

# Real-world data: who gets which anti-diabetic drug in the UK and why?

## Do kidneys matter?

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 @roxytonin

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Are SGLT2is as effective in routine care as  
they are in clinical trials?

# THE LANCET

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## Real-world studies no substitute for RCTs in establishing efficacy

[Hertzel C Gerstein](#)  • [John McMurray](#) • [Rury R Holman](#)

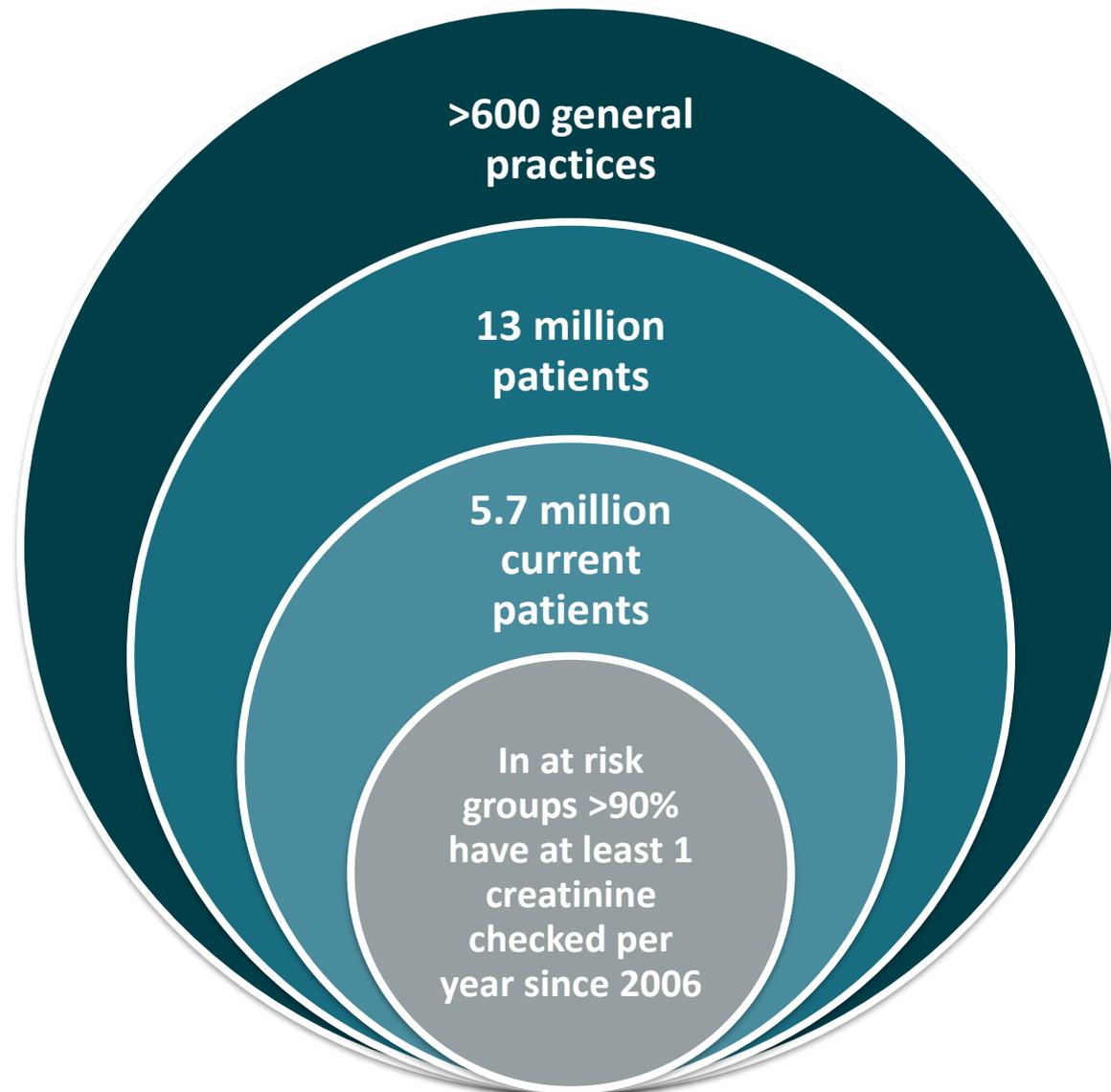
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Check for updates

# 'Real world data'





# NICE guidance for treatment of type II DM

## ADULT WITH TYPE 2 DIABETES WHO CAN TAKE METFORMIN

### If HbA1c rises to 48 mmol/mol (6.5%) on lifestyle interventions:

- Offer standard-release metformin
- Support the person to aim for an HbA1c level of 48 mmol/mol (6.5%)

If standard-release metformin is not tolerated, consider a trial of modified-release metformin

### FIRST INTENSIFICATION

#### If HbA1c rises to 58 mmol/mol (7.5%):

- Consider dual therapy with:
  - metformin and a DPP-4i
  - metformin and pioglitazone<sup>a</sup>
  - metformin and an SU
  - metformin and an SGLT-2<sup>b</sup>
- Support the person to aim for an HbA1c level of 53 mmol/mol (7.0%)

If triple therapy is not effective, not tolerated or contraindicated, consider combination therapy with metformin, an SU and a GLP-1 mimetic<sup>c</sup> for adults with type 2 diabetes who:

- have a BMI of 35 kg/m<sup>2</sup> or higher (adjust accordingly for people from black, Asian and other minority ethnic groups) and specific psychological or other medical problems associated with obesity or
- have a BMI lower than 35 kg/m<sup>2</sup>, and for whom insulin therapy would have significant occupational implications, or weight loss would benefit other significant obesity-related comorbidities

### SECOND INTENSIFICATION

#### If HbA1c rises to 58 mmol/mol (7.5%):

- Consider:
  - triple therapy with:
    - o metformin, a DPP-4i and an SU
    - o metformin, pioglitazone<sup>a</sup> and an SU
    - o metformin, pioglitazone<sup>a</sup> or an SU, and an SGLT-2<sup>b</sup>
  - insulin-based treatment
- Support the person to aim for an HbA1c level of 53 mmol/mol (7.0%)

# NICE guidance for treatment of type II DM

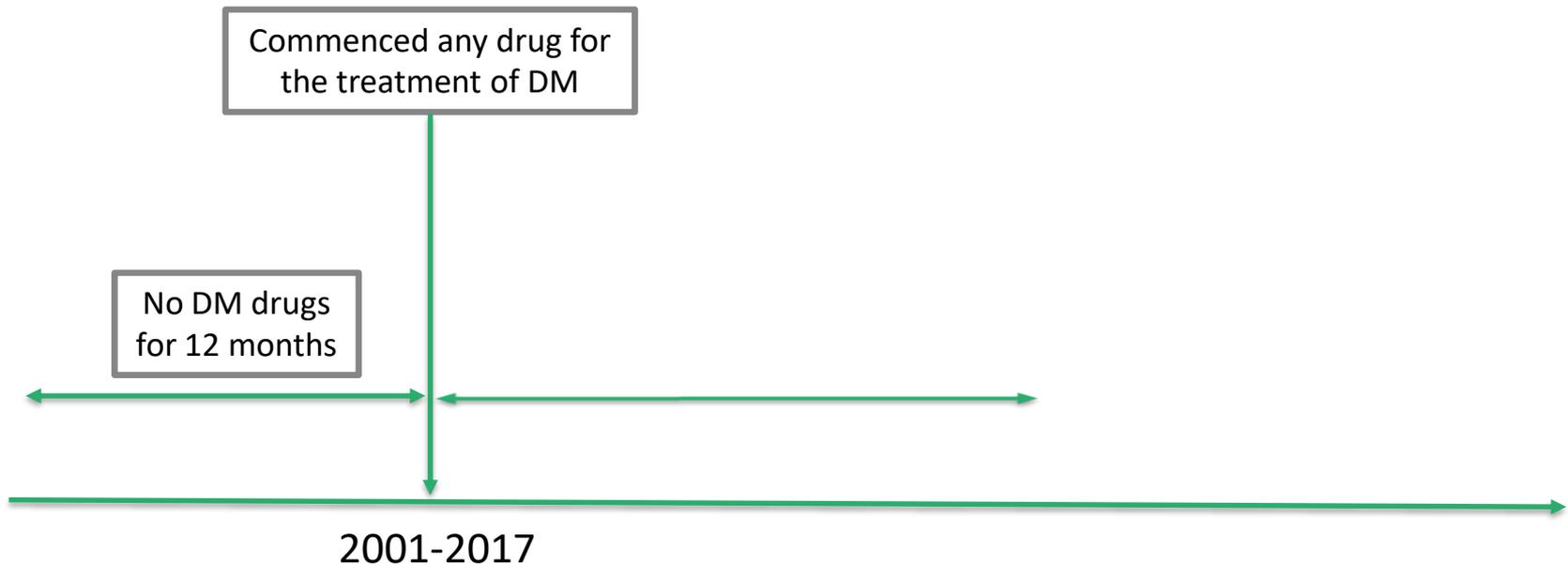
## ADULT WITH TYPE 2 DIABETES WHO CAN TAKE METFORMIN

**If HbA1c rises to 48 mmol/mol (6.5%) on lifestyle interventions:**

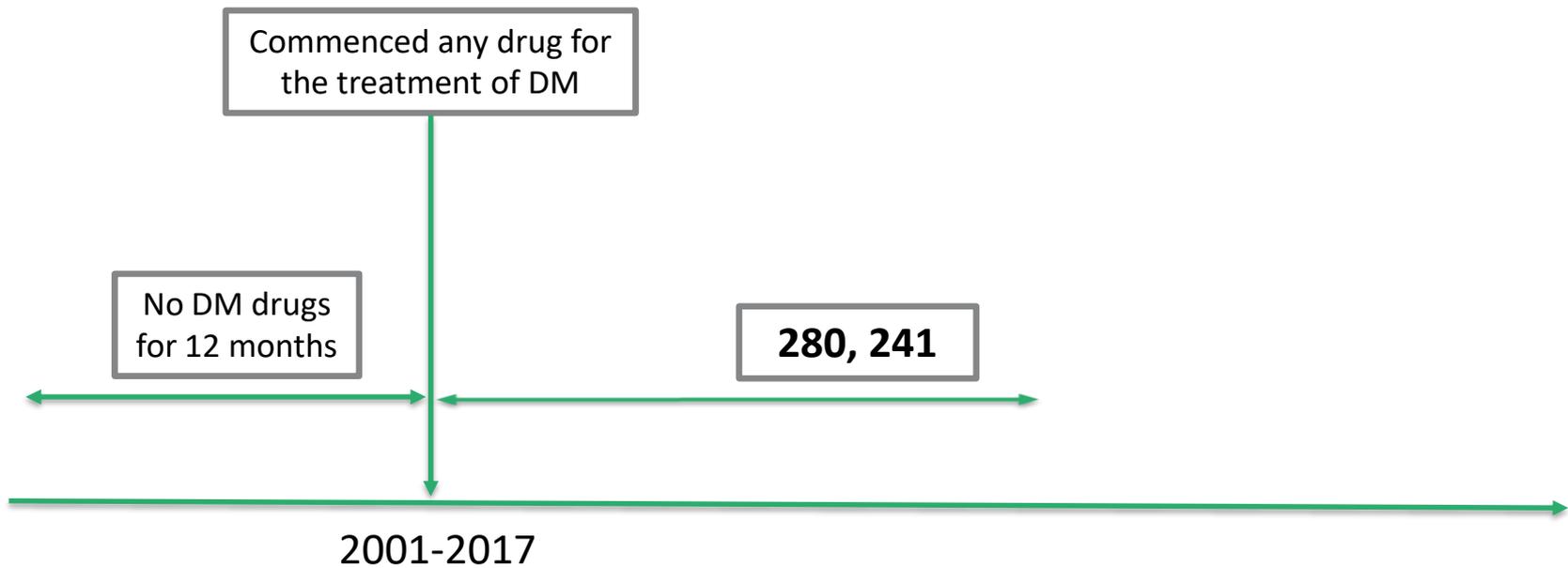
- Offer standard-release metformin
- Support the person to aim for an HbA1c level of 48 mmol/mol (6.5%)

# Changing use of antidiabetic drugs in the UK: trends in prescribing 2000–2017

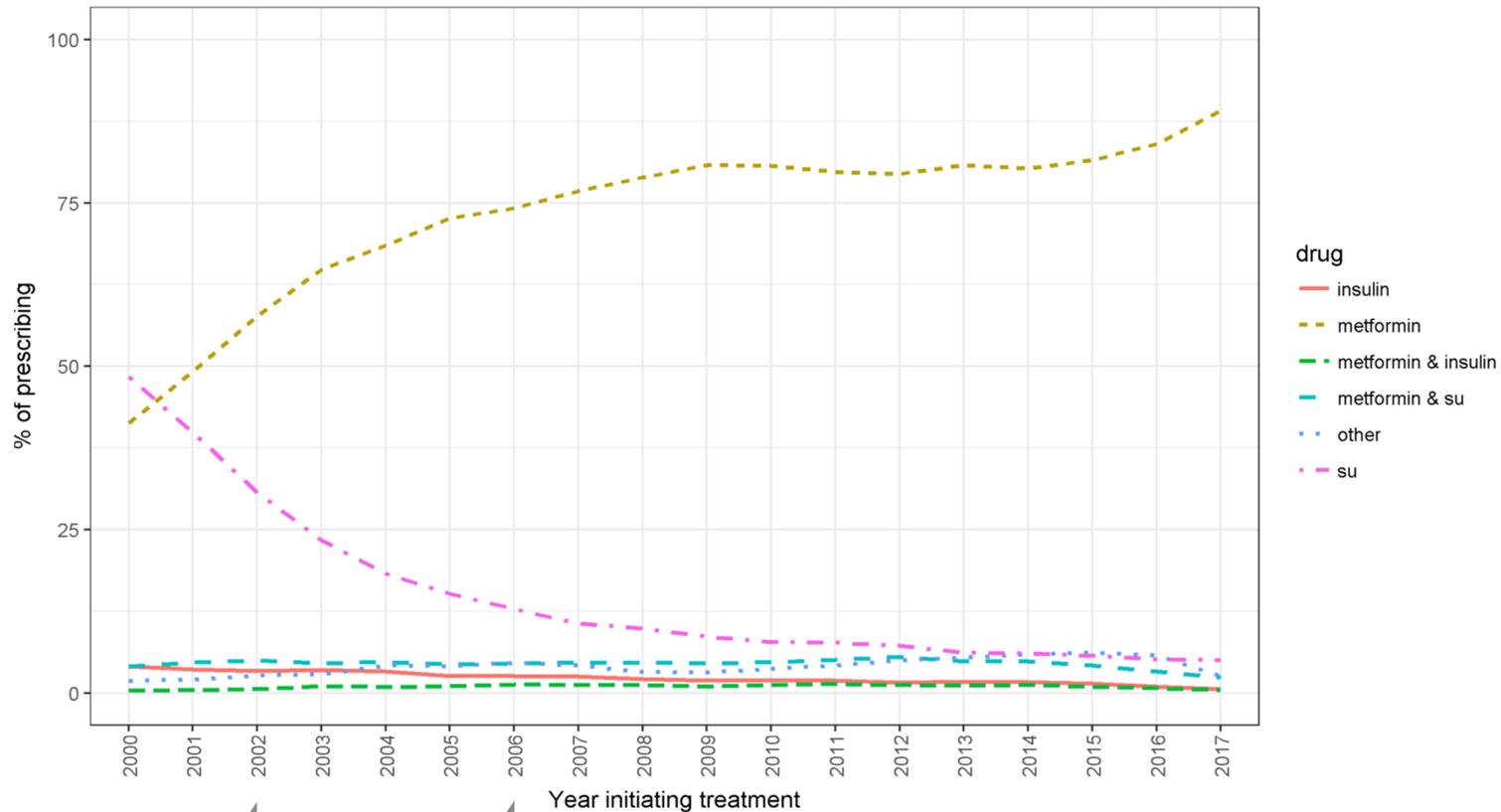
# Identification of the drug initiation cohort



# Identification of the drug initiation cohort



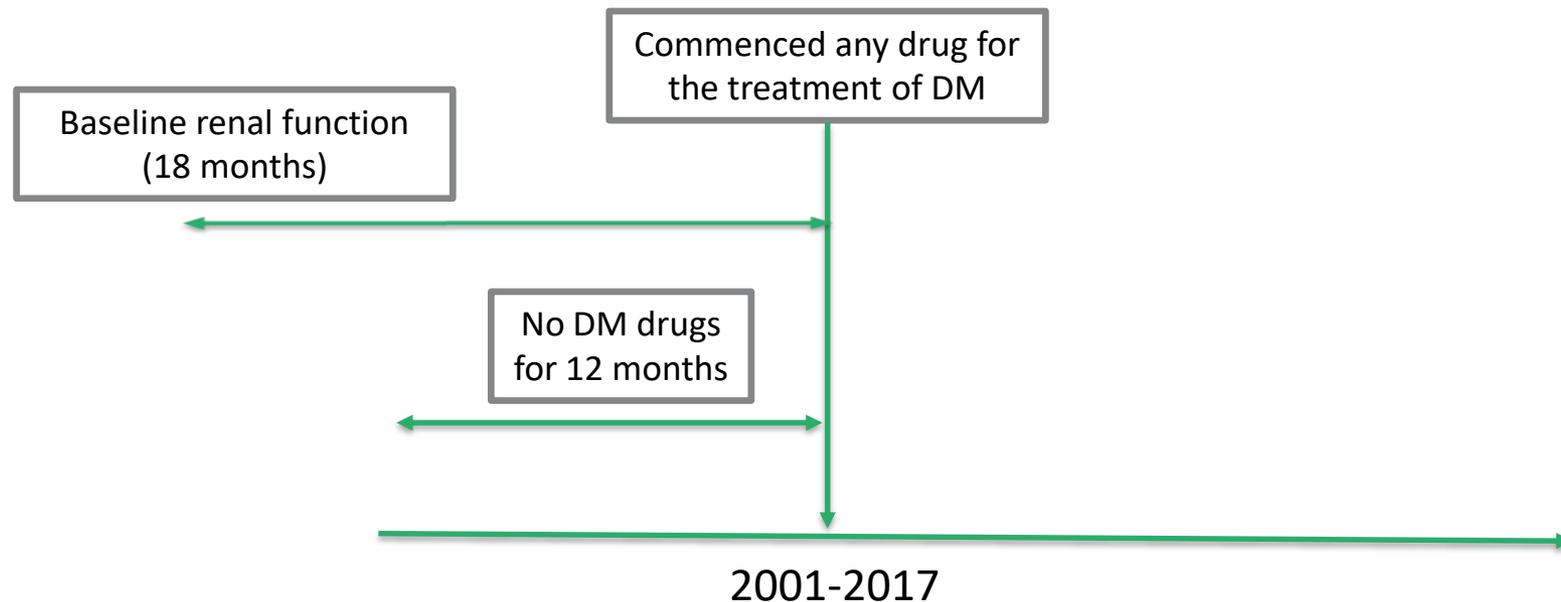
# Drug prescribing at drug initiation for T2DM 2000–2017



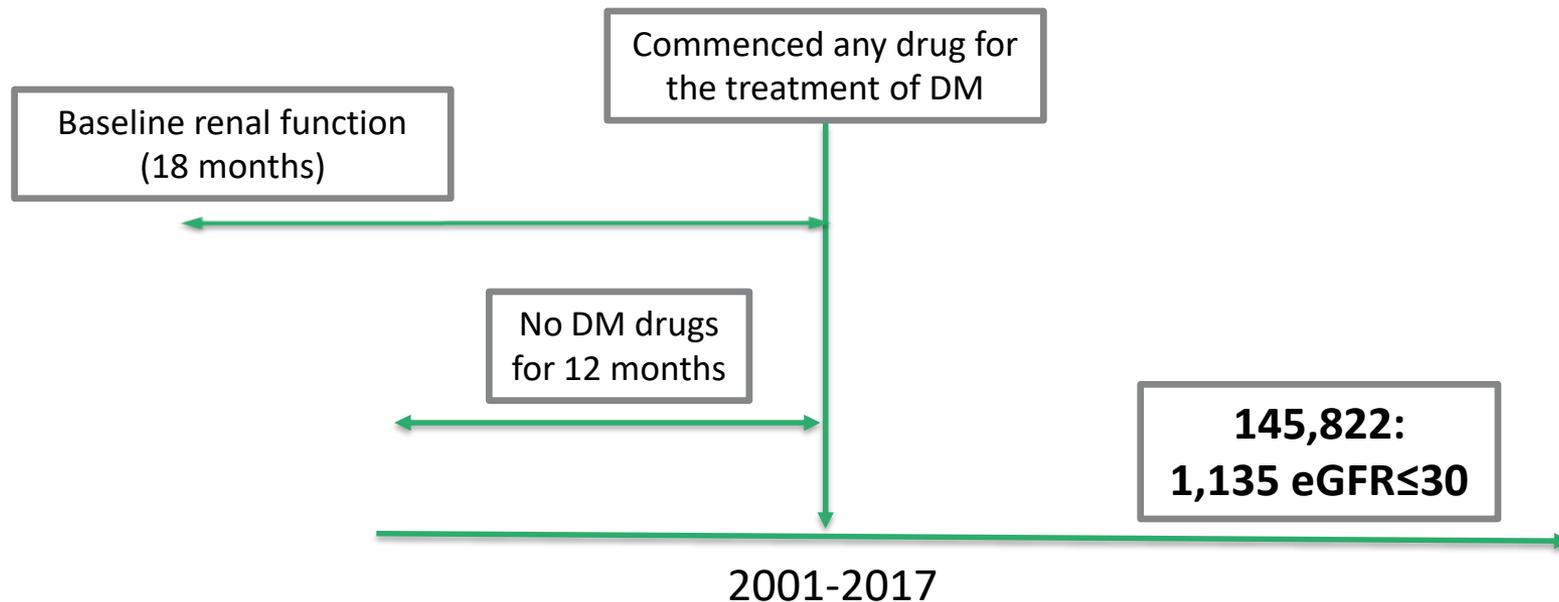
2002: First national guidance for treatment of T2DM, first line metformin.  
Stop metformin if serum creatinine >130µmol/l

2006: First CKD register for QOF  
2006: National automatic reporting of eGFR in pathology report  
2006: CG66: Stop metformin at serum creatinine >150 µmol/l or eGFR <30 ml/min/1.73m<sup>2</sup>

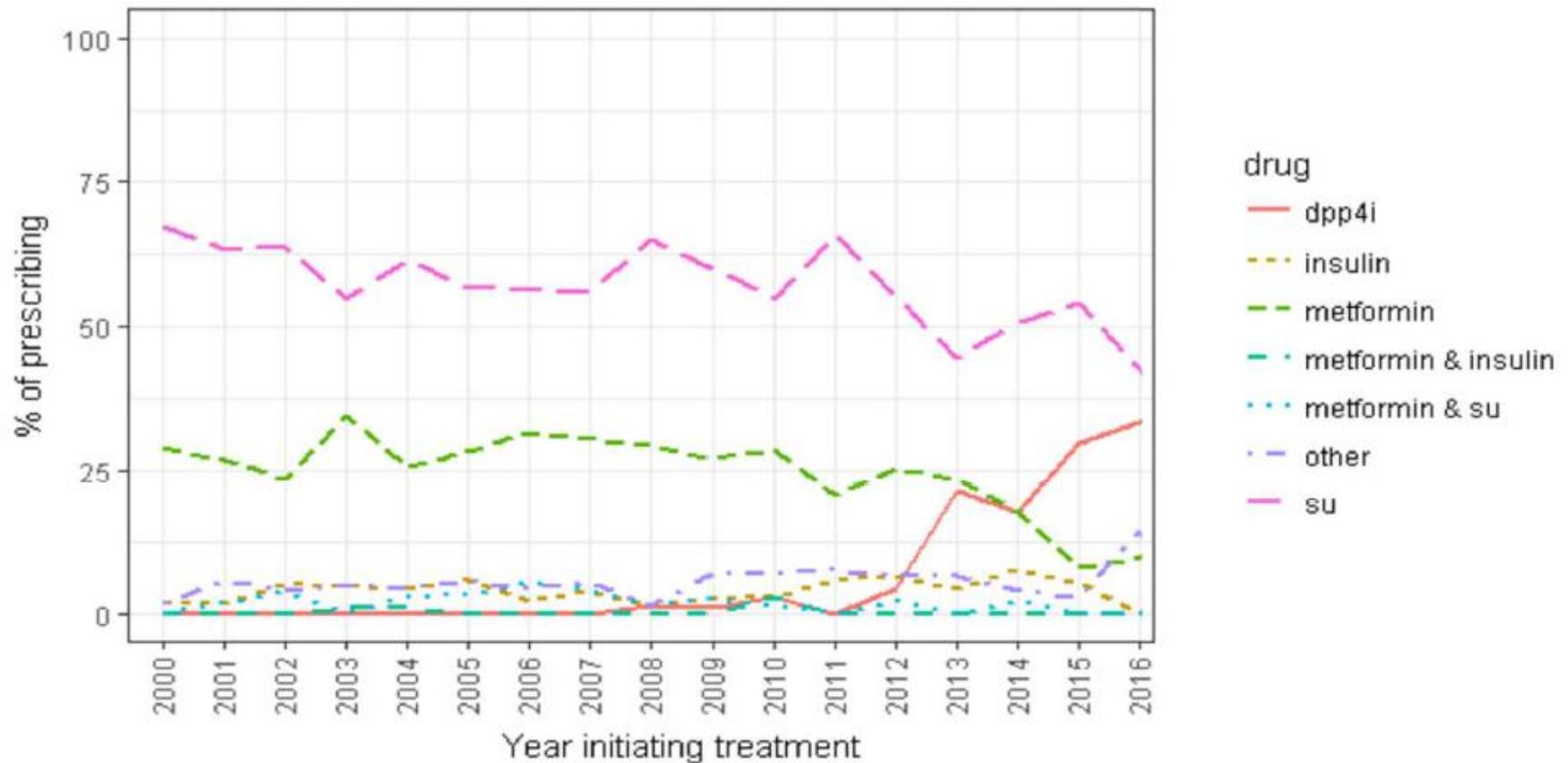
# Identification of the drug initiation cohort: people with impaired renal function



# Identification of the drug initiation cohort: people with impaired renal function



# Drug prescribing at T2DM drug initiation: people with $eGFR < 30 \text{mls/min/1.73m}^2$



# NICE guidance for treatment of type II DM

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**If HbA1c rises to 48 mmol/mol (6.5%) on lifestyle interventions:**

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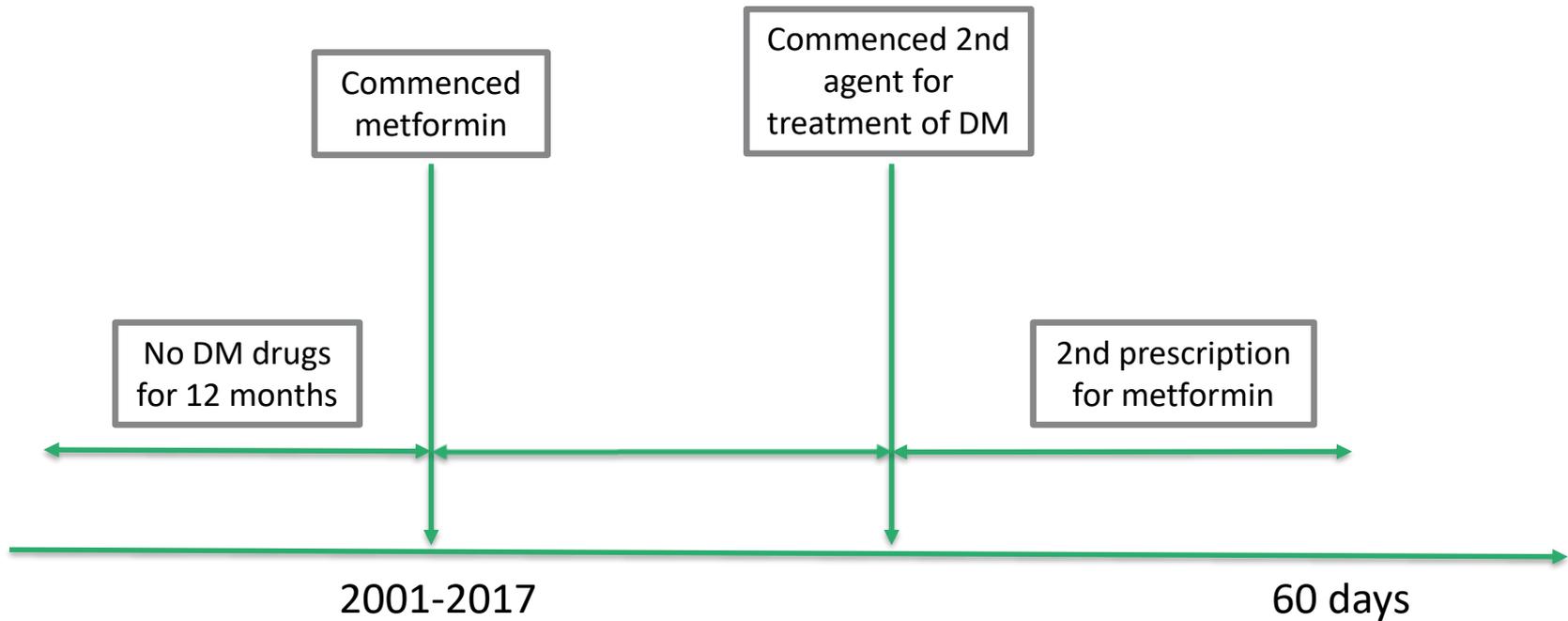


### FIRST INTENSIFICATION

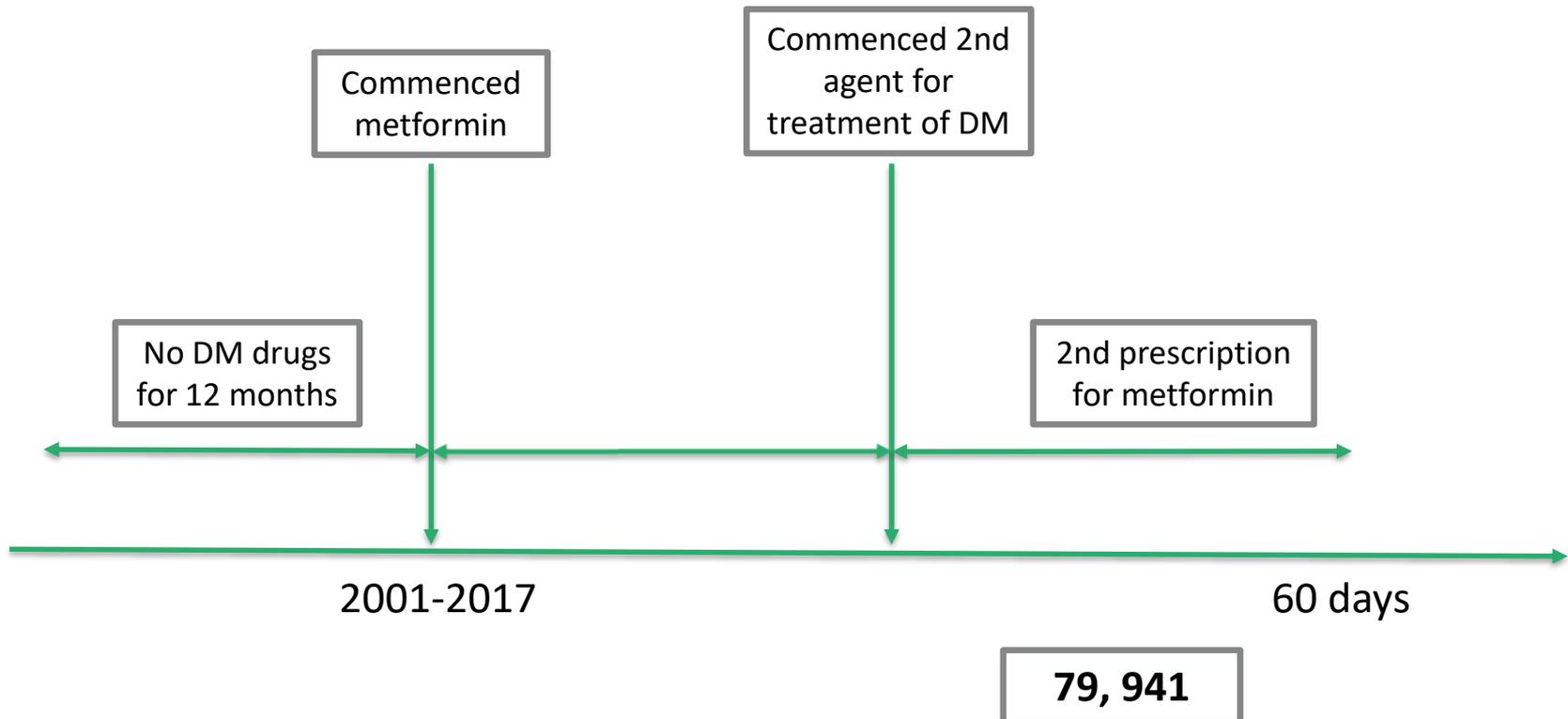
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  - *metformin and an SGLT-2<sup>b</sup>*
- Support the person to aim for an HbA1c level of 53 mmol/mol (7.0%)

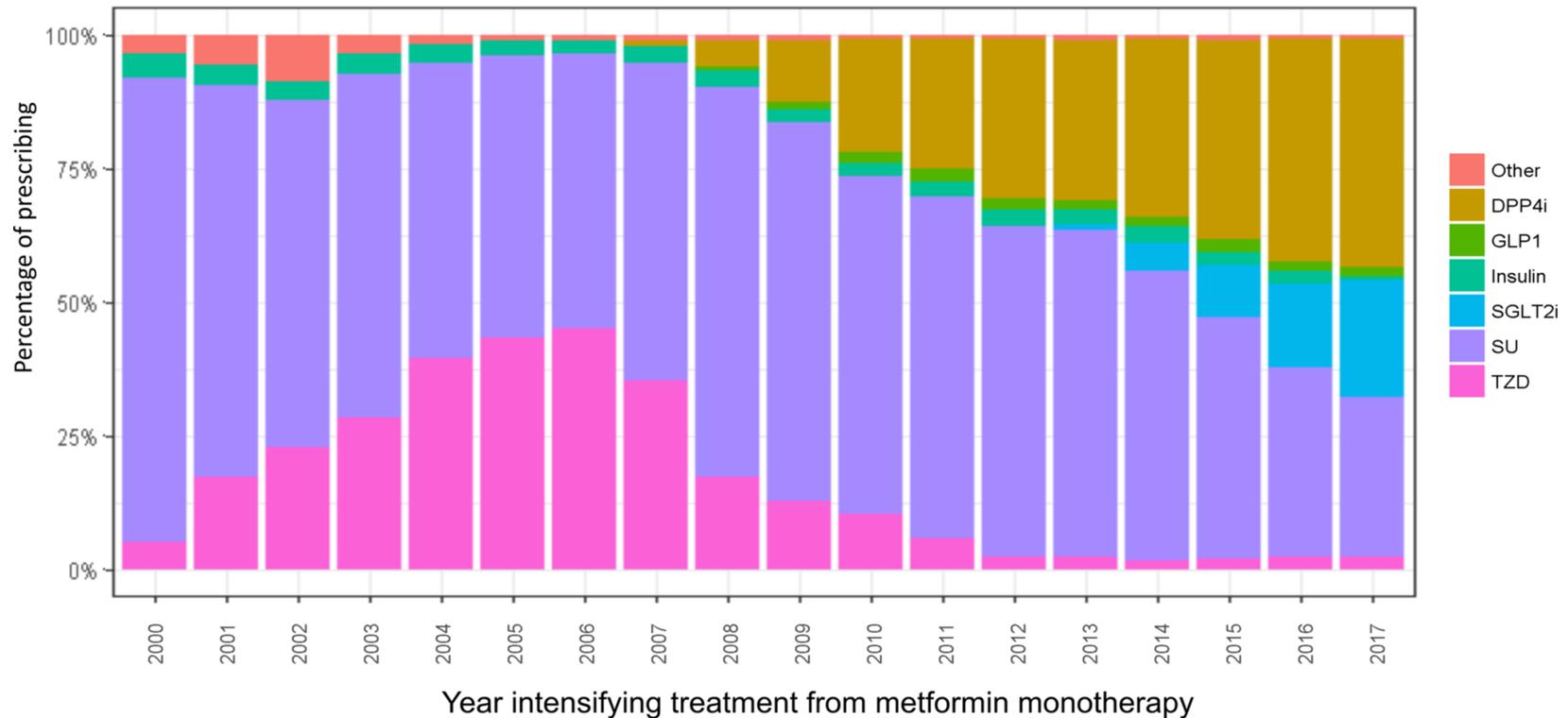
# Identification of the drug intensification cohort



# Identification of the drug intensification cohort



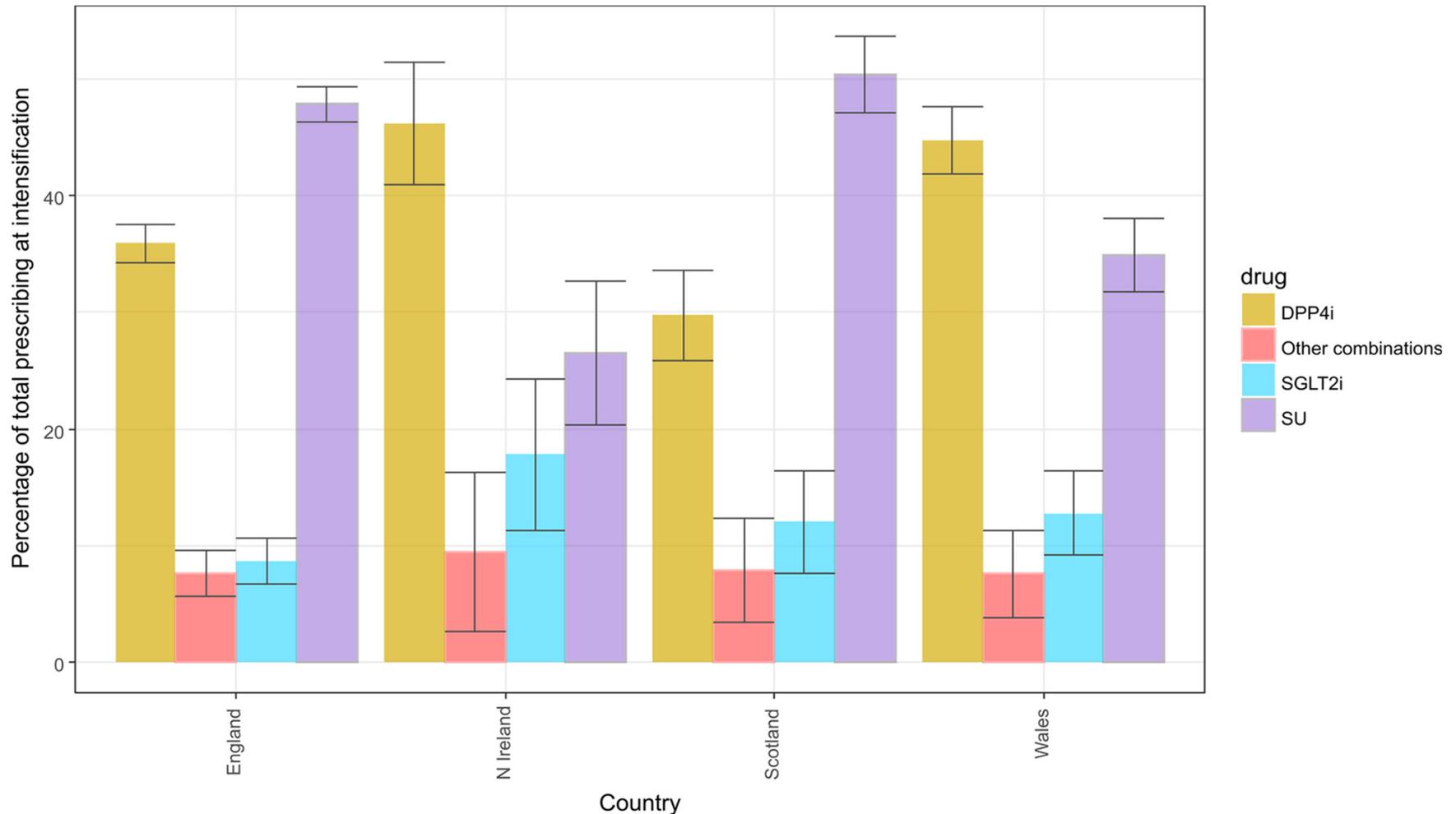
# First-stage intensification prescribing as a percentage of total prescribing 2000–2017



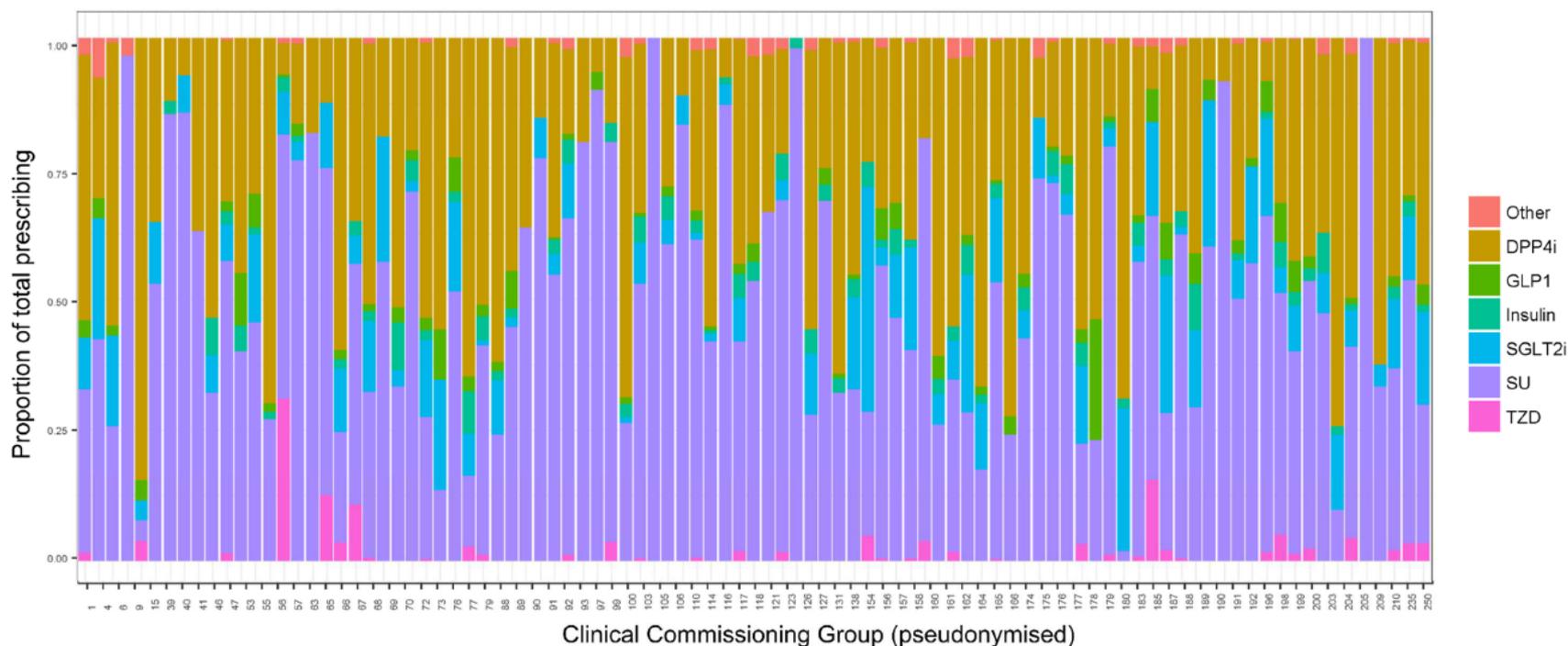
**Notable regulatory events**

- 2012: EU approval Dapagliflozin (SGLT2i)
- 2011: EU review of Pioglitazone (TZD)
- 2010: EU suspension of Rosiglitazone (TZD) approval
- 2009: Systematic review indicating increased risk of MI with Rosiglitazone
- 2007: EU approval for Sitagliptin and then Vildagliptin (DPP4i)

# Proportions of patients prescribed SGLT2i, DPP4i, SU and other drugs at first-stage intensification by region, 2014–2017



# Patterns of prescribing at the first stage of drug intensification across CCGs, 2014-2017



# Summary

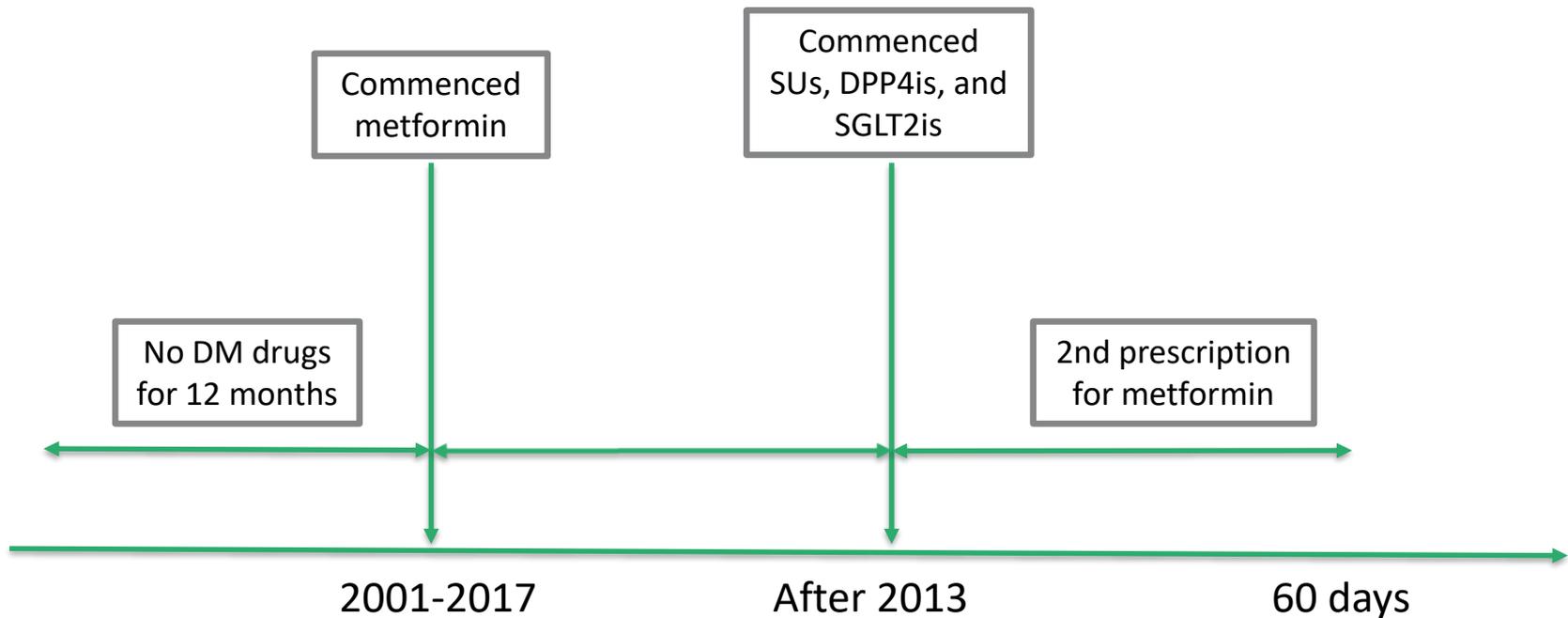
There is marked variation in prescribing:

- Over time
- By region
- By CCG

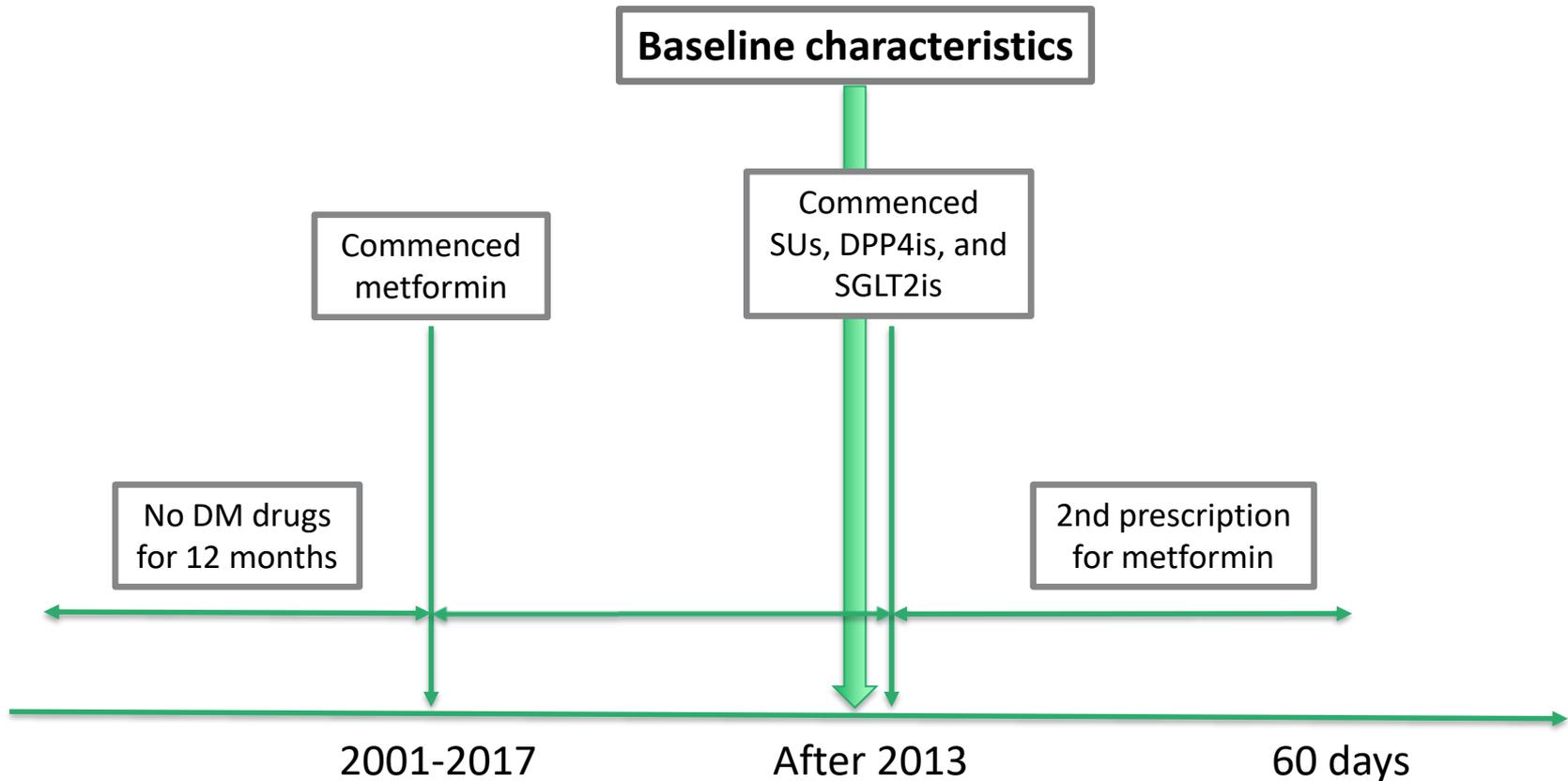
What individual patient factors influence prescribing?

Factors associated with choice of  
intensification treatment for type 2 diabetes  
after metformin monotherapy:  
a cohort study in UK primary care

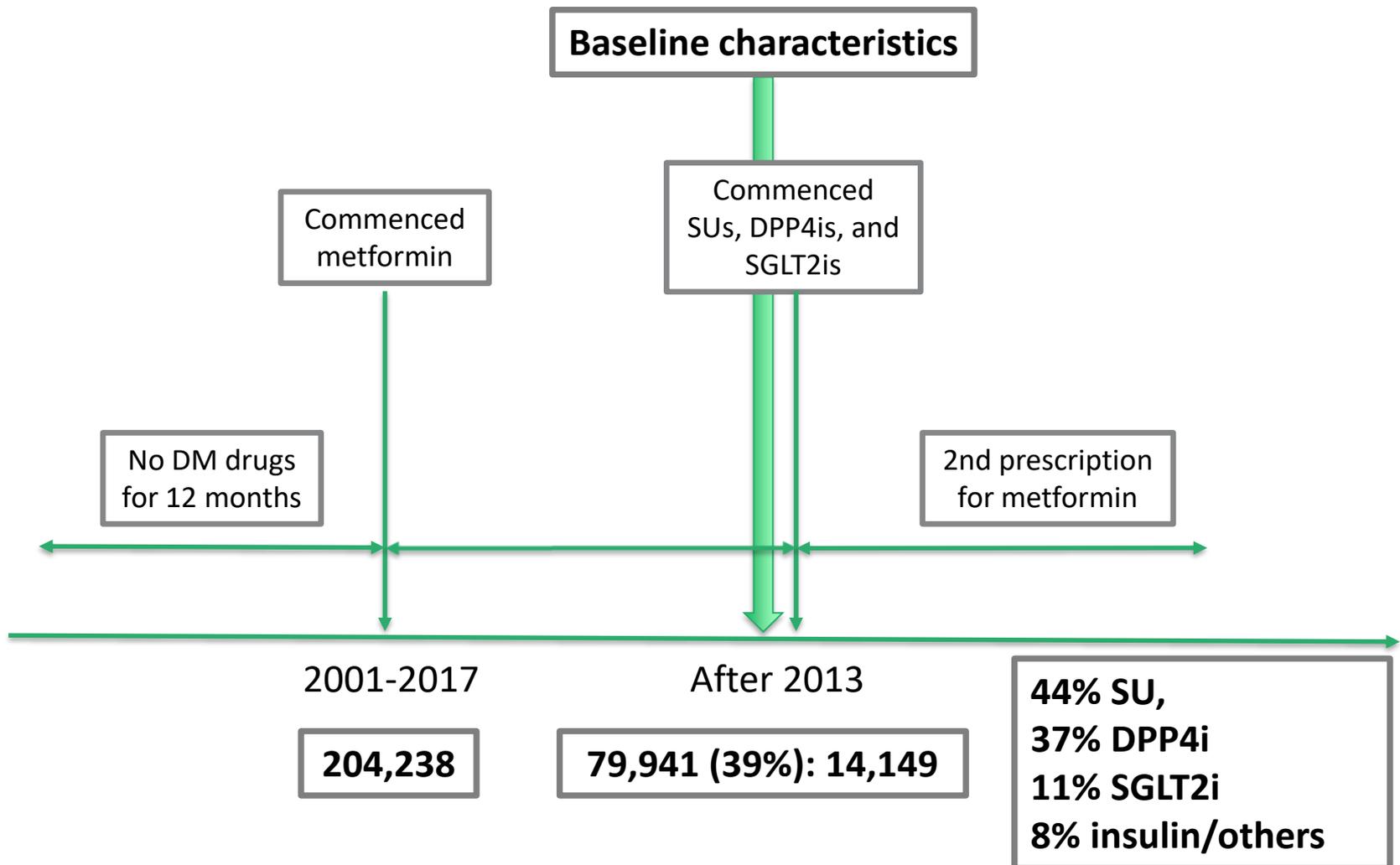
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Baseline characteristics

Commenced  
SUs, DPP4is, and  
SGLT2is, SAK 10r

We used multinomial logistic regression modelling:  
The OR for the explanatory variables shows the association  
between each variable and each drug class at first-stage  
intensification compared with SU

No DM drugs  
for 12 months

2nd prescription  
for metformin

2001-2017

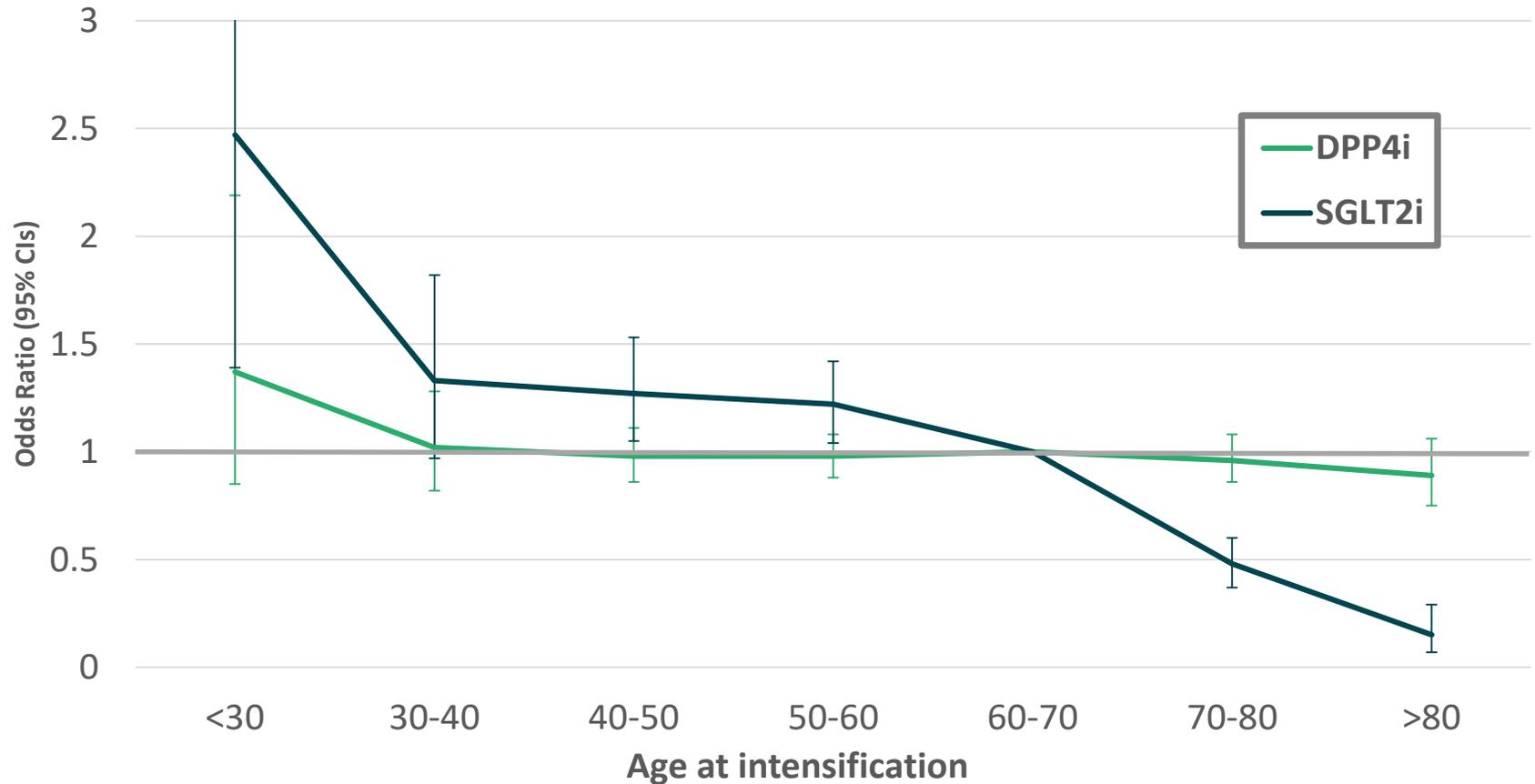
After 2013

60 days

# Factors associated with choice of intensification treatment for type 2 diabetes after metformin monotherapy: a cohort study in UK primary care

	DPP4i	SGLT2i
Age	☹️	☹️
Female sex	☹️	
HbA1c: ≤53		
HbA1c: 53-75	😊	
HbA1c: >75	☹️	☹️
Low eGFR		☹️
Time taking metformin	😊	😊
Cardiovascular disease		
Retinopathy		
BMI	😊	😊😊😊
Current Smoking		☹️
Ethnicity: South Asian	☹️	☹️
Ethnicity: Black	☹️	☹️

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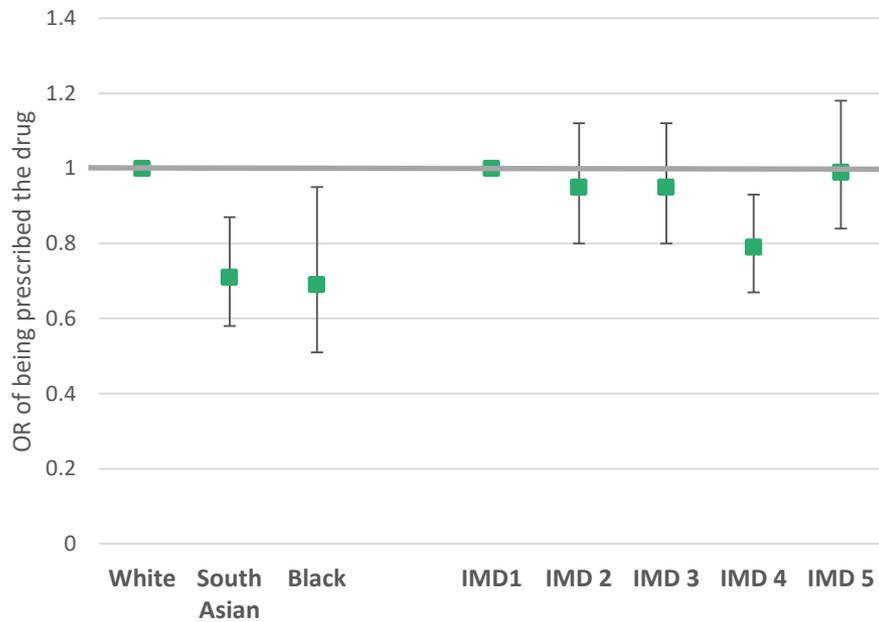


# Factors associated with choice of intensification treatment for type 2 diabetes after metformin monotherapy: a cohort study in UK primary care

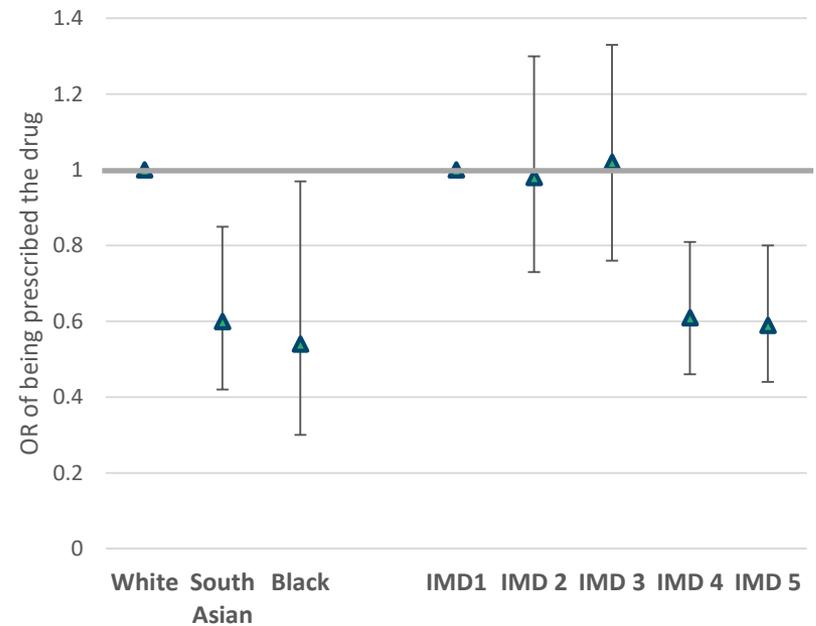
	DPP4i	SGLT2i
Age	☹️	☹️
Female sex	☹️	
HbA1c: ≤53		
HbA1c: 53-75	😊	
HbA1c: >75	☹️	☹️
Low eGFR		☹️
Time taking metformin	😊	😊
Cardiovascular disease		
Retinopathy		
BMI	😊	😊😊😊
Current Smoking		☹️
Ethnicity: South Asian	☹️	☹️
Ethnicity: Black	☹️	☹️

# Factors associated with choice of intensification treatment for type 2 diabetes after metformin monotherapy: a cohort study in UK primary care

## DPP4 inhibitors



## SGLT2 inhibitors



# Summary

Some anticipated clinical factors are associated with drug choice:

- Renal function
- BMI
- Poor glycaemic control

But non-clinical factors are also *independently* associated with prescribing

- Sex
- Age
- Ethnicity
- Socioeconomic status
- Smoking

Some anticipated clinical factors are associated with drug choice:

- Renal function
- BMI
- Poor glycaemic control

But non-clinical factors are also *independently* associated with prescribing

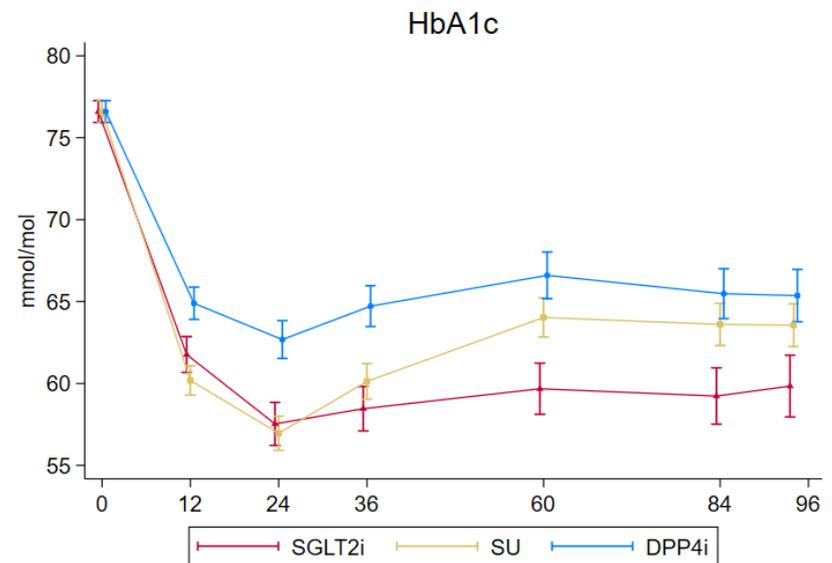
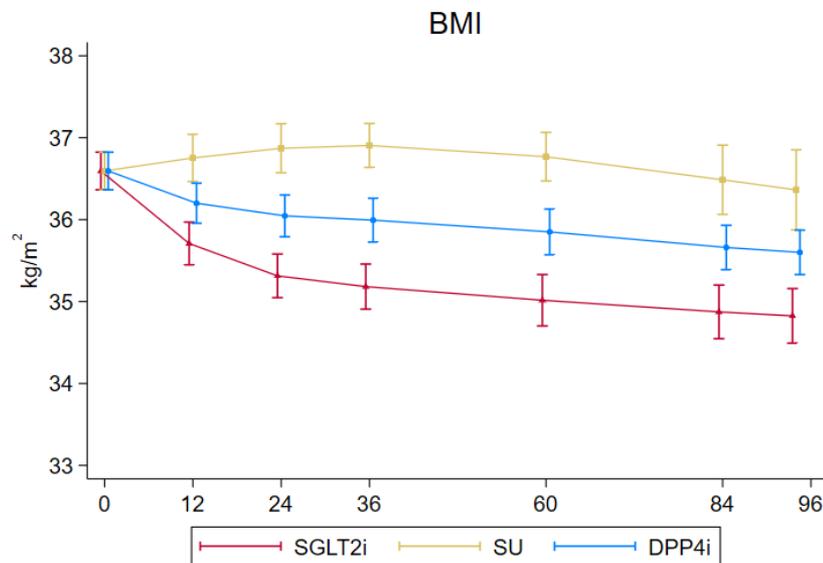
- Sex
- Age
- Ethnicity
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**What does this mean for real world data about comparative efficacy of newer anti-diabetic drugs?**

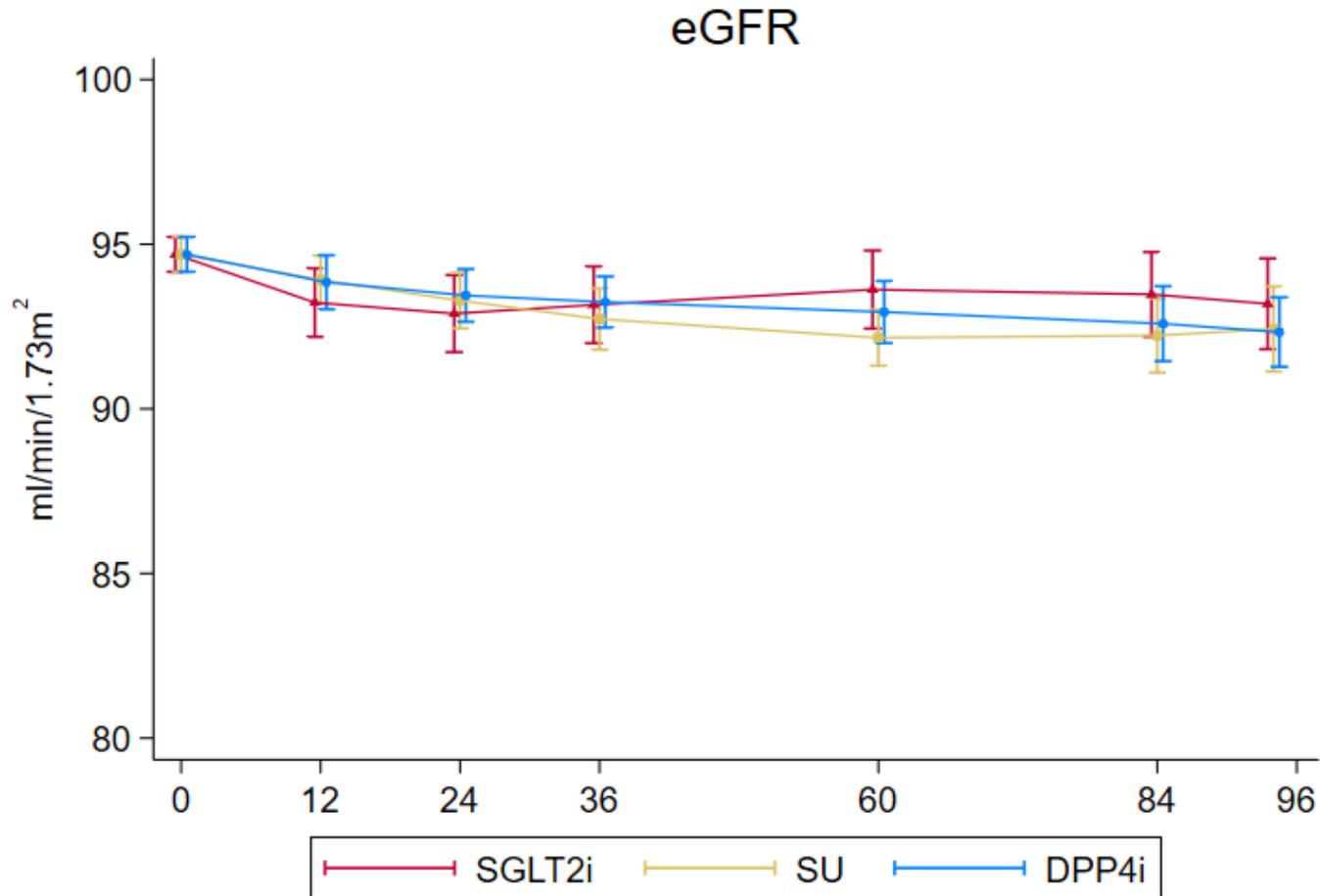


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# Comparative effect of new anti-diabetic therapies on clinical measures in UK primary care



# Comparative effect of new anti-diabetic therapies on clinical measures in UK primary care



# Conclusion: Prescribing for type 2 DM in the UK

## **For initial prescribing:**

- Increased concordance with NICE Guidelines
- 1/10 people prescribed Metformin still seem to have CKD stage 4/5

## **For first stage intensification**

- Free choice of agent according to NICE guidance
- Marked variation by region and CCG
- Choice of agent influenced by multiple factors – white people of higher SES more likely to receive new agents

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# Any questions?



Thanks to all in #teamkidney