| **Author YearStudy Name** | **Study Design** | **No. of Centers, Country** | **Study DurationMean Followup** | **Interventions** | **Baseline Demographics** | **Inclusion/Exclusion Criteria** | **Number Screened, Eligible, Enrolled, Analyzed** | **Outcomes Assessed** |
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| **ADDITION**  |
| Griffin, 201168; Simmons 201269; van der Donk 2013138ADDITION-Europe | RCT | 343 general practicesDenmark, UK, the Netherlands | Mean followup: 5.3 years | A. Intensive multifactorial treatment (n=1678)Glucose target: HbA1c ≤7.0%BMI target: ≤27 kg/m2Blood pressure target: ≤135/85 mm HgCholesterol target: ≤5.0 mmol/L in patients with no history of CVD; ≤4.5 mmol/L in patients with history of CVDLifestyle educationB. Routine care (n=1379)Standard level of care according to each center's recommendations | **A vs. B**Mean age 60 vs. 60 years41% vs. 43% female96% vs. 93% white (other races/ ethnicities not reported)Duration of diabetes: N/A; screen-detectedHbA1c 6.5 v 6.6%SBP 149 vs. 150 mmHgDBP 86 vs. 87 mmHgTC 5.5 vs. 5.6 mmol/LBMI 31.6 vs. 31.6 kg/m27% vs. 6% history of MI28% vs. 27% smoker | Newly diagnosed type 2 diabetes without: contraindications or intolerance to study medication, conditions likely to invalidate ability to give informed consent, malignant disease with a poor prognosis, pregnancy or lactation | Screened: N/AEligible: N/AEnrolled: 3057Analyzed: 3055 | Cardiovascular event (composite outcome including CV mortality, nonfatal MI, nonfatal stroke, revascularization, nontraumatic amputation) |
| Charles, 2011135ADDITION-Denmark | RCT | 190 general practicesDenmark | Duration: 5 yearsMean followup: 6 years | A. Intensive multifactorial treatment (n=702)Glucose target: HbA1c ≤7.0%BMI target: ≤27 kg/m2Blood pressure target: ≤120/80 mmHgCholesterol target: ≤5.0 mmol/L in patients with no history of CVD; ≤4.5 mmol/L in patients with history of CVDLifestyle educationB. Routine care (n=459)Standard level of care in Denmark  | **A vs. B**Mean age 60 vs. 60 years41% vs. 40% femaleRace not reportedDuration of diabetes: N/A; screen-detectedSBP 149.8 vs. 147.0 mmHgDBP 88.3 vs. 87.3 mmHgWeight (men) 93.7 vs. 94.2 kgWeight (women) 82.8 vs. 84.6 kgBMI (men) 30.4 vs. 30.4BMI (women) 31.2 vs. 31.5HDL 1.4 vs. 1.4 mmol/L TC 5.8 vs. 5.6 mmol/L | Newly diagnosed type 2 diabetes without: contraindications or intolerance to study medication, conditions likely to invalidate ability to give informed consent, malignant disease with a poor prognosis, pregnancy or lactation | Screened: 1,533Eligible: 1,278Enrolled: 1,161Analyzed: Varied by outcome | Neuropathy |
| van den Donk, 2010136; Janssen, 2009137ADDITION-Netherlands | RCT | 79 general practicesThe Netherlands | Mean duration: 4.7 years (for certain outcomes) | A. Intensive multifactorial treatment: Glucose target: HbA1c <7.0%Blood pressure target: ≤120/80 mm HgCholesterol target: <5.0 mmol/L or <4.5 mmol/L in patients with known history of CVD+ lifestyle education (n=255)B. Routine care: Glucose target: HbA1c <8.5%Blood pressure target: <150/85 mmHgCholesterol target: Any participant with CVD risk >25% within 10 years; patients with known CVD <5.0 mmol/L (n=243) | **A vs. B**Mean age 60 vs. 60 years44% vs. 48% female99% vs. 98% whiteDuration of diabetes: N/A; screen-detectedSBP 163 vs. 166 mmHgDBP 89 vs. 90 mmHgHDL 1.1 vs. 1.1 mmol/LTC 5.6 vs. 5.6 mmol/LBMI 30.4 vs. 31.2 kg/m2 | Screen-detected diabetes without: contraindications or intolerance to study medication, conditions likely to invalidate ability to give informed consent, malignant disease with a poor prognosis | Screened: NREligible: 586Enrolled: 498Analyzed: 498 | Quality of life -Medical Outcomes Study 36-Item Short Form Health Survey (SF-36; scale 0-100, higher score = better QoL)European Quality of Life-5 Dimensions (EQ5D; scale -0.5 to 1; higher score = better QoL)Diabetes Treatment Satisfaction Questionnaire (DTSQ; scale 0-36; higher score = greater treatment satisfaction)Problem Areas in Diabetes scale (PAID; scale 0-100; higher score = more emotional distress, lower QoL) |

| **Author YearStudy Name** | **Treatment: Mean Baseline and Achieved Values**  | **Clinical Health Outcomes** | **Adverse Events** | **Quality Rating** | **Funding Source** |
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| **ADDITION**  |
| Griffin, 201168; Simmons 201269, van der Donk 2013138ADDITION - Europe | **A vs. B**HbA1c -Baseline: 7.0% vs. 7.0%Achieved: 6.6% vs. 6.7%Blood pressure -Baseline: 149/86 vs. 150/87 mmHgAchieved: 135/80 vs. 138/81 mmHgTotal cholesterol -Baseline: 5.5 vs. 5.6 mmol/LAchieved: 4.2 vs. 4.4 mmol/LBMI -Baseline: 31.6 vs. 31.6 kg/m2Achieved: 31.1 vs. 31.0 kg/m2 | **A vs. B**First CV event: 121/1678 (7%) vs. 117/1377 (8%); RR 0.85 (95% CI 0.67 to 1.08); HR 0.83 (95% CI 0.65 to 1.05)All-cause mortality: 104/1678 (6%) vs. 92/1377 (7%); RR 0.93 (95% CI 0.71 to 1.22); HR 0.91 (95% CI 0.69 to 1.21)CV mortality: 26/1678 (2%) vs. 22/1377 (2%); RR 0.97 (95% CI 0.55 to 1.70); HR 0.88 (95% CI 0.51 to 1.51)MI: 29/1678 (2%) vs. 32/1377 (2%); RR 0.74 (95% CI 0.45 to 1.22); HR 0.70 (95% CI 0.41 to 1.21)Stroke: 22/1678(1%) vs. 19/1377 (1%); RR 0.95 (95% CI 0.52 to 1.74); HR 0.98 (95% CI 0.57 to 1.71)Revascularization: 44/1678 (3%) vs. 44/1377 (3%); RR 0.82 (95% CI 0.54 to 1.24); HR 0.79 (95% CI 0.53 to 1.18)A vs. B; stratified by country (n/N not reported):CV events --Denmark: HR 0.83 (95% CI 0.59 to 1.16)-UK: HR 0.80 (95% CI 0.55 to 1.17)-The Netherlands: HR 0.96 (95% CI 0.45 to 2.03)All-cause mortality --Denmark: HR 1.15 (95% CI 0.80 to 1.66)-UK: HR 0.59 (95% CI 0.35 to 0.98)-The Netherlands: HR 0.85 (95% CI 0.35 to 2.06)CV mortality --Denmark: HR 1.46 (95% CI 0.69 to 3.12)-UK: HR 0.45 (95% CI 0.19 to 1.06)-The Netherlands: HR 0.97 (95% CI 0.14 to 6.82)MI --Denmark: HR 0.55 (95% CI 0.28 to 1.09)-UK: HR 1.09 (95% CI 0.40 to 2.94)-The Netherlands: HR 0.95 (95% CI 0.14 to 6.52)Stroke --Denmark: HR 0.84 (95% CI 0.34 to 2.04)-UK: HR 1.11 (95% CI 0.52 to 2.35)-The Netherlands: HR 0.95 (95% CI 0.14 to 6.56)Revascularization --Denmark: HR 0.81 (95% CI 0.49 to 1.35)-UK: HR 0.68 (95% CI 0.32 to 1.46)-The Netherlands: HR 0.95 (95% CI 0.30 to 3.00) | None reported | Fair | Novo Nordisk; GlaxoSmithKline; Pfizer |
| Griffin, 201168; Simmons 201269, van der Donk 2013138ADDITION - Europe (cont.) |  | Second CV event -CVD mortality: 5/1678 (0.3%) vs. 3/1377 (0.2%); RR 0.82 (95% CI 0.54 to 1.24)MI: 0/1678 (0%) vs. 5/1377 (0.3%); RR 0.07 (95% CI 0.004 to 1.35)Stroke: 1/1678 (0.06%) vs. 1/1377 (0.07%); RR 0.82 (95% CI 0.05 to 13)Revascularization: 27/1678 (2%) vs. 28/1377 (2%); RR 0.79 (95% CI 0.47 to 1.34)Amputation: 0/1678 (0%) vs. 1/1377 (0.07%); RR 0.27 (95% CI 0.01 to 6.72)Pooled risk second event: HR 0.70 (95% CI 0.43 to 1.12)Third CV event -CVD mortality: 1/1678 (0.05%) vs. 3/1377 (0.2%); RR 0.27 (95% CI 0.03 to 2.63)MI: 0/1678 (0%) vs. 3/1377 (0.2%); RR 0.12 (95% CI 0.006 to 2.27)Stroke: 2/1678 (0.01%) vs. 0/1377 (0%); RR 4.10 (95% CI 0.20 to 85)Revascularization: 4/1678 (0.2%) vs. 11/1377 (0.8%); RR 0.30 (95% CI 0.10 to 0.94)Amputation: 1/1678 (0.05%) vs. 0/1377 (0%); RR 2.46 (95% CI 0.10 to 60)Pooled risk third event: HR 0.30 (95% CI 0.10 to 0.97)Pooled risk any event: HR 0.77 (95% CI 0.58 to 1.02)*Individual outcome RRs calculated; pooled HRs reported in text*Quality of life measures - A (n=1,574) vs. B (n=1,287), mean between-group difference at followupSF-36 mental component score (scale 0 to 100): -0.01 (95% CI -0.03 to 0.02)SF-36 physical component score (scale 0 to 100): -0.01 (95% CI -1.2 to 1.0)Euroquel Visual Analog Scale score (scale 0 to 100): -1.17 (95% CI -4.2 to 1.9)Euroquel 5 Dimensions score (scale -0.6 to 1.0): -0.01 (95% CI -0.03 to 0.02)Well-Being Questionnaire - General score (scale 0 to 36): -0.32 (95% CI -1.31 to 0.66)Well-Being Questionnaire - Negative score (scale 0 to 12): 0.01 (95% CI -.025 to 0.27)Well-Being Questionnaire - Positive score (scale 0 to 12): -0.19 (95% CI -0.53 to 0.15) | None reported | Fair | Not reported. |
| Griffin, 201168; Simmons 201269, van der Donk 2013138ADDITION - Europe (cont.) |  | Well-Being Questionnaire - Energy score (scale 0 to 12): -0.04 (95% CI -0.38 to 0.31)Audit of Diabetes-Dependent Quality of Life score (scale -9 to 3): -0.04 (95% CI -0.20 to 0.13) Diabetes Treatment Satisfaction Questionnaire score (scale 0 to 36): -0.85 (95% CI -1.76 to 0.07) | None reported | Fair | Not reported |
| Charles, 2011135ADDITION - Denmark | **A vs. B**HbA1c -Baseline: 6.4% vs. 6.4%Achieved: No significant change in either group (data not reported)Blood pressure -Baseline: 147/87 vs. 150/88 mmHgAchieved: Significant reduction in both groups (data not reported)Total cholesterol -Baseline: 5.5 vs. 5.6 mmol/LAchieved: Significant reduction in both groups (data not reported)BMI -Baseline: 31.5 vs. 31.2 kg/m2Achieved: No significant change in either group (data not reported) | **A vs. B**Ankle brachial index ≤0.9%: 37/507 (7.3%) vs. 30/329 (9.1%); RR 0.80 (95% CI 0.50 to 1.27)Measures of peripheral diabetic neuropathy:-Light touch 1/8: 69/387 (17.8%) vs. 47/231 (20.3%); RR 0.88 (95% CI 0.63 to 1.22)-VDT >95% percentile: 53/235 (22.6%) vs. 35/136 (25.7%); RR 0.88 (95% CI 0.60 to 1.27)-Light touch + VDT: 69/229 (30.1%) vs. 47/135 (34.8%): RR 0.87 (95% CI 0.64 to 1.17) -MNSI Qst, cut ≥7: 57/656 (8.7%) vs. 40/430 (9.3%); RR 0.93 (95% CI 0.64 to 1.37) Pain: 27/581 (4.6%) vs. 18/400 (4.5%); RR 1.03 (95% CI 0.58 to 1.85)  | None reported | Fair | NovoNordisk, Glaxo Smith Kline, Merck |
| van den Donk, 2010136; Janssen, 2009137ADDITION - Netherlands |  **A vs. B (at 1 year followup)**HbA1c -Baseline: 7.3% vs. 7.4%Achieved: 6.5% vs. 7.2%Blood pressure -Baseline: 166/90 vs. 163/83 mm HgAchieved: 133/78 vs. 144/82 mm HgTotal cholesterol -Baseline: 5.6 vs. 5.6 mmol/LAchieved: 4.4 vs. 5.1 mmol/L | **A vs. B**SF-36 at 1 year:-General health: 63.3 (SD 18.4) vs. 64.4 (SD 18.1); p=0.63-Vitality: 64.8 (SD 20.4) vs. 67.1 (SD 18.4); p=0.81-Mental health: 75.9 (SD 17.9) vs. 79.0 (SD 15.6); p=0.56-Physical functioning: 80.1 (SD 21.2) vs. 78.1 (SD 23.2); p=0.22-Role physical: 80.3 (SD 35.0) vs. 81.1 (SD 33.5); p=0.93-Bodily pain: 79.2 (SD 22.7) vs. 82.2 (22.4); p=0.97-Social functioning: 83.0 (SD 22.0) vs. 85.7 (SD 19.2); p=0.37-Role emotional: 86.2 (SD 30.9) vs. 89.9 (SD 26.0); p=0.25SF-36 at 3 years:-General health: 64.2 (SE 1.5) vs. 65.8 (SE 1.5); p=0.45-Vitality: 65.6 (SE 1.6) vs. 67.7 (SE 1.6); p=0.35-Mental health: 75.9 (SE 1.4) vs. 79.7 (SE 1.2); p=0.04-Physical functioning: 77.3 (SE 1.8) vs. 79.1 (SE 1.7); p=0.46-Role physical: 76.6 (SE 2.7) vs. 83.4 (SE 2.4); p=0.06-Bodily pain: 78.0 (SE 1.8) vs. 81.1 (SE 1.6); p=0.20-Social functioning: 83.2 (SE 1.7) vs. 86.2 (SE 1.6); p=0.20-Role emotional: 84.8 (SE 2.4) vs. 87.0 (SE 2.4); p=0.52EQ5D at 3 years: 0.81 (SE 0.02) vs. 0.82 (SE 0.02); p=0.72DTSQ at 5 years: 32.7 (SE 0.3) vs. 32.7 (SE 0.3); p=1.00PAID at 5 years: 9.8 (SE 1.0) vs. 8.4 (SE 0.9); p=0.30 | Serious AEs (hypoglycemic event requiring assistance): 1/255 (0.4%) vs. 0/243 (0%); RR 2.86 (95% CI 0.12 to 70) | Fair | NovoNordisk, Glaxo Smith Kline, Merck |

**Abbreviations:** ADDITION = Anglo-Danish-Dutch Study of Intensive Treatment in People With Screen-Detected Diabetes; BMI = body mass index; CI = confidence interval; CV = cardiovascular; CVD = cardiovascular disease; DTSQ = Diabetes Treatment Satisfaction Questionnaire; HbA = glycated hemoglobin; HR = heart rate; QoL = quality of life; RR = relative risk; SD = standard deviation; UK = United Kingdom