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Quality of prescribing in chronic kidney disease and type 2 diabetes

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Appendix 4: Supplemental data chapter 5

Table S5.1: Results of all rounds of the RAND/UCLA method

List of indicators (<i>italic reflects indicators removed during consensus meeting, between brackets reflects the original numbering</i>)	Round 1					
	Correct reflection of guidelines	Correct definitions				
		A	B	C	D	E
<i>Glucose lowering drugs</i>						
<i>(1A.) The percentage of patients with T2D that reached the target level for HbA_{1c} (≤53 mmol/mol) without glucose lowering drugs</i>	7.5-	9+	8-	9+		
<i>(1B.) The percentage of patients with T2D between 18 and 55 years that reached the target level for HbA_{1c} (≤53 mmol/mol) with glucose lowering drugs</i>	8-	5.5-	8+	9+		
<i>(1C.) The percentage of patients with T2D between 55 and 70 years that reached the target level for HbA_{1c} (≤53 mmol/mol) with glucose lowering drugs</i>	8.5+	6.5-	8+	9+		
1. (2.) The percentage of patients with T2D between 18 and 70 years with an elevated HbA _{1c} level (>53 mmol/mol) in the previous year, that started with glucose lowering drugs or that reached the HbA _{1c} target level (≤53 mmol/mol)	8+	7+	7.5-	7.5-	9+	
2. (3.) The percentage of patients with T2D between 18 and 70 years treated with monotherapy metformin and with an elevated HbA _{1c} level (>53 mmol/mol) in the previous year, that is intensified with glucose lowering drugs or that reached the HbA _{1c} target level (≤53 mmol/mol)	8-	8+	6.5-	6.5-	8.5+	9+
3. (4A.) The percentage of patients with T2D between 18 and 70 years treated with two or more non-insulin glucose lowering drugs and with an elevated HbA _{1c} level (>53 mmol/mol) in the previous year, that started with insulin or that reached the HbA _{1c} target level (≤53 mmol/mol)	8+	9+	8-	7.5-	8.5+	9+
<i>4B. The percentage of patients with T2D 70 years or older and a diabetes duration of less than 10 years treated with two or more non-insulin glucose lowering drugs and with an elevated HbA_{1c} level (>58 mmol/mol) in the previous year, that started with insulin or that reached the HbA_{1c} target level (≤58 mmol/mol)</i>	8+	9+	8+	8+	8.5+	9+
<i>4C. The percentage of patients with T2D 70 years or older and a diabetes duration of 10 or more years treated with two or more non-insulin glucose lowering drugs and with an elevated HbA_{1c} level (>64 mmol/mol) in the previous year, that started with insulin or that reached the HbA_{1c} target level (≤64 mmol/mol)</i>	8+	9+	8+	8+	8.5+	8.5+
4. The percentage of patients with T2D 18 years or older that started with metformin among all starters of oral glucose lowering drugs						

Consensus meeting		Round 3		
Health gain for patient		Correct reflection of guidelines	Health gain for patient	Necessary aspect
6.5-	Removed			
7+	Removed			
7+	Removed			
7+	· Age restriction to 70 years	9+	8+	7.5+
7+	· Age restriction to 70 years	9+	8+	8+
7.5+	No changes	8.5+	8+	8+
6.5-	Removed			
7+	Removed			
	New	9+	8+	8+

A

Table S5.1: Results of all rounds of the RAND/UCLA method (continued)

List of indicators (<i>italic</i> reflects indicators removed during consensus meeting, between brackets reflects the original numbering)	Round 1					
	Correct reflection of guidelines	Correct definitions				
		A	B	C	D	E
5. (5.) The percentage of patients with T2D 18 years or older treated with glucose lowering drugs that is prescribed metformin	8+	9+	9+	9+		
6. The percentage of patients with T2D 18 years or older treated with metformin that started with an SU-derivative among all starters of a second non-insulin glucose lowering drugs						
6. (6.) The percentage of patients with T2D 18 years or older treated with two non-insulin glucose lowering drugs that is prescribed a combination of metformin and an SU-derivative	7.5+	9+	9+	9+	9+	
7. (7.) The percentage of patients with T2D 18 years or older that started with gliclazide among all starters of an SU-derivative	8-	9+	9+	9+		
<i>Lipid lowering drugs</i>						
8. (11.) The percentage of patients with T2D between 55 and 80 years that is prescribed a statin	5.5-	8.5+	9+	3-		
9. (12.) The percentage of patients with T2D between 18 and 80 years with an elevated LDL-cholesterol level (>2.5 mmol/l) in the previous year, that started with a statin or that reached the LDL-cholesterol target level (≤2.5 mmol/l)	5.5-	7.5-	3-	9+	9+	
10. (13.) The percentage of patients with T2D between 18 and 80 years treated with simvastatin and with an elevated LDL-cholesterol level (>2.5 mmol/l) in the previous year, that switched to atorvastatin or rosuvastatin or that reached the LDL-cholesterol target level (≤2.5 mmol/l)	8.5+	9+	7+	9+	9+	
14. The percentage of patients with T2D that started with simvastatin among all starters with statins	8.5+	9+	9+	8.5+		
<i>Blood pressure lowering drugs</i>						
12A (15A.) The percentage of patients with T2D between 18 and 55 years with an elevated systolic blood pressure (>160 mmHg) in the previous year, that started with antihypertensives or that reached the systolic blood pressure target level (≤160 mmHg)	8+	8.5+	5.5-	9+	9+	
12B. (15B.) The percentage of patients with T2D between 55 and 70 years with an elevated systolic blood pressure (>140 mmHg) in the previous year, that started with antihypertensives or that reached the systolic blood pressure target level (≤140 mmHg)	8+	8.5+	8.5-	9+	9+	

Consensus meeting		Round 3		
Health gain for patient		Correct reflection of guidelines	Health gain for patient	Necessary aspect
8+	<ul style="list-style-type: none"> Old indicator 5 was split in two indicators, one on starters of oral glucose lowering drugs (ind 4) and one on prevalent use of metformin in all users of glucose lowering drug (ind 5) 	9+	8.5+	8+
	New	9+	6.5+	7+
5.5-	No changes	9+	7+	7.5+
6.5-	<ul style="list-style-type: none"> Changed to starters of a SU-derivative 	9+	8+	8+
8.5+	<ul style="list-style-type: none"> Age restriction to 55-80 years 	8.5+	9+	9+
8+	<ul style="list-style-type: none"> Age restriction to younger than 80 years Removed criteria 'cardiovascular risk' 	8.5+	8.5+	8+
7+	<ul style="list-style-type: none"> Age restriction to younger than 80 years Removed criteria 'cardiovascular risk' 	8+	7.5+	7.5+
6-	Removed			
8.5+	<ul style="list-style-type: none"> Target level of 140 mmHg changed into 160 mmHg 	8.5+	9+	9+
9+	<ul style="list-style-type: none"> Age restricted to younger than 70 years 	8.5+	8+	8.5+

Table S5.1: Results of all rounds of the RAND/UCLA method (continued)

List of indicators (<i>italic</i> reflects indicators removed during consensus meeting, between brackets reflects the original numbering)	Round 1					
	Correct reflection of guidelines	Correct definitions				
		A	B	C	D	E
<i>15C.</i> The percentage of patients with T2D 80 years or older with an elevated systolic blood pressure (>160 mmHg) in the previous year, that started with antihypertensives or reached the blood pressure target level (≤160 mmHg)	8+	9+	8.5+	6.5-	9+	
11. The percentage of patients with T2D between 18 and 70 years with an elevated systolic blood pressure (>140 mmHg) in the previous year, that started with antihypertensives or reached the systolic blood pressure target level (≤140 mmHg)						
12. (16.) The percentage of patients with T2D between 18 and 70 years treated with monotherapy antihypertensives and with an elevated systolic blood pressure (>140 mmHg) in the previous year, that is intensified with antihypertensives or that reached the systolic blood pressure target level (≤140 mmHg)	8+	9+	9+	7.5+	9+	
<i>Albuminuria lowering drugs</i>						
13. (18.) The percentage of patients with T2D 18 years or older treated with two or more antihypertensives that is prescribed an ACE-i or ARB	9+	9+	9+	9+		
14. (19.) The percentage of patients with T2D between 18 and 70 years with micro- or macro-albuminuria [†] in the previous year, that started with an ACE-i or ARB or that returned to normo-albuminuria [†]	8.5+	7.5+	9+	9+	9+	
15. (20.) The percentage of patients with T2D 18 years or older treated with antihypertensives and with micro- or macro-albuminuria [†] that is prescribed an ACE-i or ARB	8+	9+	9+	9+	9+	
16. The percentage of patients with T2D 18 years or older that started with an ACE-i among all patients that started with RAAS treatment						
<i>Medication safety</i>						
17. (8.) The percentage of patients with T2D 18 years or older treated with SU-derivatives that is prescribed glibenclamide	9+	9+	9+	9+		
18. (9.) The percentage of patients with T2D 18 years or older with an eGFR <30 ml/min/1.73m ² that is prescribed metformin	8.5+	9+	9+	8.5+		

Consensus meeting		Round 3		
Health gain for patient		Correct reflection of guidelines	Health gain for patient	Necessary aspect
6.5-	Removed			
	New, combination of 12A en 12B after round 3	8+	8+	8+
8+	· Age restricted to younger than 70 years	8+	8+	8+
7.5+	No changes	9+	8.5+	8.5+
7.5+	Age restriction to younger than 70 years	9+	8.5+	9+
8+	No changes	9+	8.5+	9+
	New	9+	7+	7+
8+	No changes	9+	9+	8.5+
7+	No changes	9+	8+	8.5+

Table S5.1: Results of all rounds of the RAND/UCLA method (continued)

List of indicators (<i>italic</i> reflects indicators removed during consensus meeting, between brackets reflects the original numbering)	Round 1					
	Correct reflection of guidelines	Correct definitions				
		A	B	C	D	E
19. The percentage of patients with T2D 80 years or older with a normal HbA _{1c} level (<53 mmol/mol) that is prescribed two or more glucose lowering drugs						
<i>10. The percentage of patients with T2D 18 years or older that is prescribed a combination of pioglitazone and insulin</i>	9+	9+	9+	9+		
<i>17. The percentage of patients with T2D 80 years or older and a systolic blood pressure <150 mmHg that is intensified with antihypertensives</i>	8+	9+	9+	9+		
<i>21. The percentage of patients with T2D 18 years or older with RAAS treatment or diuretics which serum potassium was measured yearly</i>	9+	9+	9+	9+	9+	
20. (22.) The percentage of patients with T2D 18 years or older treated with RAAS inhibitors that is prescribed a combination of an ACE-i and ARB (dual RAAS blockade)	9+	9+	9+			
<i>Vaccination</i>						
<i>23. The percentage of patients with T2D 18 years or older that is vaccinated for the flu</i>	9+	9+	9+			
<i>Therapy adherence</i>						
<i>24. The percentage of patients with T2D 18 years or older that received less than three repeat prescriptions for glucose lowering drugs</i>	6-	9+	9+			
<i>25. The percentage of patients with T2D 18 years or older that received less than three repeat prescriptions for lipid lowering medication</i>	6-	9+	9+			
<i>26. The percentage of patients with T2D 18 years or older that received less than three repeat prescriptions for antihypertensives</i>	6.5-	8.5+	9+			

T2D: type 2 diabetes; HbA_{1c}: glycated haemoglobin; SU-derivative: sulphonylurea derivatives; LDL-cholesterol; low-density lipoprotein-cholesterol; ACE-i: angiotensin-converting-enzyme inhibitor; ARB: angiotensin-II-receptor-blocker; RAAS: renin-angiotensin-aldosterone system; eGFR: estimated glomerular filtration rate.

† Micro/macro-albuminuria is defined as an albumin/creatinine ratio ≥2.5 mg/mmol for males and ≥3.5 mg/mmol for females. Normo-albuminuria is defined as an albumin/creatinine ratio <2.5 mg/mmol for males and <3.5 mg/mmol for females.

Consensus meeting		Round 3		
Health gain for patient		Correct reflection of guidelines	Health gain for patient	Necessary aspect
	New	9+	8.5+	9+
8+	Removed			
8+	Removed			
8+	Removed			
7.5+	· Denominator changed into RAAS treatment (regardless the amount)	9+	9+	9+
6-	Removed			
5-	Removed			
5-	Removed			
4-	Removed			

A

Table S5.2: Operational definitions for selected prescribing quality indicators

Overall	Operationalization
Age	Determined on 1 January 2012
Gender	Determined on 1 January 2012
T2D	Determined on 1 January 2012: diagnosis code T90 (ICPC)
Indicators	
<i>Glucose lowering drugs</i>	
1. The percentage of patients with T2D between 18 and 70 years with an elevated HbA _{1c} level in the previous year, that started with glucose lowering drugs or that reached the HbA _{1c} target level	<ul style="list-style-type: none"> • Elevated HbA_{1c}: most recent measurement in previous year (2011) >53 mmol/mol • Target level HbA_{1c}: most recent measurement in current year (2012) ≤53 mmol/mol • Start with glucose lowering drugs: <ul style="list-style-type: none"> o No prescriptions (ATC codes: A10A, A10B) in (last 4 months of) previous year (2011) and o ≥1 prescription (ATC codes: A10A, A10B) in (last 4 months of) current year (2012)
2. The percentage of patients with T2D between 18 and 70 years treated with monotherapy metformin and with an elevated HbA _{1c} level in the previous year, that is intensified with glucose lowering drugs or that reached the HbA _{1c} target level	<ul style="list-style-type: none"> • Elevated HbA_{1c}: most recent measurement in previous year (2011) >53 mmol/mol • Target level HbA_{1c}: most recent measurement in current year (2012) ≤53 mmol/mol • Metformin monotherapy: ≥1 prescription (ATC code: A10BA02) in (last 4 months of) previous year (2011) without any prescription for A10A, A10BB, A10BD, A10BF, A10BG, A10BH, A10BX in (last 4 months of) previous year (2011) • Intensified treatment: ≥1 prescriptions (ATC codes: A10A, A10BA02, A10BB, A10BD, A10BF, A10BG, A10BH, A10BX) in (last 4 months of) current year (2012)
3. The percentage of patients with T2D between 18 and 70 years treated with two or more non-insulin glucose lowering drugs and with an elevated HbA _{1c} level in the previous year, that started with insulin or that reached the HbA _{1c} target level	<ul style="list-style-type: none"> • Elevated HbA_{1c}: most recent measurement in previous year (2011) >53 mmol/mol • Target level HbA_{1c}: most recent measurement in current year (2012) ≤53 mmol/mol • Two or more non-insulin glucose lowering drugs: ≥1 prescription for ≥2 drug classes (ATC codes: A10BA, A10BB, A10BF, A10BG, A10BH, A10BX) or ≥1 prescription for drug class (ATC code: A10BD) in (last 4 months of) previous year (2011) • Start with insulin: <ul style="list-style-type: none"> o No prescriptions (ATC code: A10A) in (last 4 months of) previous year (2011) and o ≥1 prescription (ATC code: A10A) in (last 4 months of) current year (2012)

Table S5.2: Operational definitions for selected prescribing quality indicators (continued)

Overall	Operationalization
4. The percentage of patients with T2D 18 years or older that started with metformin among all starters of oral glucose lowering drugs (exclusion criterion: eGFR <30 ml/min/1.73 m ²)	<ul style="list-style-type: none"> • Start with metformin: <ul style="list-style-type: none"> o No prescriptions (ATC code: A10BA02) in (last 4 months of) previous year (2011) and o ≥1 prescription (ATC code: A10BA02) in (last 4 months of) current year (2012) • Start with oral glucose lowering drugs: <ul style="list-style-type: none"> o No prescriptions (ATC code: A10B) in (last 4 months of) previous year (2011) and o ≥1 oral glucose lowering drug prescriptions (ATC code: A10B) in (last 4 months of) current year (2012) • eGFR <30 ml/min/1.73 m² based on CKD-EPI formula using most recent serum creatinine measurement in current year (2012)
5. The percentage of patients with T2D 18 years or older treated with glucose lowering drugs that is prescribed metformin (exclusion criterion: eGFR <30 ml/min/1.73m ²)	<ul style="list-style-type: none"> • Metformin treatment: ≥1 prescription (ATC codes: A10BA02, A10BD02, A10BD03, A10BD05, A10BD07, C10BD08, A10BD10, A10BD11, A10BD13, A10BD14, A10BD15, A10BD16, A10BD17, A10BD18) in (last 4 months of) current year (2012) • Glucose lowering drugs: ≥1 prescription (ATC codes: A10A, A10B) in (last 4 months of) current year (2012) • eGFR <30 ml/min/1.73 m² based on CKD-EPI formula using most recent serum creatinine measurement in current year (2012)
6. The percentage of patients with T2D 18 years or older treated with two non-insulin glucose lowering drugs that is prescribed a combination of metformin and an SU-derivative (exclusion criterion: eGFR <30 ml/min/1.73m ²)	<ul style="list-style-type: none"> • Metformin treatment: ≥1 prescription (ATC codes: A10BA02, A10BD02, A10BD03, A10BD05, A10BD07, A10BD08, A10BD10, A10BD11, A10BD13, A10BD14, A10BD15, A10BD16, A10BD17, A10BD18, A10BD20) in (last 4 months of) the current year (2012) • SU-derivate treatment: ≥1 prescription (ATC codes: A10BB, A10BD02, A10BD04, A10BD06) in (last 4 months) of the current year (2012) • Two non-insulin glucose lowering drugs: <ul style="list-style-type: none"> o ≥1 prescription for 2 drug classes (ATC codes: A10BA, A10BB, A10BF, A10BG, A10BH, A10BX) or o ≥1 prescription for drug class (ATC code: A10BD) in (last 4 months of) current year (2012) • eGFR < 30 ml/min/1.73m² based on CKD-EPI formula using most recent serum creatinine measurement in current year (2012)

Table S5.2: Operational definitions for selected prescribing quality indicators (continued)

Overall	Operationalization
7. The percentage of patients with T2D 18 years or older that started with gliclazide among all starters of an SU-derivative	<ul style="list-style-type: none"> • Start SU-derivate: <ul style="list-style-type: none"> o No prescriptions (ATC codes: A10BB, A10BD02, A10BD04, A10BD06) in (last 4 months of) previous year (2011) and o ≥ 1 prescription (ATC codes: A10BB, A10BD02, A10BD04, A10BD06) in (last 4 months of) current year (2012) • Gliclazide therapy: ≥ 1 prescription (ATC code: A10BB09) in (last 4 months of) current year (2012)
<i>Lipid lowering drugs</i>	
8. The percentage of patients with T2D between 55 and 80 years that is prescribed a statin	<ul style="list-style-type: none"> • Statin treatment: ≥ 1 prescription (ATC code: C10AA) in (last 4 months of) current year (2012)
9. The percentage of patients with T2D between 18 and 80 years with an elevated LDL-cholesterol level in the previous year, that started with a statin or that reached the LDL-cholesterol target level	<ul style="list-style-type: none"> • Elevated LDL-cholesterol: most recent measurement in previous year (2011) >2.5 mmol/l • Target level LDL-cholesterol: most recent measurement in current year (2012) ≤ 2.5 mmol/l • Start statin: <ul style="list-style-type: none"> o No prescriptions (ATC code: C10AA) in (last 4 months of) previous year (2011) and o ≥ 1 prescription (ATC code: C10AA) in (last 4 months of) current year (2012)
10. The percentage of patients with T2D between 18 and 80 years treated with simvastatin and with an elevated LDL-cholesterol level in the previous year, that switched to atorvastatin or rosuvastatin or that reached the LDL-cholesterol target level	<ul style="list-style-type: none"> • Elevated LDL-cholesterol: most recent measurement in previous year (2011) >2.5 mmol/l • Target level LDL-cholesterol: most recent measurement in current year (2012) ≤ 2.5 mmol/l • Simvastatin therapy: ≥ 1 prescription (ATC codes: C10AA01, C10BA02, C10BA04, C10BX01, C10BX04) in (last 4 months of) previous year (2011) • Atorvastatin therapy: ≥ 1 prescription (ATC codes: C10AA05, C10BA05, C10BX06, C10BX08) in the last 4 months of current year (2012) • Rosuvastatin therapy: ≥ 1 prescription (ATC codes: C10AA07, C10BA06, C10BX05, C10BX07, C10BX09) in (last 4 months of) current year (2012)
<i>Blood pressure lowering drugs</i>	
11. The percentage of patients with T2D between 18 and 70 years with an elevated systolic blood pressure in the previous year, that started with antihypertensives or that reached the systolic blood pressure target level	<ul style="list-style-type: none"> • Elevated systolic blood pressure: most recent measure in previous year (2011) >140 mmHg • Target level systolic blood pressure: most recent measure in current year (2012) ≤ 140 mmHg • Start antihypertensives: <ul style="list-style-type: none"> o No prescriptions (ATC codes: C02, C03, C07, C08, C09) in (last 4 months of) previous year (2011) and o ≥ 1 prescriptions (ATC codes: C02, C03, C07, C08, C09) in (last 4 months of) current year (2012)

Table S5.2: Operational definitions for selected prescribing quality indicators (continued)

Overall	Operationalization
12. The percentage of patients with T2D between 18 and 70 years treated with monotherapy antihypertensives and with an elevated systolic blood pressure in the previous year, that is intensified with antihypertensives or that reached the systolic blood pressure target level	<ul style="list-style-type: none"> · Elevated blood pressure: most recent measure in previous year (2011) >140 mmHg · Target level blood pressure: most recent measure in current year (2012) ≤140 mmHg · Intensified antihypertensive treatment: <ul style="list-style-type: none"> o ≥1 prescription for 2 drug classes (ATC codes: C02, C03, C07, C08, C09, excluding ATC codes for combinations) in (last 4 months of) previous year (2011) or o ≥1 prescription for combinations (ATC codes: C03EA01, C03EA03, C07BB02, C07BB07, C07CA03, C07CB03, C09B, C09D, C09XA52) in (last 4 months of) current year (2012)
<i>Albuminuria lowering drugs</i>	
13. The percentage of patients with T2D 18 years or older treated with two or more antihypertensives that is prescribed an ACE-i or ARB	<ul style="list-style-type: none"> · Two or more antihypertensives: <ul style="list-style-type: none"> o ≥ 1 prescriptions for 2 drug classes (ATC codes: C02, C03, C07, C08, C09, excluding ATC codes for combinations) in (last 4 months of) current year (2012) or o ≥1 prescription for combinations (ATC codes: C03EA01, C03EA03, C07BB02, C07BB07, C07CA03, C07CB03, C09B, C09D, C09XA52) in (last 4 months of) current year (2012) · ACE-i/ARB therapy: ≥1 prescriptions (ATC codes: C09A, C09B, C09C, C09D) in (last 4 months of) current year (2012)
14. The percentage of patients with T2D between 18 and 70 years with micro- or macro-albuminuria in the previous year, that started with an ACE-i or ARB or that returned to normo-albuminuria	<ul style="list-style-type: none"> · Micro- or macro-albuminuria: most recent ACR measurement in previous year (2011): >2.5 mg/mmol for males and >3.5 mg/mmol for females · Normo-albuminuria: most recent ACR measurement in current year (2012): ≤2.5 for males and ≤3.5 for females · Start ACE-i/ARB treatment: <ul style="list-style-type: none"> o No prescriptions (ATC codes: C09A, C09B, C09C, C09D) in (last 4 months of) previous year (2011) and o ≥ 1 prescription (ATC codes: C09A, C09B, C09C, C09D) in (last 4 months of) current year (2012)
15. The percentage of patients with T2D 18 years or older treated with antihypertensives and with micro- or macro-albuminuria that is prescribed an ACE-i or ARB	<ul style="list-style-type: none"> · Micro- or macro-albuminuria: most recent ACR measurement in previous year (2011): >2.5 mg/mmol for males and >3.5 mg/mmol for females · Antihypertensive treatment: ≥1 prescription (ATC codes: C02, C03, C07, C08, C09) in (last 4 months of) current year (2012) · ACE-i/ARB treatment: ≥1 prescription (ATC codes: C02, C03, C07, C08, C09) in (last 4 months of) current year (2012)

Table S5.2: Operational definitions for selected prescribing quality indicators (continued)

Overall	Operationalization
16. The percentage of patients with T2D 18 years or older that started with an ACE-i among all patients that started with RAAS treatment	<ul style="list-style-type: none"> • Start RAAS treatment: <ul style="list-style-type: none"> o No prescriptions (ATC code: C09) in (last 4 months of) previous year (2011) and o ≥ 1 prescription (ATC code: C09) in (last 4 months of) current year (2012) • Start ACE-i treatment: <ul style="list-style-type: none"> o No prescriptions (ATC code: C09A, C09B) in (last 4 months of) current year (2012) and o ≥ 1 prescription (ATC codes: C09A, C09B) in (last 4 months of) current year (2012)
<i>Medication safety</i>	
17. The percentage of patients with T2D 18 years or older treated with SU-derivatives that is prescribed glibenclamide	<ul style="list-style-type: none"> • SU-derivate treatment: ≥ 1 prescriptions (ATC codes: A10BB, A10BD02, A10BD04, A10BD06) in (last 4 months of) current year (2012) • Glibenclamide therapy: ≥ 1 prescriptions (ATC code A10BB01) in (last 4 months of) current year (2012)
18. The percentage of patients with T2D 18 years or older with an eGFR < 30 ml/min/1.73m ² that is prescribed metformin	<ul style="list-style-type: none"> • Metformin treatment: ≥ 1 prescriptions (ATC codes: A10BA02, A10BD02, A10BD05, A10BD07, A10BD08, A10BD10, A10BD11, A10BD13, A10BD14, A10BD15, A10BD16, A10BD17, A10BD18) in (last 4 months of) current year (2012) • eGFR < 30 ml/min/1.73m² based on CKD-EPI formula using last serum creatinin measurement in current year (2012)
19. The percentage of patients with T2D 80 years or older with a normal HbA _{1c} level that is prescribed two or more glucose lowering drugs	<ul style="list-style-type: none"> • Normal HbA_{1c} level: most recent measurement in current year (2012) < 53 mmol/mol • Two or more glucose lowering drugs: <ul style="list-style-type: none"> o ≥ 1 prescription for 2 drug classes (ATC codes: A10A, A10BA, A10BB, A10BF, A10BG, A10BH, A10BX) in (last 4 months of) current year (2012) or o ≥ 1 prescription for drug class (ATC code: A10BD) in (last 4 months of) current year (2012)
20. The percentage of patients with T2D 18 years or older treated with RAAS inhibitors that is prescribed a combination of an ACE-i and ARB (dual RAAS blockade)	<ul style="list-style-type: none"> • RAAS treatment: ≥ 1 prescription (ATC code: C09) in the last 4 months of current year (2012) • Combination ACE-i and ARB: <ul style="list-style-type: none"> o ≥ 1 prescription (ATC codes: C09A, C09B) in (last 4 months of) current year (2012) and o ≥ 1 prescription (ATC codes: C09C, C09D) in (last 4 months of) current year (2012)

T2D: type 2 diabetes; ICPC: International Classification of Primary Care; HbA_{1c}: glycated haemoglobin; ATC: Anatomical Therapeutic Chemical Classification System; eGFR: estimated glomerular filtration rate; CKD-EPI: Chronic Kidney Disease Epidemiology Collaboration; SU-derivative: sulphonylurea derivatives; LDL-cholesterol: low-density lipoprotein-cholesterol; ACE-i: angiotensin-converting-enzyme inhibitor; ARB: angiotensin-II-receptor-blocker; ACR: albumin/creatinine ratio; RAAS: renin-angiotensin-aldosterone system.

A

Table S5.3A: Sensitivity analysis including patients with missing measurements in previous year (2011) in start and intensification indicators in ZODIAC

List of indicators

Glucose lowering drugs

1. The percentage of patients with T2D between 18 and 70 years with an elevated HbA_{1c} level (>53 mmol/mol) in the previous year, that started with glucose lowering drugs or that reached the HbA_{1c} target level (≤53 mmol/mol)
2. The percentage of patients with T2D between 18 and 70 years treated with monotherapy metformin and with an elevated HbA_{1c} level (>53 mmol/mol) in the previous year, that is intensified with glucose lowering drugs or that reached the HbA_{1c} target level (≤53 mmol/mol)
3. The percentage of patients with T2D between 18 and 70 years treated with two or more non-insulin glucose lowering drugs and with an elevated HbA_{1c} level (>53 mmol/mol) in the previous year, that started with insulin or that reached the HbA_{1c} target level (≤53 mmol/mol)

Lipid lowering drugs

9. The percentage of patients with T2D between 18 and 80 years with an elevated LDL-cholesterol level (>2.5 mmol/l) in the previous year, that started with a statin or that reached the LDL-cholesterol target level (≤2.5 mmol/l)
10. The percentage of patients with T2D between 18 and 80 years treated with simvastatin and with an elevated LDL-cholesterol level (>2.5 mmol/l) in the previous year, that switched to atorvastatin or rosuvastatin or that reached the LDL-cholesterol target level (≤2.5 mmol/l)

Blood pressure lowering drugs

11. The percentage of patients with T2D between 18 and 70 years with an elevated systolic blood pressure (>140 mmHg) in the previous year, that started with antihypertensives or that reached the systolic blood pressure target level (≤140 mmHg)
12. The percentage of patients with T2D between 18 and 70 years treated with monotherapy antihypertensives and with an elevated systolic blood pressure (>140 mmHg) in the previous year, that is intensified with antihypertensives or that reached the systolic blood pressure target level (≤140 mmHg)

Albuminuria lowering drugs

14. The percentage of patients with T2D between 18 and 70 years with micro- or macro-albuminuria[†] in the previous year, that started with an ACE-i or ARB or that returned to normo-albuminuria[†]

ZODIAC: Zwolle Outpatient Diabetes project Integrating Available Care; T2D: type 2 diabetes; HbA_{1c}: glycated haemoglobin; LDL-cholesterol: low-density lipoprotein-cholesterol; ACE-i: angiotensin-converting-enzyme inhibitor; ARB: angiotensin-II-receptor-blocker.

ZODIAC without missings (original analysis)					ZODIAC with missings (sensitivity analysis)				
Outcome score (%)	Nominator/denominator	Percentage of eligible patients	N eligible patients needed for comparison	Minimal number of T2D patients needed for reliable comparison	Outcome score (%)	Nominator/denominator	Percentage of eligible patients	N eligible patients needed for comparison	Minimal number of T2D patients needed for reliable comparison
80.9	178/220	0.4	60	15,323	97.1	7,288/7,507	13.2	11	83
66.1	846/1,280	2.3	87	3,821	68.7	1,028/1,496	2.6	83	3,136
42.9	687/1,603	2.8	95	3,335	44.7	777/1,739	3.1	95	3,102
33.1	1,436/4,342	7.6	86	1,113	64.4	9,513/14,773	26.0	89	339
45.5	1,587/3,488	6.1	96	1,552	50.2	2,058/4,099	7.2	97	1,332
63.4	724/1,142	2.0	90	4,435	88.6	7,481/8,441	14.9	39	261
57.1	816/1,428	2.5	95	3,743	58.2	901/1,549	2.7	94	3,429
61.0	326/534	0.9	95	9,719	92.5	7,124/7,700	13.6	27	197

† Micro/macro-albuminuria is defined as an albumin/creatinine ratio ≥ 2.5 mg/mmol for males and ≥ 3.5 mg/mmol for females. Normo-albuminuria is defined as an albumin/creatinine ratio < 2.5 mg/mmol for males and < 3.5 mg/mmol for females.

Table S5.3B: Sensitivity analysis including patients with missing measurements in previous year (2011) in start and intensification indicators in GIANTT

List of indicators

Glucose lowering drugs

1. The percentage of patients with T2D between 18 and 70 years with an elevated HbA_{1c} level (>53 mmol/mol) in the previous year, that started with glucose lowering drugs or that reached the HbA_{1c} target level (≤53 mmol/mol)
2. The percentage of patients with T2D between 18 and 70 years treated with monotherapy metformin and with an elevated HbA_{1c} level (>53 mmol/mol) in the previous year, that is intensified with glucose lowering drugs or that reached the HbA_{1c} target level (≤53 mmol/mol)
3. The percentage of patients with T2D between 18 and 70 years treated with two or more non-insulin glucose lowering drugs and with an elevated HbA_{1c} level (>53 mmol/mol) in the previous year, that started with insulin or that reached the HbA_{1c} target level (≤53 mmol/mol)

Lipid lowering drugs

9. The percentage of patients with T2D between 18 and 80 years with an elevated LDL-cholesterol level (>2.5 mmol/l) in the previous year, that started with a statin or that reached the LDL-cholesterol target level (≤2.5 mmol/l)
10. The percentage of patients with T2D between 18 and 80 years treated with simvastatin and with an elevated LDL-cholesterol level (>2.5 mmol/l) in the previous year, that switched to atorvastatin or rosuvastatin or that reached the LDL-cholesterol target level (≤2.5 mmol/l)

Blood pressure lowering drugs

11. The percentage of patients with T2D between 18 and 70 years with an elevated systolic blood pressure (>140 mmHg) in the previous year, that started with antihypertensives or that reached the systolic blood pressure target level (≤140 mmHg)
12. The percentage of patients with T2D between 18 and 70 years treated with monotherapy antihypertensives and with an elevated systolic blood pressure (>140 mmHg) in the previous year, that is intensified with antihypertensives or that reached the systolic blood pressure target level (≤140 mmHg)

Albuminuria lowering drugs

14. The percentage of patients with T2D between 18 and 70 years with micro- or macro-albuminuria[†] in the previous year, that started with an ACE-i or ARB or that returned to normo-albuminuria[†]

GIANTT: Groningen Initiative to Analyse Type 2 diabetes Treatment; T2D: type 2 diabetes; HbA_{1c}: glycated haemoglobin; LDL-cholesterol: low-density lipoprotein-cholesterol; ACE-i: angiotensin-converting-enzyme inhibitor; ARB: angiotensin-II-receptor-blocker.

GIANTT without missings (original analysis)					GIANTT with missings (sensitivity analysis)				
Outcome score (%)	Nominator/denominator	Percentage of eligible patients	N eligible patients needed for comparison	Minimal number of T2D patients needed for reliable comparison	Outcome score (%)	Nominator/denominator	Percentage of eligible patients	N eligible patients needed for comparison	Minimal number of T2D patients needed for reliable comparison
73.1	174/238	0.9	76	8,353	83.7	497/594	2.3	53	2,326
61.1	618/1,012	3.8	92	2,376	64.4	796/1,236	4.7	89	1,876
38.8	446/1,150	4.4	92	2,088	40.3	512/1,271	4.8	93	1,914
32.1	1,100/3,429	13.0	84	643	35.1	1,610/4,588	17.4	88	502
46.3	1,105/2,389	9.1	96	1,053	54.4	1,873/3,443	13.1	96	729
56.9	562/988	3.8	95	2,511	66.1	1,056/1,597	6.1	87	1,419
55.3	588/1,064	4.0	95	2,350	58.4	832/1,424	5.4	94	1,725
59.5	132/222	0.8	93	10,980	90.4	1,524/1,686	6.4	34	521

† Micro/macro-albuminuria is defined as an albumin/creatinine ratio ≥ 2.5 mg/mmol for males and ≥ 3.5 mg/mmol for females. Normo-albuminuria is defined as an albumin/creatinine ratio < 2.5 mg/mmol for males and < 3.5 mg/mmol for females.

Table S5.4: Sensitivity analysis using any medication in a year instead of prescribed in the last four months of the year in GIANTT

List of indicators

Glucose lowering drugs

1. The percentage of patients with T2D between 18 and 70 years with an elevated HbA_{1c} level (>53 mmol/mol) in the previous year, that started with glucose lowering drugs or that reached the HbA_{1c} target level (≤53 mmol/mol)
2. The percentage of patients with T2D between 18 and 70 years treated with monotherapy metformin and with an elevated HbA_{1c} level (>53 mmol/mol) in the previous year, that is intensified with glucose lowering drugs or that reached the HbA_{1c} target level (≤53 mmol/mol)
3. The percentage of patients with T2D between 18 and 70 years treated with two or more non-insulin glucose lowering drugs and with an elevated HbA_{1c} level (>53 mmol/mol) in the previous year, that started with insulin or that reached the HbA_{1c} target level (≤53 mmol/mol)
4. The percentage of patients with T2D 18 years or older that started with metformin among all starters of oral glucose lowering drugs
5. The percentage of patients with T2D 18 years or older treated with glucose lowering drugs that is prescribed metformin
6. The percentage of patients with T2D 18 years or older treated with two non-insulin glucose lowering drugs that is prescribed a combination of metformin and an SU-derivative
7. The percentage of patients with T2D 18 years or older that started with gliclazide among all starters of an SU-derivative

Lipid lowering drugs

8. The percentage of patients with T2D between 55 and 80 years that is prescribed a statin
9. The percentage of patients with T2D between 18 and 80 years with an elevated LDL-cholesterol level (>2.5 mmol/l) in the previous year, that started with a statin or that reached the LDL-cholesterol target level (≤2.5 mmol/l)
10. The percentage of patients with T2D between 18 and 80 years treated with simvastatin and with an elevated LDL-cholesterol level (>2.5 mmol/l) in the previous year, that switched to atorvastatin or rosuvastatin or that reached the LDL-cholesterol target level (≤2.5 mmol/l)

Blood pressure lowering drugs

11. The percentage of patients with T2D between 18 and 70 years with an elevated systolic blood pressure (>140 mmHg) in the previous year, that started with antihypertensives or that reached the systolic blood pressure target level (≤140 mmHg)
 12. The percentage of patients with T2D between 18 and 70 years treated with monotherapy antihypertensives and with an elevated systolic blood pressure (>140 mmHg) in the previous year, that is intensified with antihypertensives or that reached the systolic blood pressure target level (≤140 mmHg)
-

Last 4 months (original analysis)					Any use (sensitivity analysis)				
Outcome score (%)	Nominator/ denominator	Percentage of eligible patients	N eligible patients needed for comparison	Minimal number of T2D patients needed for reliable comparison	Outcome score (%)	Nominator/ denominator	Percentage of eligible patients	N eligible patients needed for comparison	Minimal number of T2D patients needed for reliable comparison
73.1	174/ 238	0.9	76	8,353	76.6	111/ 145	0.6	70	12,518
61.1	618/ 1,012	3.8	92	2,376	62.7	582/ 928	3.5	90	2,548
38.8	446/ 1150	4.4	92	2,088	40.9	492/ 1,202	4.6	93	2,034
78.7	841/ 1,069	4.1	65	1,688	84.9	685/ 807	3.1	50	1,608
86.3	14,984/ 17,353	65.9	46	69	87.3	15,757/ 18,054	68.6	43	63
87.0	4,865/ 5,589	21.2	44	205	87.9	5,305/ 6,038	22.9	41	179
67.5	666/ 986	3.7	85	2,249	68.0	633/ 931	3.5	84	2,364
71.7	13,123/ 18,301	69.5	78	113	76.2	13,937/ 18,301	69.5	70	101
32.1	1,100/ 3,429	13.0	84	643	33.3	1,013/ 3,040	11.5	86	740
46.3	1,105/ 2,389	9.1	96	1,053	48.4	1,373/ 2,837	10.8	96	891
56.9	562/ 988	3.8	95	2,511	56.9	509/ 894	3.4	95	2,774
55.3	588/ 1,064	4.0	95	2,350	54.2	556/ 1,026	3.9	96	2,447

Table S5.4: Sensitivity analysis using any medication in a year instead of prescribed in the last four months of the year in GIANTT (continued)

List of indicators

Albuminuria lowering drugs

- 13. The percentage of patients with T2D 18 years or older treated with two or more antihypertensives that is prescribed an ACE-i or ARB
- 14. The percentage of patients with T2D between 18 and 70 years with micro- or macro-albuminuria[†] in the previous year, that started with an ACE-i or ARB or that returned to normo-albuminuria[†]
- 15. The percentage of patients with T2D 18 years or older treated with antihypertensives and with micro- or macro-albuminuria[†] that is prescribed an ACE-i or ARB
- 16. The percentage of patients with T2D 18 years or older that started with an ACE-i among all patients that started with RAAS treatment

Medication safety

- 17. The percentage of patients with T2D 18 years or older treated with SU-derivatives that is prescribed glibenclamide
- 20. The percentage of patients with T2D 18 years or older treated with RAAS inhibitors that is prescribed a combination of an ACE-i and ARB (dual RAAS blockade)

GIANTT: Groningen Initiative to Analyse Type 2 diabetes Treatment; T2D: type 2 diabetes; HbA_{1c}: glycated haemoglobin; SU-derivative: sulphonylurea derivatives; LDL-cholesterol: low-density lipoprotein-cholesterol; ACE-i: angiotensin-converting-enzyme inhibitor; ARB: angiotensin-II-receptor-blocker; RAAS: renin-angiotensin-aldosterone system.

† Micro/macro-albuminuria is defined as an albumin/creatinine ratio ≥ 2.5 mg/mmol for males and ≥ 3.5 mg/mmol for females. Normo-albuminuria is defined as an albumin/creatinine ratio < 2.5 mg/mmol for males and < 3.5 mg/mmol for females.

Last 4 months (original analysis)					Any use (sensitivity analysis)				
Outcome score (%)	Nominator/ denominator	Percentage of eligible patients	N eligible patients needed for comparison	Minimal number of T2D patients needed for reliable comparison	Outcome score (%)	Nominator/ denominator	Percentage of eligible patients	N eligible patients needed for comparison	Minimal number of T2D patients needed for reliable comparison
87.4	12,789/ 14,627	55.6	43	77	88.7	13,817/ 15,573	59.2	39	65
59.5	132/ 222	0.8	93	10,980	62.0	124/ 200	0.8	91	11,912
84.5	2,451/ 2,901	11.0	51	457	87.1	2,604/ 2,991	11.4	44	381
70.5	920/ 1,305	5.0	80	1,612	79.9	908/ 1,137	4.3	62	1,431
2.1	163/ 7,859	29.9	781	2,614	2.2	187/ 8,644	32.8	814 [†]	2,476
3.2	502/ 15,714	59.7	1,189	1,991	5.0	835/ 16,657	63.3	74 [‡]	116