Time-dependent markers of comorbidity severity and change are associated with increased risk of mortality in heart failure:

A large database study in the general population in England

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Background

- Heart failure (HF) is a common chronic disease with increasing prevalence

- HF prognosis is poor, varies across individuals and changes over time

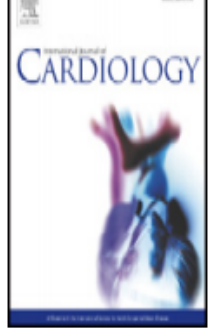- Comorbidity is common in HF and the presence of comorbidity is known to influence prognosis

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Non-cardiovascular comorbidity, severity and prognosis in non-selected heart failure populations: A systematic review and meta-analysis☆

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Diabetes 1.34 (1.24, 1.46)	COPD 1.39 (1.21, 1.60)	CKD 1.52 (1.34, 1.71)

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Background

- Chronic disease comorbidity changes over time

- Current evidence
  - Renal disease which incorporates change
  - Limited to hospital settings and selected HF groups

- Little evidence of comorbidity severity and change on prognostic outcomes

Hypothesis

- In the general HF population, comorbidity stratification by increasing severity and longitudinal change would be associated with worse mortality.

Objectives

To investigate associations between:

- recent comorbidity severity and mortality risk.

- recent change in comorbidity severity and mortality risk.

Methods

- Study population
    - Incident cohort of HF patients aged ≥ 40 years

    - Clinical Practice Research Datalink (CPRD) with first consultation code for heart failure

    - Cohort entry 1st January 2002 and 1st March 2012.

Methods: Exposures

Diabetes

Consultation code or prescription

Severity (drugs measure)

None

Oral hypoglycaemic drugs

Insulin only

Severity change

No drug category change

Increase in drug category

Decrease in drug category

Methods: Exposures

CKD

eGFR<60 ml/min/m2

Severity (physiological measure)

>105

90-105

60-89 (ref)

45-59

30-44

15-29

<15

Severity change

Classification 2

Percentage change

>25% decrease

6-25% decrease

Any % increase

0-5% decrease (ref)

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Methods

- **Confounders:**

  – Person and social (age, gender, deprivation)

  – Clinical factors (BMI, BP, Cholesterol, Haemoglobin)

  – Lifestyle factors (alcohol, smoking)

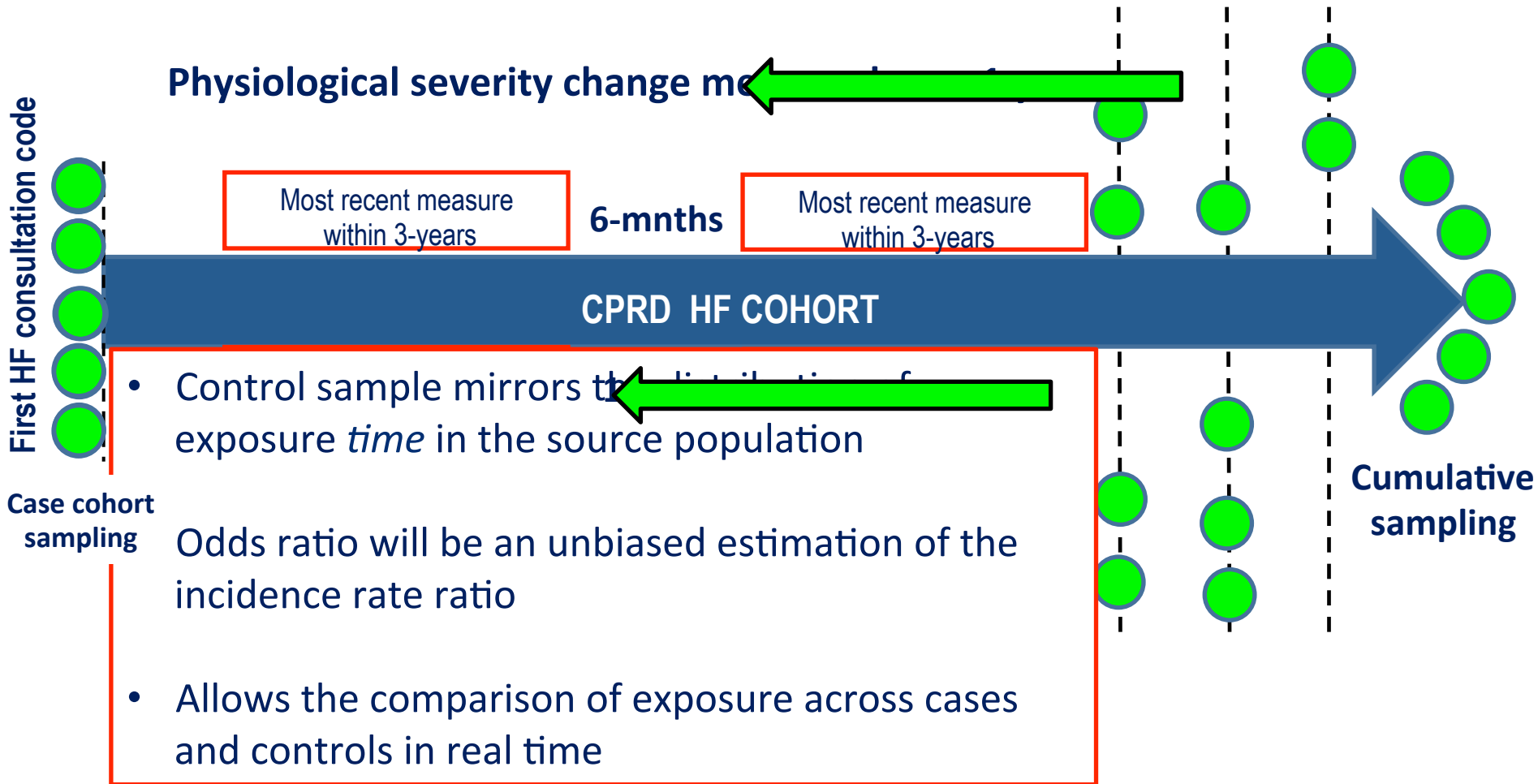 – HF medications (ACEi, ARB, B-blocker, diuretic).

- **Outcomes:**

  – All-cause mortality

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Analysis

- Nested case-control study

- Risk set sampling

- Cases matched to 4 controls on follow-up and calendar time

Risk set sampling

First HF consultation code

Physiological severity change measure

| Most recent measure within 3-years | **6-mnths** | Most recent measure within 3-years |

CPRD HF COHORT

Case cohort sampling

- Control sample mirrors the distribution of exposure *time* in the source population

Odds ratio will be an unbiased estimation of the incidence rate ratio

- Allows the comparison of exposure across cases and controls in real time

Cumulative sampling

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Analysis

- Imputation of missing confounders

- Tested continuous variables for linearity

- Investigated collinearity
  - One variable selected if >50%
  - Continuous variables centred at their means if quadratic extension included

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Analysis

- **Conditional Logistic Regression**

    – Unadjusted and adjusted for all confounders

    – For CKD change further adjustment for baseline renal function

Results

- 50,114 HF patients

- Follow-up, 0-12 years (2.57 years [0.81-4.96])

- Age median 78 years [IQR 71-85]

- 47.1% female

- 26,729 (53.3%) died; 106,916 controls

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- **Diabetes prevalence**

  Baseline: 10,533 (21%)

  Matched: 31,962 (23.9%)

  90% recent HbA1c (4 months; IQR 1.7-6.6)

  82% second measure (10 months; IQR 7.4-12.2)

- **CKD prevalence**

  Baseline: 20,084 (49.8%)
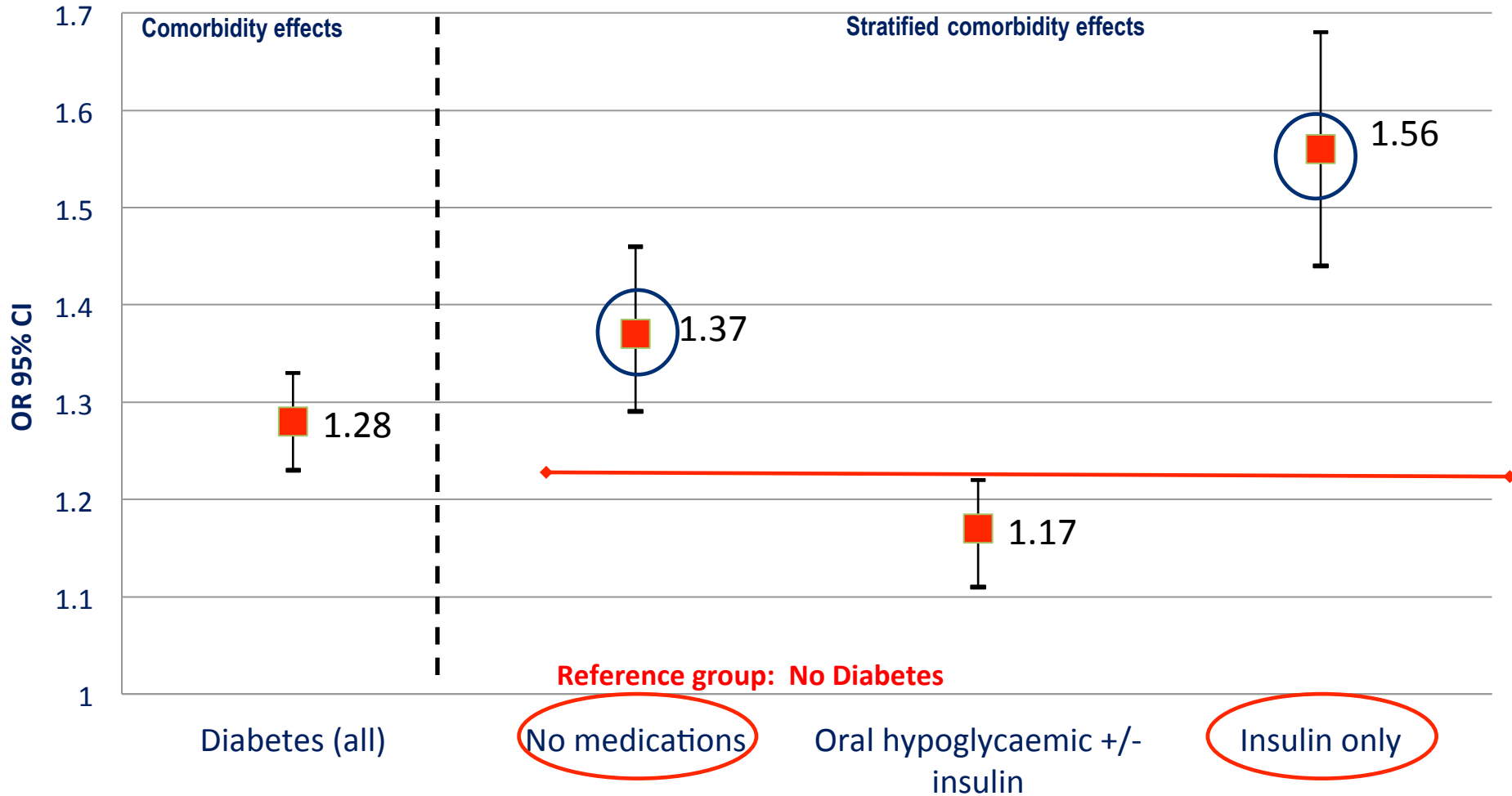
  Matched: 66,301 (55.4%)

  90% recent eGFR (3 months; IQR 1.2-7.2)

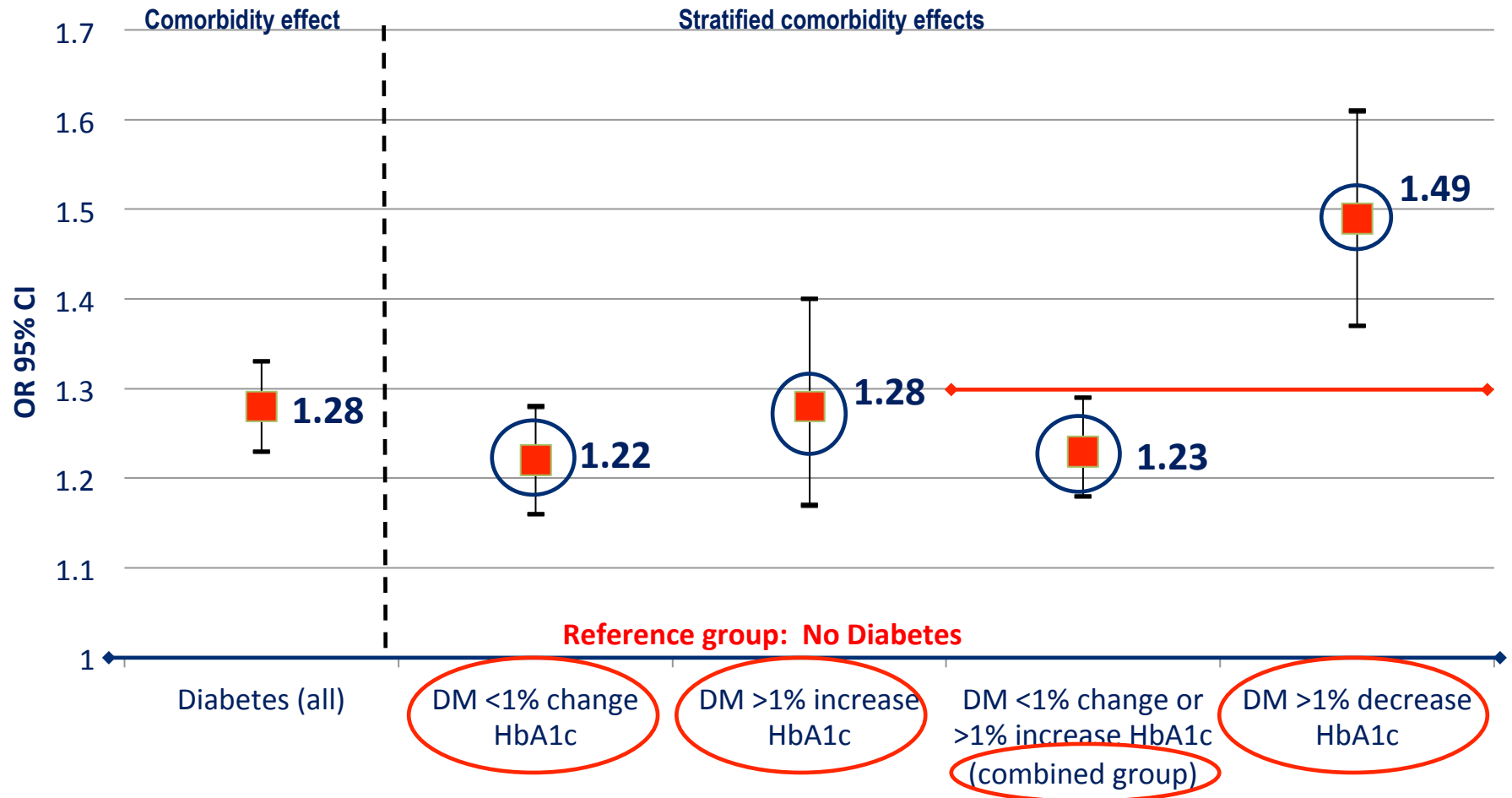 79% second measure (10 months; IQR 7.2-13.5)
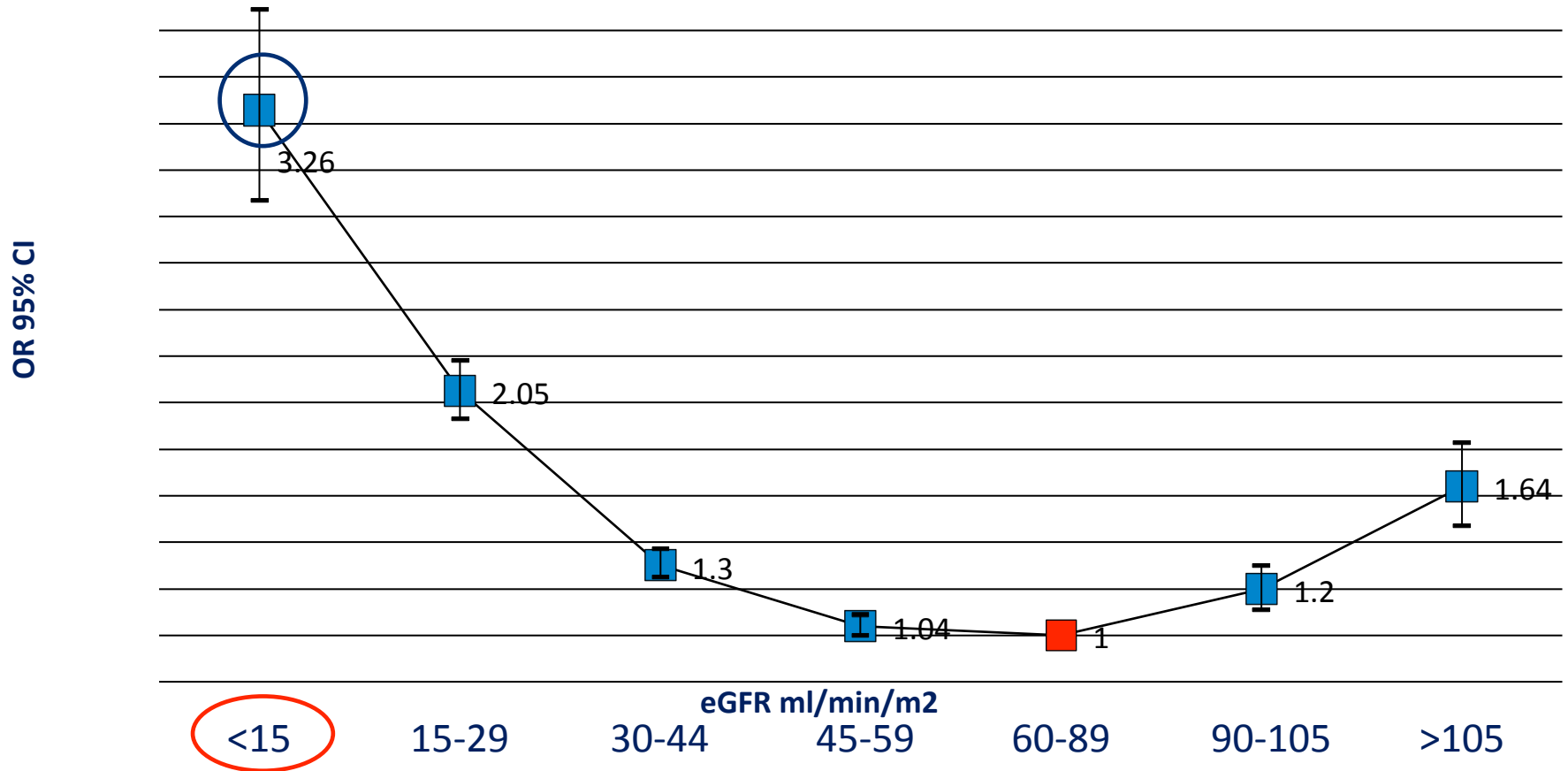
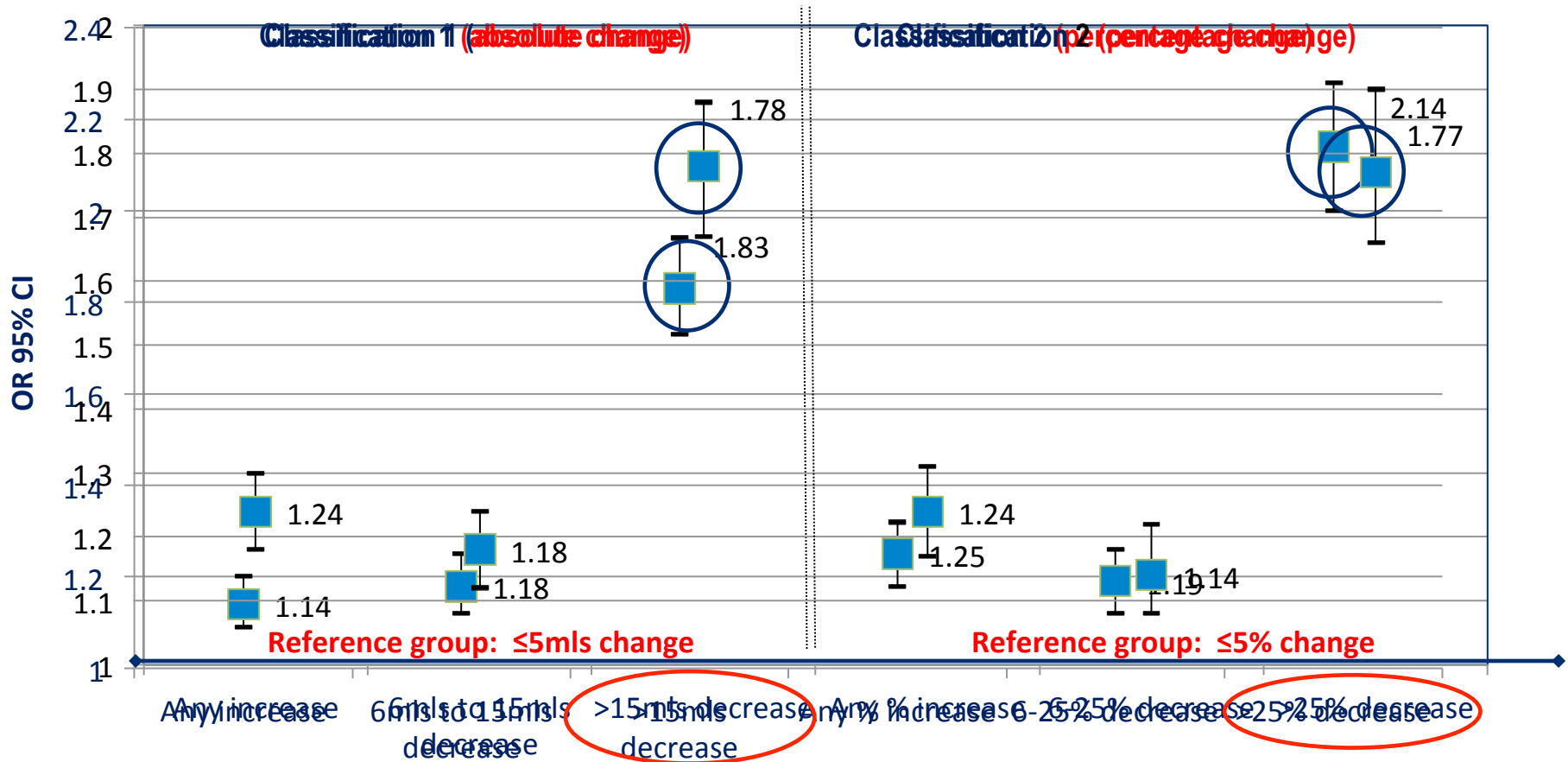# Diabetes HbA1c Severity
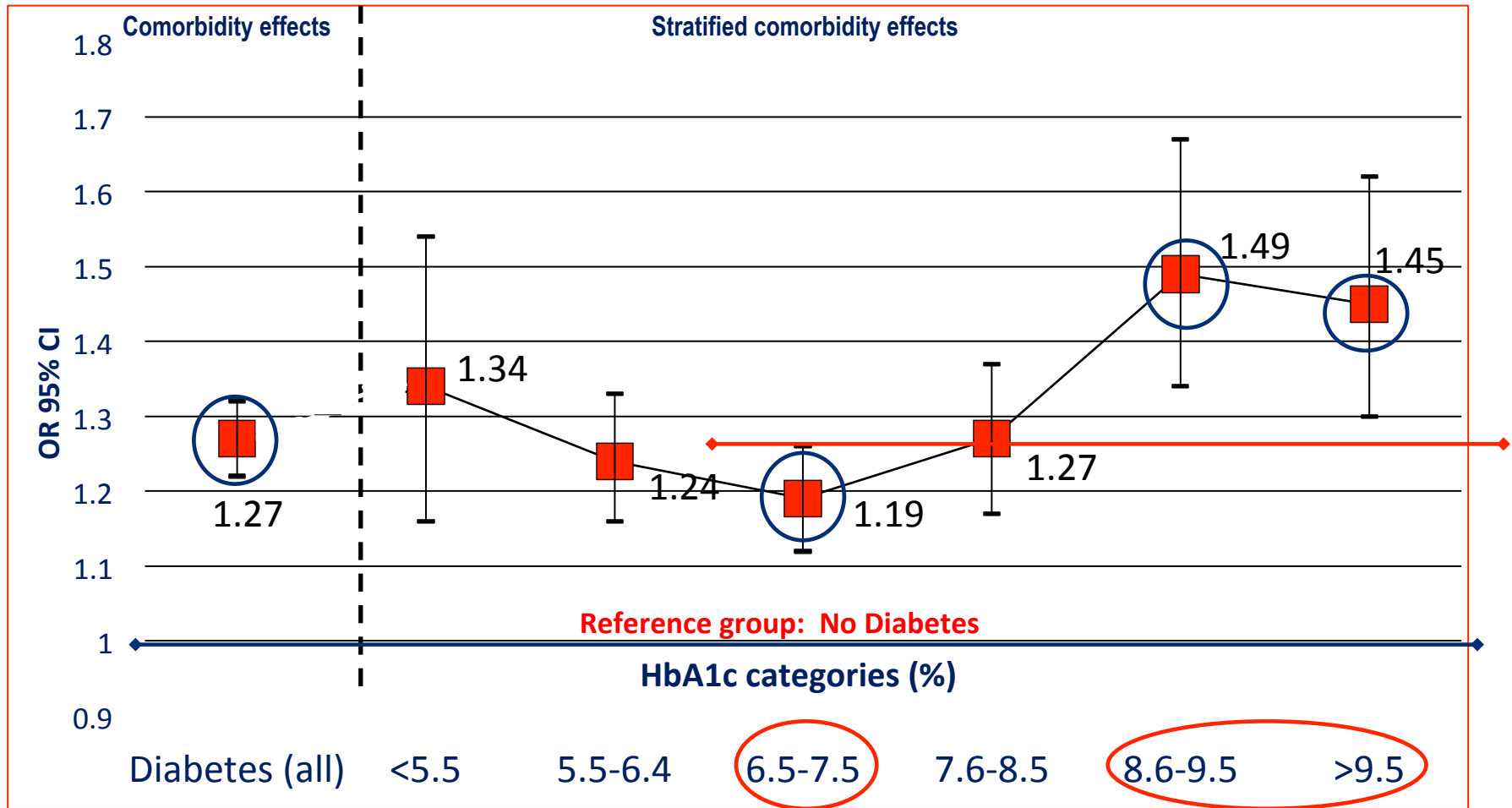
Diabetes Drug Severity

Diabetes HbA1c Severity Change

CKD severity

CKD Severity Change

Conclusions

- In the general population of HF, diabetes and CKD comorbidities are associated with an increased risk of mortality.

- This risk is significantly stratified by measures of recent comorbidity severity and change.

- This has important implications for developing new HF comorbidity interventions to improve outcomes in the general population

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7

Acknowledgements

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