Determinants of sub-optimal glycaemic control among patients enrolled in a medicine dispensing programme in KwaZulu-Natal: A cohort study, 2018–2021

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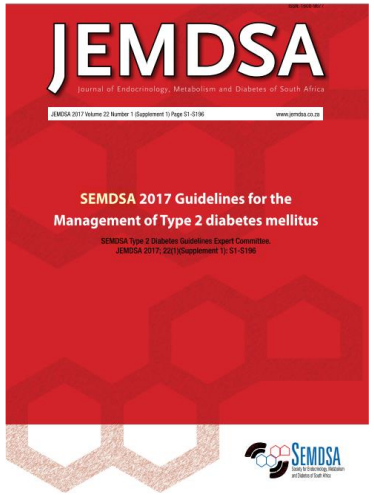
Introduction

- Type 2 Diabetes Mellitus (T2DM) is a growing public health concern in South Africa[1]
- In 2022, diabetes was ranked the leading cause of death (first in females, fourth in males)[1]
- In 2021, 4.2 million were living with diabetes[2]
- People living with type 2 diabetes mellitus (T2DM), need to monitor their glycaemic levels regularly[2,3]



- Optimal Target: **HbA1c ≤7%**[3]
- Testing frequency:

→ 6-monthly if optimally controlled[3]

→ 3-monthly if sub-optimally controlled[3]

- Optimal control/good blood sugar levels reduces the risk for diabetes-related complications[2,3]

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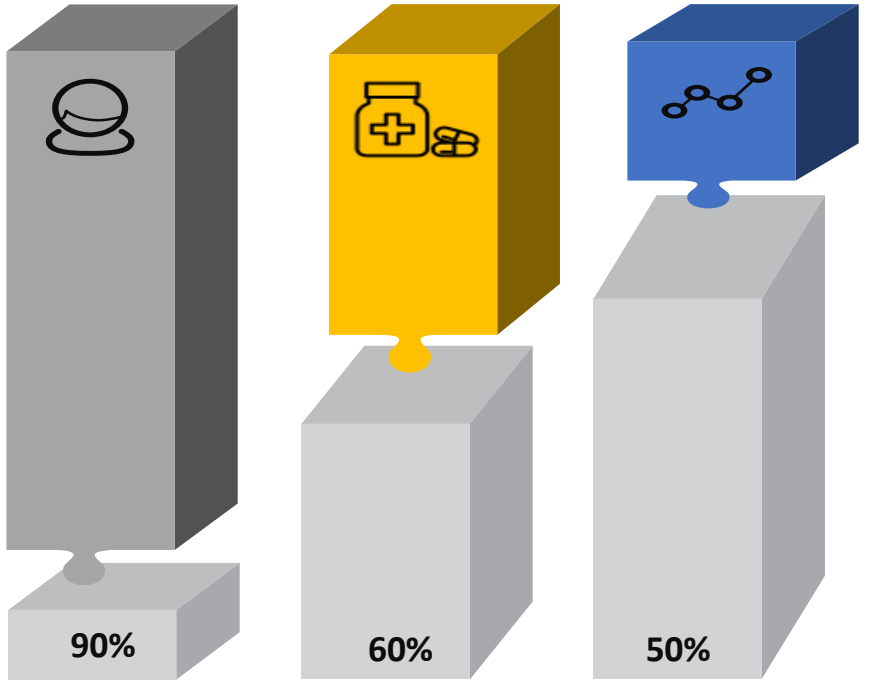
National targets for diabetes for 2030

Screening
90% of all people over 18 will know whether or not they have raised blood glucose[1]

Treatment
60% of people with raised blood glucose will receive intervention[1]

?

Controlled
50% of people receiving interventions are controlled[1]



- The Central Chronic Medicine Dispensing and Distribution (CCMDD) programme does not monitor clinical measures such as HbA1c after enrollment[4]
- The National Health Laboratory Services (NHLS) Central Data Warehouse (CDW) houses laboratory results for 80% of the public health sector
- We had an opportunity to determine gaps in the diabetes care cascade, by linking CCMDD & NHLS data

Aim

To determine the proportion of T2DM CCMDD-enrolled patients with optimal glycaemic control at enrollment and the rate and predictors of becoming sub-optimally controlled

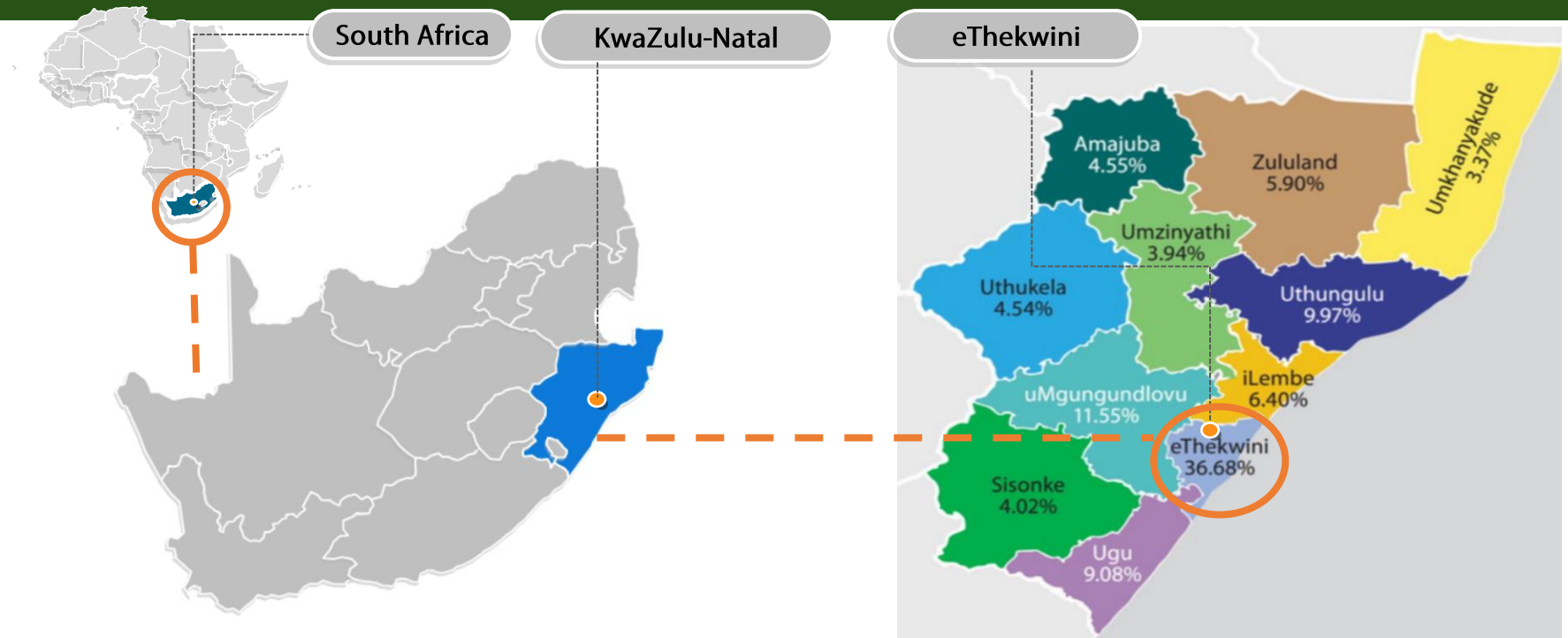
Objectives

CCMDD pick-up point, South Africa[5]

1. To determine proportions of T2DM CCMDD-enrolled patients optimally controlled at enrollment, in eThekwini, KwaZulu-Natal (KZN), between April 2018–December 2021

2. To determine the rate and predictors of becoming sub-optimally controlled for T2DM CCMDD-enrolled patients, in eThekwini, KZN, between April 2018–December 2021

Study setting



Maps of eThekwini district[7], KwaZulu-Natal, and South Africa (Africa & South Africa graphs source: https://www.slideegg.com)

- KZN province has the second-highest diabetes incidence[6]
- 1/3rd (36,68%) of all KZN's diabetes-related clinical visits occurred in eThekwini (2014-2016)[7]
- eThekwini is a densely populated Metro (2019): 3 987 648 (34.7% of the KZN population)[8]
- 220 approved CCMDD chronic medication pick-up points[8]

Study methodology

Study design

A retrospective longitudinal cohort study

Study population

CCMDD-enrolled patients in eThekwini, South Africa from 2018–2021

Ethics

Full ethical approval obtained from Wits HREC (no. M220232)

Exclusion criteria

CCMDD patients with missing HbA1c data in
NHLS
CDW

Patients sub-optimally controlled at their baseline HbA1c & those with no repeat HbA1c tests available

Data management

- Stata v17
- CCMDD data merged with NHLS lab data (HbA1c)
- Data was cleaned
- Variables were created/coded

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Study methodology

Outcome definitions

Glycaemic control:

- Optimal→HbA1c ≤7%
- Sub-optimal→HbA1c >7.1%

Time to failure:
First change of status to sub-optimal or end of study period

Predictor variables

- Age & sex
- Diabetes severity (mono vs dual therapy, facility type, T2DM-related complications)
- Comorbidity
- Quality of care (HbA1c testing frequency-SEMDSA guideline)

Descriptive analysis

Summarise characteristics (% or median, IQR) by each predictor variable for the survival analysis cohort

Survival analysis

Those with a repeat test:

- Univariate analysis: Kaplan-Meier curves & log-rank test→no. cases, no. sub-optimal events, time at risk, IR & 25th percentile of survival time
- Multivariate analysis: Extended Cox model

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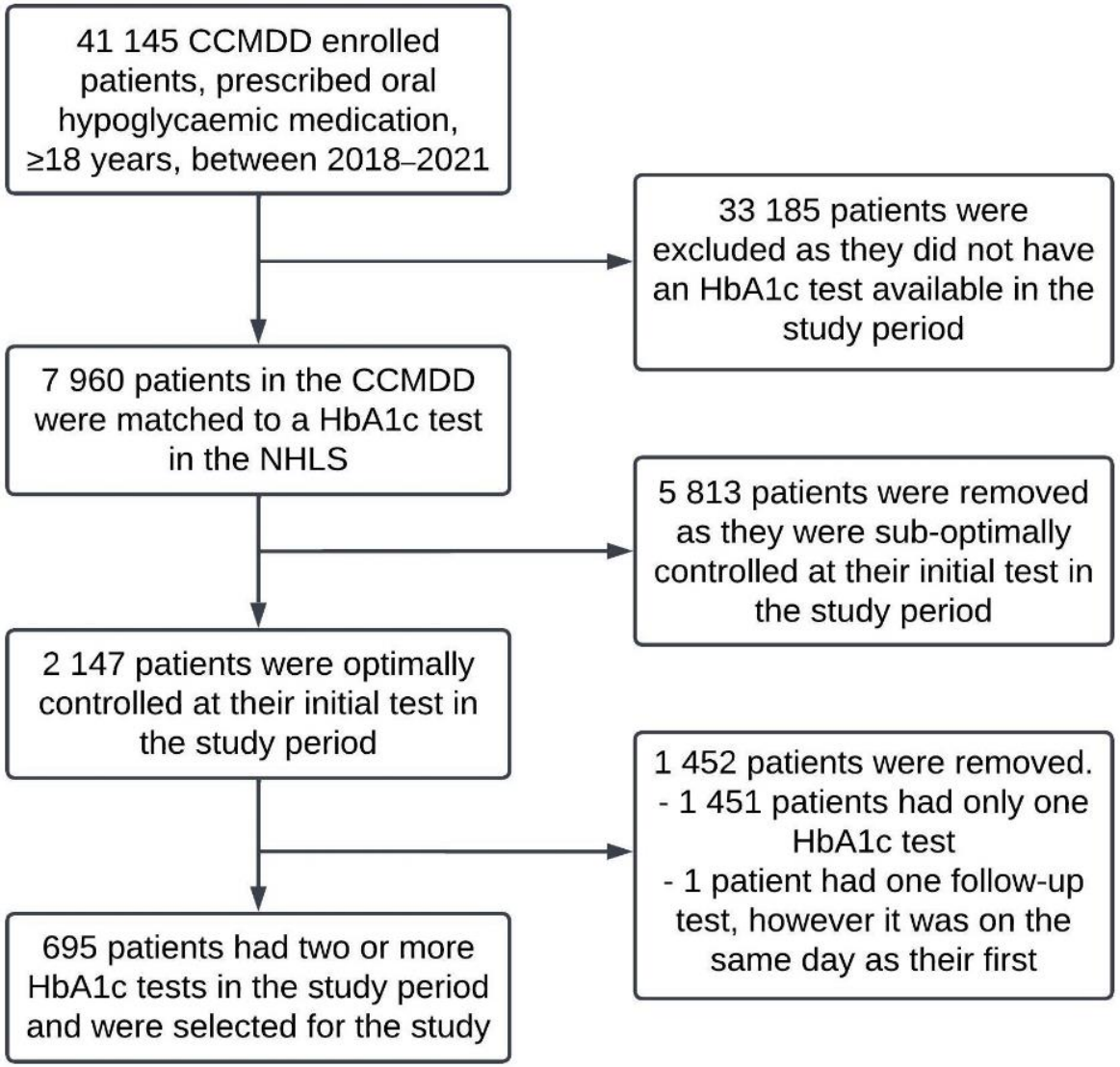
Results: Flow chart of study population selection (N=7960)



Over the study period (April 2018–December 2021) there were:

- 41 145 CCMDD enrolled patients in eThekwini
- 19% (7 960/41 145) had a non-missing HbA1c test result data from the NHLS CDW within a 6-month window of the study period (i.e. October 2017–June 2022)
- 27% (2 147/7 960) of those with a non-missing HbA1c test had optimal glycaemic control at baseline
- 32% (695/2 147) of those optimally controlled at baseline, had ≥1 repeat HbA1c test result, after the baseline test

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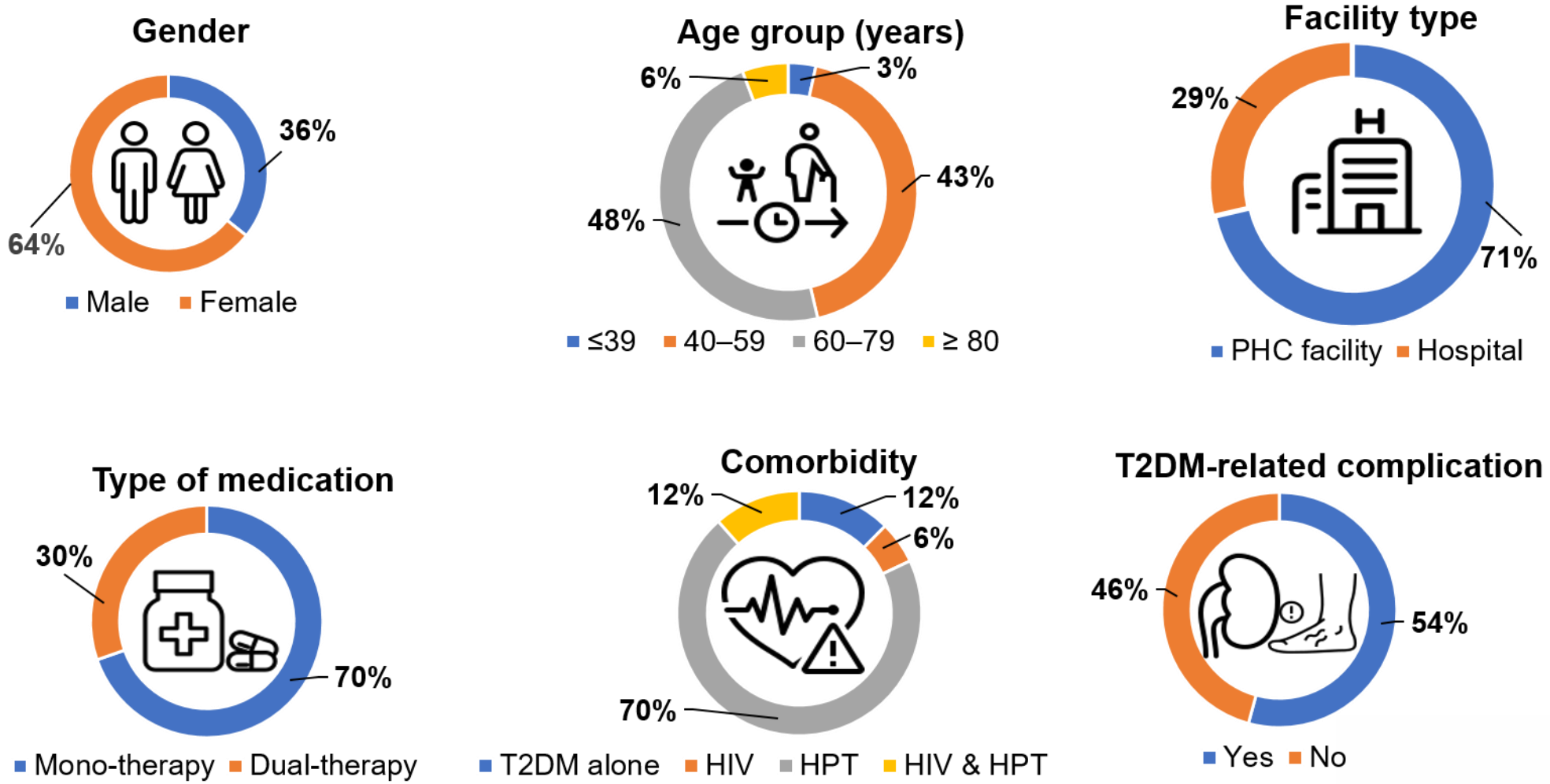
Description of patient characteristics for CCMDD cohort, eThekwini, KZN: April 2018–December 2021 (N=695)



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Description of patient characteristics for CCMDD cohort, eThekwini, KZN: 19 April 2018–30 December 2021 (N=695)

Characteristic	Total (N=695)	Sub-optimal event (N=242)	Remained Optimal (N=453)
Median Age (IQR)	61 (53– 69)	59 (51–68)	61 (54–69)
Median HbA1c (%)	6.7 (6.1–7.3)	7.5 (7.2– 8.6)	6.3 (6.0–6.6)
Median months between HbA1c tests (IQR)	13 (10–19)	13 (10–20)	12 (10–19)
Median months between CCMDD enrolment date and baseline HbA1c test date (IQR)	-3 (-13–10)	-4 (-15–6)	-2 (-13–11)
Median number HbA1c tests (IQR; min-max)	2 (2–2; 2–13)	2 (2–2; 2–6)	2 (2–2; 2–13)
Median analysis time in years (IQR; min-max)	4.7(3.8– 4.7; 0.4–4.7)	3.2(2.0–3.9; 0.4–4.7)	4.7(4.7–4.7; 4.7–4.7)

- Of the 695 patients→ 23 HbA1c tests were in the period of the level 4-5 COVID-19 lockdown in South Africa (i.e. 27th March 2020–1 June 2020).
- The median time between test during the lockdown period was **11.8** (95% CI: 6.4–14.9) versus **12.1**(95% CI: 8.9–20.1) months in lesser level, or non-lockdown periods.

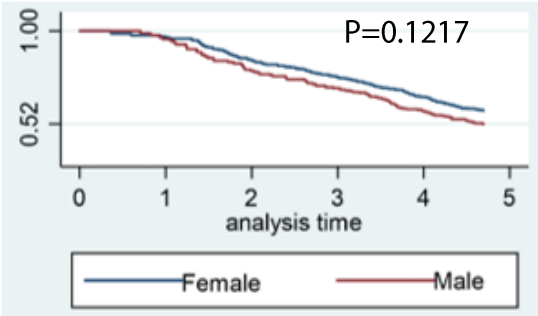
Univariate survival analysis (Kaplan-Meier and log-rank test values) for the CCMDD cohort, eThekwini, KZN, South Africa: April 2018–Dec 2021 (N=695)

Characteristic	Number of cases	Number of sub-optimal events	Time at risk (years)	Incidence rate of sub-optimal glycaemic control per 1000 person-years (95% CI)	25th percentile of survival time (years)†	p-value
Sex						0.1217§
Male	248	95	612.73	155.04 (126.80–189.58)	2.61	
Female	447	147	1 155.89	127.17 (108.19–149.49)	3.16	
Age						0.3238
17–39 years	24	10	68.44	146.11 (78.61–271.55)	3.62	
40–59 years	298	113	740.70	152.60 (126.87–183.45)	2.69	
60–79 years	333	110	857.87	128.22 (106.37–154.57)	2.86	
≥80 years	40	9	101.60	88.58 (46.09–170.25)	3.53	
Type of facility						**0.0257***§
PHC facility[a]	496	180	1180.09	**152.53** (131.80–176.52)	2.91	
Hospital	199	62	588.52	105.35 (82.13–135.12)	3.03	
T2DM-related complication						0.3447
Nephropathy or neuropathy	377	125	969.34	128.95 (108.22–153.66)	2.71	
None recorded	318	117	799.27	146.38 (122.12–175.46)	3.18	
Type of therapy						**0.0006****§
Monotherapy	484	150	1269.52	118.15 (100.68–138.66)	3.41	
Dual-therapy	211	92	499.10	**184.33** (150.27–226.12	2.12	
Comorbidity						0.8315
T2DM[b] alone	86	28	217.91	128.50 (88.72–186.10)	3.18	
T2DM and HIV[c]	39	16	101.36	157.86 (96.71–257.67)	1.92	
T2DM and HPT[d]	490	168	1256.94	133.66 (114.90–155.48)	2.88	
T2DM, HIV and HPT	80	30	192.41	155.91 (109.01–222.99)	3.34	
Months enrolled in CCMDD						0.7485
≤6 months	230	79	609.44	129.63 (103.98–161.61)	2.74	
7–12 months	69	23	180.80	127.21 (84.54–191.43)	3.60	
≥13 months	388	138	957.67	144.10 (121.96–170.26)	2.71	
HbA1c testing frequency adheres to SEMDSA guideline‡						**0.0064****§
Yes	63	9	150.34	59.86 (31.15–115.05)	4.44	
No	632	233	1 618.28	**143.98** (126.63–163.71)	2.86	
Total	**695**	**242**	**1768.62**	**136.83**	**2.88**	

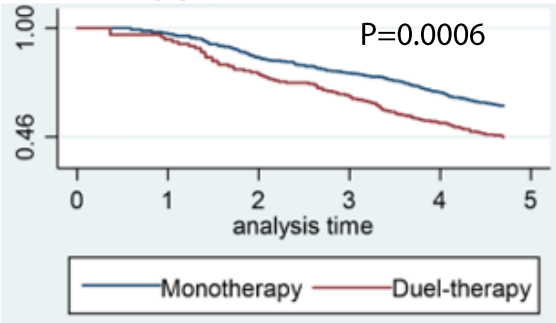
Kaplan-Meier curves for the probability of maintaining optimal glycaemic control for the CCMDD programme cohort, eThekwini, KZN, South Africa: October 2017– June 2022 (n= 695)

Significant predictors: log-rank test p-values <0.25 (Included in final Cox model)

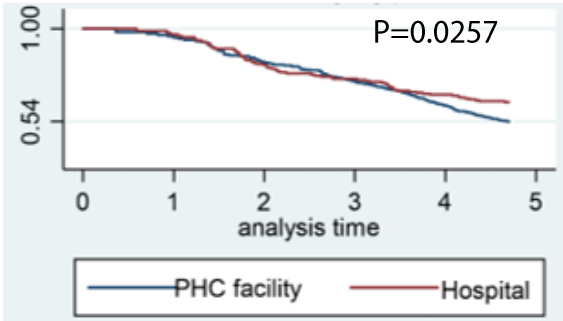
A: Gender



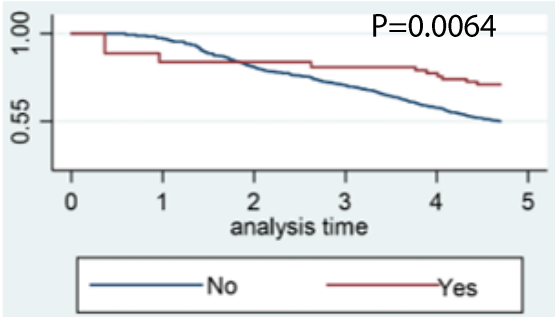
B: Therapy



C: Facility type

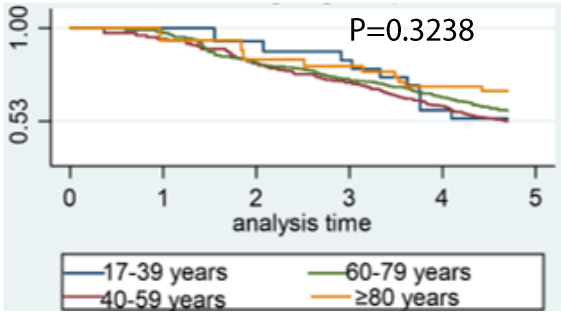


D: Guideline Adherence

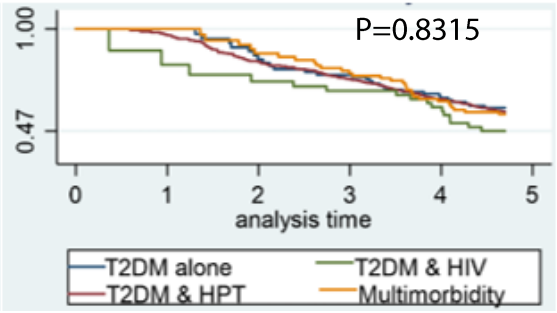


Non-significant: log-rank test with p-values >0.25 (Excluded from final Cox model)

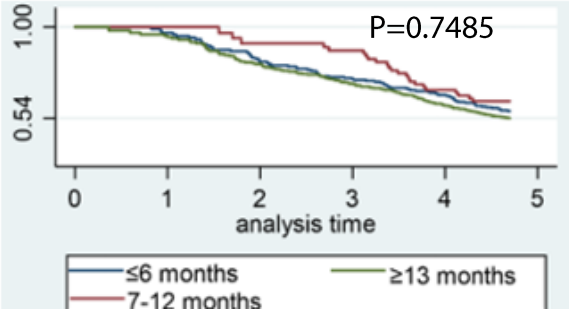
E: Age group



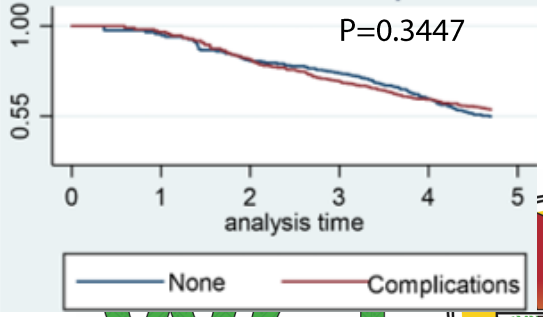
F: Comorbidity



G: Enrolment duration



H: T2DM-related complications



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Multivariable Cox regression model for factors associated with developing sub-optimal glycaemic control for the Central Chronic Medicines Dispensing and Distribution programme cohort, eThekwini, KZN, South Africa: 19th April 2018-30th Dec 2021(N=695)

Characteristic	Co-efficient	Adjusted Hazard ratio (95% CI)	p-value
Main model			
Gender			
Male	0.194 (-0.064–0.453)	1.214 (0.938–1.572)	0.141
Female	1	1	
Facility type			
Type of therapy			
Monotherapy	1	1	
Dual-therapy	0.407 (0.147–0.668)	1.503 (1.158–1.950)	0.002**
HbA1c testing frequency adheres to SEMDSA guideline†			
Yes	-0.770 (-1.441– -0.100)	0.463 (0.237–0.905)	0.024*
No	1	1	
Time-varying coefficient model			
Facility type x ln(t)			
PHC	1	1	
Hospital	-0.690 (-1.313– -0.065)	0.502 (0.269–0.937)	0.031*

The aHR for those using dual therapy was 50% higher than the hazard among those using monotherapy

Multivariable Cox regression model for factors associated with developing sub-optimal glycaemic control for the Central Chronic Medicines Dispensing and Distribution programme cohort, eThekwini, KZN, South Africa: 19th April 2018-30th Dec 2021(N=695)

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Female	1	1	
Facility type			
PHC	1	1	
Hospital	0.372 (-0.276–1.020)	1.450 (0.759–2.771)	0.261

The aHR for those who were tested in accordance with testing frequency guidelines was 54% lower than the hazard among those who weren't testing in accordance with guidelines

HbA1c testing frequency adheres to SEMDSA guideline†			
Yes	-0.770 (-1.441– -0.100)	0.463 (0.237–0.905)	0.024*
No	1	1	
Time-varying coefficient model			
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Time-varying coefficient model			
Facility type x ln(t)			
PHC	1	1	
Hospital	-0.690 (-1.313– -0.065)	0.502 (0.269–0.937)	0.031*

The combined effect was 27% decreased hazard for those attending hospitals vs. PHC (calculated using the main model and time-varying coefficient (i.e., 1- $e^{(0.372-0.690)}$) = 0.272)

Discussion

1. Only 27% of patients receiving oral diabetes medication through the CCMDD, in eThekwini, had **optimal glycaemic control** (i.e. not meeting 50% target for those controlled on T2DM medication)

→ Similarly, only 29% of CCMDD-enrolled patients in Tshwane, Gauteng province (2019) had optimal glycaemic control[10]

2. Adherence to SEMDSA guidelines for HbA1c testing frequency was poor in this cohort

- 81% of the cohort had **no HbA1c** tests performed over the 3-year study period
- The median interval between tests was 12 (optimally-controlled) & 13 months (sub-optimally controlled)

→ Similarly, in Gauteng Province (2015–2018) a study of HbA1c laboratory data (NHLS) found that 74% of patients with an initial HbA1c had no follow-up results & HbA1c testing intervals didn't comply with SEMDSA guidelines[9]

- Adherence was protective against developing sub-optimal control

→Similarly, to findings from studies in Australian (2013–2018) and the UK (2014)[11,12]

3. Patients prescribed dual-therapy had a higher hazard for developing sub-optimal glycaemic control

→ Similarly, a study in Lebanon that found that PLWT2DM who used dual-therapy had twice the odds of being uncontrolled, compared to those using mono-therapy[13]

4. Those attending hospitals, versus PHC, were at an increased hazard for developing sub-optimal control at baseline, but this effect decreased over time

→ Similarly in Gauteng (2015–2018) → those attending hospital vs PHC facilities was protectively associated optimal control for those that began sub-optimally controlled[9]

Recommendations for CCMDD & Department of Health

- Monitor glycaemic control status of CCMDD patients within the programme by creating a data feedback loop between CCMDD and NHLS CDW:

  ∴ patients who change state from optimal to sub-optimal can be flagged to exit the programme

  ∴ allowing for intensification of clinical visits from 6 to 3-monthly

  ∴ creating more opportunities to intervene, educate & prevent clinical and patient inertia

  ∴ improving glycaemic control & T2DM-related health outcomes

- Build management into CCMDD by adding point of care testing (i.e. HbA1c or FPG) at CCMDD pick-up points ∴ off-loading over-burdened facilities

- Add a self-efficacy score as an enrolment criterion, to assist the CCMDD programme to determine those who are suitable for enrollment

- Train health care providers on SEMDSA guidelines for T2DM care

- Perform facility-based audits & further qualitative research studies to establish if barriers to care exist for HbA1c testing at eThekwini public healthcare facilities

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WITS School of Public Health

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

Thank you

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Limitations & Strengths

Limitations

- There were limited HbA1c test results available in the CDW for the study time period, thus the survival analysis results may need to be interpreted with caution.

- Factors known to be associated with T2DM were not available in either dataset & were not able to be included in the analysis, which may cause unaccounted for confounding or modifying effects, which may have distorted our results
  e.g. race, other co-morbid conditions, obesity measures, lifestyle factors, socioeconomic factors, genetic factors, health literacy level, medication compliance, self-efficacy, & duration of diabetes

Strengths

- Good representation for the general CCMDD-enrolled population in eThekwini- we used data from T2DM patients spread across 13 hospitals and 107 PHC facilities in eThekwini

- Despite the CCMDD being a large public health programme, this was the first time CCMDD-enrolled patients were linked to their clinical HbA1c results, to monitor and evaluate glycaemic control over time

Description of HbA1c samples for the CCMD programme cohort receiving oral hypoglycaemic medication for T2DM, eThekwini, KZN, South Africa: 19th April 2018-30th Dec 2021 (N = 7 960)

	Number of HbA1c tests per patient			
Characteristic	**1**	**2**	**≥3†**	**Total**
HbA1c samples N (%)	7 960 (65.8%)	2 646 (21.9%)	1 496 (12.4%)	12 102 (100%)
Sub-optimally controlled N (%)	5 984 (75.2%)	1 964 (74.2%)	1 181 (78.9%)	9 129 (75.4%)
Median HbA1c result (IQR)	8.1 (7.0–10.0)	8.1 (6.9–9.9)	8.4 (7.1–10.1)	8.2 (7.0- 10.0)
Median months between 1st HbA1c test & CCMDD enrolment date (IQR)	4 (-8–18)	12 (-1– 26)	18 (5–31)	7 (-6–22)
Median months between HbA1c tests (IQR)	-	12 (8–19)	9 (6–13)	12 (8–18)
Median age in years (IQR)	60 (52–67)	60 (52–67)	60 (52–67)	60 (52–67)

- For the 7 960 CCMDD-enrolled patients, there were 12 102 HbA1c tests performed
- 66% (7 960/12 102) were 1st observations, 22% (2 646/ 12 102) were 2nd observations and 12% (1 496/ 12 102) were ≥ 3rd observations for a unique patient.
- Overall: median age of patients was 60 years (IQR: 52-67), the median interval between tests = 12 months (IQR: 8–18), the median HbA1c was 8.2% (IQR: 7.0–10.0).

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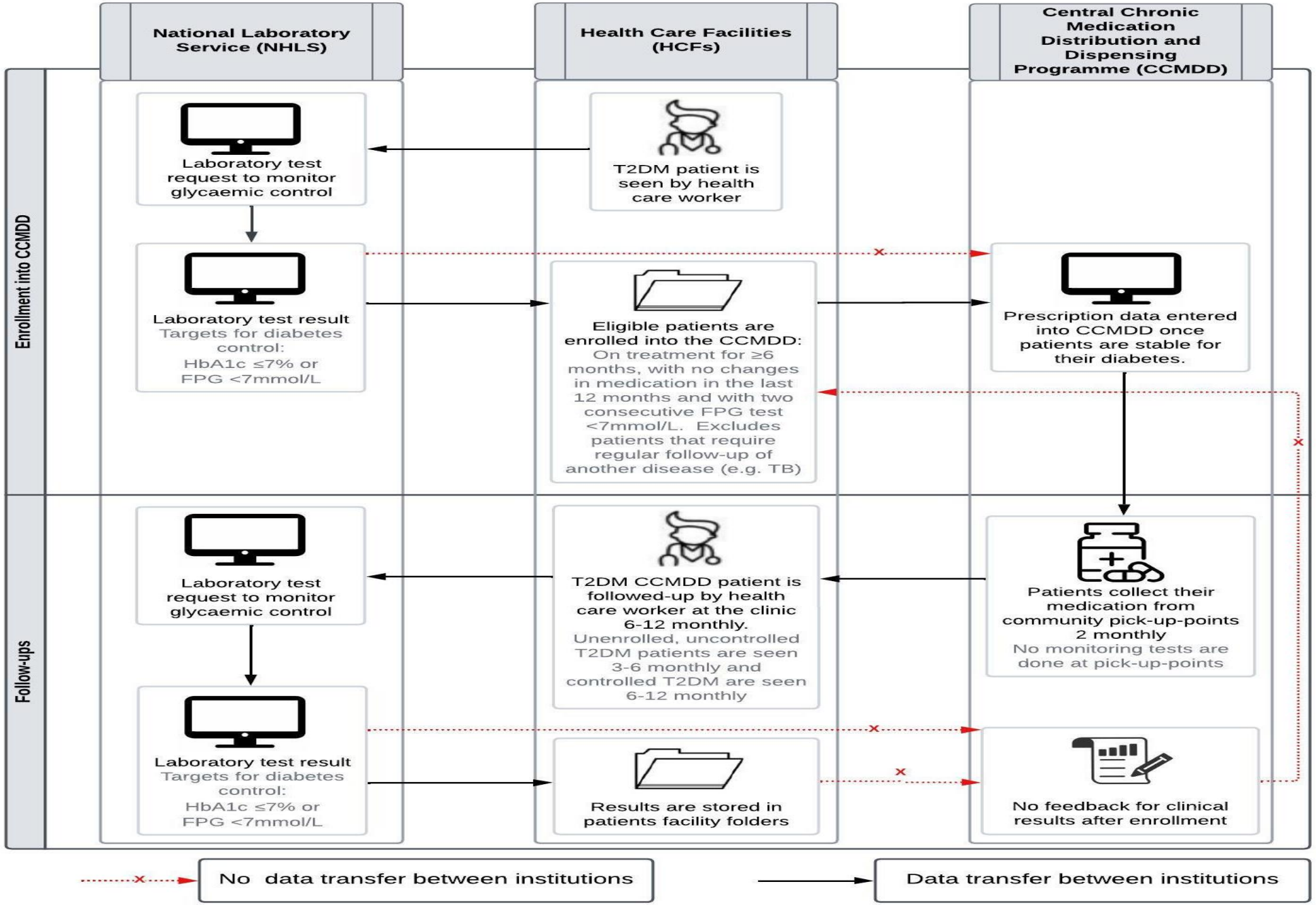
National Laboratory Service (NHLS)
Health Care Facilities (HCFs)
Central Chronic Medication Distribution and Dispensing Programme (CCMDD)
Enrollment into CCMDD
Follow-ups
Laboratory test request to monitor glycaemic control
T2DM patient is seen by health care worker
Laboratory test result
Targets for diabetes control:
HbA1c ≤7% or
FPG <7mmol/L
Eligible patients are enrolled into the CCMDD:
On treatment for ≥6 months, with no changes in medication in the last 12 months and with two consecutive FPG test <7mmol/L. Excludes patients that require regular follow-up of another disease (e.g. TB)
Prescription data entered into CCMDD once patients are stable for their diabetes.
Laboratory test request to monitor glycaemic control
T2DM CCMDD patient is followed-up by health care worker at the clinic 6-12 monthly.
Unenrolled, uncontrolled T2DM patients are seen 3-6 monthly and controlled T2DM are seen 6-12 monthly
Patients collect their medication from community pick-up-points 2 monthly
No monitoring tests are done at pick-up-points
Laboratory test result
Targets for diabetes control:
HbA1c ≤7% or
FPG <7mmol/L
Results are stored in patients facility folders
No feedback for clinical results after enrollment
No data transfer between institutions
Data transfer between institutions