JAMA | Original Investigation

Lifestyle and Metformin Interventions and Risk of Multimorbidity in Adults With Prediabetes

Marcel E. Salive, MD; Ashley H. Tjaden, PhD; Jesse R. Ames, MS; Jill P. Crandall, MD; Dana Dabelea, MD, PhD; Helen P. Hazuda, PhD; Brandy M. Heckman-Stoddard, PhD; Peter J. Huckfeldt, PhD; Shihchen Kuo, RPh, PhD; Elsa S. Strotmeyer, PhD; Marinella Temprosa, PhD; Elizabeth M. Venditti, PhD; for the DPP Research Group

IMPORTANCE Studying how to prevent or delay not just 1 disease but multiple chronic conditions is of great importance for public health; however, few interventions have demonstrated success during long-term follow-up.

OBJECTIVE To examine the association of lifestyle or metformin compared with placebo on long-term multimorbidity in adults with prediabetes.

DESIGN, SETTING, AND PARTICIPANTS Observational follow-up cohort study of a randomized clinical trial conducted at 27 sites in the United States from June 1, 1996, to December 31, 2021. From June 1, 1996, through May 28, 1999, 3234 adults at high risk of diabetes enrolled in the 3-year Diabetes Prevention Program (DPP). They were subsequently enrolled in the DPP Outcomes Study (DPPOS). Of this cohort, Centers for Medicare & Medicaid Services (CMS) morbidity data were available through 2021 for 1173 participants who provided consent. Data were analyzed from June 5, 2024, to November 7, 2025.

EXPOSURES Participants in DPP were randomly assigned to intensive lifestyle intervention, metformin, or placebo. During DPPOS, medications were unmasked with discontinuation of placebo; metformin was continued. Group booster classes were offered to the lifestyle group semiannually and all participants were offered lifestyle classes quarterly until 2014.

MAIN OUTCOMES AND MEASURES The primary outcome was multimorbidity (presence of ≥2 of 15 prevalent conditions, defined in CMS' Chronic Condition Data Warehouse and adapted for Medicare Advantage encounters). Cox proportional hazard models were applied to estimate associations between randomized treatment groups and time to development of outcomes.

RESULTS Of the 1173 participants (median age, 74 years [IQR, 70-80]; 795 [68%] were female), 997 (85%) experienced greater than or equal to 2 conditions (median, 5 [IQR, 3-7]) by the end of follow-up (316 of 385 [82%], 327 of 385 [85%], and 350 of 403 [87%], respectively, among lifestyle, metformin, and placebo groups). The risk of multimorbidity was lower among lifestyle compared with placebo participants (hazard ratio [HR], 0.79; 95% CI, 0.68-0.93) after adjustment for relevant covariates. There was no difference between participants in the metformin and placebo groups (HR, 0.91; 95% CI, 0.78-1.07). These relationships persisted when diabetes was excluded from the multimorbidity definition. When restricted to dyads of the costliest conditions, the association with lifestyle vs placebo yielded an HR of 0.57 (95% CI, 0.38-0.85).

CONCLUSIONS AND RELEVANCE Among adults with prediabetes at baseline, lifestyle intervention, but not metformin, was associated with a lower burden of multimorbidity. Lifestyle programs may persistently lower the development of chronic conditions.

TRIAL REGISTRATION ClinicalTrials.gov Identifier: DPP, NCT00004992; DPPOS, NCT00038727

Editorial

Supplemental content

Author Affiliations: Author affiliations are listed at the end of this article.

Group Information: Members of the DPP Research Group are listed in Supplement 2.

Corresponding Author: Marcel E. Salive, MD, DPPOS Coordinating Center, The George Washington University Biostatistics Center, 6710A Rockledge Dr, Ste 250, Bethesda, MD 20817 (dppmail@bsc.gwu.edu).

JAMA. doi:10.1001/jama.2026.8492
Published online June 15, 2026.

Multimorbidity, defined as the coexistence of 2 or more chronic conditions, is prevalent owing to declining mortality rates, population aging, and disease accumulation.[1-4] Estimates of multimorbidity prevalence among US adults aged 65 years and older range from 67% to 91%,[1,5] and multimorbidity can require complex, costly interventions.[5] Preventing or delaying multimorbidity with aging is important, yet few interventions have succeeded.

Randomized clinical trials, including the Diabetes Prevention Program (DPP),[6] have studied the development of specific chronic diseases and associated adverse outcomes. Although prevention of multimorbidity is compelling, methodological concerns include the difficulty and cost of assessing the accumulation of chronic conditions, requiring decades of follow-up, and the lack of a standardized definition.[1,7] Lifestyle interventions demonstrated reductions of multimorbidity after 2 years in the Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER) trial[8] and 8 years in the Action for Health in Diabetes (Look AHEAD)[9] trial, both relatively short assessment periods.

Given the success of metformin and lifestyle interventions at preventing or delaying diabetes[6,10,11] and metabolic syndrome[12] in both the short and long term, we sought to determine whether these interventions could prevent or delay multimorbidity in addition to diabetes alone. This question is supported by scientific and clinical consensus statements and clinical trials that seek to understand and influence healthy aging across decades.[13-16] Although DPP interventions have not shown significant long-term associations with microvascular or cardiovascular disease, cancer, or mortality,[17-19] the odds of frailty were found to be 37% lower for lifestyle compared with metformin and placebo 12 to 14 years after randomization.[20]

The current study examines the association of randomization to lifestyle and metformin interventions compared with placebo on the long-term (21-year) incidence and prevalence of multimorbidity, total number of chronic conditions, and high-cost condition dyads.[21]

Key Points

Question What are the associations of lifestyle and metformin interventions compared with placebo on the occurrence of multimorbidity in adults with prediabetes?

Findings In 1173 participants enrolled in Medicare and followed up for 21 years after enrolling in a randomized clinical trial, 82%, 85%, and 87% experienced multimorbidity among lifestyle, metformin, and placebo groups, respectively. The risk of multimorbidity was significantly lower in the group randomly assigned to lifestyle intervention compared with the placebo group after adjustment for relevant covariates, and there was no significant difference between the metformin and placebo groups.

Meaning Among adults with prediabetes at baseline, lifestyle intervention, but not metformin, was associated with a lower risk of multimorbidity during 21 years of follow-up.

Methods

Data Sources and Study Population

We conducted an observational follow-up cohort study spanning 21 years, using data from DPP and DPP Outcomes Study (DPPOS) participants who were enrolled in Medicare and consented to the linkage of their Centers for Medicare & Medicaid Services (CMS) claims. The DPP cohort consisted of individuals from 27 US clinical sites, recruited from June 1, 1996, through May 28, 1999, at high risk for developing type 2 diabetes.[6,22,23] The original trial, which ended in 2001 after a mean of 3.2 years (SD, 0.9 years), determined whether intensive lifestyle or metformin intervention compared with placebo was effective in preventing or delaying the onset of type 2 diabetes. The study cohort has been followed up in the DPPOS since 2002.[6,10,24] Protocols are publicly available at https://dppos.bsc.gwu.edu/web/dppos/about; design and methods are detailed elsewhere. Protocols were approved by the local institutional review boards of the participating study centers, and all participants provided written informed consent.[25] The study was conducted according to the guidelines set out in the Declaration of Helsinki and all procedures involving research study participants. This report follows the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines for cohort studies.[26]

Primary Exposures

During the DPP trial,[6] participants were randomized to lifestyle intervention, metformin, or placebo. Lifestyle participants were offered 16 individual sessions followed by monthly sessions for approximately 2 years. The behavior change program targeted reduced calories and fat (<25% kcal from fat) and at least 150 minutes of physical activity a week to achieve greater than or equal to 7% weight loss from baseline.[27,28] Metformin participants were assigned 850 mg metformin (masked) twice daily as tolerated, and placebo participants were assigned a matching placebo pill twice daily. After DPP trial completion, all participants were offered the intensive lifestyle curriculum[27] in groups during a 6-month bridge period[29] and invited to consent to the DPPOS. Until 2014, all DPPOS participants were offered quarterly group lifestyle sessions, and participants originally randomized to the lifestyle group were offered booster sessions twice annually. During DPPOS, placebo was discontinued and metformin (850 mg twice daily, as tolerated) was continued open label until the end of 2020 for participants originally assigned to this group.

Primary Outcomes Measures

Multimorbidity was defined using 15 common chronic conditions in the Medicare claims database: hypertension, heart failure, coronary artery disease/ischemic heart disease, cardiac arrhythmias, hyperlipidemia, stroke, arthritis, asthma, cancer, chronic kidney disease, chronic obstructive pulmonary disease, dementia/Alzheimer disease, depression, diabetes, and osteoporosis.[1] For fee-for-service claims, flags that indicated any report of the condition from the 2021 Master Beneficiary Summary File in the CMS Chronic Condition Data Warehouse listing 30 chronic conditions were used to identify the presence of claims relevant to any of these 15 conditions (1999-2021).[30]

These conditions reflect the most prevalent chronic conditions according to algorithms validated from research literature and criteria used by other federal sources.[30] For Medicare Advantage claims, algorithms from the CMS Chronic Condition Data Warehouse used encounter data claim diagnosis and procedure codes, reference periods, and the number and type of qualifying claims to identify the presence of the same 15 chronic conditions for data available from 2015 through 2021. Participants were categorized as having the condition if they met the definition with either fee-for-service or Medicare Advantage claims through December 31, 2021 (median, 10.1 years [IQR, 5.5-15.9] from the start of Medicare coverage or baseline DPP visit, whichever was later).

Multimorbidity was defined as a binary outcome (<2 or ≥2 conditions) and as a count outcome (number of conditions). In sensitivity analyses, the claims-based diabetes diagnosis was excluded from the definition. High-cost multimorbidity dyads were defined based on highest mean per capita Medicare fee-for-service spending in 2010 (stroke/chronic kidney disease, stroke/chronic obstructive pulmonary disease, stroke/heart failure, stroke/asthma, and chronic obstructive pulmonary disease/chronic kidney disease).[21]

Covariates

Age, sex, race and ethnicity, income, smoking status, and alcohol use were self-reported at baseline. Hemoglobin A_{1c} and baseline fasting glucose were measured according to the DPP protocol[6]; time-weighted hemoglobin A_{1c} level was calculated from semiannual visit measurements using numeric integration from the R package sfsmisc (version 1.1-19; R Foundation for Statistical Computing). According to protocol, DPP-ascertained diabetes required repeat laboratory testing for confirmation.[22] Duration of metformin use includes both study-provided and nonstudy metformin use. For DPP-ascertained variables, February 23, 2020 (median, 21 years since randomization; IQR, 21.0-22.4), was chosen as the closing date for analysis because of disruptions in clinic visits from the COVID-19 pandemic, which complicated longitudinal data analyses.

Statistical Analyses

Descriptive statistics characterized the study population at baseline (1996-1999) by original randomized group, and the analytic cohort was compared with the full DPP cohort. Three-way comparisons were performed with Kruskal-Wallis tests for continuous variables and Pearson χ^2 tests for categorical variables. The prevalence of multiple chronic conditions and counts of chronic conditions were calculated by randomized group.

Cox proportional hazard models were used to estimate the association of randomized group with risk of developing multimorbidity, defined as time to 2 or 3 chronic conditions, and risk of developing a high-cost dyad. For the purposes of these time-to-event models, the observation period for each participant started with either their baseline DPP visit (72 of 1173 [6.1%]) or their Medicare coverage start date (1101 [93.9%]), whichever was later, and ended at the end of 2021 (median observed follow-up time, 10.1 years; IQR, 5.5-15.9). Three models were fit using this approach: (1) adjusting for age at randomization, sex, and race and ethnicity; (2) additionally adjusting for smoking status, alcohol use, and body mass index (BMI; calculated as weight in kilograms divided by height in meters squared); and (3) additionally adjusting for fasting glucose level at baseline. To estimate the association between diabetes development and the burden of multiple chronic conditions (excluding diabetes), DPP-ascertained diabetes status was added to the Cox models as a time-varying covariate. To test for heterogeneity in the association of randomized group and the burden of multiple chronic conditions in prespecified subgroups (age at randomization, sex, race and ethnicity, BMI, and primary CMS data source [Medicare Advantage or fee for service]), models were fit including interaction terms with randomized group. To confirm the robustness of the analysis, we also fit logistic regression models for prevalence of multimorbidity defined as 2 or more conditions, with the same adjustments as the Cox models.

In a third approach, multimorbidity was treated as a count (number of chronic conditions), and zero-inflated Poisson regression was used to estimate the association of randomized group with the burden of multimorbidity. Three models were fit using this approach, each using a zero-inflation model that incorporated age at randomization, sex, race and ethnicity, and Medicare Advantage status, and then adjusting for each of the sets of covariates as in the first approach. Each fully adjusted model was implemented with and without diabetes (from CMS claims) as a condition. Model fit was assessed with R DHARMa version 0.4.6.

To confirm the robustness of the findings for the duration of study follow-up, we repeated survival analyses using DPP-ascertained chronic conditions. Data were available for 13 of the 15 chronic conditions (eTable 1 in Supplement 1). In these Cox models, the observation period for each participant started with their baseline DPP visit and was censored in February 2020. All randomized participants were included in the analyses, excluding those who had met the definition of having multimorbidity at baseline.

All statistical analyses were conducted in R version 4.4.1. Nominal *P* values reflect 2-sided statistical tests with a significance level of .05. The study was conducted from June 1, 1996, to December 31, 2021. Data were analyzed from June 5, 2024, to November 7, 2025.

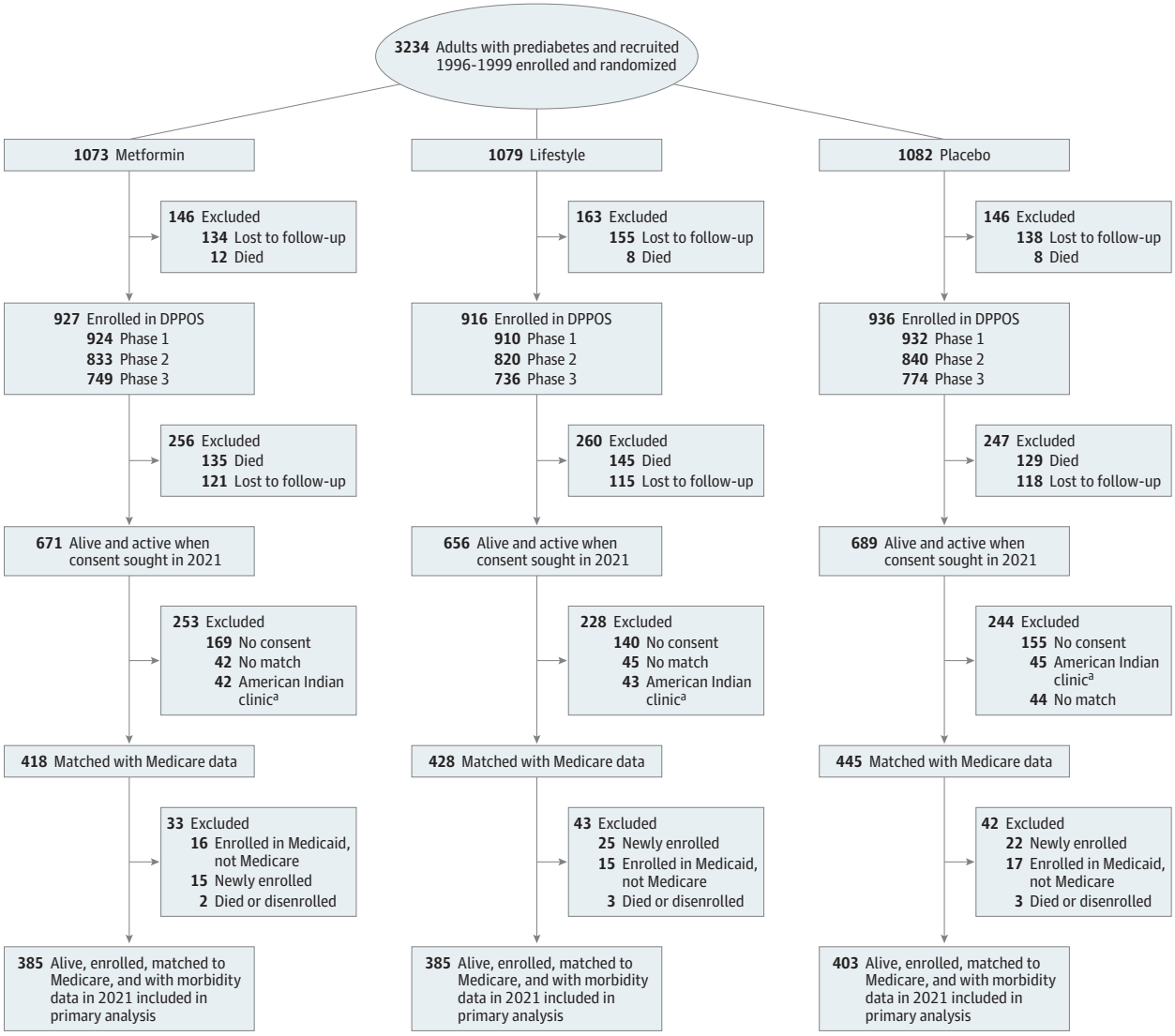
Results

Participant Characteristics

Of 3234 DPP participants, 1422 consented to CMS database matching, and their data were sent to the National Institute on Aging Data LINKAGE Program (**Figure 1**). Of these participants, the analytic sample was restricted to 1173 Medicare enrollees whose morbidity data were available in 2021 (eFigure 1 in Supplement 1).

Table 1 details baseline sociodemographic and clinical features of the 1173 participants overall and by randomized treatment group (placebo n = 403; metformin n = 385; lifestyle n = 385). Participants' median age was 51 years (IQR, 46.4-56.7 years), median BMI was 32.1, 6 (0.5%) were American Indian, 68 (5.8%) were Asian/Pacific Islander, 194 (16.5%) were

Figure 1. Flowchart of Selection of the Analytic Sample From the Diabetes Prevention Program (DPP) and DPP Outcomes Study (DPPOS)



[a]American Indian clinics did not consent to linkage of their data with external data sources.

Hispanic, 250 (21.3%) were non-Hispanic Black, 655 (56%) were non-Hispanic White, 378 (32%) were male, and 795 (68%) were female. At 2021 outcome ascertainment, the median age was 74 years (IQR, 70-80 years). Differences between DPP participants at baseline who were and were not included in analyses are provided in eTable 2 in Supplement 1. The included group was a few years older, had fewer individuals with other race, had lower BMI and waist circumference, and reported less alcohol consumption, higher education, and higher income status than the group that was not included.

Prevalence of Multimorbidity (Unadjusted Comparisons)

Overall, 85% of the cohort (993 of 1173) exhibited greater than or equal to 2 CMS-ascertained chronic conditions (primary definition of multimorbidity) at the end of follow-up; differences between randomized groups were nonsignificant. Groups differed when multimorbidity, which was lowest in the lifestyle group (**Table 2**), was treated as binary (<3 or ≥3 conditions). The median condition count was 5 (IQR, 3-7) for both placebo and metformin and 4 (IQR, 2-6) for lifestyle. Table 2 shows the percentage of individuals with each of 15 chronic conditions overall and by randomized group. The multimorbidity proportion with greater than or equal to 2 conditions differed in placebo (350 of 403 [87%]), metformin (327 of 385 [85%]), and lifestyle (316 of 385 [82%]) groups, and the proportion with greater than or equal to 3 conditions differed in placebo (326 of 403 [81%]), metformin (310 of 385 [81%]), and lifestyle (279 of 385 [72%]) groups. Overall, the top 3 chronic conditions were hyperlipidemia (886 of 1173 [76%]), hypertension (883 [75%]), and diabetes (782 [67%]). Although lifestyle modification prevented or delayed the onset of DPP-ascertained diabetes, 231 of 385 participants

Table 1. Baseline and Follow-Up Clinical and Demographic Characteristics of Participants by DPP Randomized Treatment Group

Characteristic	Intervention, No. (%)		
	Metformin (n = 385)	Lifestyle (n = 385)	Placebo (n = 403)
Baseline/randomization characteristics[a]			
Age at randomization, median (IQR), y	51 (47-57)	52 (46-57)	50 (46-56)
Race[b]			
American Indian	1 (0.3)	2 (0.5)	3 (0.7)
Asian/Pacific Islander	18 (4.7)	33 (8.6)	17 (4.2)
Hispanic	56 (14.5)	67 (17.4)	71 (17.6)
Non-Hispanic Black	84 (21.8)	78 (20.3)	88 (21.8)
Non-Hispanic White	226 (58.7)	205 (53.2)	224 (55.6)
Sex			
Female	253 (66)	261 (68)	281 (70)
Male	132 (34)	124 (32)	122 (30)
Education, y			
≤12	84 (22)	94 (24)	102 (25)
13-16	182 (47)	184 (48)	182 (45)
≥17	119 (31)	107 (28)	119 (30)
Yearly income at randomization, $[c]			
15 000 to <20 000	38 (10)	40 (10)	46 (11)
20 000 to <35 000	49 (13)	58 (15)	71 (18)
35 000 to <50 000	81 (21)	71 (18)	67 (17)
50 000 to <75 000	87 (23)	100 (26)	83 (21)
≥75 000	110 (29)	87 (23)	102 (25)
Refused to answer	20 (5.2)	29 (7.5)	34 (8.4)
Smoking status, No. (%)[d]			
Never	239 (62)	231 (60)	225 (56)
Formerly	131 (34)	134 (35)	140 (35)
Currently	15 (4)	20 (5)	38 (9)
Alcohol consumption, No. (%)			
None	162 (42)	176 (46)	188 (47)
<1 drink/wk	82 (21)	91 (24)	88 (22)
1 drink/wk to 1 drink/d	106 (28)	92 (24)	102 (25)
≥1 drink/d	30 (8)	19 (5)	17 (4)
BMI, median (IQR)[d]	31.9 (28.2-36.5)	31.8 (28.5-36.3)	32.9 (29.1-37.5)
Waist, median (IQR), cm	102 (94-111)	101 (93-109)	103 (93-113)
Height, median (IQR), cm	167 (161-174)	167 (161-173)	165 (160-173)
Fasting glucose level, median (IQR), mg/dL	105 (100-113)	105 (100-112)	106 (100-111)
HbA_{1c}, %			
<5.7	153 (40)	159 (41)	137 (34)
5.7-6.3	190 (49)	182 (47)	211 (52)
≥6.4	41 (11)	43 (11)	53 (13)
Follow-up characteristics (2021)			
Metformin use, median (IQR), y	18 (9-22)	0 (0-7)	3 (0-10)
Physical activity: average MET h/wk, median (IQR)[e]	18 (6-52)	16 (5-49)	15 (5-46)
Medicare Advantage for ≥12 mo	185 (48)	177 (46)	185 (46)

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); DPP, Diabetes Prevention Program; HbA_{1c}, hemoglobin A_{1c}; MET, metabolic equivalent of task.

SI conversion factors: To convert glucose to mmol/L, multiply by 0.0555; to convert HbA_{1c} to mmol/mol, use the equation (10.93 × HbA_{1c}) − 23.50.

[a] The DPP baseline/randomization reflects data collected during randomization (1996-1999).

[b] For race and ethnicity, participants were asked to self-select Hispanic compared with non-Hispanic and separately American Indian, Asian/Pacific Islander, Black, and White based on the 1990 US Census questionnaire about race and ethnicity.

[c] Annual income reported in 1996 to 1999 dollars.

[d] $P < .05$ for differences between treatment groups. To address this result and ensure these imbalances did not confound findings, both variables were included as covariates in the models.

[e] Self-reported leisure physical activity via the Modifiable Activity Questionnaire collected annually.

Table 2. Prevalence of Chronic Conditions Among Participants Through the End of 2021 by DPP Randomized Treatment Assignment[a]

Characteristic	No. (%)			Difference, % (95% CI)			*P* value[b]
	Metformin (n = 385)	Lifestyle (n = 385)	Placebo (n = 403)	Metformin vs lifestyle	Metformin vs placebo	Lifestyle vs placebo	
Multimorbidity (≥2 conditions)	327 (85)	316 (82)	350 (87)	2.9 (−2.6 to 8.4)	−1.9 (−7.0 to 3.2)	−4.8 (−10.1 to 0.5)	.18
Multimorbidity (≥3 conditions)	310 (81)	279 (72)	326 (81)	8.1 (1.8 to 14.3)	−0.4 (−6.1 to 5.4)	−8.4 (−14.6 to −2.3)	.006
No. of conditions, count, median (IQR)	5 (3 to 7)	4 (2 to 6)	5 (3 to 7)	0.4 (0 to 0.8)	−0.1 (−0.5 to 0.3)	−0.5 (−0.8 to −0.1)	.08
High-cost condition dyad[c]	48 (12)	40 (10)	65 (16)	2.1 (−2.7 to 6.8)	−3.7 (−8.8 to 1.5)	−5.7 (−10.7 to −0.8)	.05
Hyperlipidemia	294 (76)	275 (71)	317 (79)	4.9 (−1.5 to 11.4)	−2.3 (−8.4 to 3.8)	−7.2 (−13.5 to −0.9)	.06
Hypertension	289 (75)	274 (71)	320 (79)	3.9 (−2.6 to 10.4)	−4.3 (−10.4 to 1.8)	−8.2 (−14.5 to −2.0)	.03
Diabetes	274 (71)	231 (60)	277 (69)	11.2 (4.2 to 18.1)	2.4 (−4.2 to 9.1)	−8.7 (−15.7 to −1.8)	.002
Rheumatoid arthritis or osteoarthritis	204 (53)	184 (48)	223 (55)	5.2 (−2.1 to 12.5)	−2.3 (−9.6 to 4.9)	−7.5 (−14.8 to −0.3)	.10
Chronic kidney disease	153 (40)	134 (35)	154 (38)	4.9 (−2.1 to 12.0)	1.5 (−5.5 to 8.6)	−3.4 (−10.4 to 3.6)	.35
Ischemic heart disease	137 (36)	118 (31)	130 (32)	4.9 (−2.0 to 11.8)	3.3 (−3.5 to 10.2)	−1.6 (−8.3 to 5.1)	.33
Depression	96 (25)	110 (29)	98 (24)	−3.6 (−10.1 to 2.9)	0.6 (−5.7 to 6.9)	4.3 (−2.2 to 10.7)	.34
Congestive heart failure	66 (17)	57 (15)	63 (16)	2.3 (−3.1 to 7.8)	1.5 (−3.9 to 6.9)	−0.8 (−6.1 to 4.4)	.67
Osteoporosis	57 (15)	56 (15)	64 (16)	0.3 (−5.0 to 5.5)	−1.1 (−6.4 to 4.2)	−1.3 (−6.6 to 3.9)	.86
Asthma	52 (14)	54 (14)	64 (16)	−0.5 (−5.6 to 4.6)	−2.4 (−7.6 to 2.8)	−1.9 (−7.1 to 3.4)	.61
Nonskin cancer	54 (14)	49 (13)	51 (13)	1.3 (−3.8 to 6.4)	1.4 (−3.6 to 6.4)	0.1 (−4.6 to 4.8)	.82
COPD	39 (10)	39 (10)	67 (17)	0 (−4.3 to 4.3)	−6.5 (−11.5 to −1.5)	−6.5 (−11.5 to −1.5)	.006
Atrial fibrillation	38 (10)	47 (12)	52 (13)	−2.3 (−7.0 to 2.3)	−3.0 (−7.7 to 1.6)	−0.7 (−5.6 to 4.2)	.38
Stroke/transient ischemic attack	42 (11)	36 (9)	41 (10)	1.6 (−3.0 to 6.1)	0.7 (−3.8 to 5.3)	−0.8 (−5.2 to 3.6)	.77
Dementia/Alzheimer disease	33 (8.6)	26 (6.8)	30 (7.4)	1.8 (−2.2 to 5.8)	1.1 (−2.9 to 5.2)	−0.7 (−4.5 to 3.1)	.63

Abbreviations: COPD, chronic obstructive pulmonary disease; DPP, Diabetes Prevention Program.

[a] Centers for Medicare & Medicaid Services comorbidities were ascertained based on reported diagnoses from 1999 to 2021 from the 2021 Master Beneficiary Summary File among fee-for-service claims and 2015 to 2021 for Medicare Advantage claims.

[b] *P* value from Kruskal-Wallis rank sum test for 3-way comparison.

[c] High-cost multimorbidity dyads were defined based on highest mean per capita Medicare fee-for-service spending in 2010 (stroke/chronic kidney disease, stroke/chronic obstructive pulmonary disease, stroke/heart failure, stroke/asthma, and chronic obstructive pulmonary disease/chronic kidney disease).

(60%) in the lifestyle group developed CMS-ascertained diabetes during follow-up compared with 277 of 403 (69%) in the placebo group.

Association of Randomized Treatment Group and Multimorbidity

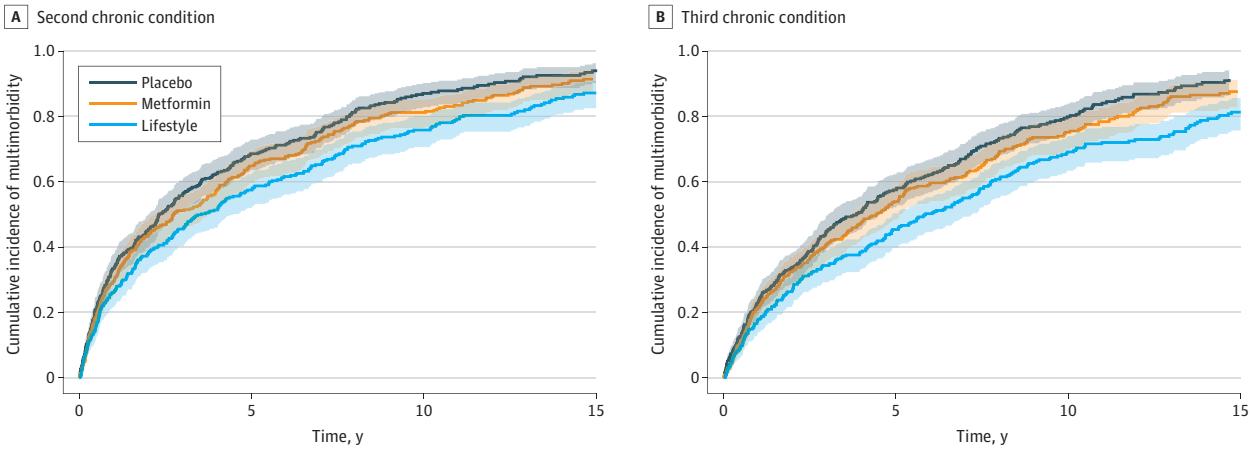
Figure 2 shows the cumulative incidence of having a second and third chronic condition by original randomized group, with the lowest incidence of multimorbidity in the lifestyle group (overall, median time to second chronic condition, 2.4 years; IQR, 0.6-6.5). The cumulative incidence of having a second and third chronic condition, after exclusion of diabetes from the definition of multimorbidity, and of having a high-cost dyad was also lowest in the lifestyle group (eFigures 1 and 2 in Supplement 1). **Figure 3** summarizes the associations of randomized groups with the onset of multimorbidity using different definitions and adjusted for baseline variables. The primary analyses showed a lower risk of multimorbidity (≥2 conditions) with lifestyle compared with placebo (hazard ratio [HR], 0.79; 95% CI, 0.68-0.93). There was no statistically significant difference between participants in the metformin and placebo groups (HR, 0.91; 95% CI, 0.78-1.07), and no interactions were detected between randomized group and age, sex, race and ethnicity, and BMI. Consistent results were observed for onset of the third chronic condition. The lifestyle group compared with the placebo group had a lower risk of having high-cost dyad conditions (HR, 0.57; 95% CI, 0.38-0.85). Sensitivity analyses removing diabetes from the chronic condition list showed results consistent with those of the main analyses (eFigures 3 and 4 and eTables 3-5 in Supplement 1).

In the model of the adjusted relative mean count of chronic conditions, using zero-inflated Poisson regression estimates as a function of randomized group, the lifestyle group had 10% fewer chronic conditions compared with placebo (relative mean count, 0.90; 95% CI, 0.84-0.97) (eFigure 5 and eTable 6 in Supplement 1). The burden of multimorbidity did not differ between metformin and placebo. In analyses comparing prevalence instead of incidence of multimorbidity, the findings were similar (eTable 7 in Supplement 1).

Association of Randomized Treatment Group and DPP-Ascertained Multimorbidity

In sensitivity analyses using DPP-ascertained multimorbidity (defined in eTable 1 in Supplement 1), results were

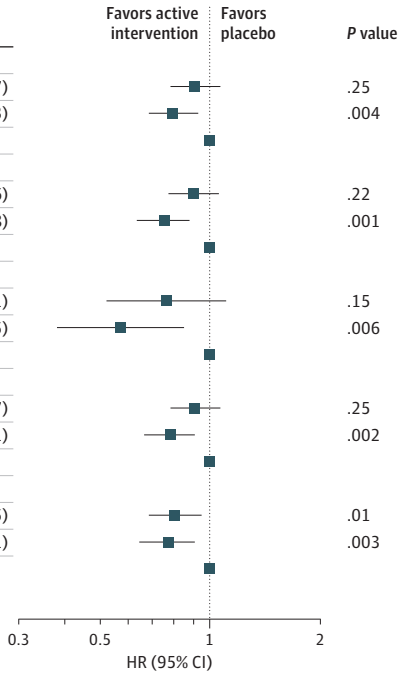
Figure 2. Time-to-Event Curves Depicting Cumulative Incidence of Multimorbidity (≥2 and ≥3 Chronic Conditions), Using Centers for Medicare & Medicaid Services–Ascertained Conditions, Stratified by Assigned Treatment



A, Time to multimorbidity (onset of second condition), defined as greater than or equal to 2 and greater than or equal to 3 chronic conditions. B, Time to multimorbidity (onset of third condition). Time 0 is the start of Medicare coverage or Diabetes Prevention Program (DPP) randomization, if randomized after the start of coverage. Median follow-up was 10.1 years (IQR, 5.5-15.9 years) from the start of Medicare coverage or baseline DPP visit, whichever was later; median time to second chronic condition was 2.4 years (IQR, 0.6-6.5 years).

Figure 3. Dot-and-Whisker Plot of Associations of Lifestyle and Metformin vs Placebo on Multimorbidity for Several Definitions

Event	No. of participants included in analysis	No. of participants with the event of interest	Risk of multimorbidity, HR (95% CI)	*P* value
2 Chronic conditions, including diabetes				
Metformin	380	321	0.91 (0.78-1.07)	.25
Lifestyle	378	306	0.79 (0.68-0.93)	.004
Placebo	395	343	1 [Reference]	
3 Chronic conditions, including diabetes				
Metformin	380	301	0.90 (0.77-1.06)	.22
Lifestyle	378	271	0.75 (0.63-0.88)	.001
Placebo	395	317	1 [Reference]	
High-cost condition dyad				
Metformin	380	48	0.76 (0.52-1.11)	.15
Lifestyle	378	39	0.57 (0.38-0.85)	.006
Placebo	395	64	1 [Reference]	
2 Chronic conditions, excluding diabetes				
Metformin	380	317	0.91 (0.78-1.07)	.25
Lifestyle	378	295	0.78 (0.66-0.91)	.002
Placebo	395	335	1 [Reference]	
3 Chronic conditions, excluding diabetes				
Metformin	380	262	0.80 (0.68-0.95)	.01
Lifestyle	378	242	0.77 (0.64-0.91)	.003
Placebo	395	282	1 [Reference]	



Adjusted hazard ratios (HRs) and 95% CIs from fully adjusted Cox regressions. Models adjusted for age (5-year increments), sex, race and ethnicity, smoking status, alcohol consumption, body mass index (calculated as weight in kilograms divided by height in meters squared; in increments of 5), and fasting glucose level (in increments of 10 mg/dL) at randomization. Median follow-up was 10.1 years (IQR, 5.5-15.9 years) from the start of Medicare coverage or baseline Diabetes Prevention Program visit, whichever was later.

consistent with the primary analyses (eFigure 5 and eTables 8 and 9 in Supplement 1). Being in the lifestyle group was associated with a lower hazard of development of DPP-ascertained multimorbidity (≥2 conditions) compared with placebo (HR, 0.73; 95% CI, 0.64-0.84). Participants who developed diabetes had a higher risk of multimorbidity (HR, 1.33; 95% CI, 1.16-1.53) independent of treatment group (eTable 9 in Supplement 1).

Discussion

In a 21-year observational study among DPP participants with Medicare insurance, randomization to lifestyle intervention compared with placebo was associated with a lower burden of multimorbidity a median of 10.1 years (IQR, 5.5-15.9 years) after Medicare coverage was started. There was a reduced risk for occurrence of the second and third condition (of the 15 examined) in the lifestyle group with adjustment for age, race and ethnicity, sex, baseline fasting glucose level, BMI, smoking status, and alcohol consumption. Results were similar when diabetes was excluded from the condition list and also for high-cost dyads. Beyond diabetes prevention, lifestyle intervention was associated with fewer chronic conditions in aging. However, randomization to metformin was not associated with a difference in multimorbidity from placebo. Findings suggest that intensive lifestyle modification may prevent or delay multimorbidity in middle and older age among adults with high risk of diabetes or with diabetes. Because lifestyle modification can be safe and cost-effective, sustaining those behaviors among Medicare beneficiaries at risk of diabetes may help to reduce health burden and health care spending.

More than 20 years after the original DPP randomized intervention exposure, 997 participants (85%) in this analysis had greater than or equal to 2 chronic conditions and 915 (78%) had greater than or equal to 3 chronic conditions (median, 5; IQR, 3-7). Compared with the placebo group, participants randomized to the lifestyle intervention had 21% lower risk for 2 chronic conditions and 25% lower risk for 3 chronic conditions. This result is consistent with the 9% to 19% reduction of multimorbidity reported for lifestyle interventions in FINGER[8] and Look AHEAD,[9] but the DPP and DPPOS have the longest duration of follow-up to date. The current findings expand on prior DPP results about diabetes prevention and included a variety of chronic conditions, such as chronic obstructive pulmonary disease, hyperlipidemia, hypertension, and possibly arthritis, although those differences were not significant individually. These results also add to evidence on interventions to reduce high-cost dyads[17] and underscore that lifestyle interventions are powerful tools to improve healthy aging.

The current study highlights the role of diabetes in multimorbidity among individuals with prediabetes. Although lifestyle modification prevented or delayed the onset of diabetes, 231 of 385 participants (60%) in the lifestyle group developed diabetes during follow-up. Participants who developed diabetes had a higher risk of multimorbidity independent of their treatment group. These risks reflect clustering of conditions with diabetes and are consistent with the comorbidity literature.[31]

Strengths of the study include initial enrollment into a randomized clinical trial, the large size and representation in the cohort, the high rates of retention and balance of the cohort according to the treatment assignment, and the long duration of follow-up. Time-to-event analysis permitted evaluation of the association with multimorbidity during 21 years of observation.

Limitations

First, by definition, multimorbidity refers to having multiple chronic conditions simultaneously rather than a discrete incidence of illness event. Thus, determining onset is ambiguous because most conditions contributing to multimorbidity are chronic diseases that develop gradually. Second, as eligible volunteers, DPP participants may not reflect general populations of individuals with prediabetes. The DPP participants had less hypertension but higher BMI at baseline vs comparable national data.[23] These data were not ascertained for American Indian center participants and those who declined consent for inclusion in this analysis. Third, events among participants who died before the consent for Medicare linkage were not accounted for. However, the included sample did not substantially differ by demographic characteristics or by assignment to the intervention. Fourth, crossover has the potential to influence the results. Adherence to study metformin declined over time, although there remained a wide difference in total metformin exposure between the groups.[19] The intensity of the lifestyle intervention was not sustained after the initial 3.2 years, and only limited lifestyle intervention was offered to all treatment groups during DPPOS, with low attendance at lifestyle classes offered during DPPOS.[32] Weight loss and physical activity were higher in the lifestyle intervention group for 6 years and then converged with that of the metformin group.[11,19] Fifth, the Medicare claims algorithms for disease ascertainment have known limitations.[33] In the diagnoses for the Medicare Advantage enrollees from encounter data, upcoding, in which a larger number of diagnoses are made relative to a comparable fee-for-service beneficiary, has been a concern.[34] However, this study addressed this problem by excluding diagnoses from electronic health record reviews, previously identified as a potential mechanism for upcoding.[35] A small proportion of participants (25 of 1173 [2.1%]) included were enrolled in Medicare before age 65 years, and although Medicare beneficiaries younger than 65 years often have more complex health needs and higher health care costs than typical beneficiaries aged 65 years or older, no differences in count of chronic conditions existed between the 2 groups in the sample.

Conclusions

Among adults with prediabetes at baseline, lifestyle intervention, but not metformin, was associated with a lower burden of multimorbidity during 21 years of follow-up. Lifestyle programs may persistently lower the development of chronic conditions.

ARTICLE INFORMATION

Accepted for Publication: April 26, 2026.

Published Online: June 15, 2026. doi:10.1001/jama.2026.8492

Author Affiliations: Division of Geriatrics and Clinical Gerontology, National Institute on Aging, Bethesda, Maryland (Salive); Biostatistics Center, Milken Institute School of Public Health, George Washington University, Bethesda, Maryland (Tjaden, Ames); Division of Endocrinology, Albert

Einstein College of Medicine, Bronx, New York (Crandall); Fleischer Institute for Diabetes and Metabolism, Albert Einstein College of Medicine, Bronx, New York (Crandall); Lifecourse Epidemiology of Adiposity and Diabetes (LEAD) Center, Colorado School of Public Health, University of Colorado Anschutz Medical Campus, Aurora (Dabelea); Department of Medicine, University of Texas Health Center San Antonio, San Antonio (Hazuda); Division of Cancer Prevention, National Cancer Institute, Rockville, Maryland (Heckman-Stoddard); Division of Health Policy and Management, School of Public Health, University of Minnesota, Minneapolis (Huckfeldt); Division of Metabolism, Endocrinology, and Diabetes, Department of Internal Medicine, University of Michigan, Ann Arbor (Kuo); Department of Epidemiology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania (Strotmeyer); Biostatistics Center and Department of Biostatistics and Bioinformatics, Milken Institute School of Public Health, George Washington University, Bethesda, Maryland (Temprosa); Department of Psychiatry, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania (Venditti).

Author Contributions: Dr Tjaden and Mr Ames had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Drs Temprosa and Venditti served as co–senior authors.
Concept and design: Salive, Tjaden, Ames, Crandall, Dabelea, Huckfeldt, Kuo, Strotmeyer, Temprosa, Venditti.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Salive, Tjaden, Ames, Temprosa, Venditti.
Critical review of the manuscript for important intellectual content: All authors.
Statistical analysis: Tjaden, Ames, Huckfeldt, Temprosa.
Obtained funding: Crandall, Dabelea, Temprosa, Venditti.
Administrative, technical, or material support: Crandall, Dabelea, Heckman-Stoddard, Temprosa, Venditti.
Supervision: Heckman-Stoddard, Temprosa, Venditti.

Conflict of Interest Disclosures: Dr Strotmeyer reported grants from Amgen and consulting fees from George Washington University during the conduct of the study. No other disclosures were reported.

Funding/Support: This study was supported by the National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health (NIH) under awards U01 DK048489, U01 DK048339, U01 DK048377, U01 DK048349, U01 DK048381, U01 DK048468, U01 DK048434, U01 DK048485, U01 DK048375, U01 DK048514, U01 DK048437, U01 DK048413, U01 DK048411, U01 DK048406, U01 DK048380, U01 DK048397, U01 DK048412, U01 DK048404, U01 DK048387, U01 DK048407, U01 DK048443, and U01 DK048400, and by the National Institute on Aging of the NIH under award 5 U19 AG078558 by providing funding during DPP and DPPOS to the clinical centers and the coordinating center for the design and conduct of the study and collection, management, analysis, and interpretation of the data. Funding was also provided by the Eunice Kennedy Shriver National Institute of Child Health and Human Development, the National Eye Institute, the National Heart, Lung, and Blood Institute, the National Cancer Institute, the Office of Research on Women's Health, the National Institute on Minority Health and Health Disparities, the Centers for Disease Control and Prevention, and the American Diabetes Association. The Southwestern American Indian centers were supported directly by the National Institute of Diabetes and Digestive and Kidney Diseases, including its Intramural Research Program, and the Indian Health Service. The General Clinical Research Center Program, National Center for Research Resources, and the Department of Veterans Affairs supported data collection at many of the clinical centers. Merck KGaA provided medication for DPPOS. DPP/DPPOS have also received donated materials, equipment, or medicines for concomitant conditions from Bristol Myers Squibb, Parke-Davis, LifeScan Inc, Health-o-Meter, Hoechst Marion Roussel, Merck-Medco Managed Care, Merck & Co, Nike Sports Marketing, SlimFast Foods, and Quaker Oats. McKesson BioServices, Matthews Media Group, and the Henry M. Jackson Foundation provided support services under subcontract with the coordinating center.

Role of the Funder/Sponsor: The sponsor of this study was represented on the Steering Committee and was involved in design and conduct of the study and the decision to submit the manuscript for publication.

Group Information: Members of the DPP Research Group are listed in Supplement 2.

Disclaimer: The participation of these individuals or the materials should not be interpreted as representing the official viewpoint of the US Department of Health and Human Services, the NIH, or the National Institute on Aging, except where noted. The opinions expressed are those of the study group and do not necessarily reflect the views of the funding agencies. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Data Sharing Statement: See Supplement 3.

Additional Contributions: The DPP Research Group acknowledges the commitment and dedication of the participants of the DPP and DPPOS.

REFERENCES

1. Salive ME. Multimorbidity in older adults. *Epidemiol Rev*. 2013;35:75-83. doi:10.1093/epirev/mxs009

2. St Sauver JL, Boyd CM, Grossardt BR, et al. Risk of developing multimorbidity across all ages in an historical cohort study: differences by sex and ethnicity. *BMJ Open*. 2015;5(2):e006413. doi:10.1136/bmjopen-2014-006413

3. Goodman RA, Ling SM, Briss PA, Parrish RG, Salive ME, Finke BS. Multimorbidity patterns in the United States: implications for research and clinical practice. *J Gerontol A Biol Sci Med Sci*. 2016;71(2):215-220. doi:10.1093/gerona/glv199

4. Rocca WA, Grossardt BR, Boyd CM, Chamberlain AM, Bobo WV, St Sauver JL. Multimorbidity, ageing and mortality: normative data and cohort study in an American population. *BMJ Open*. 2021;11(3):e042633. doi:10.1136/bmjopen-2020-042633

5. Dorr DA, Markwardt S, Bobo M, et al. The extent and burden of high multimorbidity on older adults in the US: a descriptive analysis of Medicare beneficiaries. *BMC Geriatr*. 2024;24(1):777. doi:10.1186/s12877-024-05329-y

6. Knowler WC, Barrett-Connor E, Fowler SE, et al; Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med*. 2002;346(6):393-403. doi:10.1056/NEJMoa012512

7. Suls J, Bayliss EA, Berry J, et al. Measuring multimorbidity: selecting the right instrument for the purpose and the data source. *Med Care*. 2021;59(8):743-756. doi:10.1097/MLR.0000000000001566

8. Marengoni A, Rizzuto D, Fratiglioni L, et al. The effect of a 2-year intervention consisting of diet, physical exercise, cognitive training, and monitoring of vascular risk on chronic morbidity—the FINGER randomized controlled trial. *J Am Med Dir Assoc*. 2018;19(4):355-360.e1. doi:10.1016/j.jamda.2017.09.020

9. Espeland MA, Justice JN, Bahnson J, et al. Eight-year changes in multimorbidity and frailty in adults with type 2 diabetes mellitus: associations with cognitive and physical function and mortality. *J Gerontol A Biol Sci Med Sci*. 2022;77(8):1691-1698. doi:10.1093/gerona/glab342

10. Knowler WC, Fowler SE, Hamman RF, et al; Diabetes Prevention Program Research Group. 10-Year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study. *Lancet*. 2009;374(9702):1677-1686. doi:10.1016/S0140-6736(09)61457-4

11. Knowler WC, Doherty L, Edelstein SL, et al; DPP/DPPOS Research Group. Long-term effects and effect heterogeneity of lifestyle and metformin interventions on type 2 diabetes incidence over 21 years in the US Diabetes Prevention Program randomised clinical trial. *Lancet Diabetes Endocrinol*. 2025;13(6):469-481. doi:10.1016/S2213-8587(25)00022-1

12. Orchard TJ, Temprosa M, Goldberg R, et al; Diabetes Prevention Program Research Group. The effect of metformin and intensive lifestyle intervention on the metabolic syndrome: the Diabetes Prevention Program randomized trial. *Ann Intern Med*. 2005;142(8):611-619. doi:10.7326/0003-4819-142-8-200504190-00009

13. Duque G, Lipsitz LA, Ferrucci L, Addie S, Carrington-Lawrence S, Kohanski R. Geroscience for the next chapter of medicine. *J Gerontol A Biol Sci Med Sci*. 2023;78(5):791-792. doi:10.1093/gerona/glad083

14. Birtcher KK, Allen LA, Anderson JL, et al; Writing Committee. 2022 ACC expert consensus decision pathway for integrating atherosclerotic cardiovascular disease and multimorbidity treatment: a framework for pragmatic, patient-centered care: a report of the American College of Cardiology Solution Set Oversight Committee. *J Am Coll Cardiol*. 2023;81(3):292-317. doi:10.1016/j.jacc.2022.08.754

15. Chartash D, Gilson A, Taylor RA, Hart LC. The scope of multimorbidity in family medicine: identifying age patterns across the lifespan. *J Am Board Fam Med*. 2024;37(2):251-260. doi:10.3122/jabfm.2023.230221R1

16. Barzilai N, Crandall JP, Kritchevsky SB, Espeland MA. Metformin as a tool to target aging. *Cell Metab*.

2016;23(6):1060-1065. doi:10.1016/j.cmet.2016.05.011

17. Lee CG, Heckman-Stoddard B, Dabelea D, et al; Diabetes Prevention Program Research Group. Effect of metformin and lifestyle interventions on mortality in the Diabetes Prevention Program and Diabetes Prevention Program Outcomes Study. *Diabetes Care*. 2021;44(12):2775-2782. doi:10.2337/dc21-1046

18. Goldberg RB, Orchard TJ, Crandall JP, et al; Diabetes Prevention Program Research Group. Effects of long-term metformin and lifestyle interventions on cardiovascular events in the Diabetes Prevention Program and its Outcome Study. *Circulation*. 2022;145(22):1632-1641. doi:10.1161/CIRCULATIONAHA.121.056756

19. Heckman-Stoddard BM, Crandall JP, Edelstein SL, et al; DPP Research Group. Randomized study of metformin and intensive lifestyle intervention on cancer incidence over 21 years of follow-up in the Diabetes Prevention Program. *Cancer Prev Res (Phila)*. 2025;18(7):401-411. doi:10.1158/1940-6207.CAPR-23-0461

20. Hazuda HP, Pan Q, Florez H, et al. Association of intensive lifestyle and metformin interventions with frailty in the Diabetes Prevention Program Outcomes Study. *J Gerontol A Biol Sci Med Sci*. 2021;76(5):929-936. doi:10.1093/gerona/glaa295

21. Bowling CB, Sloane R, Pieper C, et al. Association of sustained blood pressure control with lower risk for high-cost multimorbidities among Medicare beneficiaries in ALLHAT. *J Gen Intern Med*. 2021;36(8):2221-2229. doi:10.1007/s11606-021-06623-w

22. Diabetes Prevention Program Research Group. The Diabetes Prevention Program: design and methods for a clinical trial in the prevention of type 2 diabetes. *Diabetes Care*. 1999;22(4):623-634. doi:10.2337/diacare.22.4.623

23. Diabetes Prevention Program Research Group. The Diabetes Prevention Program: baseline characteristics of the randomized cohort. *Diabetes Care*. 2000;23(11):1619-1629. doi:10.2337/diacare.23.11.1619

24. Diabetes Prevention Program Research Group. Long-term effects of lifestyle intervention or metformin on diabetes development and microvascular complications over 15-year follow-up: the Diabetes Prevention Program Outcomes Study. *Lancet Diabetes Endocrinol*. 2015;3(11):866-875. doi:10.1016/S2213-8587(15)00291-0

25. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human participants. *JAMA*. 2025;333(1):71-74. doi:10.1001/jama.2024.21972

26. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; for the STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *J Clin Epidemiol*. 2008;61(4):344-349. doi:10.1016/j.jclinepi.2007.11.008

27. Diabetes Prevention Program (DPP) Research Group. The Diabetes Prevention Program (DPP): description of lifestyle intervention. *Diabetes Care*. 2002;25(12):2165-2171. doi:10.2337/diacare.25.12.2165

28. Hamman RF, Wing RR, Edelstein SL, et al. Effect of weight loss with lifestyle intervention on risk of diabetes. *Diabetes Care*. 2006;29(9):2102-2107. doi:10.2337/dc06-0560

29. Venditti EM, Bray GA, Carrion-Petersen ML, et al; Diabetes Prevention Program Research Group. First versus repeat treatment with a lifestyle intervention program: attendance and weight loss outcomes. *Int J Obes (Lond)*. 2008;32(10):1537-1544. doi:10.1038/ijo.2008.134

30. Centers for Medicare & Medicaid Services. 30 CCW chronic conditions algorithms: MBSF_CHRONIC_{*YYYY*} file. Updated August 2025. Accessed May 23, 2024. https://www2.ccwdata.org/documents/10280/19139421/chr-chronic-condition-algorithms.pdf

31. Cicek M, Buckley J, Pearson-Stuttard J, Gregg EW. Characterizing multimorbidity from type 2 diabetes: insights from clustering approaches. *Endocrinol Metab Clin North Am*. 2021;50(3):531-558. doi:10.1016/j.ecl.2021.05.012

32. Apolzan JW, Venditti EM, Edelstein SL, et al; Diabetes Prevention Program Research Group. Long-term weight loss with metformin or lifestyle intervention in the Diabetes Prevention Program Outcomes Study. *Ann Intern Med*. 2019;170(10):682-690. doi:10.7326/M18-1605

33. Weir REJ Jr, Lyttle CS, Meltzer DO, Dong TS, Ruhnke GW. The relative ability of comorbidity ascertainment methodologies to predict in-hospital mortality among hospitalized community-acquired pneumonia patients. *Med Care*. 2018;56(11):950-955. doi:10.1097/MLR.0000000000000989

34. Medicare Payment Advisory Commission. March 2024 report to the Congress: Medicare Payment Policy. Published March 15, 2024. Accessed May 21, 2025. https://www.medpac.gov/document/march-2024-report-to-the-congress-medicare-payment-policy/

35. Meyers DJ, Trivedi AN. Medicare Advantage chart reviews are associated with billions in additional payments for some plans. *Med Care*. 2021;59(2):96-100. doi:10.1097/MLR.0000000000001412