1/
Hey #NephTwitter!
Welcome to a 🆕 #tweetorial #xtorial #skeetorial brought to you by @KIReports.
Want more, check out the blog here:

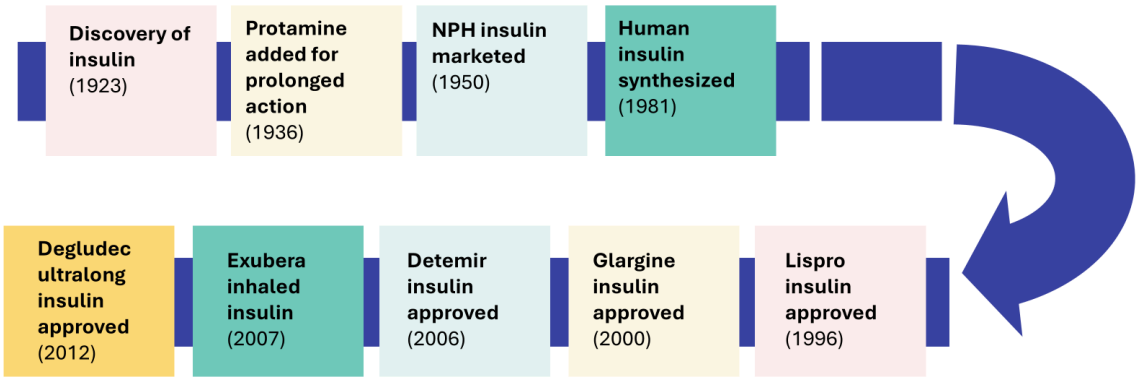
2/
Our author is @brian_rifkin (Nephrologist & T1D for 30 yrs)
Our topic: What are the trends of diabetic nephropathy (DN) in T1D patients
#MedTwitter #Nephtwitter #NephSKy

3/
There are no conflicts of interest. Please also check out #KIReportsCommunity educational #blogposts lead by @sophia_kidney at https://www.kireportscommunity.org/. FOLLOW US at @KIReports for more expert #MedEd in #kidneydisease. #FOAMed

4/
Drs Banting, Macleod and Best discovered insulin over a century ago in Toronto Canada, and won the 1923 Nobel prize in Physiology and Medicine for their discovery. #Type1Diabetes

5/

Mering and Minkowski, in 1889, had discovered the role of the pancreas in the pathogenesis of diabetes and T1D was further characterized by the autoimmune destruction of pancreatic Beta-cells leading to an absolute insulin deficiency.



6/
How does hyperglycemia lead to organ damage and DN?

1. Alterations in pH
2. Ketosis and cell starvation
3. DNA damage
4. Protein glycation

7/

Answer is D. Elevated plasma glucose levels lead to multi-organ failure. Protein glycation & formation of advanced glycation end products (AGEs), play an important role in the pathogenesis of diabetic complications like retinopathy, nephropathy, and neuropathy.

8/
The Diabetic Control of Complications Trial (DCCT) in the 1990s showed the many benefits of intensive glucose control in decreasing the incidence of diabetic retinopathy, neuropathy and nephropathy.
www.nejm.org/doi/full/10.1056/NEJM199309303291401

9/
Unfortunately even though insulin & insulin delivery for patients with T1D has seen innovation, medication breakthroughs in the treatment of DN over the last decade have not kept pace with those for T2D patients. This has led to little change in the prognosis of DN in T1D.

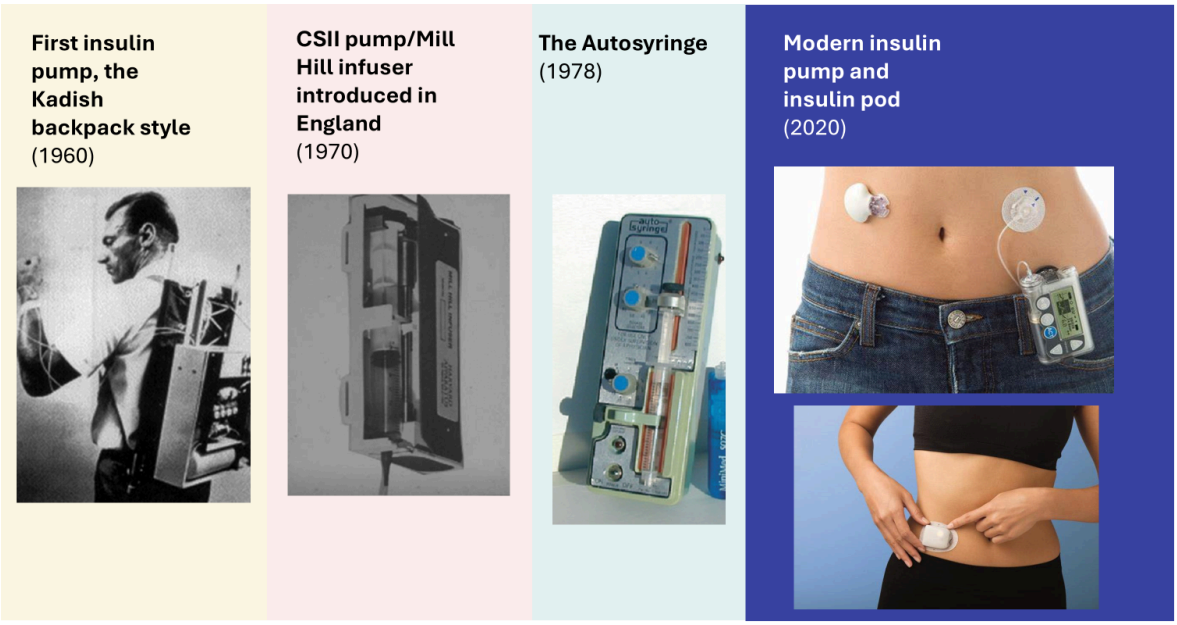
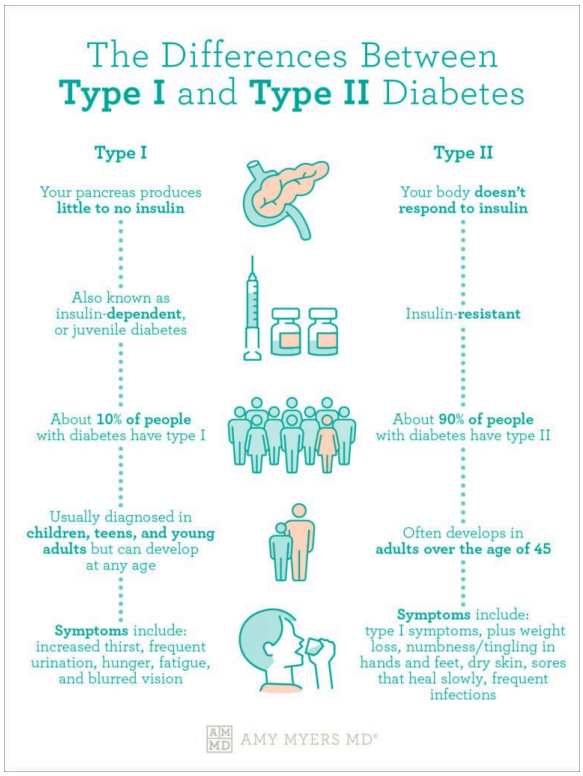
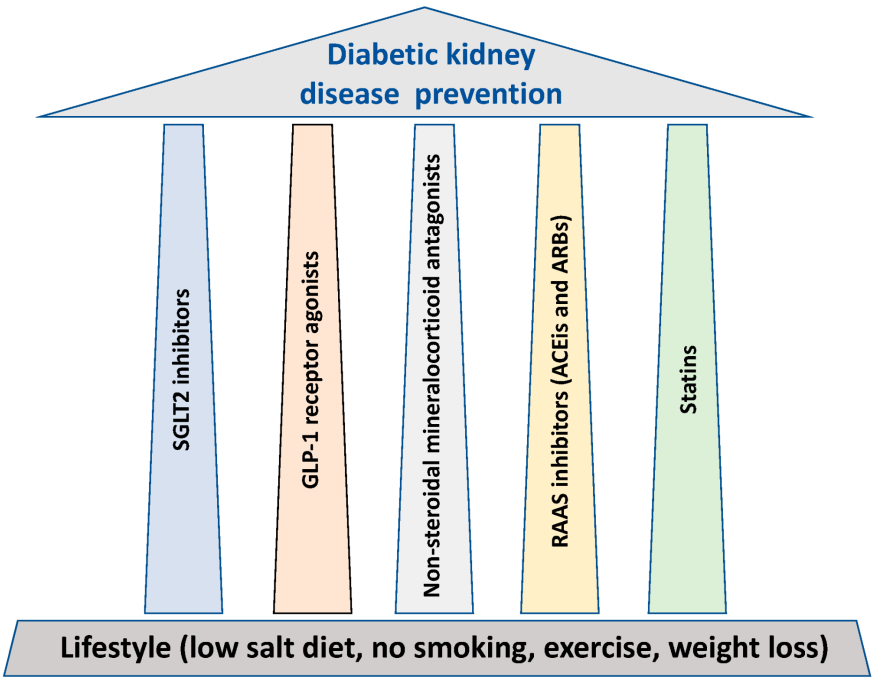


Fig 4. History of the insulin pump adapted from: Alsaleh FM, Smith FJ, Keady S, Taylor KM. Insulin pumps: from inception to the present and toward the future. J Clin Pharm Ther. 2010 Apr;35(2):127-38.

10/
People with T2D compose roughly 90% of the world's patients with diabetes. Not surprisingly, newer therapeutics for preventing diabetic nephropathy (DN) have been aimed almost exclusively at this group.



11/
Many of the pillars of DN treatment (e.g. SGLT2 inhibitors, GLP-1 RA, NS-MRAs), that have shown overwhelming benefits in patients with DN, have excluded persons with T1D from trials.



12/

At least 1 trial with sotagliflozin, an SGLT2i, in patients with T1D showed improved glycemic control but also ⬆️ risk of diabetic ketoacidosis (DKA), making their use restricted (FDA unapproved) except to the most compliant & knowledgeable patients.
https://www.nejm.org/doi/10.1056/NEJMoa1708337?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200www.ncbi.nlm.nih.gov

Table 2. Efficacy End Points.

End Point	Sotagliflozin (N=699)	Placebo (N=703)	Difference (95% CI)	P Value
	no./total no. (%)		*percentage points*	
Patients with glycated hemoglobin <7.0% and no severe hypoglycemia or diabetic ketoacidosis				
All patients	200/699 (28.6)	107/703 (15.2)	13.4 (9.0 to 17.8)	<0.001
Patients who used insulin pump	88/275 (32.0)	45/280 (16.1)	15.9 (8.6 to 23.3)	<0.001
Patients who did not use insulin pump	112/424 (26.4)	62/423 (14.7)	11.8 (6.1 to 17.4)	<0.001
Patients with glycated hemoglobin ≥7.0% and ≥1 episode of severe hypoglycemia*	16/699 (2.3)	13/703 (1.8)	0.4 (−1.0 to 1.9)	0.56
Patients with glycated hemoglobin ≥7.0% and ≥1 episode of diabetic ketoacidosis*	18/699 (2.6)	4/703 (0.6)	2.0 (0.7 to 3.3)	0.003

* These results are from a post hoc analysis that was performed with the use of asymptotic methods to summarize the differences in binomial proportions without stratification according to randomization factors. The small number of events suggested that stratified tests would not be sensible. This category included patients who had an event of interest and a glycated hemoglobin value of 7.0% or higher at week 24 or missing data at the 24-week assessment.

13/

What percentage of T1D are prescribed (unapproved) GPL-1RA or SGLT2i medications?

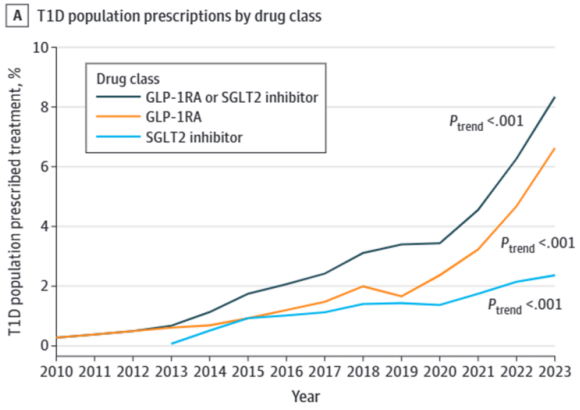
1. 0%
2. 3%
3. 9%
4. 20%

14/

Answer is C. 945,000 T1D pts were identified in an EHR review of US pts. 6.6% were prescribed GLP1-RAs & 2.4% SGLT2i in 2023, a significant ⬆️ from the prior decade, but still significantly ⬇️ than T2D. There is a definite need for therapeutics for DN in T1D that is yet unmet.

www.jamanetwork.com/journals/jama/article-abstract/2825312

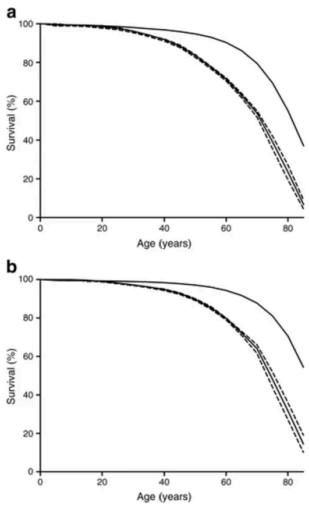
Figure. Trends in Drugs Prescribed Among People With Type 1 Diabetes (T1D), 2010-2023



15/

The presence of T1D has been shown to decrease the life expectancy of a patient by 10-12 years on average, however, there does appear to be an improving trend over the last several decades.

Life Expectancy Type 1 Diabetes in Australia 1997-2010



Percentage survival by age for (**a**) men and (**b**) women with type 1 diabetes compared with the general population during 1997–2010. Solid line, general population; solid line with a dotted line on each side, type 1 diabetic patients, the dotted lines represent the 95% CIs

16/
Poulsen et al's publication in @KIReports looked at the experience of a registry based cohort of T1D and DN in a single center in Copenhagen, Denmark (2000-2020).
www.kireports.org/article/S2468-0249(24)01938-7/fulltext

17/
591 patients were identified with new onset DN.
💉The median age of diagnosis of T1D was 23 yrs, with the median onset of DN of 53 yrs.
🚨Glucose control was suboptimal, however, with a median HbA1C of 73 mmol/mol (8.8%).
👍Impressively, 73% of patients received RASi.

18/
Not surprisingly, those with worse laboratory findings, requiring more medications to achieve specified therapeutic goals, had worse outcomes. A subset of 283 patients underwent mGFR studies. There was no apparent improvement in mGFR trajectories during the study period.

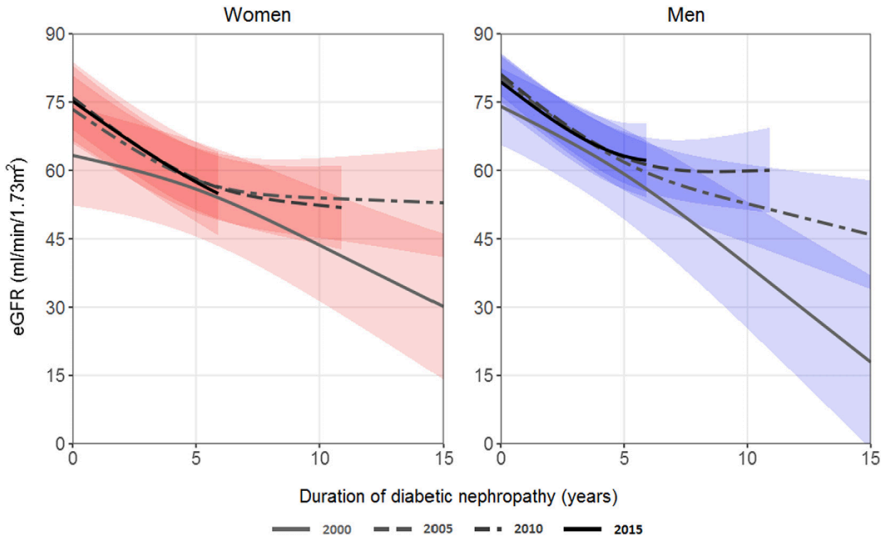


Figure 1. Development in eGFR trajectories after DN onset between 2000 and 2020. Estimated eGFR trajectories for women (red) and men (blue) with DN onset at age of 53 years in 2000 (solid grey line), 2005 (dashed line), 2010 (dashed dotted line) and 2015 (black solid line). The depicted trajectories are from the adjusted model with the following median baseline values: albuminuria (454 mg/g or mg/24 h); $HbA1_c$ (75 mmol/mol); hemoglobin (8.2 mmol/l); LDL-cholesterol (2.5 mmol/l); triglyceride (1.2 mmol/l); systolic blood pressure (142 mm Hg); BMI (25 kg /m^2); and exposure to RAS inhibitor, antihypertensive, and lipid-lowering medication. DN, diabetic nephropathy; eGFR, estimated glomerular filtration rate in ml/min per 1.73 m^2.

19/

The crude mortality rate per 100-person years was 2.4 for DN, 7.2 for kidney failure and 18.7 for CVD with kidney failure. The risk of developing kidney failure was increased 71% in T1D with a history of CVD.

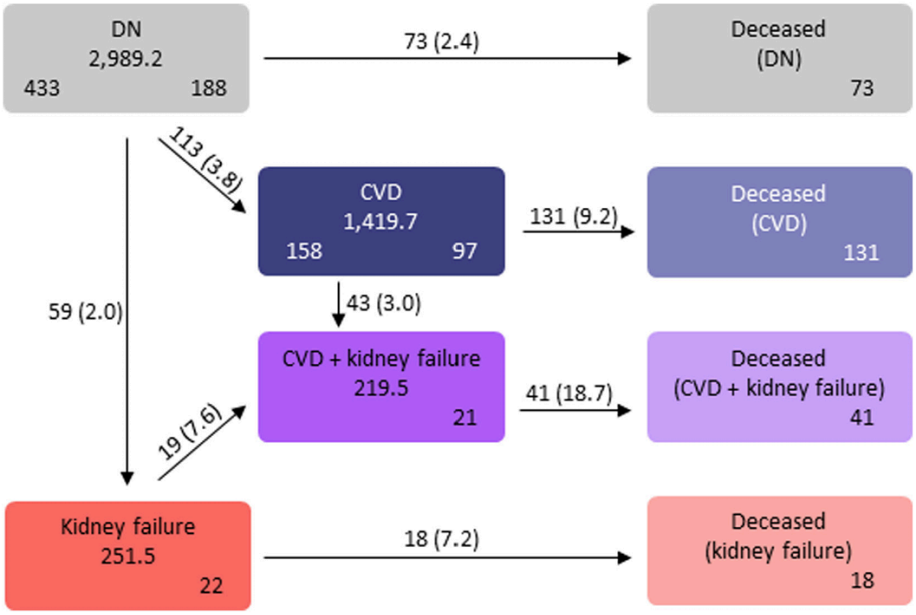


Figure 3. Multistate model. Disease states and transitions between states. Box numbers indicate the following: centered, person-years spent in this state; bottom-left, number of persons starting follow-up in this state; bottom-right, number of persons ending follow-up in this state. Arrow numbers indicate transitions (rate per 100 person-years). CVD, cardiovascular disease; DN, diabetic nephropathy.

20/
The risk of developing CVD, kidney disease, and death were high and negatively impacted by male sex, the presence of cardiovascular and poor risk factor control (lipid, A1C, BP, BMI, ⬆️med usage).

21/
The avg ⬇️ in eGFR was approx 4 ml/min/yr in the preceding two decades (1980-2000). The current study found an average decline of 3 ml/min/yr in women & 3.2 ml/min/yr in men (2000-2015). Based on this data, the overall prognosis for DN in T1D does not appear to have improved.

22/
Unfortunately, patients with T1D have been seemingly left in the dust, unable to partake in many of these treatments. There should be a certain urgency to address the needs of T1D patients as vigorously as T2D patients, until such a day as there is a cure.

23/ This has been another @KIReports tweetorial by @brian_rifkin. Please share this #tweetorial with your followers and friends! Thanks to *** for great feedback! #NephTwitter #NephSky