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Take CaRe of Me Programme:

Gaps in Early Diagnosis of Cardiorenal Complications Among Individuals With Type 2 Diabetes

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Introduction

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- Nearly half of people with T2D have cardio-renal-metabolic complications (CAD: 32% and CKD: 20%) — which are associated with increased risk of mortality.[1,2,3] However, there are gaps in early identification and prevention of cardiorenal complications in T2D.
- Major guidelines including the ADA, ESC and KDIGO emphasise the need for early screening of cardiorenal complications, followed by timely initiation of SGLT2i or GLP-1RA in patients with high-risk factors or established ASCVD, CKD, or HF, independent of baseline HbA_{1c}.[4,5,6,7]
- **'Take CaRe of Me', a subset of DISCOVER CaReMe Registry**, evaluated the real-world burden, screening implementation and treatment patterns of cardiorenal complications among individuals with T2D in primary care settings in emerging countries.

World Health Organization

Executive summary. The selection and Use of Essential Medicines 2021
Report of the 23rd WHO Expert Committee on the Selection and Use of Essential Medicines

Section 18.5.2 Oral hypoglycemic agents

The Expert Committee recommended inclusion of the sodium-glucose cotransporter-2 (SGLT2) inhibitor empagliflozin (with canagliflozin and dapagliflozin as therapeutic alternatives) on the core list of the EML as add on treatment for adults with type 2 diabetes with or at high risk of cardiovascular disease and/or diabetic nephropathy. This recommendation was based on high-quality evidence of reduced risk of all-cause mortality, major cardiovascular adverse events, and adverse renal outcomes, and a reasonable safety profile.

ADA, American Diabetes Association; ASCVD, atherosclerotic cardiovascular disease; CAD, coronary artery disease; CKD, chronic kidney disease; EASD, European Association for the Study of Diabetes; EML, List of Essential Medicines; ESC, European Society of Cardiology; GLP-1-RA, glucagon-like peptide-1 receptor agonist; HbA_{1c}, glycated haemoglobin; HF, heart failure; KDIGO, Kidney Disease: Improving Global Outcomes; SGLT2i, sodium–glucose cotransporter 2 inhibitor; T2D, Type 2 diabetes

1. International Diabetes Federation, 9 edition. IDF diabetes atlas Fact sheet, 2019. **2.** Arnold SV, et al. Diabetes, Obesity and Metabolism. 2018 Aug;20(8):2000-3. **3.** Birkeland KI, et al. Diabetes, obesity and metabolism. 2020 Sep;22(9):1607-18. **4.** American Diabetes Association. Standards of Medical care in Diabetes 2021; 126. **5.** 2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD. **6.** KDIGO 2020 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease. Kidney Int. 2020;98(4S):S1–S115. **7.** World Health Organization. Model List of Essential Medicines – 22nd List, 2021. Geneva: World Health Organization; 2021 (WHO/MHP/HPS/EML/2021.02).

Study Design

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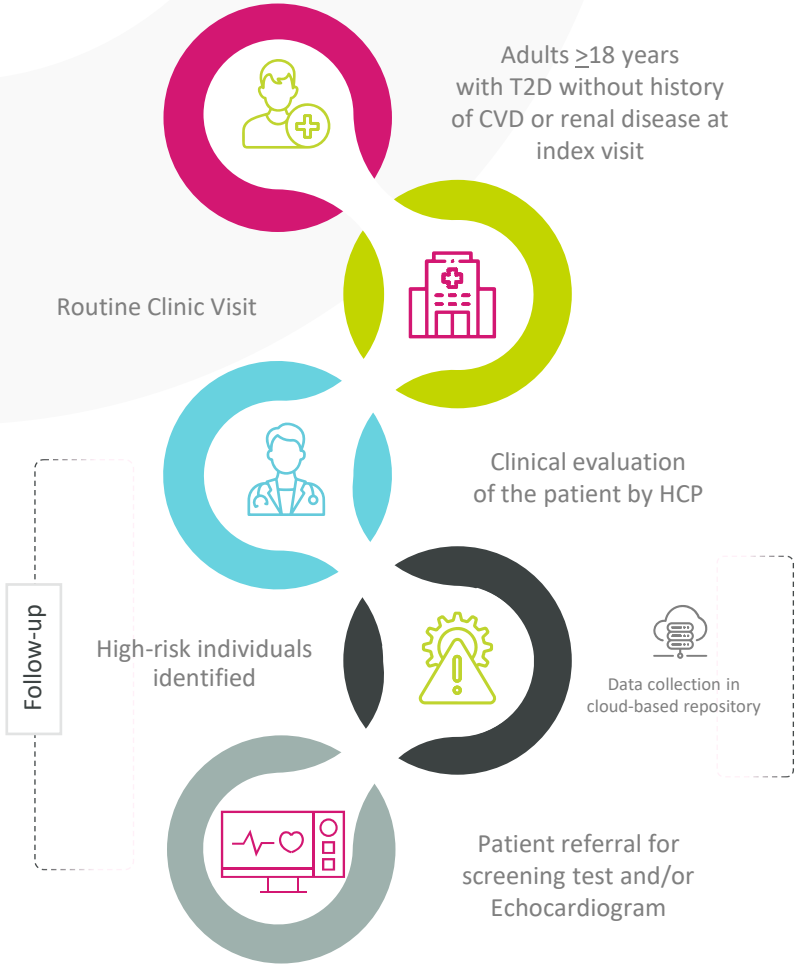
Take CaRe of Me program: An ongoing, international, prospective, study for diagnosis and management of early cardiorenal complications in T2D



Identification of high/ very high-risk individuals

European Society of Cardiology (ESC) 2019 Cardiovascular risk categories

Urine Albumin: Creatinine Ratio >30mg/g

ESC 2019 Cardiovascular risk categories[8]

Very-high-risk	People with any of the following: Documented ASCVD, either clinical or unequivocal on imaging. Documented ASCVD includes previous ACS (MI or unstable angina), stable angina, coronary revascularization (PCI, CABG, and other arterial revascularization procedures), stroke and TIA, and peripheral arterial disease. Unequivocally documented ASCVD on imaging includes those findings that are known to be predictive of clinical events, such as significant plaque on coronary angiography or CT scan (multivessel coronary disease with two major epicardial arteries having >50% stenosis), or on carotid ultrasound. DM with target organ damage,[a] or at least three major risk factors, or early onset of T1DM of long duration (>20 years). Severe CKD (eGFR <30 mL/min/1.73 m^2). A calculated SCORE ≥10% for 10-year risk of fatal CVD. FH with ASCVD or with another major risk factor.
High-risk	People with: Markedly elevated single risk factors, in particular TC >8 mmol/L (>310 mg/dL), LDL-C >4.9 mmol/L (>190 mg/dL), or BP ≥180/110 mmHg. Patients with FH without other major risk factors. Patients with DM without target organ damage,[a] with DM duration ≥10 years or another additional risk factor. Moderate CKD (eGFR 3059 mL/min/1.73 m^2). A calculated SCORE ≥5% and <10% for 10-year risk of fatal CVD.

ASCVD, atherosclerotic cardiovascular disease; CABG, coronary artery bypass graft; CKD, Chronic kidney disease; CT, Computed tomography; eGFR, estimated glomerular filtration rate; FH, Familial hypercholesterolaemia; HCP, Health care professional; LDL-C, low density lipoprotein-cholesterol; PCI, Percutaneous coronary intervention, T2D, Type 2 diabetes; T1DM, Type 1 diabetes; TC, Total Cholesterol, TIA, transient ischemic attack

8. Mach F et al. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk: The Task Force for the management of dyslipidaemias of the ESC and EAS. European heart journal. 2020 Jan 1;41(1):111-88.

Results

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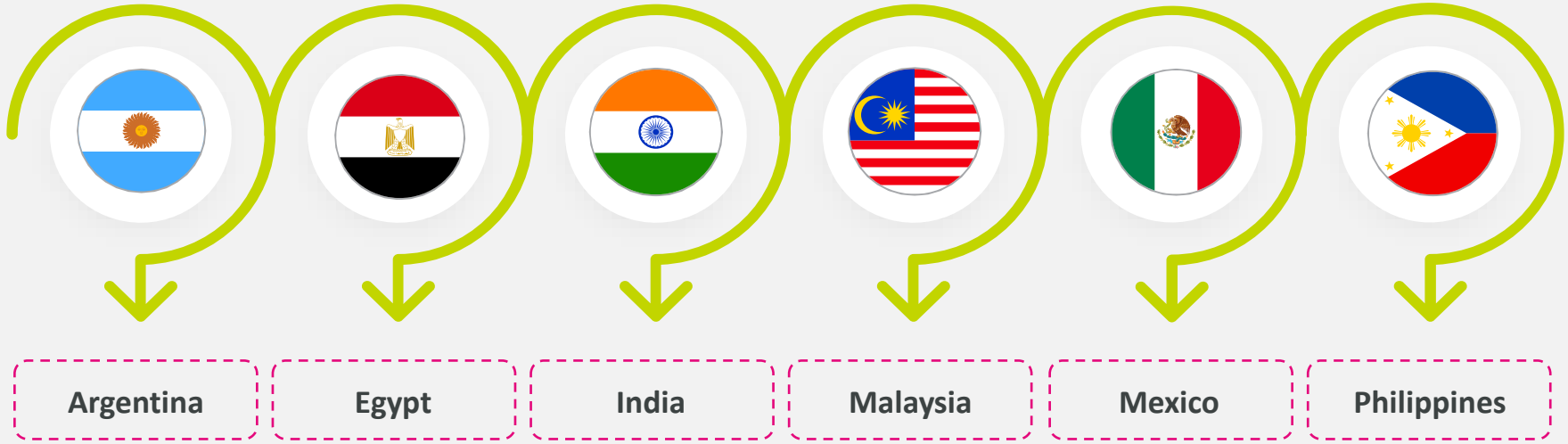
We present preliminary results of 4686 patients enrolled from Dec 2020 to May 2021 from six emerging countries



Demographic profile	
Mean age (±SD)	55.7±11.3 years
Male gender	46.2%

Target for final analysis: **12000**

Results: Baseline Clinical Characteristics

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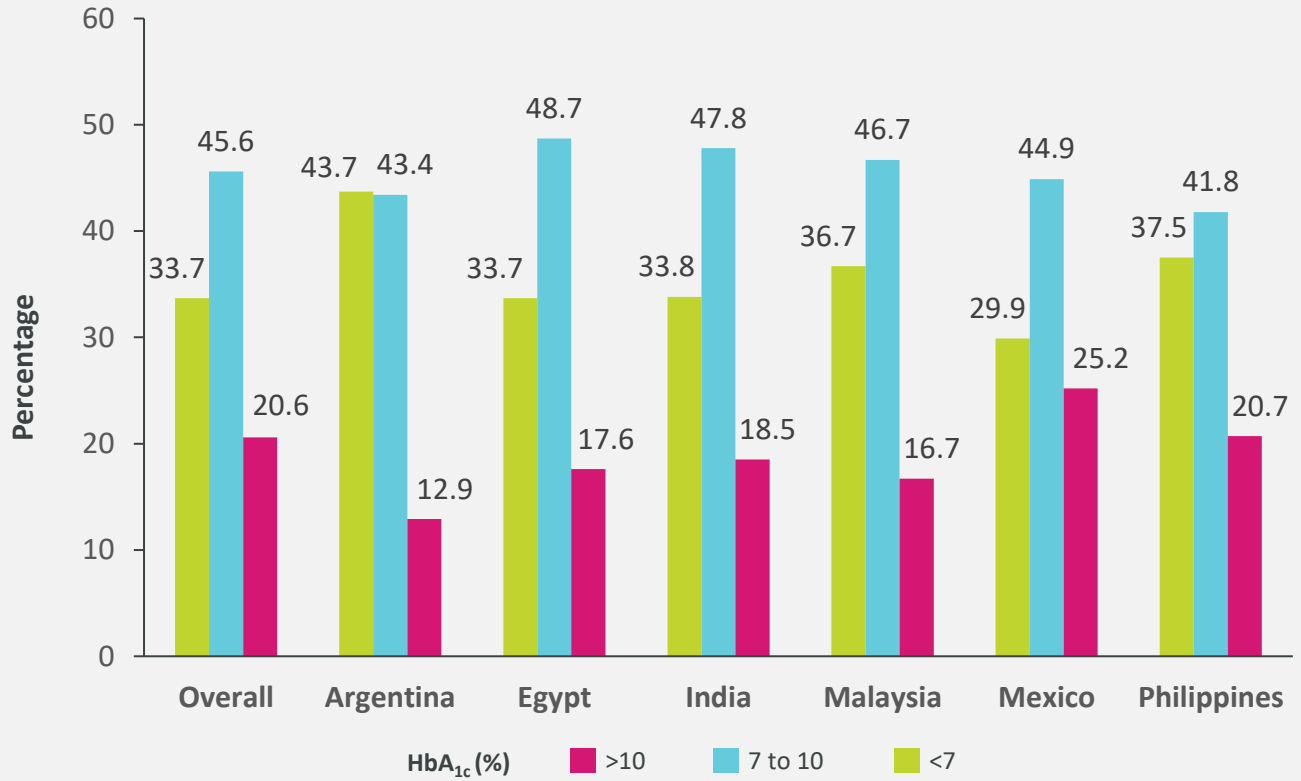
5% had HFpEF and none had HFrEF

Diabetes related	
Mean (±SD) T2D duration	8.4±7.2 years
Patients with T2D duration <5 years	40.1%
Mean (±SD) HbA_{1c}	8.3±3.0%
Patients having HbA_{1c} >7%	66.3%

Based on Echocardiography	
Left ventricular hypertrophy	20.6%
Left atrial enlargement	16.5%
Diastolic dysfunction	8.9%
Valvular diseases	8.6%



T2D, Type 2 diabetes; HbA_{1c}, glycated haemoglobin; SD, standard deviation; HFrEF, Heart Failure With Reduced Ejection Fraction; HFpEF, Heart failure with preserved ejection fraction

Baseline: Cardiorenal Complications

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- Mean (±SD) eGFR of the cohort: 94.6±23.2 mL/min/1.73m^2 (N=479);
  Mean (±SD) UACR: 62.9±181.9 mg/g (N=3869)
- High/very high CV risk as per ESC 2019: 37.0%
- High renal risk (UACR >30mg/g): 32.7%

	Overall	Argentina	Egypt	India	Malaysia	Mexico	Philippines
UACR (mg/g)*, n (%)	***N=3869***	***N=339***	***N=157***	***N=1509***	***N=29***	***N=1561***	***N=274***
A1 (<30)	2605(67.3)	244(72)	100(63.7)	927(61.4)	17(58.6)	1171(75%)	146(53.3)
A2 (30-300)	1104(28.5)	89(26.3)	52(33.1)	508(33.7)	**11(37.9)**	332(21.3)	**112(40.9)**
A3 (>300)	160(4.1)	6(1.8)	5(3.2)	74(4.9)	**1(3.4)**	58(3.7)	**16(5.8)**
CV risk*, n (%)	***N=4686***	***N=399***	***N=196***	***N=1671***	***N=30***	***N=1618***	***N=772***
Low	2592(55.3)	190(47.6)	87(44.4)	825(49.4)	15(50)	972(60.1)	503(65.2)
Moderate	362(7.7)	11(2.8)	14(7.1)	196(11.7)	2(6.7)	87(5.4)	52(6.7)
High/Very High	1732(37)	**198(49.6)**	**95(48.5)**	650(38.9)	13(43.3)	559(34.5)	217(28.1)

*Risk defined per UACR and ESC 2019 *Highest frequencies are presented in purple

ESC, European Society of Cardiology; UACR, Urine albumin:creatinine ratio; CV, Cardiovascular; eGFR, Estimated Glomerular Filtration Rate

All Lines of Anti-diabetic Treatment Therapy in Patients with Cardiorenal Complications

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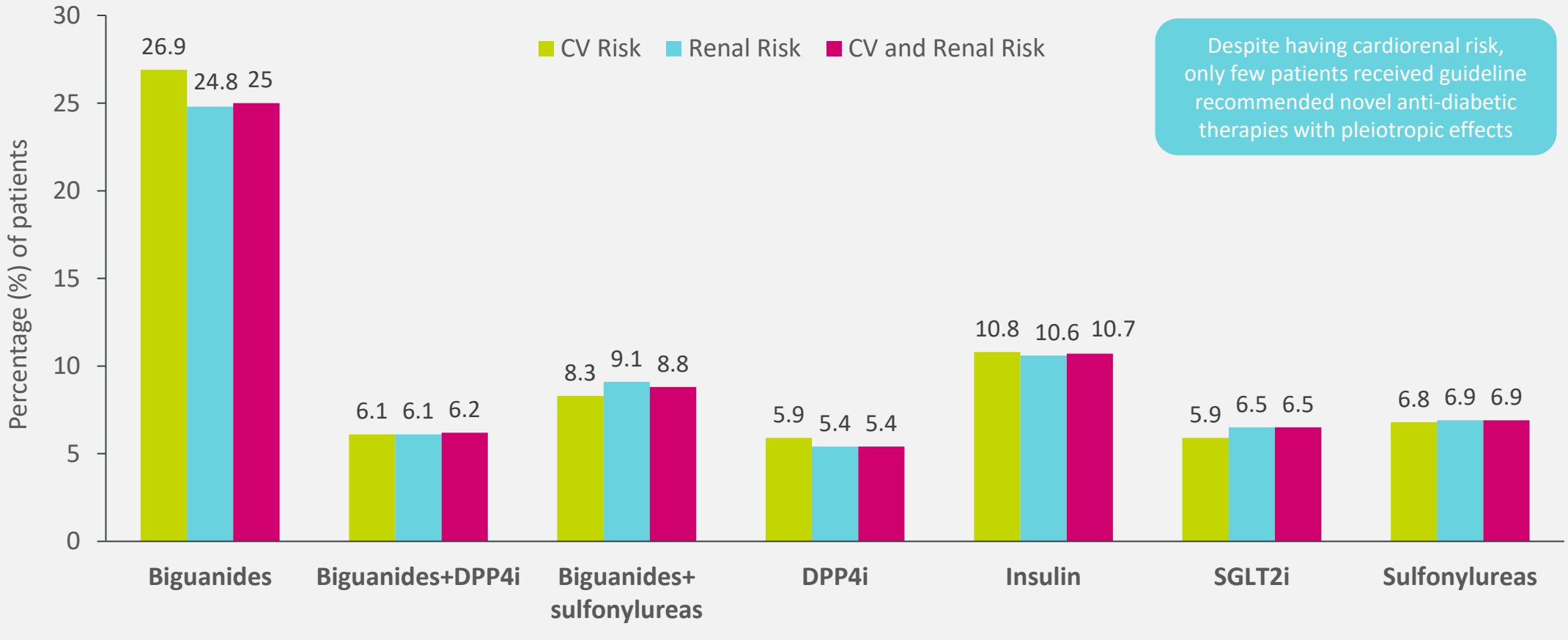

Despite having cardiorenal risk, only few patients received guideline recommended novel anti-diabetic therapies with pleiotropic effects

Data cutoff for >5% of patients receiving either therapy
CV, cardiovascular; DPP-4i, dipeptidyl peptidase-4 inhibitor; SGLT2i, sodium-glucose co-transporter-2 inhibitor

High-risk Patients Receiving Novel Cardioprotective Drugs as First-line Antidiabetic Therapy

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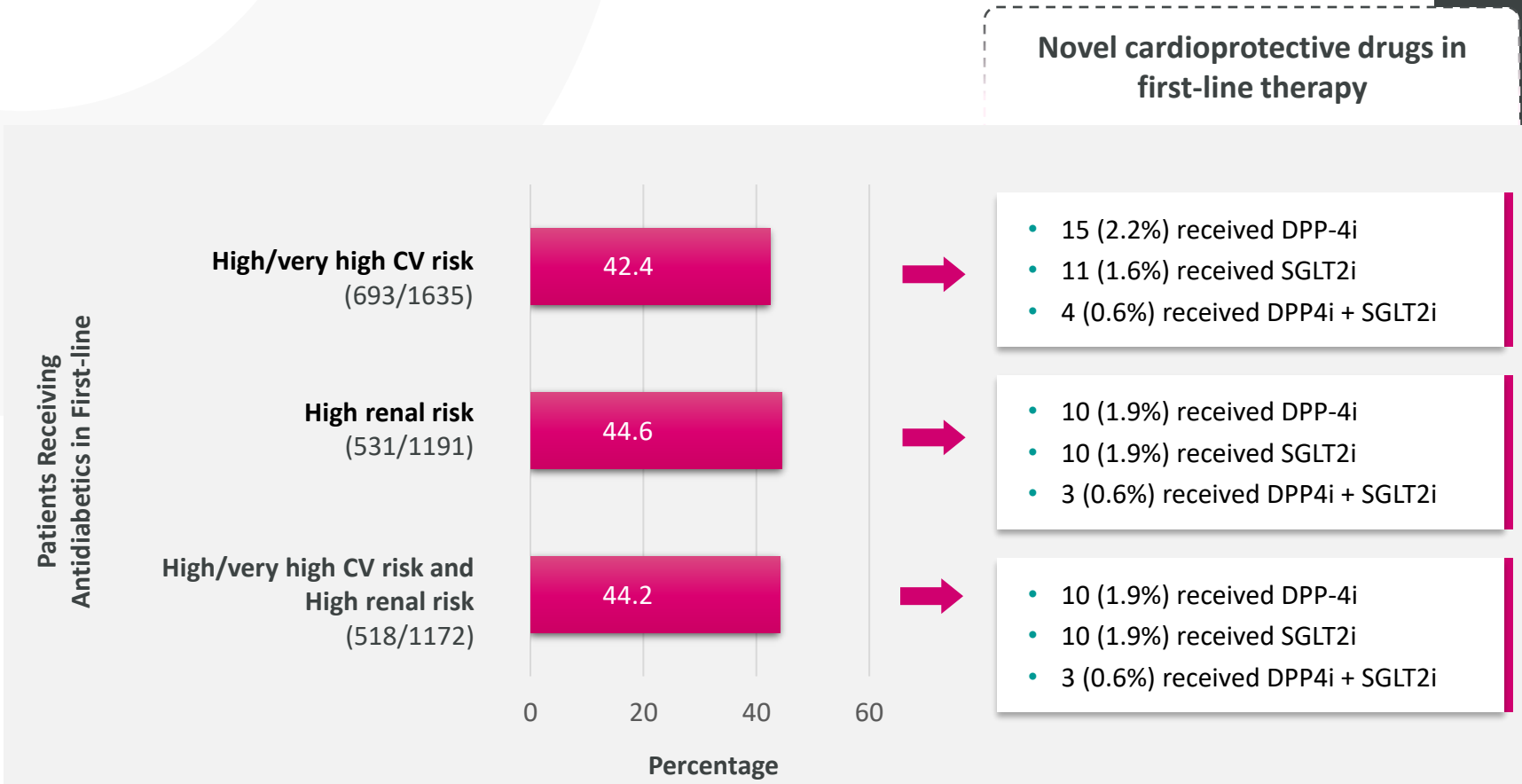


Novel cardioprotective drugs in first-line therapy

- 15 (2.2%) received DPP-4i
- 11 (1.6%) received SGLT2i
- 4 (0.6%) received DPP4i + SGLT2i

- 10 (1.9%) received DPP-4i
- 10 (1.9%) received SGLT2i
- 3 (0.6%) received DPP4i + SGLT2i

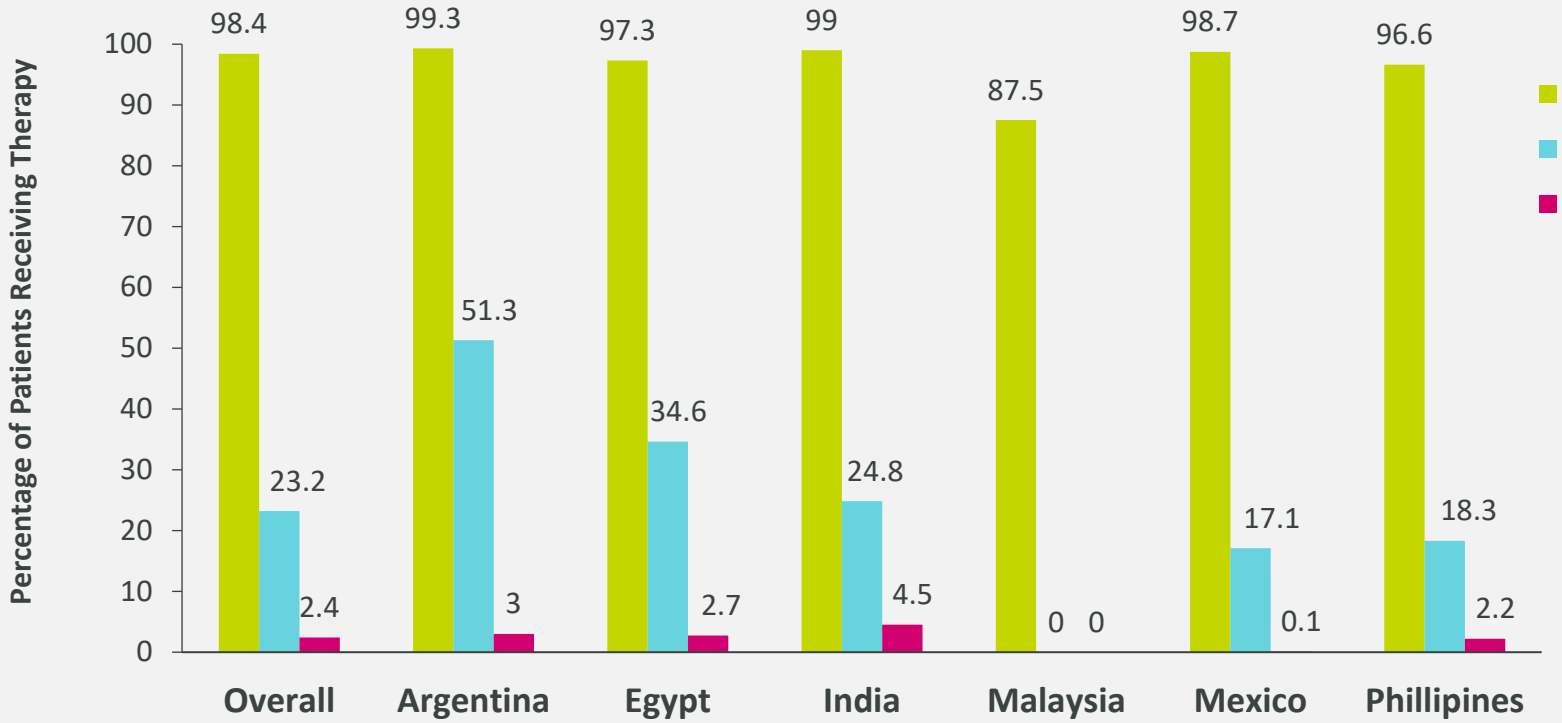
- 10 (1.9%) received DPP-4i
- 10 (1.9%) received SGLT2i
- 3 (0.6%) received DPP4i + SGLT2i

Stark difference in real-world practice patterns and guideline recommendations warrant call for action for early initiation of SGLT2i and GLP1-RA

CV, Cardiovascular; DPP-4i, dipeptidyl peptidase-4 inhibitors; GLP1-RA, Glucagon-like peptide-1 receptor agonists; SGLT2i, sodium-glucose cotransporter-2 inhibitors

Concomitant Therapies in Overall Patient Cohort

1407 (32.3%) patients had high cholesterol (>180mg/dL) and 2048 (51.4%) patients had high LDL (>70mg/dL) levels



- Majority patients received anti-lipid therapy
- 17.1-51.3% received anti-hypertensive therapy
- Less than 5% received anti-platelet therapy

LDL, low density lipoproteins

Discussion and Conclusion

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In about one-third of patients with T2D, silent cardiorenal complications can be diagnosed when screened per the guideline recommendations

Although 37% of patients had very high or high CV risk, just 1.8% of T2D patients were receiving an oral antidiabetic drug that can reduce CV risk

Although 32.7% patients had high renal risk, just 1.9% of T2D patients were receiving an oral antidiabetic drug that can reduce renal risk

Gaps in real-world treatment necessitate strategic approaches to enhance utilization of cardiorenal protective antidiabetic therapies in concordance with recent guidelines

T2D, Type 2 diabetes; CV, Cardiovascular

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Thank You!