RCTs mainly including patients with DM2

Study name registration number Design	**Setting** Place, setting and time	**Population** Inclusion / Exclusion criteria	Characteristics	**Intervention vs. Control** Description with duration	**Outcomes** Primary and secondary	**Results** Longest follow-up period with intervention effects (IG vs. CG) with SD, 95%-CI or p value
Educational strategies						
Abaza 2017 NCT02868320 RCT	Egypt, urban, tertiary care, 03-07/2015	DM2, mobile phone, capable to read SMS or live with someone who could read	n=73 56 % females age (yrs): 51.5±9.2 majority had had diabetes for > 1 yr hypertension: 41.1 % on insulin: 19.2 % DM complication: 80.8 % HbA1c (%): 9.7±2.7	Diabetes awareness program: paper-based educations material plus IG (n=34): daily messages and weekly reminders addressing various diabetes care categories vs. CG (n=39): paper-based educations material Duration: 12 wks.	Primary: change in Hba1C Secondary: Random blood glucose levels, body weight, adherence of treatment and medication, diabetes self-efficacy and knowledge, rate of hospital/ER visits, frequency of measurements, regular exercise, patients confidence in healthcare provider and satisfaction, healthcare provider's reputation	After 3 months: HbA1c (%): • No differences: 8.73 ±1.98 vs. 8.84±2.40, MD_a: 0.290 (-0.402 to 0.983; p = 0.406) • Benefit with IG: 47 vs. 15 % achieved the targeted 1% drop (p = 0.003) Random blood glucose (mg/dl): • No difference: 181±65 vs. 201±87 (p=0.288) Treatment adherence (scores): • Benefit with IG in SCI 3.42±0.48 vs. 2.52±0.49 (p<0.001) and Morisky: 3.76±0.55 vs. 2.74±1.07 (p<0.001) Hospital /ER admission (%): No differences: 0 vs. 10.3 (p=0.118)
Adibe 2013 RCT	Nigeria, urban, tertiary care	DM2, age≥ 18 yrs with oral hypoglycemic and / or insulin therapy no pregnancy	n=220 58 % females age (yrs): 52.6±7.9 duration of diabetes (yrs): 4.7±2.5, 60.5% with diabetes > 5 yrs on insulin: 13.6 % hypertension: 60.5 %	IG (n=110): structured self-care education and training program by pharmacists and nurses vs. CG (n=110): usual / conventional care Duration: 12 months	Primary: incremental cost-utility ratio, net monetary benefit Other: quality of life	After 12 months: Quality of life: • Benefit with IG: 0.86 ± 0.12 vs. 0.64 ± 0.10 (p=0.0001) improved single attributes except "hearing" functioning of the patients Costs: • benefit of $0.76±0.15 vs. $0.64± 0.15 QALY/patient and year; MD: $ 0.12 (0.07 to 0.16) • incremental cost-utility ratio of $571 per QALY
Adjei 2015	Ghana, urban	DM	n=200 64.5% female	IG: (n=100): electronical reminder for	Primary: Compliance with appointment dates	After 6 months: Adherence to appointment schedules

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RCT			age (yrs): < 50 yrs: 63 % > 50 yrs: 37 % fasting glucose (mmol/l): 10.4±3.8	clinical appointments of patients + alert system for abnormal laboratory results vs. CG: (n=100): usual diabetes care, paper based method Duration: 6 months	Other: metabolic risk factors, BMI	(%) Benefit for IG: 97.8 vs. 89.4 (p=0.010) Fasting glucose (mmol/l): Benefit for IG: 8.04±2.14 vs. 8.85±2.63; MD 0.4 (-0.59 to -0.36, p=0.022)
Amendezo 2017 NCT02032108 RCT	Rwanda, urban, tertiary care	DM2>3mths, age>21yrs no pregnancy or severe co-morbid illnesses.	n=251 69.3% females age (yrs): 50.9 ±10.9 BMI (kg/m²): 27.9 (27.0-28.5) duration of diabetes : <10 yrs: 73.7%, >10 yrs: 16.3% HbA1c (%): 8.98±8.6-9.3	IG (n=115): standard care plus monthly lifestyle education sessions of 45 min duration vs. CG (n=108): standard care Duration: 12 months	Primary: difference in HbA1c Secondary: fasting glucose, systolic and diastolic blood pressure, BMI	after 12 months: HbA1c (%): Benefit for IG with median reductions of -1.70 (-2.09 to-1.31) vs. -0.52 (-0.95 to -0.10); MD: -0.72 (-1.14 to -0.30; p< 0.001) Fasting glucose (mmol/L): 6.9 (6.45 to 7.36) vs. 9.02 (8.18 to 9.87) (p<0.001)
Chraibi 2017 NCT01589653 RCT	Egypt, Indonesia, Morocco, Saudi Arabia, Vietnam 05/2012-07/2015	DM2 with diagnosis ≥ 12 months, age≥18 , currently being treated with NPH Insulin for ≥ 3 months + metformin (1000-1500 mg) for ≥ 2 months, HbA1c ≥ 7.0% ≤10%, BMI ≤ 40.0 kg/m^2 no treatment with thiazolidinedione, glucagon-like peptide-1 receptor agonists, pramlintide within the last 3 months , >1 IU/kg NPH insulin daily; previous use of premixed or bolus insulin, > 1 severe hypoglycemic episode during	n=155 74.9 % female age (yrs): 54.5 ±10.0 BMI (kg/m²): 29.05±4.9 HbA1c (%): 8.6 ±0.83 fasting glucose (mmol/L): 8.97 duration of diabetes (yrs): 9.5±5.8 African patients: • Egypt: 25.75 % • Morocco: 27.7 % Diabetic nephropathy / neuropathy / retinopathy (%): 3.2 / 16.1 / 3.2	IG (n=76): patient driven titration of Biphasic insulin aspart 30 twice daily, 3 clinic visits vs. CG (n=79): physician driven titration twice daily, 6 clinic visits Titration in both arms according to the titration protocol bases on self-measured plasma glucose values, measured twice daily on 3 preceding days, telephone contact whenever deemed	Primary: change in HbA1c Secondary: proportion of patients achieving the ADA target of HbA1c <7.0 % and the HbA1c target of <6.5 % after 20 weeks, FPG changes, hypoglycemic episodes,	Change over 5 months: HbA1c (%): • Decreased in both arms with non-inferiority between groups: MD -0.23 (-0.54 to 0.08) • More patients reached HbA1c <7.0%: 40.8 vs. 29.1 %, RR: 1.79 (0.87 to 3.65) and <6.5%: 25 vs. 19 %; RR: 1.52 (0.67 to 3.46) • More patients reached target HbA1c levels without severe or minor hypoglycemic episodes: <7.0%: 38 vs. 27.8 %, RR: 1.52 (0.61 to 3.79), <6.5%: 18 vs. 14.8 %; RR 1.13 (0.36 to 3.52) FPG (mmol/l): • Decreased in both arms with no difference between groups: 0.95±0.28

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		the previous 12 month, impaired kidney or hepatic function, proliferative retinopathy or maculopathy requiring treatment	Macroangiopathy (%): 5.2	necessary Duration: 20 weeks		vs. 0.67±0.28; MD: -0.28 (-1.07 to 0.52) Costs • Less frequent clinic visits to healthcare professionals in IG: 4.8±0.65 vs. 7.5±1.42 visits/patient Complications: • hypoglycemic episodes: no difference: 608.4 vs. 789.2 / 100 patient-years of exposure; RR: 0.74 (0.44; 1.23) treatment-emergent AEs: no difference: 324.2 vs. 302.2 events / 100 patient-years of exposure
Debussche 2018 NCT01485913 RCT	Mali, urban, secondary care, 07/2011-02/2013	DM2, age 30-80 yrs, HbA1c ≥ 8 %, no DM1, severe diabetes complications or concomitant illnesses that threatened their functional or vital prognosis	n=151 76.2% female age (yrs): 52.5±9.8 BMI (kg/m²):28.6±5.4	IG (n=76): peer-led structured patient education received culturally tailored structured patient education (3 courses of 4 sessions) delivered in the community by five trained peer educators vs. CG (n=75): conventional care alone Duration:1 yr	Primary: HbA1c Secondary: anthropometric indicators (weight and BMI, waist circumference), SBP, DBP, anti-diabetic and anti-hypertensive treatment, knowledge score, dietary practices	Change to 12 months HbA1c (%): • Benefit in IG: MD 1.05 % (-1.54;-0.56) vs. -0.15 % (-0.56; 0.26) (p = 0.006)
Essien 2017 PACTR201302 00047835 RCT	Nigeria, urban, tertiary care, 09/2013-05/2014	DM1 or DM2, age: ≥ 18 yrs, HbA1c> 8.5 %, able to engage in moderate exercise, no eye disease that would limit the ability to read	n=118 60.2 % female age (yrs): 52.7±10.5 BMI (kg/m²): 28.9±7.5 HbA1c (%):10.7±1.6 type of diabetes • DM1: 14.4 % • DM2: 85.6 %	IG: (n=59): intensive and systematic disease self-management education programme (invitation and encouragement by clinical staff to attend 12 structured teaching sessions) vs.	Primary: HbA1c	After 6 months: HbA1c (%): 8.4 (8 to 8.9) vs. 10.2 (9.8 to 10.7); MD_a: -1.8 (-2.4 to -1.2); (p < 0.0001)

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				CG (n=59): conventional disease-self-management education Duration: 6 months		
Fairall 2016 ISRCTN20283604 Cluster-RCT	South Africa, urban/rural, primary care, 03/2011 – 11 / 2011	age ≥ 18 yrs , clinics providing service for NCD Patients with DM, hypertension, chronic respiratory disease or depression, with self-reported hypoglycaemic (in case of DM)	n= 38 public sector primary care clinics, 4393 patients, n=1842 with DM 73 % female age (yrs):median, IQR): 52 (42-61) vs. 52 (44-62) BMI (kg/m²): 30±8 HbA1c (%):9 (4-17), in HbA1c in DM≥ 7 %: 77 %	IG (n=2166, 851 with DM): Nurses were trained to use a primary care programme to support and expand nurses`role in NCD care and contains a clinical management tool with enhances prescribing provisions vs. CG (n=2227, 991 with DM): Nurses continued to use the Lung Health and HIV/AIDS approach with usual training Duration: 14 months	Primary (for DM): treatment intensification (addition or increase in dose of metformin and/or sulphonylurea, insulin, ACE-inhibitor, aspirin, statin	over 14 months HbA1c (%): • <7 %: 41 vs. 38 %; RR 1.08 (0.77 to 1.52; p=0.638) • 7-10 %: 69 vs. 55 %; RR 1.30 (1.16 to 1.47; p<0.001) • >10 %: 71 vs. 73 %; RR 0.97 (0.81 to 1.16; p=0.703) Treatment intensification rates* (%): • 57% vs. 50%, RRa: 1.11 (0.99 to 1.26) (p=0.083) for patients with DM
Hailu 2018 NCT03185689 RCT	Ethiopia, urban, 02/2016-10/2017	DM2, age > 18 yrs no DM1 or GDM, pregnant women, severe cognitive or physical impairment, and terminally ill people	n=220 33 % female age (yrs): 54.5±10 BMI (kg/m²):25±4 HbA1c (%):10.5±4	IG (n= 116): Nurse-led disease-management education: 6 sessions, supported with illustrative pictures handbooks and fliers, customized to local conditions by trained nurses vs. CG (n=104): usual follow-up care Duration: 9 months	Primary: patients with target HbA1c (≤ 7 %) Secondary: systolic and diastolic blood pressure, fasting glycose, BMI, waist circumference	Change over 9 months: HbA1c (%): • No difference: 45 % vs. 50 % with target values (p=0.21), MD: 2.88% (-3.85 to -1.92) vs. 2.57% (-3.47 to -1.67) fasting glucose (mg/dl): • Benefit with IG: 36 % vs.25 % with target values, MD: -27 (-45 to -9; p=0.003)

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Labhardt 2011 NCT00744458 Cluster-RCT	Cameroon rural, primary care, 08/2008-02/2010	newly detected adult patients with DM2 and ⁄or hypertension in the catchment area of nurse-led health centres, staffed, equipped and trained to care for DM2 and hypertension	n=33 facilities, 221 patients 64% females age (yrs): 59.8±12.7 diabetes: 15.4 % Overweight (BMI 25-29.9 kg/m^2): 28.5 % Obesity (BMI> 30 kg/m²): 20.4 %	IG 1 (11 centres, n=55): incentive group free treatment for 1 months for patients who regularly attended follow up visits vs. IG 2 (11 centres, n=77): letter group: reminder letters in case of a missed follow-up visit vs. CG (11 centres, n=89): no additional intervention Duration: 12 months	Primary: Patient retention at 1 yr (≥ 12 follow-up visits within 12 months) Secondary: Adherence with timely attendance of follow-up visit schemes and changes in blood pressure and blood glucose levels.	After 12 months: Retention rates (%): • Benefit for IG1 and IG2 vs.CG: 60 vs. 65 vs. 29 %; MD 34 (21 to 46) with no differences between IG1 and IG2; MD -5 (-22 to 12) Loss to follow-up: • Benefit for IG1 and IG2: IG1 vs. CG: HR 0.44 (0.27 to 0.72; p< 0.001) • IG2 vs. CG: HR 0.38 (0.24 to 0.61; p<0.001) Adherence (%): • Benefit for IG1 and IG2: 38 vs. 35 vs. 10; MD 26 (14 to 42), IG1 vs CG: MD 28(13 to 37); IG2 vs. CG: MD 25 (13 to 37) • no difference between IG1 and IG2: MD 3 (-14 to 20) FPG: No differences between groups
Mash 2014 Cluster RCT	South Africa, urban, primary care, 12/2010 -12/2012	DM2 with any therapy attending community health centres in the working class areas of Cape Town Metropole no DM1, dementia, mental illness or acute illness	n=34 public sector community health centres, 1570 patients 73.8% females age (yrs): 56.1±11.6 HbA1c (%): 9.1±2.3	IG (17 health centres, n=710): 4 monthly sessions lasting 60 min with group education about diabetes topics (understanding diabetes and medication, living a healthy lifestyle and preventing complications), delivered by a health promotion officer vs. CG (17 health centres, n=860): usual care: ad hoc advice during consultations and	Primary: improvement of diabetes self-care activities (5 % weight loss, and a 1 % reduction in HbA1c level) Secondary: improved diabetes specific self-efficacy, locus of control, mean blood pressure, mean weight loss, mean waist circumference, mean HbA1c, mean total cholesterol levels, quality of life	After 12 months: HbA1c (%): No differences: 8.4±2.0 vs. 8.8±2.2; MD_a: 0.01 (-0.27 to 0.28; p=0.967) Adherence (self-care activities): No differences in scores of physical activity, use of diet plan or medication, foot care or frequency of smoking Quality of life: No differences in physical functioning, role or social functioning, mental or general health and pain Costs: Incremental cost effectiveness ratio: 1862 Dollar/ QALY gained

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				occasional educational talks in waiting room Duration: 12 months		
Muchiri 2015 RCT	South Africa, rural, primary care, 04/2010-11/2011	DM2, age 40-70 yrs attending community health centres, HbA1c≥ 8 %, blood sugar levels ≥ 10 mmol/l, duration of diabetes ≥ 1 yr no insulin therapy, pregnant women, full time employed	n=82 86.6 % female age (yrs): 59±7.4 BMI(kg/m²): 30.9±6.9 HbA1c (%): 11.1±2.0 duration of diabetes (yrs): 6	IG (n=41): education materials+ 8 weekly group educational sessions about diabetes and nutrition, follow-up sessions+vegetable gardening CG (n=41): education materials Duration: 12 months	Primary: HbA1c Secondary: Other clinical outcomes (BMI, blood pressure and blood lipids), HbA1c, dietary behaviours	over 12 months HbA1c (%): • no difference: 9.8±1.92 vs. 10.4±1.92; MD −0.63 (-0.26 to 1.50; p=0.16)
Owolabi 2019 PACTR201810599931422 RCT	South Africa urban/rural, primary care 07/2018-04/2019	DM, age ≥18 yrs, DM diagnosed at least in the last 6 months, currently receiving treatment at the selected clinics, on stable medication for ≥ 3 months prior to recruitment, uncontrolled glycaemic control, in possession of a mobile phone, able to retrieve and read SMSs and willing to receive SMSs health or mental conditions that could interfere with the study, pregnant or planning to get pregnant within the next 6 months, debilitated or handicapped in such a way that obtaining anthropometric measurements could be	n=216 84.3 % females age (yrs): 60.6±11.6 DM2 (%): 94 Treated with oral pills (%): 75.5 Duration of DM (yrs): 9.1±7.4 Duration of DM treatment (yrs): 8.8±7.2 Hypertension (%): 83.0 Random blood glucose (mmol/L): 14.34±3.9 BMI(kg/m²): 32.2±6.2	IG (n=108): daily SMS text-messaging SMS at an agreed time of the day, according to their needs, care plan and goal with motivational and support messages, advice on lifestyle behaviours (e.g. diets, physical activity, smoking cessation, medication and appointment reminders) vs. CG (n=108): usual diabetes care Duration: 6 months	Primary: Morning random blood sugar Secondary: co-morbid outcomes (hypertension and obesity), obtained through blood pressure measurement, anthropometric measurements (body weight, BMI) acceptability, feasibility	Over 6 months: Blood glucose levels (mmol/L): -1.58±5.29 vs. -1.95±4.69; MD 0.51(-0.8 to 1.82), MD_a 0.26 (-0.81 to 1.32)

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		challenging				
Sodipo 2017 RCT	Nigeria, primary care, 03/2013-11/2013	DM2 ≥ 18 yrs. on antidiabetic medication no patients with emergencies, chronic complications such as nephropathy, neuropathy etc., those already using glucometer	n=120 gender: 50% female age (yrs): 59±10.95 HbA1c (%): 8.7±2.45 fasting glucose (mg/dl): 152±60.9 duration of diabetes (yrs): 50%> 3yrs	IG (n=60): Self-monitoring of blood glucose before and after meals 3 days a week for 12 weeks CG (n=60); non SMBG Duration: 12 wks	HbA1C, fasting glucose	after 3 months: HbA1c (%): No difference: 7.2±2.0 vs.7.7±2.0 (p= 0.174) fasting glucose (mg/dl): No difference: 123.2±35.1 vs. 137.6±50.1 (p=0.087)
Steyn 2013 Cluster-RCT	South Africa, urban, primary care, 1999-2000	public sector primary health care clinics (CHC) with ≥ 25 diabetes and ≥ hypertension patients age ≥15yrs, a documented attendee at the particular CHC with ≥ 4 visits during the previous year for hypertension or diabetes who received treatment for these conditions at each visit no patients being unable to answer a questionnaire	18 community health centres n=1096, of them n= 456 with DM age (yrs): 58.3 ± 11 gender:74 % females BMI (kg/m$^{2)}$: 30.7 ± 6.2 Type of Diabetes: • DM1: 5.8% • DM2: 91.35% uncertain DM type: 2.85%	IG (9 clinics, n=229): introduction of structured clinical record with guidelines prompts after training of doctors in their use and suggestions to incorporate them in regular patient records, contact over 1 year vs. CG (9 clinics, n= 227): usual care with passively disseminated guidelines Duration: 1 year	primary: HbA1C in the diabetes group secondary: uncontrolled glycaemia (HbA1c ≥7%) in the diabetes group.	After 3 months: HbA1c (%): IG: 8.8% vs. 8.8%; MDa -1.0 (-1.1 to -0.9) HbA1c ≥7% (%): no relevant difference: 64.1 vs. 62.6; MD 0.90 (0.53 to 1.53)
Takenga 2014 RCT	Congo, urban	DM2, 35-75 yrs	n=40 20 % females age (yrs): 53.3 ± 10.1 HbA1c (%): 8.63	IG (n=20): self-management of diabetes with Mobil DIAB (telemedical approach) vs. CG (n=20): conventional therapy without telemedical system	primary: HbA1c	after 2 months: HbA1c (%): Benefit for IG: 6.73±1.59 vs. vs. 8.6±1.35 (MD -1.87 (-2.91 to -0.83)

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				Duration: 60 days		
Tawfik 2016 RCT	Egypt, urban, primary care, 05/2015-09/2015	DM2 for ≥ 1 yr, 40-79 yrs attending an outpatient clinic no patients who were already using a similar medication chart, severe or terminal health conditions, or patients with behavioural health issue that could make it difficult to understand the communication	n=255 53.7 % females age (yrs): 55.7±8.35 HbA1c (%): 8.14±1.3 duration of diabetes (yrs): 8.3±1.3	IG (n=127): comprehensive cardiovascular risk communication vs. CG (n=128): standard usual care Duration: 3 months	Primary: HbA1c Secondary: Cardiovascular risk perception, diabetes self-care, cardiovascular risk scores	After 3 months: HbA1c (%): Benefit for IG: 7.5±0.8 vs. 8.12±0.9; MD -0.62 (-0.85 to -0.39) controlled HbA1c (%): 32.7 vs. 29.9
Thuita 2020 PACTR201910518676391 RCT	Kenya Secondary care recruitment 08/2016 - 10/2016	DM2, 20-79 yrs with regular attendance of an outpatient clinic Pregnancy, complications such as renal failure, congestive heart failure, or stroke	n=153 59.5 % females age (yrs). 56±11.6 Family history of DM (%): 46.6 Poor glycaemic control (%) with HbA1c>7%: 77.8 DM for 1-5 yrs (%): 58.2 % Years with DM: 6.7±6.9 Oral medications (%): 82.4 BMP (kg/m2): 27±4.6 HbA1c (%): 8.49±1.9 fasting glucose (mmol/l): 11.0±3.3	IG2 (n=51): nutrition education programme for 2 hrs /week with peer-to-peer support vs. IG1 (n=51): Education programme vs. CG (n=51): Standard care Duration: 8 weeks	Primary: metabolic syndrome prevalence (MetS) Other: anthropometry and clinical data, blood pressure, blood glucose and lipid profile, physical activity levels, food intake	After 6 months: Metabolic syndrome prevalence: lower with IG2: Harmonized criteria:52.1 vs.69.4 vs. 91.3 (p<0.001) WHO: 58.3 vs. 77.6 vs. 89.1 (p=0.003) HbA1c (%): Mean change: no differences -2.04±2.70 vs. 1.48±2.73 vs. -0.73±2.71 High HbA1c: no differences: 47.9 vs. 29.0 vs. 34.8 % fasting glucose (mmol/l): no differences: -2.59±0.66 vs. -2.95±0.64 vs. -1.55±0.68 high fasting glucose: 79.2 vs. 83.7 vs. 91.3 %

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Webb 2015 NCT01275040 Cluster RCT	South Africa, urban, primary care, 06/2010-03/2011	primary health care clinics, patients with clinical diagnosis of DM2 or DM1 for ≥5yrs, age ≥ 18 yrs	n= 12 primary health care clinics n= 599 gender:68.5 % female age (yrs): 57.8±10.5 HbA1c (%): 8.73±2.3 HbA1c ≥ 7 %: 73 % BMI (kg/m$^{2)}$: 30.8±6.7 Typ of diabetes: • DM1: 3.7 %, • DM2: 70.3 % • unknown: 26 % duration of Diabetes: • < 5 yrs: 47.3 % • 5-10 yrs: 22.0 % • > 10 yrs: 20.2 % • unknown: 10.5 %	IG (n=328): mobile screening team visits primary care clinic and provides education and active screening for diabetic complications (foot, kidney, cardiac and renal complications) vs. CG(n=273): no mobile screening team, routine care with similar education for patients. and health care workers Duration: 1 yr	Primary: HbA1c, detected neuropathy, nephropathy and retinopathy, HbA1c categories Secondary: detected complications, referred patients for complication assessment or care, blood pressure and lipid control, costs, LDL cholesterol, creatinine	after 12 months HbA1c (%): no difference: 8.54±2.11 vs. 8,76 ±2.2, MD-0.22 (-0.64, 0.20) screening rate for complications: in IG 60% increase of screening in all complication indicator groups, in both groups testing of HbA1c and renal complications (serum-creatinine) increased , but no significant difference , screening for eye complications, only increased significantly in IG no significant difference in the proportion of actions taken beween IG and CG (p=0.83)
Strategies to enhance physical activity						
Asuako 2017 RCT	Ghana, urban, tertiary care, 08/2015-03/2016	DM, age: 20-68 yrs, ambulant patients, without diabetes complications with < 150 minutes /wk of moderate physical activity no SBP > 140 or DBP> 90 mmHg, bilateral or unilateral lower or upper limbs amputation, use of insulin pump	n=12 83% female age (yrs): 83% were 46-55 yrs. BMI (kg/m²):25.4±4.5 fasting glucose (mmol/l):9.33 ± 5.7 type of diabetes: DM1: 17 % DM2: 83 % duration of diabetes (yrs): • 1-5 yrs: 25 % • 6-10 yrs: 50 % • 10 yrs: 25 %	IG (n=7): walking aerobic exercise sessions without treadmills (3/week) vs. CG (n=5): only activity of daily living Both continued regular medical/clinical routines Duration: 8 weeks	FPG, Lipid profile, body weight, BMI	Change over 2 months: FPG (mmol/l): Benefit for IG: 6.27 ± 0.91 vs. 8.00 ± 0.96; MD 1.73 (-1.88 to -1.59; p<0.001)

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Fayehun 2018	Nigeria, urban 06/2014-11/2014	DM2, age 18-64 yrs, Diagnosed ≥ 12 months, non-insulin dependent, on dietary control ± hypoglycemic agents, able to walk without limitations no pregnant women, smokers, prescription of medications that might impair ability to walk	n= 46 63 % female age (yrs): 54±7.7 (33-64) BMI (kg/m²): 22.4±3.3 HbA1c (%): 6.6 (5.3-9.0) duration of diabetes (yrs):<7 yrs: 70 %, >7 yrs 30 %	IG (n=23): Goal to accumulate 10000 steps per day vs. CG (n=23): normal activity habits Duration: 10 weeks	Primary: HbA1c Secondary: step count	Change over 2.5 months: HbA1c (%): Benefit for IG: 6.26 (6.19 to 6.33) vs. 6.82 (6.69 to 6.95); MD_a: -0.74 (-1.32 to -0.02; p=0.015)
Maharaj 2016 RCT	Nigeria, rural 07/2013-06/2014	DM2, non- insulin dependent, blood glucose levels 6 - 13 mmol/l no cardiac, abdominal or spinal surgery ≤ 6 months, history of fractures of lower limbs, spine, weakness, deformities, loss of sensation in the feet, retinopathy, nephropathy	n=90 52 % females age (yrs): 39.4 ± 8.6 (30-58) BMI (kg/m²): 27.7±5.8 HbA1c (%): 8.79±2.11 duration of diabetes (yrs): 2.5±2.1	IG (n=45): rebound exercise 3 times/week for 20-30 min, moderate intensity of 40-60 % of HR maximum vs. CG (n=45): watched videos and read health magazines Duration: 9 weeks	Primary: HbA1c , FPG, BMI Other: Heart and respiratory rates, blood pressure, oxygen saturation	After 9 weeks HbA1c (%): Benefit for IG: 7.12±1.19 vs. 8.36±1.25; MD_a: 0.904 (0.832 to 0.984; p=0.017) FPG (mmol/l): Benefit for IG: 6.92±1.21 vs. 8.73±1.23; MD_a: 0.787 (0.7345- 0.841; p=0.002)
van Rooijen 2004 RCT	South Africa, urban 03/2002-11/2002	black women with DM2, age 40-65yrs, duration of DM ≥12 months no chest pain on effort, possible previous myocardial infarction and intermittent claudication, cerebro-vascular incidents, arthritis, retinopathy	n=158 gender:100 % females age (yrs): 54-55 HbA1c (%): 9.35	IG (n=80): education+ incremental daily home exercise, use of daily physical activity records+6 fortnightly supervised aerobic exercise classes vs. CG(n=77): education+ relaxation exercise Duration: 12wks	Primary: HbA1c, BMI Secondary: walking distance (6 min walk)	Change over 3 months: HbA1c (%): no difference: 8.99±2.59 vs. 8.26±1.97
Yan 2014	Mozambique,	DM2, male, age 40-70 yrs, diagnosis for ≥ 12 months	n=41 100% male	IG (n=31): low or vigorous intensity	plasma glucose, HbA1c	Change over 3 months: HbA1c (%):

Study name registration number Design	**Setting** Place, setting and time	**Population** Inclusion / Exclusion criteria	Characteristics	**Intervention vs. Control** Description with duration	**Outcomes** Primary and secondary	**Results** Longest follow-up period with intervention effects (IG vs. CG) with SD, 95%-CI or p value
RCT	urban	no known diseases other than DM2 and hypertension, no diagnosed cardiovascular diseases	age(yrs): 54±2.5 HbA1c: 8.6±0.7 plasma glucose (mmol/l): 9.65±1.2 BMI (kg/m$^{2)}$: 27.1 ± 1.0	exercise 3-5 times/week vs. CG(n=10): walked 1 hour per day as part of their daily lifestyle Duration:12 wks		reduction in both groups with no differences between groups: 7.7±0.4 vs. 7.7±0.8 Plasma glucose (mmol/l): 9.6 ± 0.7 vs. 11.1 ± 1.3
Pharmacological strategies						
Distiller 2014 RCT	South Africa	DM2 for ≥ 1 year with total insulin requirement of >200 U/d for ≥ 3 months, BMI > 30 kg/m^2, HbA1c> 7,5 %, on long-term metformin therapy (1.7–2.5 g/d) no pregnant or with childbearing potential, endocrinopathy, chronic inflammatory or systematic autoimmune disorder, CVD, active carcinoma, chronic illness, renal dysfunction, gastroparesis, no corticosteroids, DPP-4 inhibitors, exenatide, liraglutide, no anticipated change in other concomitant medication or insulin resistence	n=28 50% female age (yrs): 51.7 (36-71) HbA1c (%): 8.95 (7.6-11.3) BMI (kg/m²): 40.8 (31.2-47)	IG (n=14): regular Insulin (500 U/ml) + metformin + exenatide (5 µg orally twice a day for 1 month and titrated to 10 µg) vs. CG (n=14): regular Insulin (500 U/ml) +metformin Duration: 6 months	Primary: HbA1c Secondary: Body weight, insulin dose, hypoglycemia	Change to 6 months: HbA1c (%): Significant improvement in both groups 8.7→7.7(p=0.002) vs. 9.2→7.5 (p=0.0001) With no difference between groups (MD: 0.28; p=0.80) Complications: Mild hypoglycaemia: 5 vs. 2 persons with 20 vs. 5 events (p ≤ 0.001)
El-Haggar 2015 RCT	Egypt, urban 01/2013-04/2014	DM2, age: 45-55 yrs, obese (BMI≥30 kg/m^2), with duration 5-10 yrs, treated with glimepiride alone no Inflammatory disease,	n=48 79 % female age (yrs): 50.1±4.6 HbA1c (%): 7.83±0.87 fasting glucose (mg/dl): 193±50	IG1 (n=16): glimepiride (3 mg/d) + 2 (1 mg twice/d) vs. IG2 (n=16): glimepiride (3 mg/d) +	not specified: glycemic markers, metabolic markers, adiponectin, interleukin-6, leukotriene B4, mast cell tryptase, lipid panel,	Changes over 12 weeks: HbA1c (%): • Highest benefit for IG1: 7.1±0.86 vs. 8.2±0.82 vs. 8.7±0.93 (p< 0.05) fasting glucose (mg/dl): • Highest benefit for IG1: 199±38 vs.

Study name registration number Design	**Setting** Place, setting and time	**Population** Inclusion / Exclusion criteria	Characteristics	**Intervention vs. Control** Description with duration	**Outcomes** Primary and secondary	**Results** Longest follow-up period with intervention effects (IG vs. CG) with SD, 95%-CI or p value
		severe hepatic or renal disease, epilepsy pregnant/lactating females	BMI (kg/m²): 37.6±4.6 duration of diabetes (yrs): 7.7 ±2.6	ketotifen (1 mg once/d) vs. CG (n=16): glimepiride (3 mg/d) alone Duration: 12 weeks	BMI	207.7± 47.6 (p< 0.05)
Malek 2015 RCT	Egypt, Algeria, Tunesia, South Africa 03/2010-05/2012	DM2, age ≥ 18 yrs, currently treated with suboptimal dose of oral anti-diabetic drugs; HbA1c 7-11 % (under metformin-monotherapy) and ≤ 10 % (under combination therapy), BMI≤40 kg/m^2 no allergies or contraindications to the product, pregnant or breastfeeding, impaired hepatic or renal function, cardiovascular history, uncontrolled hypertension, proliferative retinopathy, macular oedema	n=403 age (yrs): 52.8±9.6 59.8 % female HbA1c (%): 8.65 BMI (kg/m^2): 29.7±4.5 duration of diabetes (yrs): 7.5±5.1	Stepwise individual insulin intensification of IG (n=200): basal-bolus insulin analogues (insulin detemir +Insulin aspart) vs. CG (n=203): thrice daily biphasic insulin aspart depending on HbA1c-values over 50 wks	Primary: HbA1c Secondary: patients achieving HbA1c < 7.0 %, prandial plasma glucose	Change over 50 weeks: HbA1c (%): Non-inferiority: 7.4 vs. 7.3; MD 0.1 (-0.1 to 0.3 (full-analysis set), MD 0.2 (-0.1 to 0.4 (per protocol) 40.3% and 44.9% achieved HbA1c<7.0% Hypoglycaemia (events/patient year): 9.4 vs. 9.8 Serious adverse events: 6.5 vs. 3.4 % with 1 treatment-related SAE in CG Adverse events: 58.5 vs. 63.1%
Strategies on food supplementation						

Study name registration number Design	**Setting** Place, setting and time	**Population** Inclusion / Exclusion criteria	Characteristics	**Intervention vs. Control** Description with duration	**Outcomes** Primary and secondary	**Results** Longest follow-up period with intervention effects (IG vs. CG) with SD, 95%-CI or p value
Ali 2019 RCT	Egypt Urban, tertiary care 09/2017 – 04/2018	DM2, oral antidiabetic agents with no change of type and dosage of antidiabetic agents in the past 3 months, ≥ 30 years insulin-dependence, pregnancy, lactation, use of Ca, multivitamins, Vitamin D supplements, use of drugs that affect Vitamin D status, dietary Ca intake > 1500 mg/d, hypo- or hyperthyroidism, smoking, use of antiepileptic drugs, sarcoidosis, tuberculosis, potentially terminal illness, inflammatory bowel disease, liver or kidney disease, malignancy	n=85 age (yrs): 54.6 ±2.8 68 % females BMI (kg/m²): 28.6±3.3 Diabetic duration (yrs): 4.4±2.1 fasting glucose (mg(dL): 168±54.4 fasting serum insulin (µIU/mL): 18.1±8.3 HbA1c(%):8.8±1.8	oral antidiabetic agents as usual + IG 1 (n=22): continuous oral Vitamin D3 (4000 IU/ d) vs. IG 2 (n=22): intermittent regimen of Vitamin D3 (50 000 IU/ week) vs. IG 3 (n=21): single IM injection of 300 000 IU of Vitamin D3 at the start of the study vs. CG (n=20): only oral antidiabetic agents Duration: 3 months	Not specified: serum creatinine, blood urea nitrogen, total and ionized Ca, serum phosphorus, fasting glucose, fasting serum insulin, 25(OH)D3 levels, HbA1c	After 3 months: fasting glucose (mg(dL): higher decrease in IG1 and IG2: -20.9±18.1 vs. -23.0±37.9 vs. -3.5±6.9 vs. 1.0±5.6 (p<0.001) fasting serum insulin (µIU/mL): higher decrease in IG1 and IG2: -4.44±5.2 vs.-5.88±4.6 vs. -1.55±9.4 vs. 0.10±1.0 (p< 0.001) HbA1c (%):higher decrease in IG1 and IG2: -0.81±0.77 vs. -0.82±0.87 vs. -0.34±1.47 vs. 0.05±0.08 (p<0.001)
Anderson 2001 RCT	Tunesia, urban	DM2 ≥ 5y, age< 65 yrs, fasting glucose > 8 mmol/l and HbA1C > 7.5 % no pregnant or lactating women, receiving trace element supplements in past 3 months, with gastric or diuretic treatment, acute renal, acute infection or recent surgery	n=110 age (yrs): 53.2 ±16.8 BMI (kg/m²): 29.1±1.0 HbA1c (%):8.82±3.25 fasting glucose (mmol/l): 11.45±0.83 duration of diabetes (months): 73.6±66	IG 1 (n=27): Zinc (30 mg/d) vs. IG 2 (n=27): Chromium (400 µg/d) vs. IG 3 (n=27): Zinc (30 mg /d) + Chromium (400 µg /d) vs. CG (n=29): placebo Duration: 6 months	Not specified: HbA1C, fasting glucose plasma concentrations of zinc, copper, selenium, urinary chromium and zinc, Plasma thiobarbituric acid reactive substances, copper-zinc-superoxid dismutase, selenium - glutathione peroxidase	Change over 6 months: HbA1c (%): 7.7±1.6 vs. 7.4±1.4 vs. 8.1±1.6 CG: not reported
Anyanwu 2016	Nigeria, urban	DM2, age 35-65 yrs on oral antidiabetics with vitamin D	n=42 57.6 % female	IG (n=21): Vitamin D3 supplements	Primary: HbA1c Other: fasting glucose,	Changes over 12 wks: HbA1c (%):

Study name registration number Design	**Setting** Place, setting and time	**Population** Inclusion / Exclusion criteria	Characteristics	**Intervention vs. Control** Description with duration	**Outcomes** Primary and secondary	**Results** Longest follow-up period with intervention effects (IG vs. CG) with SD, 95%-CI or p value
RCT .		deficiency and poor glycemic control (HbA1c > 6.5 %) no patients on insulin, pregnancy, renal insufficiency, chronic liver disease or alanine transferase > 5 times upper reference limit, tuberculosis, diarrheal, or malabsorption state	age (yrs): 51.8±2.05 HbA1c (%): 7.88 fasting glucose (mg/dl): 152.8±56.5	(3000 IU/d) vs. CG(n=21): placebo Duration: 12 weeks	levels of serum Vitamin D, calcium, albumin, phosphate, creatinine, and alanine transaminase	• MD (IG vs. CG): -0.66 (-0.161 to 0.29) vs 0.38 (-0.08 to 0.84); • MD: -1.04 (-2.09 to 0.01) • change from poor glycemic control (HbA1c>6.5 %) to normal HbA1c (%): benefit for IF: 33.3 vs. -9.1 (p<0.05) fasting glucose (mg/dl): 137.2±33.6 vs. 154±67.5 patient adherence (tablet counts, %): 62.2 vs. 59.9
El Gayar 2019 **RCT**	Egypt, urban, outpatients 01/2017-01/2018	DM2 for < 6 months, 30-60 yrs, HbA1c level < 9%, BMI≥30 kg/m^2 no insulin therapy, any injectable or oral antidiabetic medication other than metformin, no smoking, consumption of alcohol or narcotic drugs, no acute illnesses at the baseline or during the study, no pregnancy or lactation, autoimmune disorder, cardiac or renal diseases, thyroid, chronic inflammatory diseases, peptic ulcer, regular consumption of ginger or other herbal drugs, hypersensitivity to ginger, consumption of lipid lowering drugs or oral contraceptive pills or any supplements 2 months before starting the study	n=80 49 % female age (yrs): 46.2 ± 9.1 HbA1c (%): 8.04±0.5 fasting glucose (mg/dl): 176.9±18.3 Fasting serum insulin (mIU/L): 19.3±3.3 BMI (kg/m^2): 32.3±1.4	diet, physical activity, and metformin IG (n=40): ginger powder supplementation (600 mg/capsule, 3 capsules/d) vs. CG (n=40): Placebo Duration: 8 weeks	Not specified: glycemic status, lipid profile and beta-cell function	After 8 wks: HbA1c (%): decrease in both groups to 6.94±0.38 vs. 7.26±0.45 Fasting serum insulin (mIU/L): decrease in both groups to 12.86±2.59 vs. 13.21±2.08 fasting glucose (mg/dl): decrease in both groups to 120.88±9.06 vs. 151.70±13.23

Study name registration number Design	**Setting** Place, setting and time	**Population** Inclusion / Exclusion criteria	Characteristics	**Intervention vs. Control** Description with duration	**Outcomes** Primary and secondary	**Results** Longest follow-up period with intervention effects (IG vs. CG) with SD, 95%-CI or p value
El-Sheikh 2019 RCT	Egypt, urban	DM2 on glimepiride alone, age ≥30 yrs no insulin sensitizers, steroids, NSAIDs, warfarin or lipid lowering medications, thyroid hormones, valproic acid or suffered from: acute or chronic inflammatory diseases, end-stage renal disease undergoing dialysis, hypothyroidism epilepsy, pregnant and breast-feeding women	n= 72 67 % female age (yrs): 50.6±8.7 HbA1c (%):9.76±1 fasting glucose (mg/dl):194.84±20.8 BMI (kg/m²): 34.4±5.45	IG (n=38): glimepiride 2 mg twice daily + L-carnitine 1 gm twice daily vs. CG (n=34): glimepiride dose 2 mg twice daily Duration: 6 months	HbA1c, fasting glucose, PPBG, fasting insulin, extracellular part of insulin regulated aminopeptidase, tumor necrosis factor-alpha, visfatin and lipid panel, BMI and homeostasis model assessment of insulin resistance	Change over 6 months: HbA1c (%): Benefit for IG: 7.41±0.5 vs. 9.5±0.78 (p<0.001) fasting glucose (mg/dl): Benefit for IG: 179.6±9.3 vs. 192.41±27.4 (p=0.018)
Matter 2020 NCT03851055 RCT	Egypt, urban, outpatients 08/2017 to 08/2018	DM, treated with insulin, 10 to 18 yrs, transfusion dependent beta-thalassemia major no other hemoglobinopathies (e.g. a-thalassemia or sickle thalassemia, disorders that may affect glucose homeostasis other than b-TM, autoimmune diseases, collagen diseases, hypo- or hyperthyroidism, infections, or tumours, or those who were taking any vitamins or food supplements < 1 month before the study and participating in a previous investigational drug study within 3 mo preceding screening	n=80 52.5% females age (yrs): 16.3±1.4 (range 12-18) fasting glucose (mg/dL): 144.5±22.4	diet schedule with optimal macronutrient distribution and pharmacologic treatment IG (n=40): zinc gluconate (2x20 mg/d) vs. CG (n=40): placebo Duration: 3 months	Primary: fasting glucose Secondary: fructosamine, fasting C-peptide, and HOMA-IR safety: any AEs (e.g. nausea, vomiting, abdominal pain, diarrhea, constipation, and reduction of appetite)	After 12 wks: fasting glucose (mg/dL): higher decrease with IG to 116.9±4.6 vs. 144.5±22.9 (p<0.001) HbA1c (%): higher in IG (no results reported) no side effects were reported
Moustafa	Egypt,	DM2, newly diagnosed	n=62	IG (n=29, 21 analysed):	Glycemic control,	After 3 months:

Study name registration number Design	**Setting** Place, setting and time	**Population** Inclusion / Exclusion criteria	Characteristics	**Intervention vs. Control** Description with duration	**Outcomes** Primary and secondary	**Results** Longest follow-up period with intervention effects (IG vs. CG) with SD, 95%-CI or p value
2019 RCT	urban, outpatients recruitment 02/2016-03/2018	(within a time duration ≤6 months), 18–60 yrs other antidiabetic medications, pregnant and lactating women, major organ dysfunction (hepatic failure, active hepatitis, liver cirrhosis or renal complications), changed their standard medications during the 12 weeks of the study	72% females HbA1c(%): 7.51±1.4 fasting glucose (mg/dl): 154.4±51.6 BMI(kg/m^2): 33.9±6.1 family history of DM (%): 78.5 retinopathy/altered vision (%): 53 GDM (%): 9.2	nigella sativa oil capsules (3x 450 mg/d) vs. CG (n=33, 23 analysed): metformin (2000 mg/d) Duration: 3 months	oxidative stress markers, biochemical parameters, weight/BMI/waist circumference, total antioxidant capacity TAC	HbA1c (%): no difference: 7.01±0.83 vs. 6.55±0.72 fasting glucose (mg/dl): no difference: 119.8±23.7 vs. 120.7±25.4 Complications: no differences in occurrence of chills, sweating, tachycardia, lethargy/ weakness, polydipsia, polyuria, dry skin, polyphagia, blurred vision, foot problems, or tingling/numbness foot problems lower in IG: 4.8% vs. 33.3%, (p = 0.025).
Ragheb 2020 NCT03437902 RCT	Egypt, urban, outpatients care 02/2019-05/2018	DM2, receiving standard oral hypoglycemic agents, ≥ 35 yrs, no history of overt vascular disease, renal or hepatic failure or antioxidant supplementation or insulin therapy, no change of oral hypoglycemic drugs	n=70 age (yrs): 54.9±8.4 70 % females BMI (kg(m^2): 32.5±5.7 HbA1c(%): 8.50±1.86 fasting glucose (mg/dl): 142.8±52.6	IG2 (n=20): Rutin (60) + vitamin C (160 mg) 3x daily vs. IG1 (n=20): Vitamin C (500 mg) 1x daily vs. CG (n=13); only usual oral antidiabetic treatment Duration: 8 weeks	Primary: HbA1c, oxidative stress marker, antioxidant capacity, insulin resistance, lipid profile Secondary: Quality of life	After 2 months: HbA1c (%): no difference 7.494 ± 1.72 vs. 8.504 ± 2.059 vs. 8.504 ± 2.059 (p=0.1882) fasting glucose (mg/dl): lower in IG2 and CG: 111.3 (IQR 93.3-135.2) vs. 144 (114.8-201) vs. 113.3 (94-152.2) (p=0.017) Quality of life (SF 36): • Benefit of physical functioning and energy domains in IG2 vs. CG (p=0.0049, p=0.0253). • Benefit of role limitation to physical health and emotional improved in IG1 vs. CG (p=0.0267,p=0.0280) • no difference between groups in the other domains (emotional well-being, social functioning, pain and general health)

Study name registration number Design	**Setting** Place, setting and time	**Population** Inclusion / Exclusion criteria	Characteristics	**Intervention vs. Control** Description with duration	**Outcomes** Primary and secondary	**Results** Longest follow-up period with intervention effects (IG vs. CG) with SD, 95%-CI or p value
Rashad 2017 RCT	Egypt, urban	DM2, 50-62 yrs no insulin medication, allergies, recent thromboses or uncontrollable hypertension	n=34 43.3 % female age (yrs): 55.5±6.15 HbA1c (%):6.75±1.2 fasting glucose (mmol/l): 8.5±1.4 postprandial plasma glucose(mmol/l): 15.6±3.3 BMI (kg/m²):28.55±4 type of diabetes duration of diabetes (yrs): 6.1 ± 2.2	IG (n=17): Balanites aegyptiaca extract (400 mg)) vs. CG: (n=17) placebo capsules (potato maltodextrin) Duration: 8 wks	glycemic markers, lipid profile, FPG	Change over 8 wks: 2h postprandial plasma glucose: benefit for IG :26.88% decrease vs. CG 2.6% increase FPG (mmol/l): benefit for IG: 7.8 ± 0.9 vs. CG: 8.5 ± 1.1
Somanah 2012 NCT01248143 RCT	Mauritius, urban/rural 11/2010-03/2011	newly diagnosed DM, age 25–60 yrs fasting glucose range: 5.1–5.9 mmol/L no secondary complications, non-smoker or stopped for > 6 months , alcoholic consumption < 2 standard drinks/day, post-menopausal women without hormone replacement treatment, no glucose-lowering, cholesterol-lowering or anti-hypertension treatment	n=127 47% female age (yrs): range 25–60 HbA1c (%): 5.99±0.4 fasting glucose (mg/dL): 93.2±8.0 BMI (kg/m^2): 26.6 ± 3.7	IG (n=44): supplementation of a fermented papaya preparation (6g/d twice daily, over 12 wks), followed by a 2 week wash out period with the same amount of water vs. CG (n=56): consumed an equivalent amount of water Duration: 14wks	HbA1C fasting glucose, Lipid profile, diet score, blood pressure, alanine aminotransferase; aspartate aminotransferase, Ferritin, c-reactive protein, uric acid, microalbumin/urinary creatinine ratio	After 14 wks: HbA1c (%): no difference (p=0.448) fasting glucose (mg/dL): • remained relatively unchanged in boths genders: • males: 96.2±17.0 vs. 87.6±11.7 • females: 95.6±15.8 vs. 94.3±5.0
Strategies on treatment of DM related complications						

Study name registration number Design	**Setting** Place, setting and time	**Population** Inclusion / Exclusion criteria	Characteristics	**Intervention vs. Control** Description with duration	**Outcomes** Primary and secondary	**Results** Longest follow-up period with intervention effects (IG vs. CG) with SD, 95%-CI or p value
El-Makaky 2020 NCT03783845 RCT	Egypt, urban/rural recruited 06/2015 to 03/2016	DM2 for >5 yrs, 40-70 yrs, HbA1c 7 to 9% at the last medical evaluation, no change in diabetes treatment over the previous 3 months, ≥ 6 permanent teeth excluding third molars, clinical attachment level and pocket depth ≥4 mm in >30 % of the sites, diagnosis of chronic periodontitis based on the presence of 4 teeth as a minimum with ≥ 1 site Pregnancy, alcoholism and smoking, Presence of any systemic disorders other than hypertension and diabetes, diabetic major complications, antimicrobial therapies or periodontal therapies in the last 6 months, allergy to metronidazole and amoxicillin	n=88 56.8 % females age (yrs): 52.6±6.8 HbA1c (%): 8.16±0.72	IG (n=44): immediate periodontal therapy: one-stage scaling and root planning, a combination of systemic antibiotics (amoxicillin 500 mg and metronidazole 400 mg 3x/day for 2 weeks), and oral hygiene instructions vs. CG(n=44): delayed periodontal therapy after 3 months Duration: 3 months	Primary: HbA1c Secondary: not named	After 3 months: HbA1c (%): benefit for IG: 7.27±0.5 vs. 8.34±0.64: MD -1.07 (-1.32 to -0.83)
El-Sharkawy 2016 NCT02794506 RCT	Egypt, urban 06/2014-03/2015.	DM2 >5 yrs, >20 teeth, chronic moderate or severe periodontitis with probing depth and clinical attachment level >5 mm, bleeding by probing, on oral hypogylcemic drug therapy > 6 months, no smoking, use of	n=50 34% female age (yrs): 50.5 ± 7.4 (38 to 63) HbA1c (%): 8.66 ±0.73 FPG (mg/dl): 183.5 ±12.547 BMI (kg/m²): 26.9± 3.1 duration of diabetes	IG (n=24): scaling and root planing (SRP)+ 400mg oral Propolis once daily vs. CG (n=26) scaling and root planing (SRP)+Placebo Duration: 6 months	Primary: HbA1c Secondary: FPG, serum N-(carboxymethyl) lysine, periodontal parameters	after 6 months HbA1c (%) Benefit for IG 7.75± 0.48 vs.8.5±0.73 (p<0.01) FPG(mg/dl) Benefit for IG

Study name registration number Design	**Setting** Place, setting and time	**Population** Inclusion / Exclusion criteria	Characteristics	**Intervention vs. Control** Description with duration	**Outcomes** Primary and secondary	**Results** Longest follow-up period with intervention effects (IG vs. CG) with SD, 95%-CI or p value
		antibiotics, non-steroidal or anti-inflammatory drugs within the last 3 months, periodontal therapy ≤ 1 year, retinopathy grade 3/4, pregnancy, no contraceptive drugs	(yrs): 8.1 ± 3.9 hypertension: 4.5% neuropathy: 1.5% retinopathy: 0.5% nephropathy: 0%			
Ghoneim 2013 RCT	Egypt, 03/2010-03/2012	DM, duration ≥ 15 yrs, bilateral diabetic macular edema (≥ 6 months) no prior treatment with intravitreal corticosteroids, peribulbar steroid injection within ≤ 6 months, pars plana vitrectomy, history of glaucoma or steroid induced IOP elevation, ischemic maculopathy, foveal tracted, IOP≥ 23 mmHg	n=19 (38 eyes) 89.5 % female age (yrs): 52.3±11.4	IG (n=19): one eye with 8 mg triamcinolone acetonide vs. CG (n=19): other eye with4 mg of triamcinolone acetonide Duration: 6 months	Primary: Visual acuity Others: Intraocular pressure (IOP), IOP lowering drugs, complications	after 6 months: Complications: • no eyes with retinal detachment, vitreous haemorrhage, intraocular reaction or endophthalmitis. • one eye in IG developed posterior subcapsular cataract.
Nteleki 2015 RCT	South Africa, urban	DM2 with neuropathic or mixed (venous and arterial) ulcers; lower extremity ulcer; stable or worsening ulcer that has been present for ≥ 4 weeks no acute cellulitis, osteomyelitis, or gangrene, renal, hepatic, hematologic, neurologic, or immune disease not related to diabetes; presence of malignant disease not in remission for > 5 years; use of oral or parenteral	n=7 with 14 lower extremity ulcers 85 % male age (yrs): 62 duration of diabetes (yrs): 16.7	standard podiatric management and IG1 (n=2): phototherapy to the regional lymphatic nodes and ulcer(s) vs. IG2 (n=3): phototherapy on the ulcer vs. CG (n=2): placebo phototherapy Duration: 12 weeks	healing rate (area and perimeter of the ulcer)	after 3 months: Healing: • The rate of healing increased in all three groups, • 67% of ulcers received some form of phototherapeutic intervention, 40% of those ulcers resolved completely over 8 weeks no AEs

Study name registration number Design	**Setting** Place, setting and time	**Population** Inclusion / Exclusion criteria	Characteristics	**Intervention vs. Control** Description with duration	**Outcomes** Primary and secondary	**Results** Longest follow-up period with intervention effects (IG vs. CG) with SD, 95%-CI or p value
		corticosteroids, immunosuppressive, or cytotoxic agents; known infection with human immunodeficiency virus or presence of AIDS; other leg ulcers				
Saeed 2013 RCT	Egypt, urban 11/2010-07/2012	DM, intractable diffuse diabetic macular edema without vitreomacular traction. central foveal thickness ≥300 µm no vitreomacular traction, active neovascularization of proliferative diabetic retinopathy, an enlarged foveal avascular zone on fluorescein angiography, neurosensory detachment on optical coherence tomography, treatment for diabetic macular edema within ≤ 3 months, previous vitreoretinal surgery, other major ocular surgery within the previous 6 months, YAG capsulotomy within ≤2 months, macular pathology	n= 34 (34 eyes) 50% females age (yrs): 55.5 ± 8.9 duration of diabetes (yrs): 24±5.4	IG (n=15): vitrectomy with removal of the posterior hyaloid, at the end of the procedure injection of intravitreal triamcinolone acetonide (IVTA, 0.1 mL, 40 mg/mL) +bevacizumab (1.25 mg) +macular grid laser photocoagulation vs. CG (n=15); same intravitreal injection combination Duration: 12 months	primary: BCVA, central foveal thickness	Changes over 12 months Complications: • Changes in BCVA and central foveal thickness at 3, 6, and 12 *(P*< 0.01), better mean BCVA in IG at 12 months. • Better mean central foveal thickness in IG at 12 months. Major adverse events: development of cataracts (3/15 vs. 6/15) and elevation of intraocular pressure (7/15 vs. 2/15)
Tsobgny-Tsague 2018 NCT02745015 RCT	Cameroon, urban, tertiary care, 12/2014-	DM2, >11teeth, severe chronic periodontitis according to the 2012 CDC-AAP classification, no periodontal treatment,	n=34 56% female age (yrs): 51.4 ± 8.8 HbA1c (%):9.3 ± 1.3 BMI (kg/m²): 28.3± 5.4	IG (n=17): immediate ultrasonic scaling, scaling and root planning +subgingival 10% povidone iodine irrigation	Primary: change in HbA1c Secondary: Plaque index, gingival bleeding index, pocket depth, clinical attachment loss	Change over 3 months: HbA1c (%): Benefit with IG: 6.7 ± 2.0 % vs. 8.1 ± 2.6 %, MD: 2.2 (p=0.029) adverse events: 1 /15 patient reported tongue

Study name registration number Design	**Setting** Place, setting and time	**Population** Inclusion / Exclusion criteria	Characteristics	**Intervention vs. Control** Description with duration	**Outcomes** Primary and secondary	**Results** Longest follow-up period with intervention effects (IG vs. CG) with SD, 95%-CI or p value
	05/2015	alteration of DM treatment 6 mths prior to the study, onset of systemic diseases or an acute condition, use of immunosuppressive medications or others drugs or presence of conditions able to alter periodontitis clinical features	duration of diabetes (months): 55.5 ± 42.6 complications: neuropathy (%): 40 nephropathy (%): 7 retinopathy (%): 7 diabetic foot (%): 3	vs. CG(n=17): periodontal treatment 3 months later Duration: 3 months		irritation following chlorhexidine moth rinse in IG
Yakoot 2019 NCT01531517 RCT	Egypt, urban 07/2011-07/2013	Adult DM2 or DM1 patients, limb-threatening diabetic foot ulcerations no life-threatening extensive gangrenous lesions that needed immediate amputations; bad general condition; shock or unstable vital signs; critically ill with severe organ/system dysfunctions or advanced malignancy.	n=119 gender:44.5% female age (yrs): 54.7 ±8.4 type of diabetes: • DM1: 22.9% • DM2: 86.2%	conservative debridement of necrotic tissue and irrigation with warm normal saline and IG (n=61): local application of ointment composed of royal jelly and panthenol vs. CG (n=58): local application of Panthenol duration: 12months	primary: complete healing secondary: reduction of infection in the ulcer site, al reaction that may be due to study drug	after 12 months rate of complete healing (%): Benefit for IG: 32.4% vs. 12%; p=0.034

ADA: American Diabetes Association; BCVA: Best-corrected visual acuity; BMI: Body mass index; CG: Control group; CI: Confidence interval; CHC: Community health centre; DBP: Diastolic blood pressure; DM: diabetes mellitus; DM1: Type 1 diabetes; DM2: type 2 diabetes; FPG: fasting plasma glucose; HbA1c: haemoglobin A1c; IG: intervention group; IQR: interquartile range; n: number of participants; NCD: Non-communicable disease; NPH: neutral protamine Hagedorn; MD: mean difference; MDa: adjusted mean difference; NCD: Non-communicable disease ;RCT: randomized controlled trial; RR: Relative risk; RRa: adjusted relative risk; SAE: Serious adverse events; SBP: Systolic blood pressure; SCI: Diabetes Self-Care Inventory; SD: Standard-deviation; SMBG: self-monitoring of blood glucose; wks: weeks; yrs: years

Supplementary Table 3: Characteristics and results of studies on patients with DM2