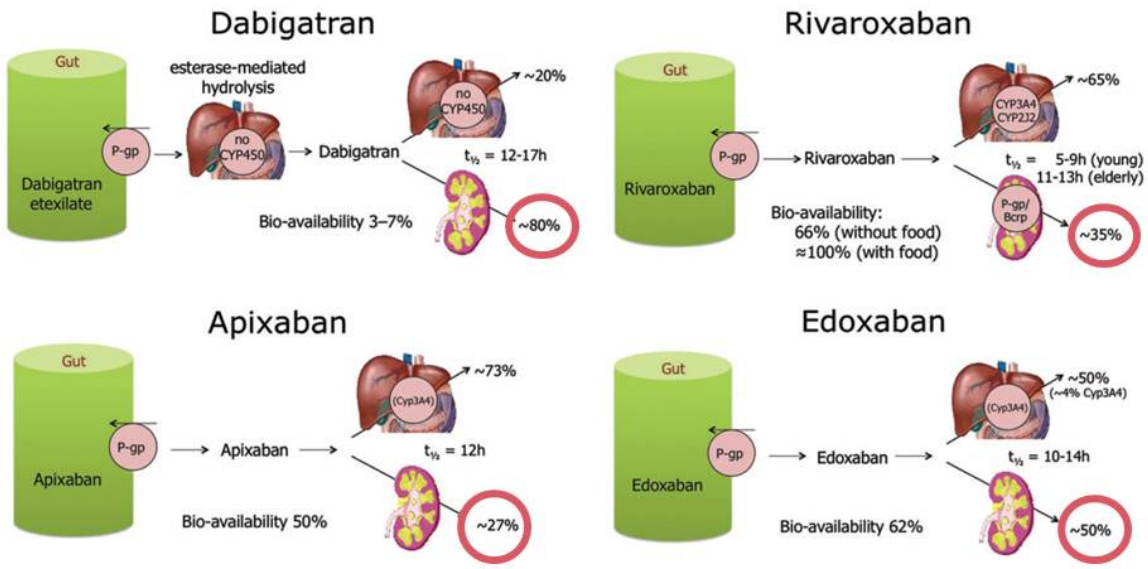
NOACs in CKD

Updated European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist anticoagulants in patients with non-valvular atrial fibrillation

Nonvitamin K-dependent Oral AntiCoagulant agents



Heidbuchel H et al. ***Europace*** 2015; 17: 1467

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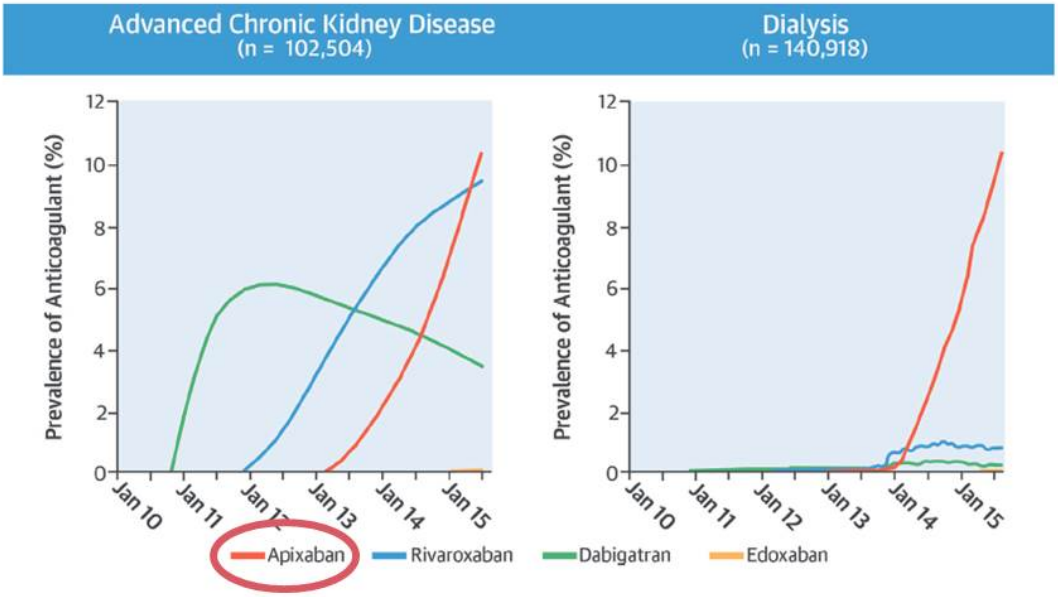
NOACs in CKD

Nonvitamin K-dependent Oral AntiCoagulant agents



Chan KE et al. ***JACC*** 2016; 67: 2888

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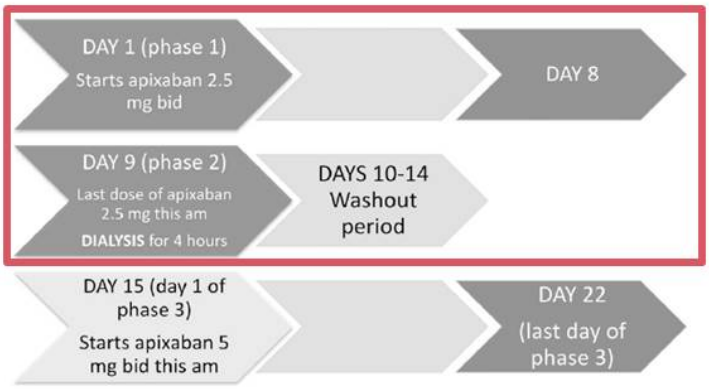
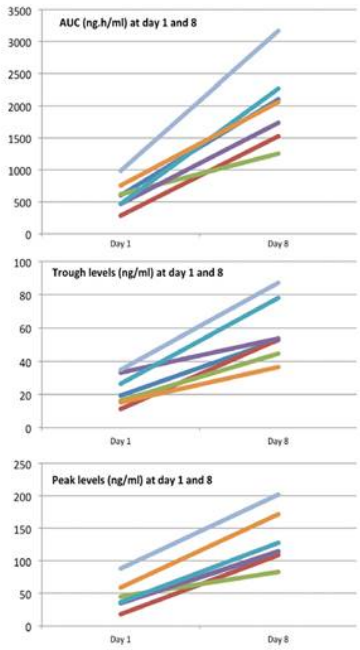
NOACs in CKD

7 patients on hemodialysis received apixaban **2.5 mg twice daily** for 8 days, blood samples were collected before and after apixaban administration on days 1 and 8





Mavrakanas TA et al. ***J Am Soc Nephrol*** 2017; 28: 2241

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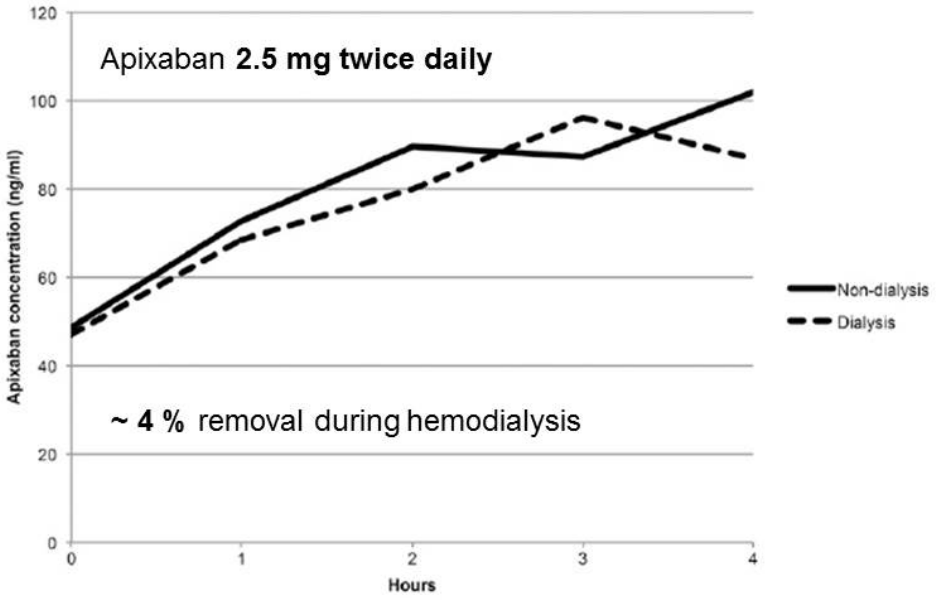
NOACs in CKD



Mavrakanas TA et al. ***J Am Soc Nephrol*** 2017; 28: 2241

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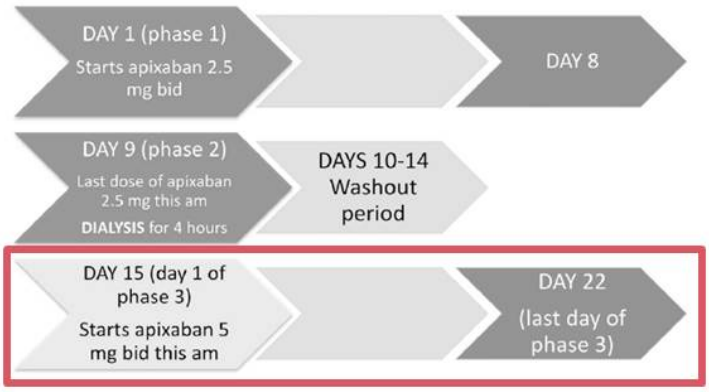
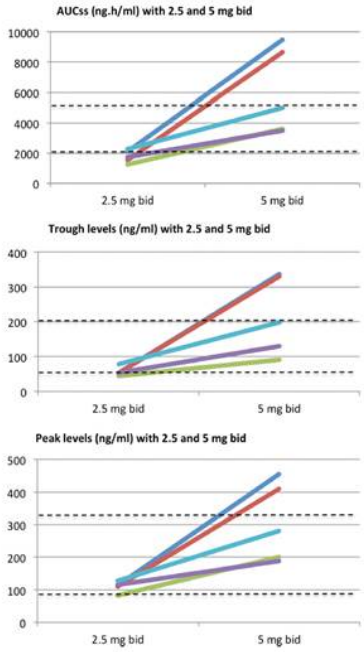
NOACs in CKD

5 patients on hemodialysis received apixaban **5 mg twice daily** for 8 days, blood samples were collected before and after apixaban administration on days 1 and 8





Mavrakanas TA et al. ***J Am Soc Nephrol*** 2017; 28: 2241

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NOACs in CKD

Apixaban 2.5 mg twice daily	Day 1	Day 8	*P* Value	Reference Levels (for the 2.5 mg twice daily dose)
AUC_{0-12}, ng h/ml	298.6 (38.0%)	1009.8 (30.7%)	<0.001	—
AUC_{0-24}, ng h/ml	597.3 (38.0%)	2019.7 (30.7%)	<0.001	1661 (1120–2620)[19]
C_{max}, ng/ml	45.2 (49.9%)	131.5 (31.1%)	<0.001	123 (69–221)[a20]
t_{max}, h	4.4 (62%)	3.6 (48%)	0.32	—
C_{min}, ng/ml	22.3 (41.2%)	58.0 (31.2%)	<0.001	56 (24–103)[19]

C_{min} according to manufacturer **79** [34-162] ng/ml

Apixaban 5 mg twice daily	Day 22	*P* Value	Reference Levels (for the 5 mg twice daily dose)
AUC_{0-12}, ng h/ml	3026.6±46.6% [2770.4]	0.03	[1474–1717][18]
AUC_{0-24}, ng h/ml	6053.2±46.6% (3505.5–9469.7)	0.03	3370 (2070–5250)[19]
C_{max}, ng/ml	307.0±39.4% (189.0–455.0)	0.02	171 (91–321)[a20]
t_{max}, h	3.8±35.6% (2.5–6.0)	0.89	—
C_{min}, ng/ml	217.5±51.9% (91.0–337.4)	0.03	107 (56–203)[19]

C_{min} according to manufacturer **103** [41-230] ng/ml

Mavrakanas TA et al. ***J Am Soc Nephrol*** 2017; 28: 2241

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NOACs in CKD

	Siontis 2018	Reed 2018	Chokesuwattanaskul 2018
Number in study	25 523	124	43 850
OR of major bleed with apixaban	0.72 (CI 0.59-0.87)	0.25(CI: 0.07-0.82)	0.42 (CI: 0.28-0.61)
OR of stroke/ embolism with apixaban	0.88 (CI: 0.69-1.12)	NA	OR = 0.56 (CI: 0.23-1.39)
Bleeding risk	Favors apixaban	Favors apixaban	Favors apixaban
Efficacy	No significant difference	No significant difference	No significant difference

Weber J et al. ***Eur J Haematol*** 2019; 102: 312

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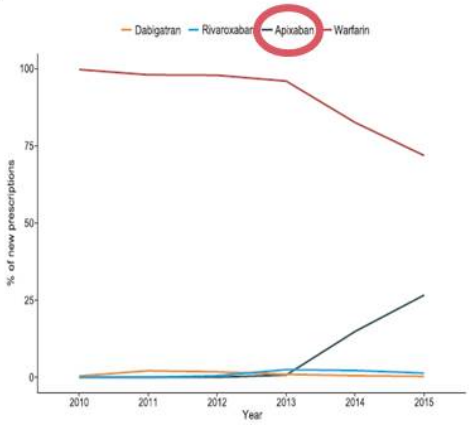
NOACs in CKD

- **Retrospective cohort study** of Medicare beneficiaries included in the United States Renal Data System (October 2010 to December 2015)
- Eligible patients were those with **end-stage kidney disease** and **atrial fibrillation** undergoing **dialysis** who initiated treatment with an oral anticoagulant



Siontis et al. ***Circulation*** 2018; 138:1519

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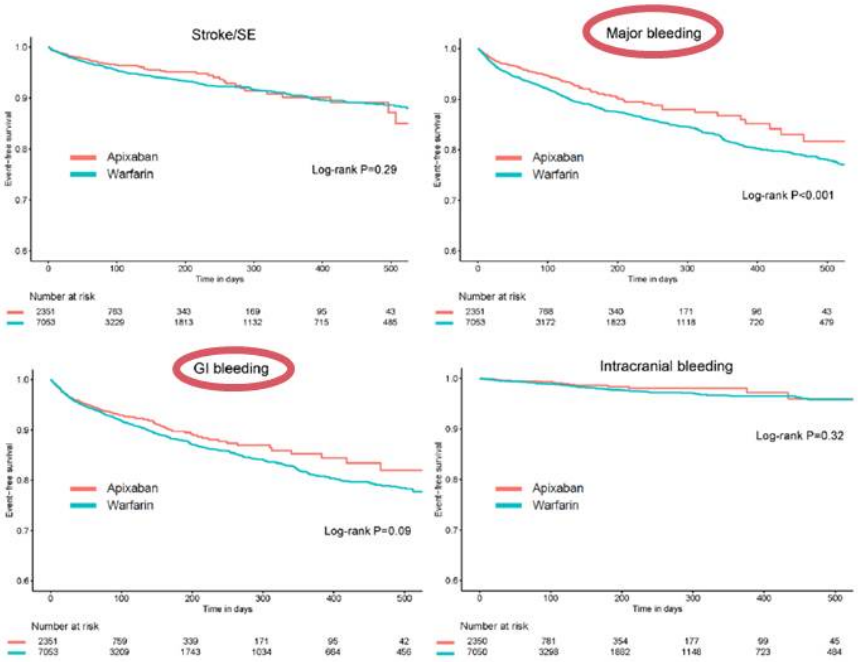
NOACs in CKD



Siontis et al. ***Circulation*** 2018; 138:1519

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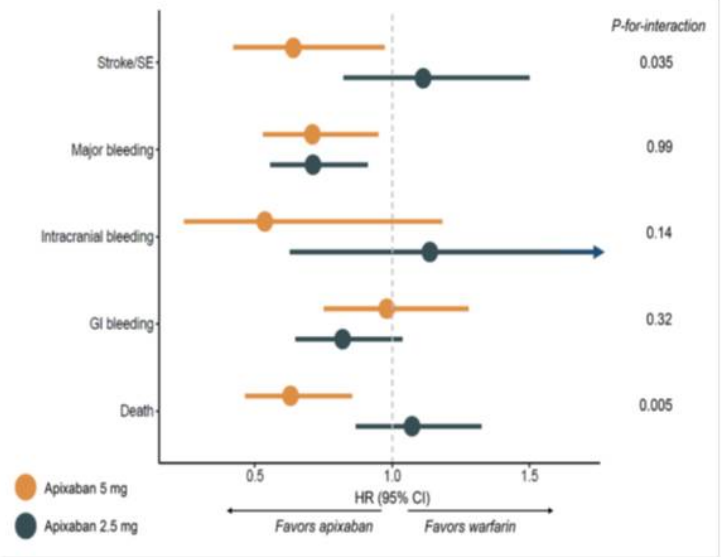
NOACs in CKD

- 1.034 (44%) patients on **5 mg** apixaban twice daily
- 1.317 (56%) patients on **2.5 mg** apixaban twice daily
- 23.172 patients on warfarin



Siontis et al. ***Circulation*** 2018; 138:1519

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NOACs in CKD

CKD Stage	GFR (mL/min)	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
1	>90	✓	✓	✓	✓
2	90-60	✓	✓	✓	✓
3	59-30	✓ ESC: GFR 30-49 mL/min ⇨ reduced dose	✓ ESC: GFR 30-49 mL/min ⇨ reduced dose	✓	✓ ESC: GFR 30-49 mL/min ⇨ reduced dose
4	29-15	FDA: reduced dose / EMA: Contra-indicated	✓ reduced dose	✓ reduced dose*	✓ reduced dose
5 5D	<15 Dialysis	Contraindicated	Contraindicated	FDA: full to reduced * dose / EMA: Contra-indicated	Contraindicated

* : If two of the following criteria are present : serum creatinine ≥ 1.5 mg/dl, age ≥ 80 years, body weight ≤ 60kg

Stamellou E & Flöge J. ***Nephrol Dial Transplant*** 2018; 33: 1683

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Aspirin and CV prevention

ARRIVE – Gaziano JM et al. ***Lancet*** 2018; 392: 1036

- 12.546 individuals with intermediate risk
- 10-year risk for CVD ~14-17%
- **No benefit**, but significantly more gastrointestinal bleeding episodes with aspirin

ASPREE – McNeil et al. ***N Engl J Med*** 2018; 379: 1499

- 19.114 elderly (> 65 years) without CVD
- **No benefit**, but significantly more major bleeding episodes and **cancer (!)** with aspirin

ASCEND Study Collaborative Group. ***N Engl J Med*** 2018; 379: 1529

- 15.480 patients with diabetes but without CVD
- **Significant benefit**, but also highly significantly more major bleeding episodes with aspirin

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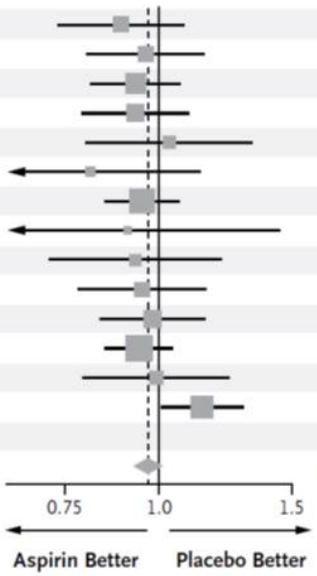
Aspirin and CV prevention

Trial (year)	Aspirin	Placebo	Hazard Ratio for All-Cause Mortality (95% CI)
	no. of deaths/total no. of participants		
BMDT (1988)	270/3429	151/1710	0.89 (0.74–1.08)
PHS (1989)	217/11,037	227/11,034	0.96 (0.80–1.14)
ETDRS (1992)	340/1856	366/1855	0.93 (0.81–1.06)
HOT (1998)	284/9399	305/9391	0.93 (0.79–1.09)
TPT (1998)	113/1268	110/1272	1.03 (0.80–1.32)
PPP (2001)	62/2226	78/2269	0.81 (0.58–1.13)
WHS (2005)	609/19,934	642/19,942	0.95 (0.85–1.06)
JPAD (2008)	34/1262	38/1277	0.91 (0.57–1.43)
POPADAD (2008)	94/638	101/638	0.93 (0.72–1.21)
AAA (2010)	176/1675	186/1675	0.95 (0.78–1.15)
JPPP (2014)	297/7220	303/7244	0.98 (0.84–1.15)
ASCEND (2018)	748/7740	792/7740	0.94 (0.85–1.04)
ARRIVE (2018)	160/6270	161/6276	0.99 (0.80–1.24)
ASPREE (2018)	558/9525	494/9589	1.14 (1.01–1.29)
Overall (I^2=0%, P=0.67)			**0.97 (0.93–1.01)**



Ridker PM et al. ***N Engl J Med*** 2018; 379: 1572

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Aspirin and CV prevention

2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

COR	LOE	Recommendations
IIb	A	1. Low-dose aspirin (75-100 mg orally daily) might be considered for the primary prevention of ASCVD among select adults 40 to 70 years of age who are at higher ASCVD risk but not at increased bleeding risk (S4.6-1–S4.6-8).
III: Harm	B-R	2. Low-dose aspirin (75-100 mg orally daily) should not be administered on a routine basis for the primary prevention of ASCVD among adults >70 years of age (S4.6-9).
III: Harm	C-LD	3. Low-dose aspirin (75-100 mg orally daily) should not be administered for the primary prevention of ASCVD among adults of any age who are at increased risk of bleeding (S4.6-10).

Arnett DK et al. ***Circulation*** 2019; Mar 17 doi:10.1161/CIR.0000000000000678

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Take-Home Message

- NOACs may be a valuable alternative to standard anticoagulation with OACs in CKD patients with respect to **safety** (bleeding complications)
- Most data exist for **apixaban**, prospective studies are on the way (AVKDIAL, RENAL-AFR, AXADIA)
- Aspirin should **not** be used routinely for primary CV prevention in patients with increased risk of bleeding (e.g. uremic patients)

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Other treatments of CV disease in CKD

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State of the Art

- Reducing low-density cholesterol with statin-based therapy reduces CV risk in CKD patients, but the utility in patients on dialysis is uncertain
- CKD patients are characterized by a high level of micro-inflammation promoting CVD
- SGLT2-inhibition is a promising drug therapy for prevention of CV events in diabetic patients, possibly also those with more advanced CKD

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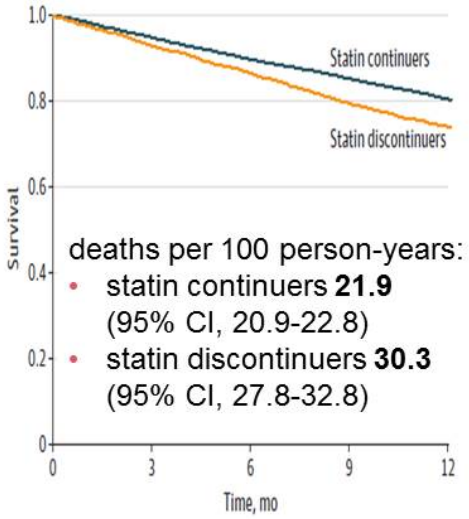
Statin use in CKD

- Retrospective cohort study of 14.298 veterans transitioning to dialysis, who received statins for 12-month before dialysis and survived the first year of dialysis
- In **continuers** statin therapy was continued for at least 6 months during the first year after dialysis initiation



No. at risk

Statin therapy continuers	11936	10959	9915	8967	8033
Statin therapy discontinuers	2362	2089	1839	1574	1351

Streja E et al. ***JAMA Network Open*** *2018 Oct 5;1(6):e182311*

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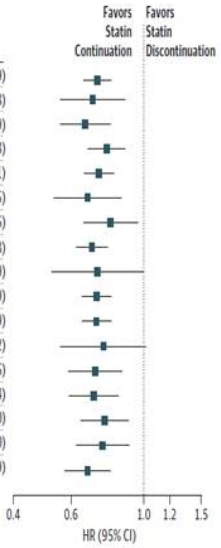
Statin use in CKD

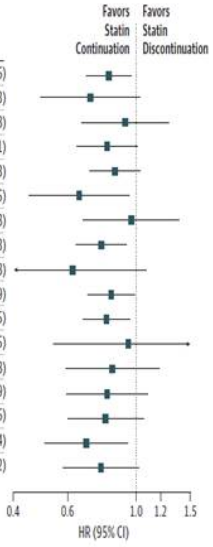
All-cause mortality

Source	Patients, No.	*P* for Interaction	HR (95% CI)
All	14298		0.72 (0.66-0.79)
Age <65 y	4146	.24	0.70 (0.56-0.88)
Age 65 to <75 y	4202		0.66 (0.56-0.79)
Age ≥75 y	5950		0.77 (0.68-0.88)
Not African American	11255	.54	0.73 (0.66-0.81)
African American	3043		0.67 (0.53-0.85)
No diabetes	3614	.21	0.79 (0.66-0.96)
Diabetes	10627		0.70 (0.63-0.78)
No CVD	2369	.98	0.72 (0.53-0.99)
CVD	11872		0.72 (0.65-0.79)
No liver disease	13228	.72	0.72 (0.65-0.79)
Liver disease	1013		0.75 (0.56-1.02)
Never smoker	3834	.68	0.71 (0.59-0.86)
Current smoker	4181		0.71 (0.60-0.84)
Past smoker	4683		0.76 (0.64-0.90)
LDL-C <70 mg/dL	4042	.38	0.75 (0.62-0.90)
LDL-C ≥70 mg/dL	5693		0.68 (0.58-0.79)



CV mortality

Source	Patients, No.	*P* for Interaction	HR (95% CI)
All	14298		0.82 (0.69-0.96)
Age <65 y	4146	.68	0.71 (0.49-1.03)
Age 65 to <75 y	4202		0.92 (0.67-1.28)
Age ≥75 y	5950		0.81 (0.65-1.01)
Not African American	11255	.23	0.85 (0.71-1.03)
African American	3043		0.65 (0.45-0.95)
No diabetes	3614	.21	0.97 (0.67-1.38)
Diabetes	10627		0.77 (0.64-0.93)
No CVD	2369	.35	0.63 (0.36-1.08)
CVD	11872		0.83 (0.70-0.99)
No liver disease	13228	.64	0.80 (0.68-0.95)
Liver disease	1013		0.95 (0.54-1.65)
Never smoker	3834	.83	0.84 (0.60-1.18)
Current smoker	4181		0.81 (0.60-1.09)
Past smoker	4683		0.80 (0.60-1.06)
LDL-C <70 mg/dL	4042	.65	0.69 (0.51-0.94)
LDL-C ≥70 mg/dL	5693		0.77 (0.58-1.02)



Streja E et al. ***JAMA Network Open*** *2018 Oct 5;1(6):e182311*

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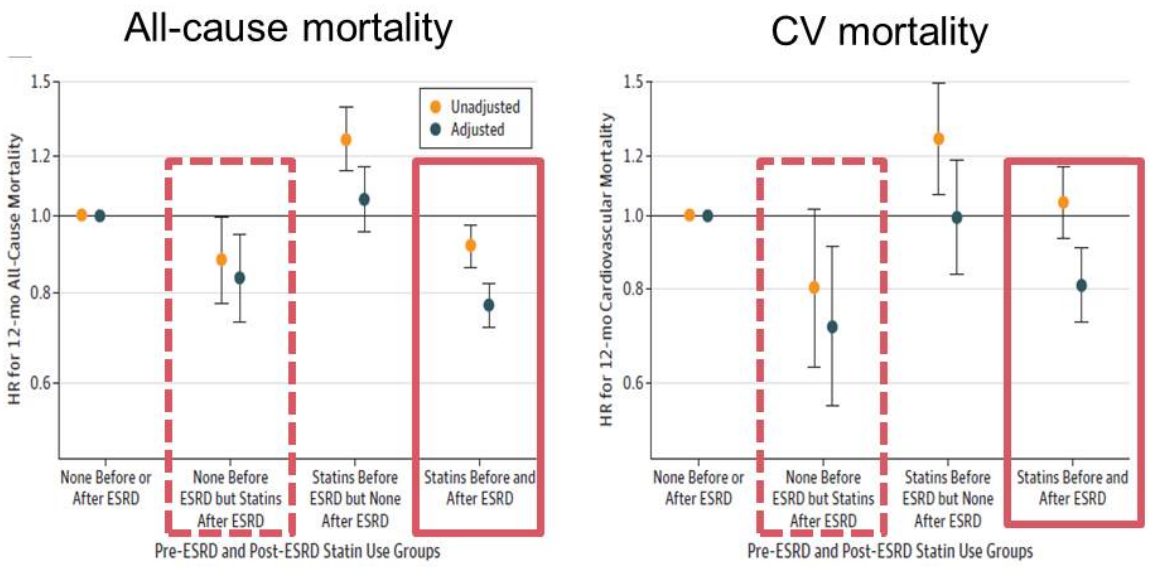
Statin use in CKD



Streja E et al. ***JAMA Network Open*** *2018 Oct 5;1(6):e182311*

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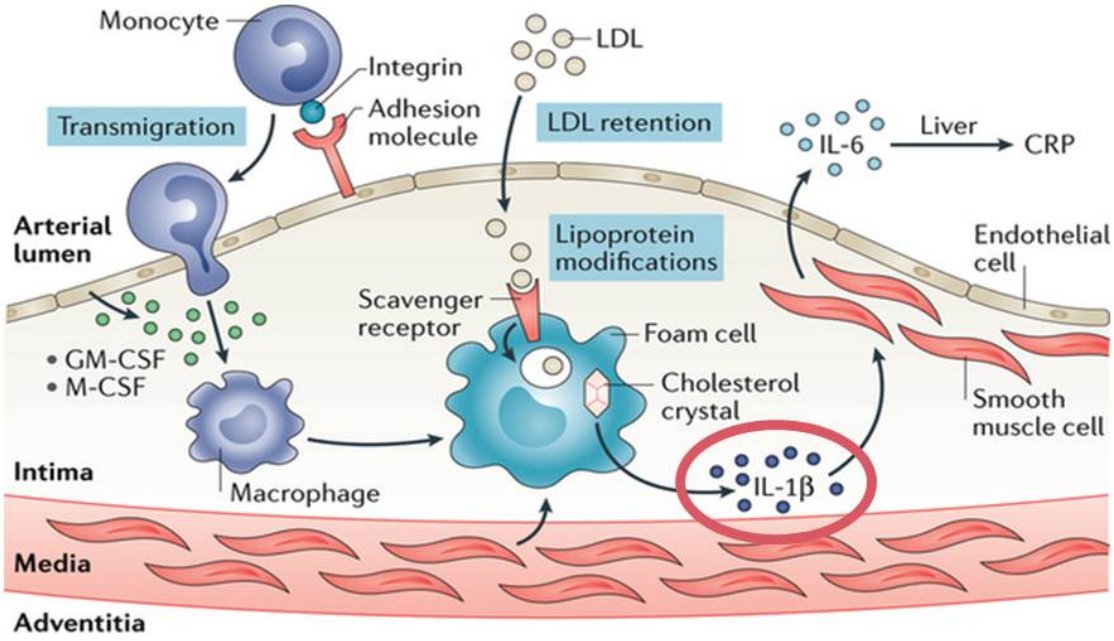
Inflammation and atherosclerosis



Gistera A & Hansson GK. ***Nat Rev Nephrol*** 2017; 13: 368

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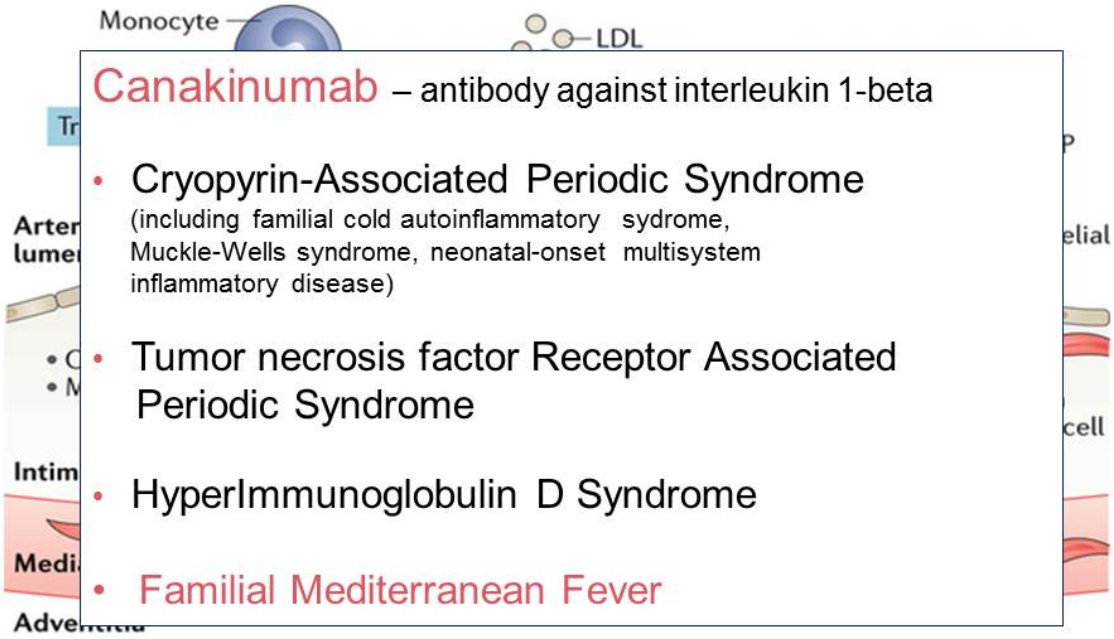
Inflammation and atherosclerosis



Canakinumab – antibody against interleukin 1-beta

- Cryopyrin-Associated Periodic Syndrome
  (including familial cold autoinflammatory sydrome, Muckle-Wells syndrome, neonatal-onset multisystem inflammatory disease)
- Tumor necrosis factor Receptor Associated Periodic Syndrome
- HyperImmunoglobulin D Syndrome
- Familial Mediterranean Fever

Gistera A & Hansson GK. ***Nat Rev Nephrol*** 2017; 13: 368

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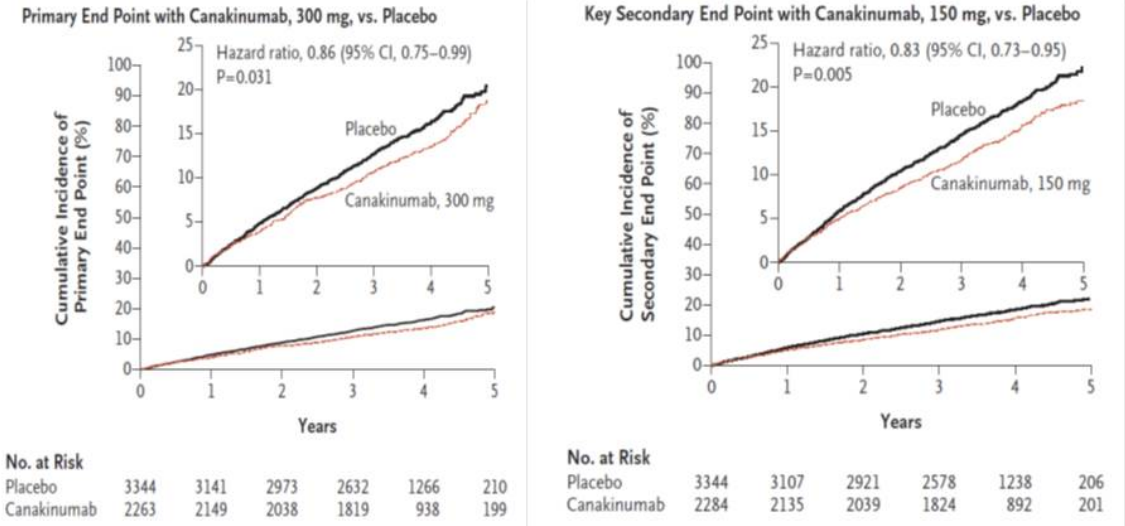
Canakinumab in CV disease

Canakinumab **AN**tiinflammatory **T**hrombosis **O**utcome **S**tudy



Ridker PM et al. ***N Engl J Med*** 2017; 377: 1119

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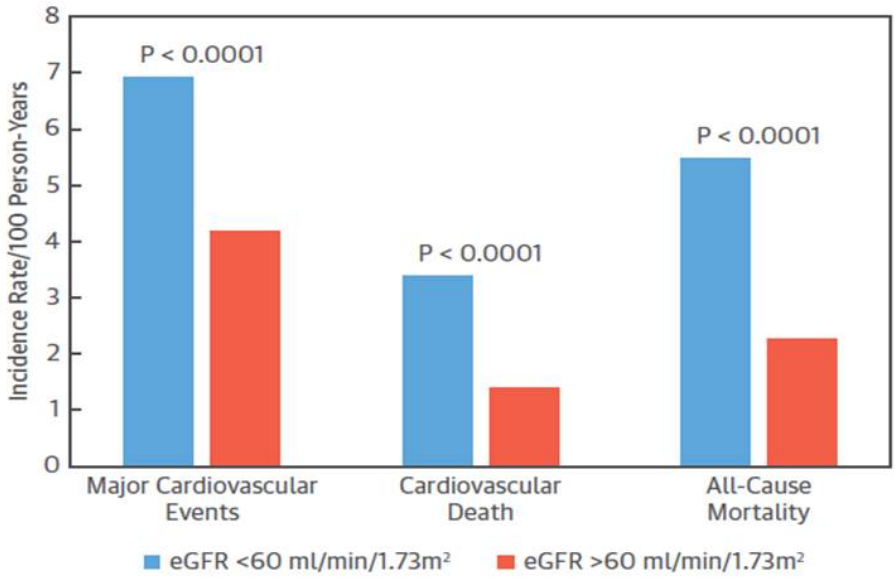
Canakinumab in CKD

Canakinumab ANtiinflammatory Thrombosis Outcome Study



Ridker PM et al. ***JACC*** 2018; 71: 2405

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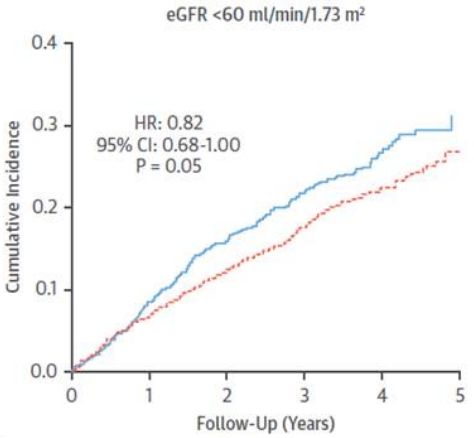
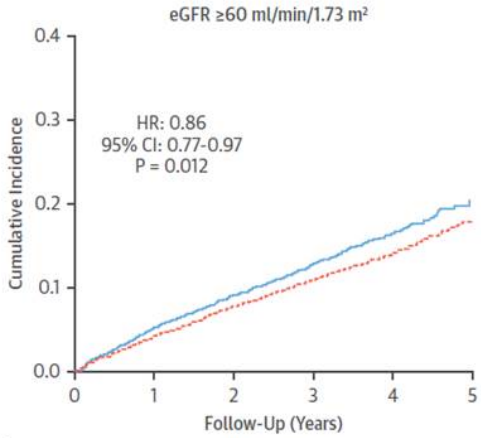
Canakinumab in CKD

Canakinumab ANtiinflammatory Thrombosis Outcome Study





No. at risk:						
Placebo	626	561	499	423	182	27
Canakinumab	1249	1139	1047	894	410	58

No. at risk:						
Placebo	2717	2546	2422	2155	1056	179
Canakinumab	5467	5177	4940	4410	2155	382

Ridker PM et al. ***JACC*** 2018; 71: 2405

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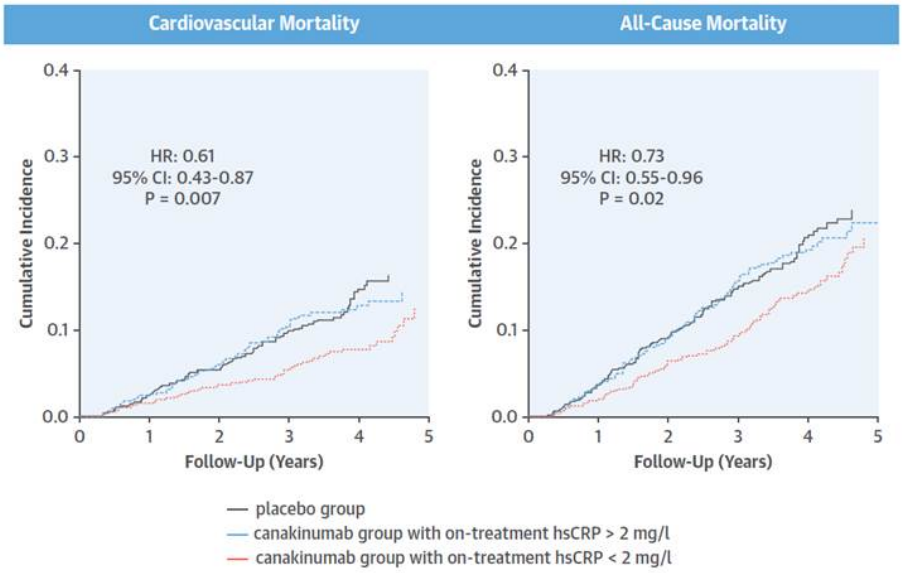
Canakinumab in CKD

Canakinumab **AN**tiinflammatory **T**hrombosis **O**utcome **S**tudy



Ridker PM et al. ***JACC*** 2018; 71: 2405

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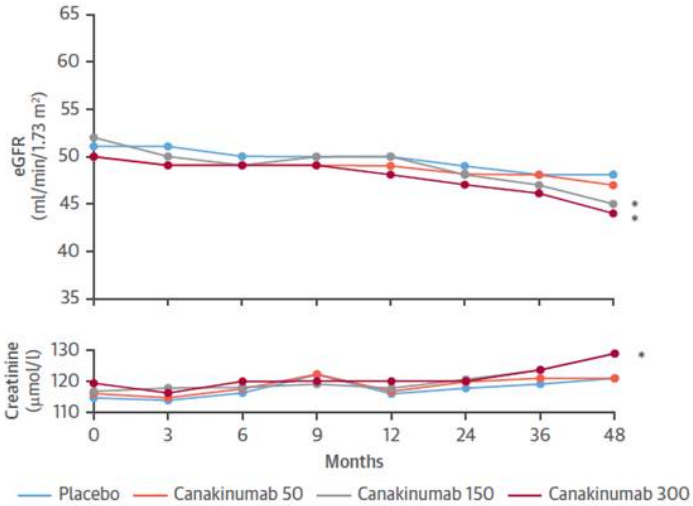
Canakinumab in CKD

Canakinumab **AN**tiinflammatory **T**hrombosis **O**utcome **S**tudy



*p < 0.05 for canakinumab 150 mg and 300 mg at 48 months for eGFR and for canakinumab 300 mg at 48 months for creatinine

Ridker PM et al. ***JACC*** 2018; 71: 2405

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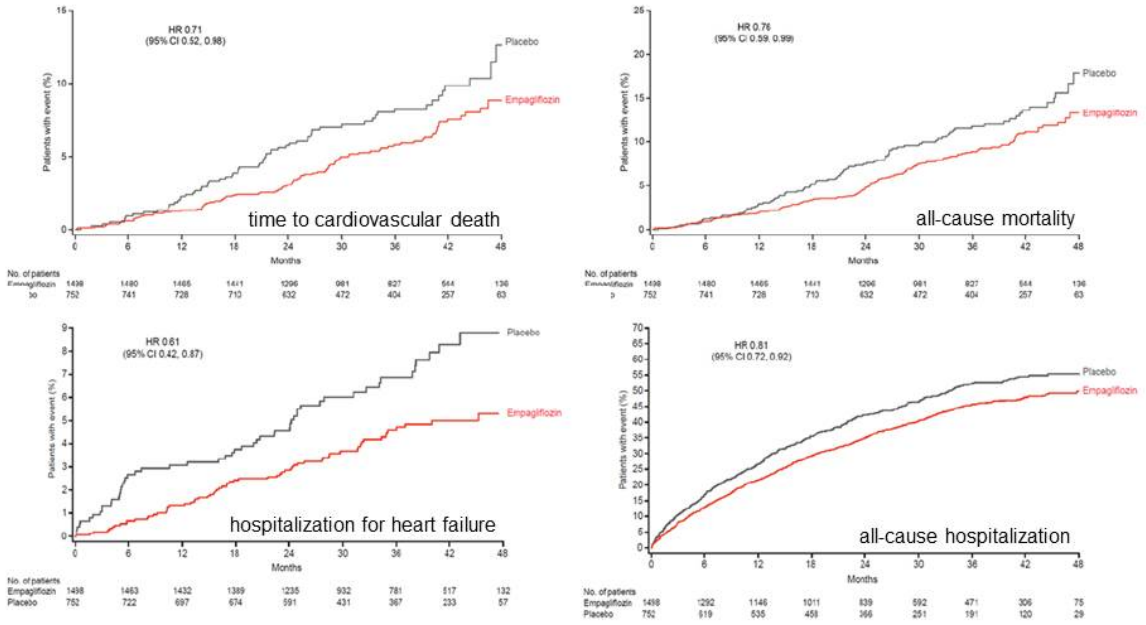
SGLT$_2$-inhibition in diabetic CKD



Wanner C et al. ***Circulation*** 2018; 137: 119

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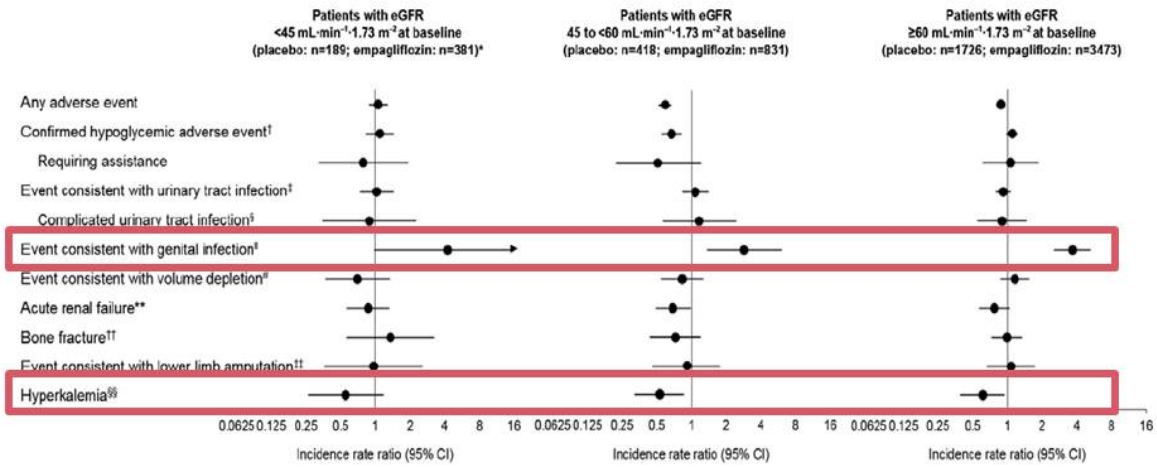
SGLT$_2$-inhibition in diabetic CKD



Wanner C et al. ***Circulation*** 2018; 137: 119

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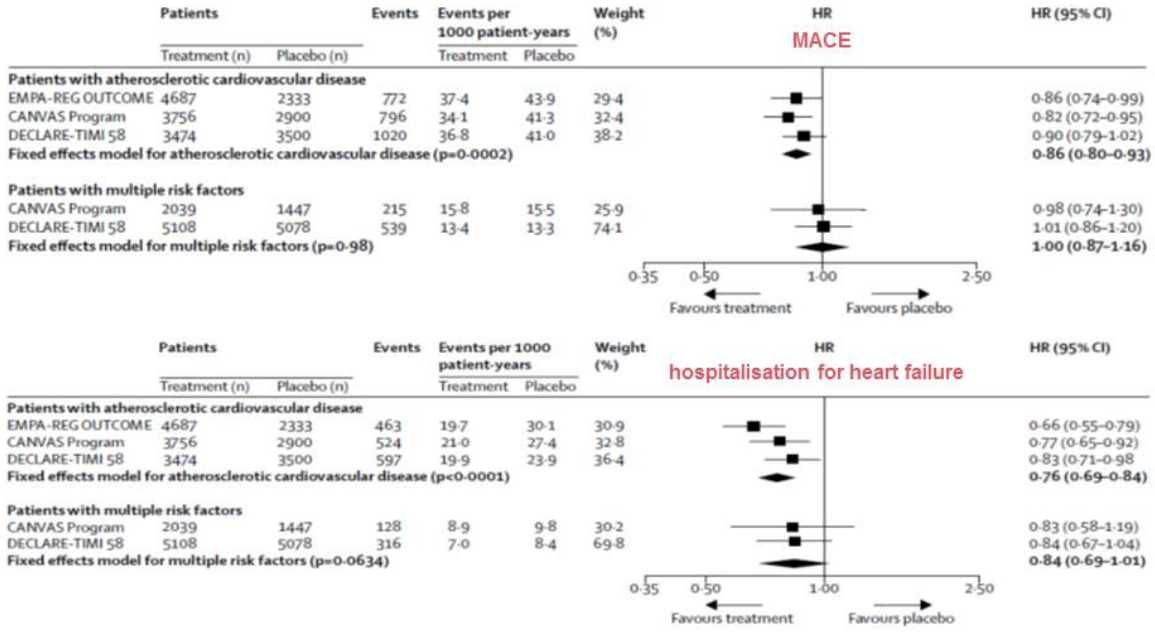
SGLT$_2$-inhibition in diabetic patients



Zelniker TA et al. ***Lancet*** 2019; 393: 31

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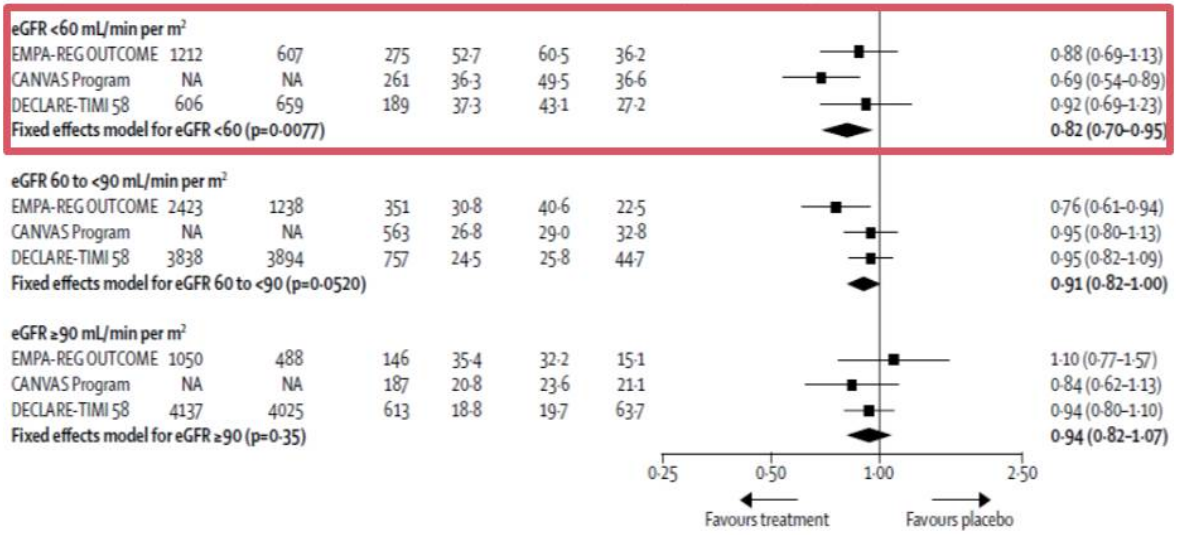
SGLT$_2$-inhibition in diabetic CKD

Major adverse cardiovascular events (**MACE**)



Zelniker TA et al. ***Lancet*** 2019; 393: 31

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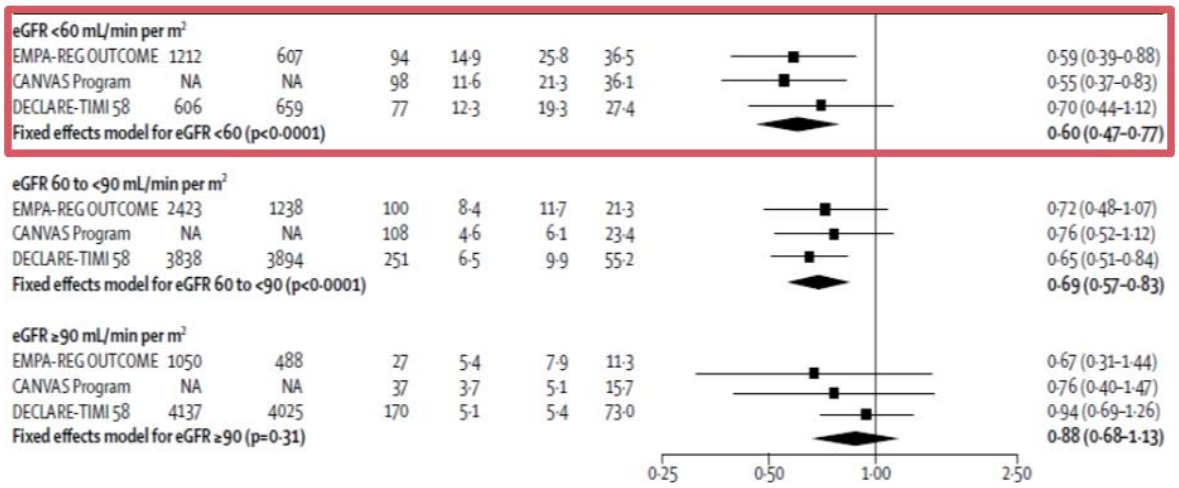
$SGLT_2$-inhibition in diabetic CKD

Hospitalisation for heart failure



Zelniker TA et al. ***Lancet*** 2019; 393: 31

Take-Home Message

- Reducing low-density cholesterol with statin-based therapy reduces CV risk in CKD patients, possibly also in patients transitioning to dialysis
- Promising pharmacological treatment targets with particular benefit on CV outcome in CKD patients may be reduction of microinflammation (inhibition of interleukin 1-beta) and $SGLT_2$-inihibition

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21. Wanner C et al. *Circulation* 2018; 137: 119
22. Zelniker TA et al. *Lancet* 2019; 393: 31

List of Abbreviations

- AF – atrial fibrillation
- CI – confidence interval
- CKD – chronic kidney disease
- CVD – cardiovascular disease
- eGFR – estimated glomerular filtration rate
- HR – hazard ratio
- MACE – major adverse cardiovascular events
- NOAC – nonvitamin K-dependent oral anticoagulant