GOOD EVIDENCE MATTERS

GEMs of the Week

SPOTLIGHT

Low-Dose Colchicine
A Small Dose, But a Big Impact on Cardiovascular Outcomes in Patients with Diabetes

Chair Placement
Does the "Nudge" Make Physician Behavior and Patient Satisfaction Budge?

Wait, Don't Intubate
Conservative Airway Management for Acute Poisoning

Could Vitamin D Supplementation Improve Primary Dysmenorrhea?

Coffee! It's Good for the Heart and Soul

COVID-19
The Virus that Gives a Sweet Tooth!

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Low-Dose Colchicine: A Small Dose, But a Big Impact on Cardiovascular Outcomes in Patients with Diabetes

Low-Dose Colchicine in Patients with Type 2 Diabetes and Recent Myocardial Infarction in the Colchicine Cardiovascular Outcomes Trial (COLCOT).

Roubille F, Bouabdallaoui N, Kouz S, et al. Low-Dose Colchicine in Patients with Type 2 Diabetes and Recent Myocardial Infarction in the Colchicine Cardiovascular Outcomes Trial (COLCOT). *Diabetes Care*. 2024;47(3):467-470. doi:10.2337/dc23-1825

KEY TAKEAWAY: Low-dose colchicine reduces cardiovascular (CV) events in patients with type 2 diabetes mellitus (T2DM) and recent myocardial infraction (MI).

STUDY DESIGN: Double-blinded randomized controlled trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Colchicine was a medication that worked to combat inflammation, particularly during acute episodes of gout. Data from the Colchicine Cardiovascular Outcomes Trial (COLCOT) suggested that colchicine had a beneficial effect in decreasing inflammation in patients with coronary artery disease (CAD). Roughly one-third of the patients who had a diagnosis of CAD also had a diagnosis of T2DM. This prespecified analysis investigated if colchicine influenced future CV events in patients with T2DM.

PATIENTS: Adults with T2DM with recent MI

INTERVENTION: Low dose colchicine initiated within 30 days of MI

CONTROL: Placebo

PRIMARY OUTCOME: Composite cardiovascular events
Secondary Outcome: Individual cardiovascular events, adverse events

METHODS (BRIEF DESCRIPTION):

- Adult patients with recent history of MI within last 30 days were included in the study.
- Patients with severe heart failure (HF), left ventricular ejection fraction (LVEF) <35%, stroke in the past three months, type 2 index MI, previous or planned coronary artery bypass surgery, inflammatory bowel disease (IBD), or chronic diarrhea were excluded from the study.
- Patients were randomized 1:1 to 0.5 mg of colchicine once daily or placebo.
- The primary outcome assessed the composite of CV events including cardiovascular death, resuscitated, cardiac arrest, MI, stroke, or urgent hospitalization for angina requiring coronary intervention.
- CV events were identified from clinical records, diagnostic tests, and adjudication by an independent clinical events committee. They were classified as present or absent (no scale-based scoring system).
- Secondary outcomes included the individual components of the composite endpoint including MI, stroke, and cardiovascular death, as well as adverse events.
- The study calculated hazard ratios (HR) with confidence intervals (CI) and p-values to determine statistical significance using the Cox proportional hazard models.

INTERVENTION (# IN THE GROUP): 462

COMPARISON (# IN THE GROUP): 497

FOLLOW-UP PERIOD: Median of 23 months

RESULTS:

Primary Outcome –

- Colchicine reduced the composite of cardiovascular events compared to placebo (hazard ratio [HR] 0.65; 95% CI, 0.44–0.96).

Secondary Outcome –

- Colchicine reduced the risk of stroke compared to placebo (HR 0.21; 95% CI, 0.05–0.96).
- Colchicine did not reduce the risk of cardiovascular death, resuscitated cardiac arrest, MI, or urgent hospitalization for angina leading to coronary revascularization compared to placebo.
- Colchicine increased nausea and pneumonia adverse events compared to placebo.
  - Nausea (2.7% vs 0.8%, respectively; *p*=.03).
  - Pneumonia (2.4% vs 0.4%, respectively; *p*=.008).
- Other related adverse events reported included gastrointestinal events, diarrhea, flatulence, decreased appetite, gastrointestinal hemorrhage, anemia, leukopenia, thrombocytopenia, infection, severe infection, diabetic foot infection, septic shock, hospitalization for heart failure, and cancer, but were not statistically significant between groups.

LIMITATIONS:

- Composite endpoint did not show significant reduction in MI or mortality.
- While this study shows secondary prevention in high-risk patients, it doesn't answer if it should be used as a general practice in high-risk patients who have major a CV event.
- The study had a short follow up period, which may not be enough to assess long term benefit and/or harm of daily colchicine treatment.
- The study was conducted in a prespecified patient population (patients with T2DM and recent MI), which may limit the ability to generalize the findings to other groups.

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Chair Placement: Does the "Nudge" Make Physician Behavior and Patient Satisfaction Budge?

Effect of Chair Placement on Physicians' Behavior and Patients' Satisfaction: Randomized Deception Trial

Iyer R, Park D, Kim J, Newman C, Young A, Sumarsono A. Effect of Chair Placement on Physicians' Behavior and Patients' Satisfaction: Randomized Deception Trial. *BMJ*. 2023;383:e076309. Published 2023 Dec 15. doi:10.1136/bmj-2023-076309

KEY TAKEAWAY: Placing chairs at bedside in hospital single-occupancy rooms increases physician sitting rates.

STUDY DESIGN: Single site double blind randomized clinical trial

LEVEL OF EVIDENCE: STEP 3 (downgraded due to not achieving the required sample size)

BRIEF BACKGROUND INFORMATION: Sitting has been shown to improve physician communication and patient satisfaction. Prior studies have shown hospitalist physicians sit in only one in five encounters. The purpose of this study was to determine if chair placement can improve physician sitting rate.

PATIENTS: Internal medicine hospitalist physicians and hospitalized adult patients

INTERVENTION: Placing chairs within three feet of patients' beds

CONTROL: Chair placed in cabinet

PRIMARY OUTCOME: Physician sitting rate

Secondary Outcome: Patient satisfaction, physician time spent in room, and physician and patient perception of time spent in room

METHODS (BRIEF DESCRIPTION):

- A total of 51 board-certified internal medicine hospitalists at one community hospital with a mean age 36 years old, and six mean years post residency were included.
- Adult hospitalized patients had a mean age of 53 years old, 54% men, 35% Hispanic, and 40% were Black.
- Patients unable to answer four orientation questions were excluded.
- Patient rooms were randomized 1:1 to chair placed three feet from bed or usual placement in cabinet.
- Patients were told the study measured satisfaction.
- Physicians were told the study explored practice variation and to allow student shadowing.
- Medical student observed physician-patient interactions, noting if physicians sat, for how long, and their behavior (time in room, introducing self, and knocking).
- After physicians left the room, medical students administered two surveys to patients: Tool to Assess Inpatient Satisfaction with Care from Hospitalists (TAISCH) and the truncated physician communication component of the Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS).
    - TAISCH measures patient satisfaction with scores ranging from 15–75. Higher scores indicate greater patient satisfaction.
    - HCAHPS measures patient experiences of hospital stays, the truncated physician communication component measures patient perceived quality of physician communication with scores ranging from 3–12. Higher scores indicate greater perceived physician communication.
- Physicians completed post-encounter surveys.

INTERVENTION (# IN THE GROUP): 60

COMPARISON (# IN THE GROUP): 65

FOLLOW-UP PERIOD: 10 months

RESULTS:

Primary Outcome –

- Chair placement at bedside increased physician sitting during the patient encounter compared to the control (odds ratio [OR] 21; 95% CI, 7.3–59).

Secondary Outcome –

- Chair placement at bedside increased patients' satisfaction measured by TAISCH scores compared to control (effect estimate 3.9; 95% CI, 0.9–7.0).
- Chair placement at bedside increased patient satisfaction measured by HCAHPS scores (OR 5.1; 95% CI, 1.1–25).
- Chair placement at bedside was not associated with increased time spent in the room, and perception of increased time in room for physicians or patients.

LIMITATIONS:

- The study did not attain the precalculated sample size estimate 253 patient encounters, resulting in its termination after achieved only 125 encounters

which could overestimate the true magnitude of effect.

- Chairs were placed immediately before each encounter unlike typical situations where they may be used by others.
- The study was conducted in a single county hospital using only single-occupancy rooms, making the findings less generalizable to other hospitals.
- HCAHPS surveys were collected electronically immediately after encounter vs the typical administration after hospitalization, which is via mail.
- The use of deception might have limited how the study was conducted.
- The study might have led to observer bias due to medical students observing the encounters.

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Wait, Don't Intubate: Conservative Airway Management for Acute Poisoning

Effect of Noninvasive Airway Management of Comatose Patients with Acute Poisoning: A Randomized Clinical Trial

Freund Y, Viglino D, Cachanado M, et al. Effect of Noninvasive Airway Management of Comatose Patients with Acute Poisoning: A Randomized Clinical Trial. *JAMA*. 2023;330(23):2267-2274. doi:10.1001/jama.2023.24391

KEY TAKEAWAY: Conservatively withholding intubations decreases in-hospital deaths, and length of stays (LOS) in both the hospital and intensive care unit (ICU) and requirement for mechanical ventilation compared to intubating patients who are comatose from acute poisoning.

STUDY DESIGN: Multicenter, nonblinded randomized controlled trial

LEVEL OF EVIDENCE: STEP 3 (downgraded due to lack of blinding)

BRIEF BACKGROUND INFORMATION: The decision to intubate comatose patients with acute poisoning and a Glasgow Coma Scale (GCS) <9 remains controversial, as it aims to prevent aspiration pneumonia but also introduces risks such as hemodynamic instability, hypoxia, and airway complications. Over 20,000 poisoned patients are intubated annually in the U.S., yet no high-quality evidence definitively supports or refutes this practice. While some observational studies suggest early intubation may reduce aspiration risk, others have found no significant impact on aspiration or mortality rates.

PATIENTS: Comatose adults (>18 years old) with suspected acute poisoning and GCS <9

INTERVENTION: Conservative airway management strategy of withholding intubation

CONTROL: Usual Care; intubation

PRIMARY OUTCOME: In-hospital death, length of ICU admission, median length of ICU stay, median length of in-hospital stays, and use of mechanical ventilation
Secondary Outcome: Median length of mechanical ventilation, intubation-related adverse events, the occurrence of pneumonia, first pass failure

METHODS (BRIEF DESCRIPTION):

- 225 patients were recruited for this study from 20 emergency departments (ED) and one ICU in France.
- Four EDs only recruited patients from the hospital, and 16 EDs recruited patients in hospital and pre-hospital medical emergency systems with an emergency medicine physician present at the scene.
- 38% were female and 62% were male, mean age 33 years old.
- Patients were randomized into an intervention group or a control group.
- Randomization was stratified by block balance using sealed envelopes.
- The intervention group underwent a conservative airway strategy of withholding intubation.
- The control group received routine practice where intubation occurred at the physician's discretion.
- The primary outcome measured in-hospital deaths mechanical ventilation, percentage of ICU admissions, median length of ICU stays, median length of in-hospital stays, truncated at 28-days.
- Secondary outcomes measured the following: median length of mechanical ventilation, intubation-related adverse events, the occurrence of pneumonia within 48-hours, and the proportion of first pass failures.

INTERVENTION (# IN THE GROUP): 116

COMPARISON (# IN THE GROUP): 109

FOLLOW-UP PERIOD: One month

RESULTS:

Primary Outcome –

- There were no reported in-hospital deaths from either group.
- Conservatively withholding intubation decreased the risk the ICU admission compared to control (46% vs 72%, respectively; odds ratio [OR] 0.23; 95% CI, 0.12–0.44).
- Conservatively withholding intubation decreased median length of ICU stay compared to control (0 vs 24 hours, respectively; rate ratio [RR] 0.39; 95% CI, 0.24–0.66).
- Conservatively withholding intubation did not significantly affect the median length of in-hospital stay compared to control (22 vs 37 hours, respectively; RR 0.74; 95% CI, 0.53–1.0).
- Conservatively withholding intubation decreased the likelihood of requiring mechanical ventilation

compared to control (21% vs 65%, respectively; OR 0.12; 95% CI, 0.06–0.24).

Secondary Outcome –

- Conservatively withholding intubation decreased median length of mechanical ventilation compared to control (21% vs 65%, respectively; RR 0.12; 95% CI, 0.06–0.24).
- Conservatively withholding intubation reduced the risk of intubation-related adverse events compared to control (6% vs 15%, respectively; OR 0.37; 95% CI, 0.15–0.95).
- Conservatively withholding intubation reduced the risk of first pass failure compared to control group (OR 0.06; 95% CI, 0.01–0.46).
- There was no significant difference in occurrence of pneumonia between the groups.

LIMITATIONS:

- The study was unblinded, which could introduce performance and detection biases.
- The findings are specific to comatose patients with acute poisoning and a GCS score of <9, which may limit applicability to other patient groups.
- While adverse events were reported, a more detailed breakdown could provide better insights into the safety profile of the intervention.

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Could Vitamin D Supplementation Improve Primary Dysmenorrhea?

Effect of Vitamin D Supplementation on Primary Dysmenorrhea: A Systematic Review and Meta-Analysis of Randomized Clinical Trials

Chen YC, Chiang YF, Lin YJ, et al. Effect of Vitamin D Supplementation on Primary Dysmenorrhea: A Systematic Review and Meta-Analysis of Randomized Clinical Trials. *Nutrients*. 2023;15(13):2830. Published 2023 Jun 21. doi:10.3390/nu15132830

KEY TAKEAWAY: Vitamin D treatment substantially reduces pain levels in women who experience dysmenorrhea.

STUDY DESIGN: Systemic review and meta-analysis of nine randomized controlled trials (RCTs) (N=695)

LEVEL OF EVIDENCE: STEP 3 (downgraded due to high heterogeneity, bias in the form of inconsistent blinding, and incomplete reporting of results)

BRIEF BACKGROUND INFORMATION: Primary dysmenorrhea is a challenging problem, with nonsteroidal anti-inflammatory drugs (NSAIDs) and oral contraceptive pills (OCPs) being current mainstays of treatment. There is growing demand for alternative treatments that do not disrupt ovulation with a favorable safety profile. This study investigated whether vitamin D could be an effective treatment for pain associated with primary dysmenorrhea.

PATIENTS: Menstruating women 13–40 years old

INTERVENTION: Vitamin D supplementation (D3)

CONTROL: Placebo or standard care

PRIMARY OUTCOME: The degree of pain relief after vitamin D treatment

Secondary Outcome: Subgroup analysis based on dose, study time, and dose interval

METHODS (BRIEF DESCRIPTION):

- A literature search was conducted for primary dysmenorrhea, restricting the search to English language from 2012–2023, and only involving RCTs.
- Persons with menstrual cycles occurring every 21–35 days, with periods lasting between 3–7 days were included in the study.
- The population had to experience menstrual pain with no underlying cause or history of uterine or ovarian disease, and a normal pelvic examination. They had to be in good health and could not receive medical treatment including calcium or magnesium-containing medications or OCPs.
- Patients with a diagnosis of secondary dysmenorrhea or other reproductive diseases, use of OCPs or intrauterine device pregnancy, or treatment with other vitamins or minerals were excluded from the study.
- Seven of the nine studies were conducted in Iran, with the other studies being conducted in Saudia Arabia and India.
- Data was analyzed by two investigators independently.
    - Some patients received 300,000 IU as a single dose. This was given five days before their putative next menses in two studies and any time in a single study for one, two or three cycles depending on the study.
    - Some patients received 50,000 IU as a regular weekly dose for eight weeks.
    - Some patients received 5,000 IU plus 1,000 mg calcium for about 20 consecutive days for three cycles.
    - Some patients received 3,000 IU plus 500 mg mefenamic acid monthly for three cycles.
    - Recent studies included over-the-counter acetaminophen or NSAIDs for ethical reasons and to mitigate confounding effects.
    - Each study utilized a placebo administered in the same manner as the control.
    - Some studies included additional agents and examined those individually.
- Menstrual pain intensity was assessed using the visual analogue scale (VAS), rated as 0–10, in eight studies. One used a numerical rating scale (NRS), rated as 0–10.
- Subgroup analyses were based on weekly average (greater or less than 50,000 IU) and total vitamin D dose (greater or less than 400,000 IU), study time (greater or less than 70 days), and dose interval (monthly or once vs weekly or daily).
- Outcomes were compared using the standardized mean difference (SMD) and 95% confidence intervals (CIs).

- The Cochrane Collaboration tool was used to assess risk of bias. With this tool, performance bias, detection bias, attrition bias and reporting bias were assessed.

INTERVENTION (# IN THE GROUP): 282

COMPARISON (# IN THE GROUP): 413

FOLLOW-UP PERIOD: 2–4 months

RESULTS:

Primary Outcome –

- Vitamin D supplementation significantly reduced menstrual pain compared to placebo in those with dysmenorrhea (9 trials, n=695; standardized mean difference [SMD] –1.4; 95% CI, –2.1 to –0.73; I^2=92%).

Secondary Outcome –

- Weekly vitamin D supplementation of ≥50,000 IU decreased pain whether it was administered for more or less than 70 days, and in any dose interval, compared to the control.
  - Total dose ≥400,000 IU (SMD −1.1; 95% CI, −1.6 to −0.49)
  - Study duration ≥70 days (SMD −0.94; 95% CI, −1.5 to −0.38)
  - Study duration <70 days (SMD −1.2; 95% CI, −2.0 to −0.33)
  - Dosed monthly or once (SMD −0.94; 95% CI, −1.5 to −0.38)
  - Dosed weekly or daily (SMD −1.2; 95% CI, −2.0 to −0.33)

LIMITATIONS:

- All the studies were conducted outside the US, which may influence generalizability to US populations.
- Two scoring systems for menstrual pain intensity were used, with NRS being easier to understand and faster to complete whereas VAS can be susceptible to errors secondary to misinterpretation of the scale length.
- High heterogeneity resulted in wide variation between dosing and subsequent serum levels.
- The inclusion of primary dysmenorrhea relied on reported medical history.
- Potential publication bias was noted as well as inconsistent blinding.
- High doses of vitamin D supplementation carry risk of hypervitaminosis if unmonitored.
- Incomplete reporting of the results negatively impacts level of evidence.

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Coffee! It's Good for the Heart and Soul

Coffee and Tea Consumption and Cardiovascular Disease and All-Cause and Cause-Specific Mortality in Individuals with Diabetes Mellitus: A Meta-Analysis of Prospective Observational Studies

Ding L, Wang HP, Zhao JY, et al. Coffee and Tea Consumption and Cardiovascular Disease and All-cause and Cause-specific Mortality in Individuals with Diabetes Mellitus: A Meta-analysis of Prospective Observational Studies. *Front Nutr*. 2025;12:1570644. Published 2025 Jun 2. doi:10.3389/fnut.2025.1570644

KEY TAKEAWAY: In patients with diabetes, higher rates of coffee consumption may lower risks of mortality and cardiovascular disease (CVD) compared to lower rates of daily coffee consumption. Higher rates of tea consumption may lower risks of mortality.

STUDY DESIGN: Meta-analysis of 17 prospective observational studies (N=160,653)

LEVEL OF EVIDENCE: STEP 3 (downgraded due to imprecision with intervention measurement)

BRIEF BACKGROUND INFORMATION: Patients with diabetes are at a higher risk for cardiovascular disease and mortality than the general population. Coffee and tea consumption have been linked to a decreased risk of CVD and mortality in the general population. This study aimed to determine if coffee or tea consumption in patients with diabetes was associated with a decrease in cardiovascular disease and mortality.

PATIENTS: Adults with diabetes mellitus

INTERVENTION: High coffee or tea consumption

CONTROL: Low coffee or tea consumption

PRIMARY OUTCOME: CVD incidence, all-cause mortality, and cause-specific mortality

Secondary Outcome: Stroke incidence, coronary artery disease incidence, dose response

METHODS (BRIEF DESCRIPTION):

- A total of 17 studies published between 2003–2025, primarily from American and European cohorts, were included.
- Studies selected were prospective observational studies that reported risks estimates associated with coffee and/or tea consumption and mortality and/or cardiovascular disease in adult diabetic patients.
- Studies were excluded if they looked at the same study population, looked at the general population instead of diabetic patients specifically, or looked at different types of caffeine intake.
- Coffee and tea consumption categories were measured differently across studies, so a linear analysis was performed that looked at risks estimates with each additional cup per day.
- The New-Castle Ottawa scale was used to grade the quality of the studies included, 12 being high grade, and five being moderate.
- Hazard ratios (HR) and 95% confidence intervals (CI) were calculated using a random effects model looking at the association of coffee and/or tea consumption over time and the risks of CVD, mortality, and stroke incidence.
- Statistical analysis was also used to look at a dose response, higher intake of coffee/tea over time, vs lower intake to risk estimates.
- The certainty of evidence was graded using the Nutri grade meta-evidence rating for each of the above outcomes.

INTERVENTION (# IN THE GROUP): Not available

COMPARISON (# IN THE GROUP): Not available

FOLLOW-UP PERIOD: Median 11 years

RESULTS:

Primary Outcome –

- Higher rates of coffee consumption were associated with a lower risk of all-cause mortality compared to lower rates of coffee consumption in patients with diabetes mellitus (hazard ratio [HR] 0.82; 95% CI, 0.73–0.91; I^2>58%).
- Higher rates of coffee consumption were associated with a lower risk of CVD incidence (HR 0.85; 95% CI, 0.75–0.97; I^2=0%).
- Higher rates of tea consumption were associated with a lower risk of all-cause mortality compared to lower rates of tea consumption (HR 0.85; 95% CI, 0.79–0.92; I^2>46%).
- There was no significant change in the risk of CVD incidence with high tea consumption (HR 0.96; 95% CI, 0.84–1.1; I^2=0%).

- There was no significant change in the risk of CVD mortality with high coffee consumption (HR 0.84; 95% CI, 0.67–1.0; I^2>58%).
- High rates of tea consumption were associated with decreased risk of CVD mortality (HR 0.86; 95% CI, 0.80–0.93; I^2=0%).
- There was no significant change in the risk of cancer mortality with high coffee or tea consumption:
  - Coffee (HR 0.96; 95% CI, 0.62–1.5; I^2>58%)
  - Tea (HR 0.95; 95% CI, 0.76–1.2; I^2=0)

Secondary Outcome –

- High coffee consumption was associated with a decreased risk of coronary heart disease (HR 0.82; 95% CI, 0.68–0.99; I^2=0%).
- There was no significant decrease in stroke incidence in patients with high coffee consumption.
- A non-linear dose response was observed with coffee consumption (and all-cause mortality, with the lowest risk of all-cause mortality found at four cups of coffee per day, and no significant risk reduction above six cups per day (HR 0.96; 95% CI, 0.93–0.98).
- A non-linear dose response was also observed with tea consumption with the lowest risk of all-cause mortality found at two cups per day of tea (HR 0.93; 95% CI, 0.88–0.96).
- For all other outcomes, there was no significant evidence of nonlinear association.

LIMITATIONS:

- The studies were observational, thus increasing the risk of residual or unmeasured confounding.
- There were inconsistencies with the quantification and assessment of coffee and tea intake between studies.
- Due to the inconsistency of the quantification of coffee and tea intake between studies, it limits the ability to assess a precise dose-response relationship on the risk effects.
- There is potential for publication bias in this study.

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COVID-19: The Virus That Gives a Sweet Tooth!

Incidence of Diabetes After SARS-CoV-2 Infection in England and the Implications of COVID-19 Vaccination: A Retrospective Cohort Study of 16 Million People

Taylor K, Eastwood S, Walker V, et al. Incidence of diabetes after SARS-CoV-2 infection in England and the implications of COVID-19 vaccination: a retrospective cohort study of 16 million people. *Lancet Diabetes Endocrinol*. 2024;12(8):558-568. doi:10.1016/S2213-8587(24)00159-1

KEY TAKEAWAY: COVID-19 increases the incidence of both type 1 and type 2 diabetes, as well as the persistence of type 2 diabetes, particularly in hospitalized patients, while vaccination serves as a protective factor.

STUDY DESIGN: Retrospective cohort study

LEVEL OF EVIDENCE: STEP 3

BRIEF BACKGROUND INFORMATION: The global impact of SARS-CoV-2 on the development of diabetes has been previously studied, showing 30–50% increased incidence of type 2 diabetes after infection. It has been difficult to find such an association with type 1 diabetes. This study aimed to examine the relationship between COVID-19 and different subtypes of diabetes, as well as the impact of COVID-19 vaccination.

PATIENTS: Adults 18–110 years old without prior diabetes diagnosis

INTERVENTION: SARS-CoV-2 diagnosis and COVID-19 vaccination status

CONTROL: People without SARS-CoV-2 diagnosis, regardless of vaccination status

PRIMARY OUTCOME: Incidence of new-onset type 1 and type 2 diabetes

Secondary Outcome: Persistent type 2 diabetes

METHODS (BRIEF DESCRIPTION):

- Adults 18–110 years old in England registered with a general practitioner using TPP software for at least six months prior to the start of the study were included.
- Individuals with a history of COVID-19 diagnosis or any diabetes phenotype prior to the start of the study were excluded.
- In the subgroup of those with development of gestational diabetes, only women were included.
- COVID-19 diagnosis was defined based on validated testing, healthcare diagnosis or death with SARS-CoV-2 infection recorded in health record.
- Cohorts were grouped based on COVID-19 vaccination status which included a pre-vaccination cohort, vaccinated cohort, and unvaccinated.
- The primary outcome measures the incidence of new-onset diabetes defined using primary care and hospital data.
    - Incidence of type 2 diabetes
        - Pre-vaccination cohort: 145,533
        - Vaccinated cohort: 34,365
        - Unvaccinated cohort: 2,781
    - Incidence of type 1 diabetes:
        - Pre-vaccination cohort: 16,047
        - Vaccinated cohort: 2,619
        - Unvaccinated cohort: 747
- The secondary outcome measured persistent type 2 diabetes as evidenced by continued treatment with ≥2 glucose-lowering prescription medications or with elevated HbA1c level >47.5 mmol four months after diagnosis.
- Adjusted hazard ratios (aHRs) were used to compare incidence after COVID-19 diagnosis with diabetes incidence before or in absence of COVID-19. Adjusted hazard ratios were meant to control for potentially confounding variables including age, sex, ethnicity, region of residence, socioeconomic deprivation, smoking status, primary care consultation rate, previous major health events, chronic conditions, body mass index (BMI), health-care worker status and residency in a care home.
- Additional subgroup analysis was performed for individuals diagnosed with type 2 diabetes.

INTERVENTION (# IN THE GROUP): Not available

COMPARISON (# IN THE GROUP): Not available

FOLLOW-UP PERIOD: January 1, 2020, to December 14, 2021

RESULTS:

Primary Outcome –

- COVID-19 exposure increased the incidence of type 2 diabetes in all cohorts compared to no COVID-19 exposure during the first four weeks:

    - Pre-vaccination cohort (adjusted hazard ratio [aHR] 4.3; 95% CI, 4.1–4.5)
    - Vaccinated cohort (aHR 1.6; 95% CI, 1.5–1.8)
    - Unvaccinated cohort (aHR 8.8; 95% CI, 7.5–10)
- COVID-19 exposure increased the incidence of type 1 diabetes in all cohorts during the first four weeks:
    - Pre-vaccination cohort (aHR 2.3; 95% CI, 1.9–2.8)
    - Vaccinated cohort (aHR 1.5; 95% CI, 1.1–2.1)
    - Unvaccinated (aHR 4.1; 95% CI, 2.9–5.7)
- COVID-19 hospitalization increased the incidence of type 2 diabetes compared to non-hospitalized COVID-19 cases across nearly all cohorts during the first four weeks:
    - Pre-vaccination cohort:
        - Hospitalized (aHR 28; 95% CI, 26–31)
        - Non-hospitalized (aHR 2.0; 95% CI, 1.8–2.1)
    - Vaccination cohort:
        - Hospitalized (aHR 21; 95% CI, 18–25)
    - Unvaccinated cohort:
        - Hospitalized (aHR 54.5; 95% CI, 45–66)
        - Non-hospitalized (aHR 2.6; 95% CI 1.9–3.5)
- COVID-19 hospitalization did not significantly the incidence of type 2 diabetes compared to non-hospitalized COVID-19 cases in the vaccination cohort during the first four weeks (aHR 1.1; 95% CI, 0.98–1.3).
- COVID-19 hospitalization increased the incidence of type 1 diabetes compared to non-hospitalized COVID-19 cases across all cohorts during the first four weeks:
    - Pre-vaccination cohort:
        - Hospitalized (aHR 51; 95% CI, 36–74)
        - Non-hospitalized (aHR 1.7; 95% CI, 1.3–2.1)
    - Vaccination cohort:
        - Hospitalized; insufficient events for estimation
        - Non-hospitalized (aHR 1.4; 95% CI 1.01–2.0)
    - Unvaccinated cohort:
        - Hospitalized; insufficient events for estimation
        - Non-hospitalized; insufficient events for estimation

Secondary Outcome –

- COVID-19 exposure increased the persistence of type 2 diabetes with 3,486 (57%) cases reported.
- COVID-19 hospitalization increased the persistence of type 2 diabetes with 837 (61%) cases reported.

LIMITATIONS:

- Causality cannot be definitively established between COVID-19 infection and subsequent diabetes incidence, given study design of retrospective cohort
- Cases of mild or asymptomatic cases of COVID-19 could not be accounted for.
- The effect of different variants of COVID-19 may have affected subsequent diabetes development.
- Treatment landscape for COVID-19 was evolving during the study time period, potentially skewing analysis.

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