GEMs
GOOD EVIDENCE MATTERS

GEMs of the Week

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Family Physicians Inquiries Network

What's in this week's issue?

Week of February 10-14, 2025

SPOTLIGHT:

Smoking Cessation: Electronic Cigarettes vs Varenicline

Smoking Cessation: Electronic Cigarettes vs Varenicline

Electronic Cigarettes vs Varenicline for Smoking Cessation in Adults: A Randomized Clinical Trial

Tuisku A, Rahkola M, Nieminen P, Toljamo T. Electronic Cigarettes vs Varenicline for Smoking Cessation in Adults: A Randomized Clinical Trial [published correction appears in JAMA Intern Med. 2024 Aug 1;184(8):993. doi: 10.1001/jamainternmed.2024.3981]. *JAMA Intern Med*. 2024;184(8):915-921. doi:10.1001/jamainternmed.2024.1822

KEY TAKEAWAY: Nicotine-containing electronic cigarettes (ECs) and varenicline are both effective options in cigarette smoking abstinence compared to placebo.

STUDY DESIGN: Randomized, placebo-controlled clinical trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Traditional cigarette use continues to be one of the leading causes of mortality. There is evidence that nicotine-containing ECs are affiliated with increased smoking cessation rates compared with nicotine replacement therapy and that they are superior to nicotine-free ECs. Long-term use of EC outcomes is still being studied, but the benefits for people who switch from traditional cigarette use outweigh the risks of harmful substances found in cigarettes. This study aimed to provide evidence of an effective way in which people can stop utilizing cigarettes.

PATIENTS: Adults who smoked daily for ≥10 years

INTERVENTION: Nicotine-containing EC or varenicline + nicotine-free ECs

CONTROL: Placebo tablets

PRIMARY OUTCOME: Confirmed smoking abstinence at 26 weeks

Secondary Outcome: Self-reported abstinence at 26 weeks, self-reported abstinence at 52 weeks, confirmed smoking abstinence at 52 weeks, adverse events

METHODS (BRIEF DESCRIPTION):

- Participants were recruited from a previous study and local newspapers.
- Participants 25–75 years old who smoked daily for 10 years with a minimum of 10 cigarettes a day for ≥5 years, were willing to quit, exhaled carbon monoxide (CO) level of ≥115ppm, and had moderate to high nicotine dependence were included in the study.
- Participants were randomized 1:1:1 into the following 3 groups:
  - The EC group received nicotine-containing EC with 18 mg/mL of nicotine tanks.
  - The varenicline group received varenicline + nicotine-free EC (0 mg/mL of nicotine). Participants took varenicline at 0.5 mg daily on days 1–3, 0.5 mg twice daily on days 4–7, and then 1 mg twice daily for the rest of the 12 weeks.
  - The placebo group received nicotine-free ECs.
- Each group underwent a 12-week intervention and observation period of up to 52 weeks to monitor for smoking cessation.
- Participants received a total of eight sessions of individualized smoking cessation counseling lasting 30 minutes with an established motivational interviewing technique.
- The primary outcome was a confirmed seven-day abstinence from cigarette smoking measured on week 26 via self-report.
- A CO level of <10 ppm was used to confirm abstinence.
- The secondary outcomes measured self-reported abstinence at 26 weeks, self-reported abstinence at 52 weeks, confirmed smoking abstinence at 52 weeks, and adverse events.
- Adverse events included death due to any cause, events grade three or four, and events leading to discontinuation, insomnia, cough, or other.

INTERVENTION (# IN THE GROUP):

- Nicotine-containing EC: 152
- Varenicline + nicotine-free EC: 153

COMPARISON (# IN THE GROUP): 153

FOLLOW-UP PERIOD: 52 weeks

RESULTS:

Primary Outcome –

- Nicotine-containing EC improved abstinence rates at 26 weeks compared to placebo (risk difference [RD] 21%; 95% CI, 10–30).
- Varenicline improved abstinence rates at 26 weeks compared to placebo (RD 24%; 95% CI, 14–34).

- Varenicline did not affect abstinence rates at 26 weeks compared to nicotine-containing ECs (RD 3%; 95% CI, –8 to 14).

Secondary Outcome –

- Nicotine-containing ECs improved self-reported abstinence at 26 weeks compared to placebo (RD 21%; 95% CI, 10–31).
- Varenicline improved self-reported abstinence at 26 weeks compared to placebo (RD 23%; 95% CI, 12–33).
- Varenicline did not affect rates at 26 weeks compared to nicotine-containing ECs.
- Nicotine-containing ECs did not improve self-reported abstinence at 52 weeks compared to placebo.
- Varenicline improved abstinence self-reported abstinence at 52 weeks compared to placebo (RD 19%; 95% CI, 8–28).
- Varenicline did not improve abstinence rates at 52 weeks compared to nicotine-containing EC.
- Nicotine-containing ECs did not improve confirmed abstinence rates at 52 weeks compared to placebo.
- Varenicline improved confirmed abstinence rates at 52 weeks compared to placebo (RD 18%; 95% CI, 8–28).
- Varenicline did not improve confirmed abstinence rates at 52 weeks compared to nicotine-containing ECs.

Adverse Events –

- Adverse events leading to discontinuation of a study treatment occurred in 9.9% of the nicotine-containing EC group, 18% in the varenicline group, and 9.2% in the placebo group.
- No adverse events in grades three or four were reported.
- Death from any cause occurred in 1.3% of the nicotine-containing EC group, 0% in the varenicline group, and 1.3% in the placebo group.

LIMITATIONS:

- Single-center trial with limited participants
- There was no systematic method to gather information on participants guessing which treatment group they were placed in.
- Limited one-year follow-up
- Long-term harm linked to test treatments
- Different types of ECs with different concentrations may not be able to be replicated.
- Verification by exhaled CO levels was limited to detecting conventional cigarette smoking within the previous 1–2 days.

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Adenotonsillectomy for Pediatric Snoring?

Adenotonsillectomy for Snoring and Mild Sleep Apnea in Children: A Randomized Clinical Trial

Redline S, Cook K, Chervin RD, et al. Adenotonsillectomy for Snoring and Mild Sleep Apnea in Children: A Randomized Clinical Trial. *JAMA*. 2023;330(21):2084-2095. doi:10.1001/jama.2023.22114

KEY TAKEAWAY: An adenotonsillectomy does not significantly improve executive functioning or attention compared to watchful waiting in children with mild sleep-disordered breathing (SDB).

STUDY DESIGN: Multi-center, single-blind randomized control trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Sleep-disordered breathing, including habitual snoring and apneic episodes, affects 6–7% of children. Untreated sleep-disordered breathing in children poses the risk of several consequences including metabolic disease, cardiovascular disease, behavioral problems, daytime sleepiness, impaired growth and neurodevelopment, and quality of life. Adenotonsillar hypertrophy in children is the most recognized risk factor for sleep-disordered breathing. Limited data exists to support the benefits of surgery for sleep-disordered breathing. This study assessed the effectiveness of surgical intervention compared to supportive care in children with mild sleep-disordered breathing.

PATIENTS: Children 3–13 years old with tonsillar hypertrophy and sleep-disordered breathing

INTERVENTION: Adenotonsillectomy

CONTROL: Watchful waiting with supportive care

PRIMARY OUTCOME: Executive functioning and attention

Secondary Outcome: Fine motor control, behavior, SDB symptom burden, sleepiness, disease-specific quality of life, global quality of life, systolic blood pressure (SBP) diastolic blood pressure (DBP), body mass index (BMI)

METHODS (BRIEF DESCRIPTION):

- Children with tonsillar hypertrophy, mild sleep-disordered breathing (habitual snoring most of the night on at least 3 nights per week for 3 months), obstructive apnea index <1 (number of complete obstructive breathing pauses per hour of sleep), obstructive AHI <3 (number of complete and partial obstructive episodes per hour of sleep), and who were considered appropriate candidate for adenotonsillectomy by an otolaryngologist were included in the study.
- Exclusion criteria included recurrent tonsilitis, BMI Z-score of >3, and severe comorbidities.
- Study participants were randomly assigned to early tonsillectomy within four months of randomization or watchful waiting with supportive care.
- All study participants received standardized education on healthy sleep and lifestyle in addition to a referral for untreated allergies or asthma.
- Assessments were conducted by staff blinded to the child's treatment assignment at baseline and 12 months after randomization via standardized polysomnography at a centralized sleep reading center.
- After a night of typical sleep at their home, each child underwent anthropometry, neurodevelopmental tests, and other clinical evaluations every six months.
- Caregivers, unblinded to the child's treatment assignment, completed standardized questionnaires at each examination.
- The primary outcomes of the study were:
  - Executive functioning was assessed via The Behavior Rating Inventory of Executive Functioning (BRIEF) using the Global Executive Composite (GEC) T score. A summary of behavioral regulation and metacognition based on mean scores of 50, with higher scores indicative of worse executive functioning.
  - Attention was measured objectively using a computer-based Go/No-go (GNG) test. This test assesses the child's ability to correctly identify targets corrected for their response bias with higher scores indicative of better attention.
- The secondary outcomes of the study were:
  - Fine motor control was measured objectively using the National Institutes of Health Toolbox 9-Hole Dexterity tests, with times for the child to complete the task averaged across each hand.

- Caregiver rating of behavior was assessed via the Childhood Behavior Checklist (CBCL), which scores specific behavior. Scores range from 24–84, with higher scores indicative of greater emotional, social, and behavioral problems.
- SDB symptom burden was assessed via the Pediatric Sleep Questionnaire-Sleep-Related Breathing Disorder scale. Scores ranged from 0–1, with a higher score indicating greater severity of sleep burden.
- Sleepiness was assessed via the Epworth Sleepiness Scale modified for children (mESS). Scores range from 0–24 with higher scores indicating greater daytime sleepiness.
- Disease-specific quality of life was assessed via the Obstructive Sleep Apnea 19 (OSA-18) assessment tool, a Likert scale that assesses the frequency of loud snoring over four weeks. Scores range from 18–126, with higher scores indicating greater negative quality of life.
- Global quality of life was assessed by the Pediatric Quality of Life Inventory (PedsQL), which was comprised of four subscales including emotional functioning, social functioning, school functioning, and physical functioning. Scores range from 0–100, with a higher score indicating a better quality of life.
- BMI was analyzed using Z scores were standardized by age and sex. Z score of ≥3 is indicative of obesity. BMI was classified as healthy weight, underweight, overweight, and obese.
- SBP and DBP were assessed via sphygmomanometer at rest.

INTERVENTION (# IN THE GROUP): 231
COMPARISON (# IN THE GROUP): 227

FOLLOW-UP PERIOD: 12 months

RESULTS:

Primary Outcome –

- Adenotonsillectomy did not result in a significant difference in improved executive functioning compared to watchful waiting at 12 months (between-group difference −0.96; 95% CI, −2.7 to 0.74).
- Adenotonsillectomy did not result in a significant difference in improved attention compared to watchful waiting at 12 months (between-group difference 0.05; 95% CI, −0.18 to 0.27).

Secondary Outcome –

- Adenotonsillectomy reduced behavioral problems in children compared to watchful waiting (effect size –3.1; 95% CI, –4.9 to –1.3).
- Adenotonsillectomy decreased SBD symptom burden compared to watchful waiting (effect size –0.16; 95% CI, –0.20 to –0.12).
- Adenotonsillectomy reduced sleepiness compared to watchful waiting (effect size –1.2; 95% CI, –2.2 to –0.21).
- Children who underwent early adenotonsillectomy experienced improvements in both disease-specific quality of life (effect size –9.75; 95% CI, –13 to –6.7) and global quality of life (effect size 4.8; 95% CI, 1.4–8.1).
- Adenotonsillectomy lowered SBP compared to watchful waiting (effect size –9.0; 95% CI, –15 to –2.5).
- Adenotonsillectomy lowered DBP compared to watchful waiting (effect size –6.5; 95% CI, –12 to –1.5).
- No significant differences were observed in fine motor control or BMI between the adenotonsillectomy and watchful waiting groups.

LIMITATIONS:

- Exclusion criteria did not specify what was considered a severe pediatric comorbidity.
- Unknown treatment and duration of children referred for allergies and asthma which may have impacted the results of outcome assessments.
- Caregivers were not blinded to interventions which may have influenced the results of outcome assessments.
- Obstructive sleep apnea is known to impact learning and memory, both of which were not assessed.

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Prostate Cancer Screening with PSA, Kallikrein Panel, and MRI

Prostate Cancer Screening with PSA, Kallikrein Panel, and MRI: The ProScreen Randomized Trial

Auvinen A, Tammela TLJ, Mirtti T, et al. Prostate Cancer Screening With PSA, Kallikrein Panel, and MRI: The ProScreen Randomized Trial. *JAMA*. 2024;331(17):1452-1459. doi:10.1001/jama.2024.3841

KEY TAKEAWAY: A small increase in prostate cancer detection occurred using a tiered prostate cancer screening protocol using prostate-specific antigen (PSA), then subsequently a panel of four prostate-specific lab tests, and finally an MRI scan with biopsy.

STUDY DESIGN: Unblinded randomized controlled trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Primary prevention screening for prostate cancer with PSA has harms and benefits. PSA screening can lead to unnecessary procedures and discomfort for patients, overdiagnoses, and underdiagnoses.

PATIENTS: Men 50–63 years old

INTERVENTION: Tiered screening

CONTROL: No invitation to tiered screening

PRIMARY OUTCOME: Number and rates of low-grade and high-grade prostate cancers detected

METHODS (BRIEF DESCRIPTION):

- Men without a diagnosis of prostate cancer who lived in Helsinki and Tampere, Finland, in 2018 were included in the study.
- Included men were randomly split into a 1:3 ratio to the screening group and the no-invitation group.
- The screening group received a PSA test, and if the PSA was >3.0 ng/ml, they were invited to do further screening tests in sequential order.
- The four-kallikrein panel includes a total, free, and intact PSA and a human-kallikrein-related peptidase 2 (hK2).
  - If the kallikrein panel was >7.5%, then the subjects received an MRI with a biopsy
- The long-term primary outcome was prostate cancer mortality.
- The outcome of this study was the diagnosis of low-grade or high-grade prostate cancer.
- The follow-up period of 10 and 15 years starts at the date of randomization of the subjects. At these times, prostate cancer mortality will be calculated.
- Depending on PSA results, participants were asked to rescreen within 2–6 years.
  - If the PSA was ≥3.0 ng/ml then the participants would be rescreened in two years, if it was between 1.5 ng/ml and 2.99 ng/ml, then the participants would be rescreened in four years, and if it was <1.5 ng/ml, the participants would be rescreened in six years.
- Currently, Finland does not formally support any prostate cancer screening program.

INTERVENTION (# IN THE GROUP): 15,299

COMPARISON (# IN THE GROUP): 45,544

FOLLOW-UP PERIOD: 10–15 years

RESULTS:

Primary Outcome –

- Invited men who underwent screening were more likely to be diagnosed with prostate cancer compared to control (2.1% vs 0.78%, respectively; risk difference [RD] 1.3; 95% CI, 0.97–1.6; NNS=77).
- All invited men, including those who did not undergo screening, were more likely to be diagnosed with prostate cancer compared to control, although the effect size was smaller (1.4% vs 0.78%, respectively; RD 0.66; 95% CI, 0.45–0.87; NNS=152).
- All invited men, including those who underwent screening, were more likely to be diagnosed with:
  - Low-grade prostate cancer defined as Gleason <7 (0.26% vs 0.14%, respectively; RD 0.11%; 95% CI, 0.03–0.20; NNT=909)
  - High-grade prostate cancer (1.1% vs 0.62%; RD 0.51; 95% CI, 0.33–0.7; NNT=196)

LIMITATIONS:

- Waiting for long-term follow-up to assess the primary outcome of prostate cancer-specific mortality.
- Results represent only one round of screening.
- The control group screening was the usual care, but the usual care in Finland differs from that in other countries.

- Since the study started in 2018, there still needs to be multiple follow-ups to determine if the primary outcome is reached.

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Should Statins Be Continued in the Elderly?

Benefits and Risks Associated with Statin Therapy for Primary Prevention in Old and Very Old Adults: Real-World Evidence from a Target Trial Emulation Study

Xu W, Lee AL, Lam CLK, Danaei G, Wan EYF. Benefits and Risks Associated With Statin Therapy for Primary Prevention in Old and Very Old Adults: Real-World Evidence From a Target Trial Emulation Study [published correction appears in Ann Intern Med. 2024 Aug;177(8):1144. doi: 10.7326/ANNALS-24-01062]. *Ann Intern Med*. 2024;177(6):701-710. doi:10.7326/M24-0004

KEY TAKEAWAY: Statins used as primary prevention decrease all-cause mortality and cardiovascular disease (CVD) in patients ≥75 years old.

STUDY DESIGN: Prospective, observational cohort with sequential target trial emulation

LEVEL OF EVIDENCE: STEP 3

BRIEF BACKGROUND INFORMATION: Current evidence is inconclusive about the benefits of statin use in patients ≥75 years old and guidelines exclude specific recommendations for this patient population. This study aimed to evaluate the benefits and risks of statins for primary prevention regardless of the statin dose.

PATIENTS: Adults ≥75 years old

INTERVENTION: Statin therapy

CONTROL: No statin therapy

PRIMARY OUTCOME: All-cause mortality and CVD
Secondary Outcome: Adverse events

METHODS (BRIEF DESCRIPTION):

- This study was conducted by obtaining electronic health records from the clinical management system of the Hong Kong Health Authority.
- Participation was limited to patients ≥75 years old who were either statin and lipid-lowering drug naïve or did not have any of these medications within the past two years per individual patient chart reviews.
- Statin therapy was defined as the use of simvastatin, atorvastatin, fluvastatin, rosuvastatin, lovastatin, pitavastatin, or pravastatin at any dose.
- Patients with a history of CVD, liver dysfunction, myopathies, and cancer were excluded from the study.
- Statin indication was defined as the following:
  - ≤1 CVD risk factor with low-density lipoprotein (LDL) >160 mg/dL
  - ≥2 CVD risk factors with LDL >130 mg/dL
  - Coronary heart disease (CHD) risk equivalents with LDL >100 mg/dL
- CHD equivalents included hypertension (HTN), hypertensive chronic kidney disease (CKD), hypertensive retinopathy, peripheral vascular disease, type 2 diabetes mellitus (T2DM), diabetic retinopathy.
- All-cause mortality and CVD incidence were measured as the primary outcome of the study and were defined as a composite outcome of myocardial infarction (MI), heart failure, and stroke.
- The secondary outcomes measured adverse events characterized by myopathies defined by clinician diagnosis and liver dysfunction defined as transaminitis.
- This study utilized a target trail emulation defined as using observational data to stimulate hypothetical randomized controlled trials.
- Adults between 6–74 years old were used to test the validity of the emulation trial by serving as a standard given the known benefits of statin therapy within this population.
- The emulated trial provided baseline characteristics ≤0.1 standardized mean difference between the three groups (60–74 years old, 75–84 years old, and ≥85 years old).

INTERVENTION (# IN THE GROUP): 97,462

COMPARISON (# IN THE GROUP): 66,453

FOLLOW-UP PERIOD: 5.6 years

RESULTS:

Primary Outcome –

- Statin therapy decreased CVD incidence for all age groups compared to patients not on statin therapy.
  - 60–74 years old (hazard ratio [HR] 0.89; 95% CI, 0.86–0.92; number needed to treat [NNT]=110)
  - 75–84 years old (HR 0.94; CI, 0.90–0.98; NNT=20)
  - ≥85 years old (HR 0.85; 95% CI, 0.77–0.94; NNT=23)

- Statin therapy decreased all-cause mortality for all age groups compared to patients not on statin therapy.
    - 60–74 years old (HR 0.87; 95% CI, 0.84–0.91; NNT=149)
    - 75–84 years old (HR 0.90; 95% CI 0.86–0.94; NNT=69)
    - ≥85 years old (HR 0.85; 95% CI, 0.78–0.93; NNT=24)

Secondary Outcome –

- There was no statistically significant difference in adverse events for patients on statin therapy compared to patients not on statin therapy for any age group.

LIMITATIONS:

- Lifestyle modifications including diet, physical activity, and genetic factors were not considered.
- Statin intensity was not taken into consideration as any dose of statin was used in this research.

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The views expressed herein are those of the author and do not necessarily reflect the official policy of the Department of the Air Force, Defense Health Agency, Department of Defense, or the US Government.

Terbinafine Still on Top for Dermatophyte Toenail Onychomycosis

Relative Impact of Traditional vs Newer Oral Antifungals for Dermatophyte Toenail Onychomycosis: A Network Meta-Analysis Study

Gupta AK, Venkataraman M, Bamimore MA. Relative impact of traditional vs. newer oral antifungals for dermatophyte toenail onychomycosis: a network meta-analysis study. *Br J Dermatol*. 2023;189(1):12-22. doi:10.1093/bjd/ljad070

KEY TAKEAWAY: Terbinafine remains a safe, effective, and most studied treatment for dermatophyte onychomycosis of toenails, however, it is also effective at higher doses and longer durations than traditionally prescribed.

STUDY DESIGN: Bayesian network meta-analysis study including 21 randomized controlled trials (RCTs) and observational studies (N=6,724)

LEVEL OF EVIDENCE: STEP 3 (downgraded due to the design of included studies)

BRIEF BACKGROUND INFORMATION: Few meta-analyses exist comparing different treatments of onychomycosis. This meta-analysis synthesizes available data to provide insight into the effectiveness of anti-fungal monotherapies. Onychomycosis is a common condition treated by primary care providers.

PATIENTS: Patients with dermatophyte toenail onychomycosis

INTERVENTION: Oral monotherapy anti-fungal

CONTROL: Other active monotherapy or placebo

PRIMARY OUTCOME: One year of mycological and complete cure rates

METHODS (BRIEF DESCRIPTION):

- Included patients were healthy adults >18 years old who had onychomycosis caused by dermatophytes.
- Across the 21 studies, 36 different monotherapy regimens were compared.
- Monotherapies were compared to other monotherapy regimens or placebo.
- Various terbinafine regimens included 250 mg to 100 mg over 6–24 weeks; some included nail abrasion or aggressive debridement.
- Other monotherapies included griseofulvin and a variety of different “azole” regimens.
- Outcomes were determined one year from the start of treatment by mycological cure (negative microscopy and culture) and complete cure (absence of signs and symptoms) rates.
- Different regimens were compared to obtain relative effects in outcomes and Surface Under the Cumulative Ranking Cure (SUCRA) values, a number.
- The SUCRA value is a number from 0–100%, the higher the number, the higher the likelihood that the therapy is in the top rank.

INTERVENTION (# IN THE GROUP): Not available

COMPARISON (# IN THE GROUP): Not available

FOLLOW-UP PERIOD: One year

RESULTS:

Primary Outcome –

- 250 mg terbinafine for 12 weeks improved mycological cure rates compared to 200 mg itraconazole (3 studies, n=589; odds ratio [OR] 2.4; 95% CI, 1.6–3.6).
- 250 mg terbinafine for 12 weeks did not improve complete cure rates compared to terbinafine 250 for 12 weeks, followed by no treatment for 12 weeks, followed by treatment for four weeks (1 study, n=107; OR 0.29; 95% CI, 0.11–0.42).

LIMITATIONS:

- Seven of the 21 studies were found to have a high risk of bias, concentrating on selection and performance biases.
- 11 of the 21 studies were at unclear risk of bias and only three were without risk of bias.
- Gender was absent for many studies and was unable to be assessed as an effect modifier.
- Few statistically significant trials that were directly compared to one another were included in the meta-analysis.
- No stratification by age as a modifier, inclusion criteria were “immunocompetent adults” only
- The majority of secondary outcomes for safety and tolerability were not available in the main body of the paper, only in the supporting information.
- Only 14 of the 76 of outcomes in the pairwise comparison were statistically significant.
- The funding source was not provided.

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Rural-Urban Divide in Diabetes Care: A Retrospective Analysis

Disparities in Diabetes Care: Differences Between Rural and Urban Patients Within a Large Health System

Foss R, Fischer K, Lampman MA, et al. Disparities in Diabetes Care: Differences Between Rural and Urban Patients Within a Large Health System. *Ann Fam Med*. 2023;21(3):234-239. doi:10.1370/afm.2962

KEY TAKEAWAY: Living in rural areas is associated with fewer patients achieving diabetes care quality goals compared to living in urban areas. Being female and older is each associated with a higher likelihood of achieving these goals.

STUDY DESIGN: Retrospective cohort study

LEVEL OF EVIDENCE: STEP 4

BRIEF BACKGROUND INFORMATION: There is growing evidence that rural populations in the US face greater healthcare challenges, particularly in the management of chronic diseases such as diabetes. Rural patients often lack access to healthcare services, which may negatively impact their ability to meet diabetes management goals. The primary objective of this study was to compare the quality of diabetes care between rural and urban patients. The secondary objective was to identify potential factors contributing to disparities in care.

PATIENTS: Adults with type 2 diabetes mellitus (T2DM)

INTERVENTION: Rural residence

CONTROL: Urban residence

PRIMARY OUTCOME: Attainment of diabetes goals

Secondary Outcome: Adjusted Clinical Group (ACG) risk score (a complexity marker), number of outpatient visits, diabetes education, nutritionist visits, endocrinology visits, insurance type, clinician credentials

METHODS (BRIEF DESCRIPTION):

- Patients in this study were gathered from an integrated health system with facilities in Minnesota, Wisconsin, and Iowa. The patients were primarily white (93%) and with a mean age of 66 years old.
- Inclusion criteria included the diagnosis of T2DM and assignment to a family medicine primary care clinician during the study period in 2019.
- Classification into rural vs urban residence was derived from the Rural-Urban Commuting Area code for each patient's primary zip code. Urban patients in this model lived in or near a city of ≥50,000 residents.
- The attainment of quality diabetes care was defined as meeting all five parameters of the D5 metric, which includes no tobacco use, A1C <8%, BP <140/90 mmHg, low-density lipoprotein (LDL) cholesterol at goal or statin use, and aspirin use as per clinical guidelines.
- The primary outcome of attainment of the D5 metric was analyzed using a generalized linear mixed model. Patient characteristics between rural and urban groups were compared using chi-squared tests for categorical variables and Kuskal-Wallis tests for continuous variables.
- ACG score >1 indicated more complex patients and a score <1 indicated less complex patients and the diabetes educator indicated that at least one visit for education.
- Having an endocrinologist visit during a given year is a sign of uncontrolled DM this association is caused by referring the patient to a specialist only in case not meeting the diabetes goal.
- Additionally, residents and fellows were included as physicians. This was measured to link for association with meeting the diabetes goals.

INTERVENTION (# IN THE GROUP): 45,279

COMPARISON (# IN THE GROUP): 24,642

FOLLOW-UP PERIOD: One year

RESULTS:

Primary Outcome –

- Rural patients were less likely to attain diabetes goals compared to urban patients (adjusted odds ratio [aOR] 0.93; 95% CI, 0.88–0.97).
- Women were more likely than men to attain diabetes goals (aOR 1.1; 95% CI, 1.03–1.1).
- Older patients (increasing per 10 years) were more likely than younger patients to attain diabetes goals (aOR 1.2; 95% CI, 1.02–1.1).

Secondary Outcome –

- Patients with access to a diabetes education visit were less likely to attain quality goals (aOR 0.92; 95% CI, 0.87–0.97).
- There was no significant difference in diabetes education visits between rural and urban patients.

- Patients with access to an endocrinology visit were less likely to attain quality goals (aOR 0.80; 95% CI, 0.73–0.86).
- Rural patients were less likely to have an endocrinology visit compared to urban patients (5.5% vs 9.3%; *p*<.001).
- Increasing outpatient visits (beyond 1 per year) was associated with a slightly higher likelihood of attaining quality goals (aOR 1.03; 95% CI, 1.03–1.04).
- Rural patients had fewer outpatient visits compared to urban patients (mean number of visits 3.2 vs 3.9, respectively; *p*<.001).
- Patients with Medicaid were less likely to attain quality goals compared to commercial insurance (aOR 0.58; 95% CI, 0.53–0.63).
- Rural patients were more likely to have Medicaid than urban patients (8.0% vs 7.3%, respectively; *p*<.001).
- Patients with Medicare were more likely to attain quality goals compared to commercial insurance (aOR 1.2; 95% CI, 1.1–1.2).
- Rural patients were more likely to have Medicare than urban patients (63% vs 61%, respectively; *p*<.001).
- Non-white patients were less likely to attain quality goals than White patients (aOR 0.83; 95% CI, 0.77–0.90).
- Rural patients were more likely to identify as White than urban patients (94% vs 91%, respectively; *p*<.001).
- There was no significant difference in the attainment of care goals between patients who had a nutrition visit and those who did not.
- Rural patients were much more likely to have an advanced practice provider as their primary care clinician compared to urban patients (26% vs 9.1%, respectively; *p*<.001).
- There was no significant difference found between advanced practice providers and physicians, though the authors note that some existing data contradicts this outcome.
- There was no significant difference between nutrition visits for rural vs urban patients.

LIMITATIONS:

- The study was retrospective therefore, a causative relationship cannot be identified.
- The large-scale design of the study may identify statistically significant differences that lack clinical meaningfulness.
- There was an inability to control for certain confounders which included patient education, individual health beliefs, physician workload, and clinic accessibility.
- The study population was primarily White and skewed toward older patients which may limit the external validity of the study.
- Data was collected during 2019 and may have been impacted by the COVID-19 pandemic.
- The negative impact of diabetes education and endocrinology found in this study was attributed to a selection bias of patients with severe disease being more likely to have a referral to these specialists.

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