No, current evidence does **not demonstrate a statistically significant reduction in MACE** with tirzepatide versus placebo in dedicated cardiovascular outcome trials; data are **limited to noninferiority versus active comparators and exploratory endpoints** from glycemic efficacy trials.

1. Introduction

The cardiovascular safety and efficacy of tirzepatide, a dual GIP/GLP-1 receptor agonist, in adults with type 2 diabetes has been a subject of intense research focus. While GLP-1 receptor agonists such as liraglutide and semaglutide have demonstrated significant reductions in major adverse cardiovascular events (MACE) compared to placebo in large dedicated cardiovascular outcome trials (CVOTs), the evidence for tirzepatide remains less definitive. The pivotal SURPASS-CVOT trial compared tirzepatide to dulaglutide (an active comparator with established CV benefit), demonstrating noninferiority but not superiority for MACE reduction, and did not include a placebo arm (Nicholls et al., 2025; Nicholls et al., 2023). Other phase 3 studies, such as SURPASS-4 and SURPASS-AP-Combo, reported MACE outcomes as exploratory or secondary endpoints rather than primary outcomes, with results indicating no excess cardiovascular risk but lacking statistical power for definitive conclusions (Del Prato et al., 2021; Gao et al., 2023). Several post hoc analyses and biomarker studies suggest favorable effects on cardiovascular risk factors and surrogate markers, but these do not substitute for hard clinical outcomes (Wilson et al., 2021; Wilson et al., 2020; Bashir, 2021). Ongoing and future trials may provide more conclusive evidence regarding tirzepatide's impact on MACE compared to placebo.

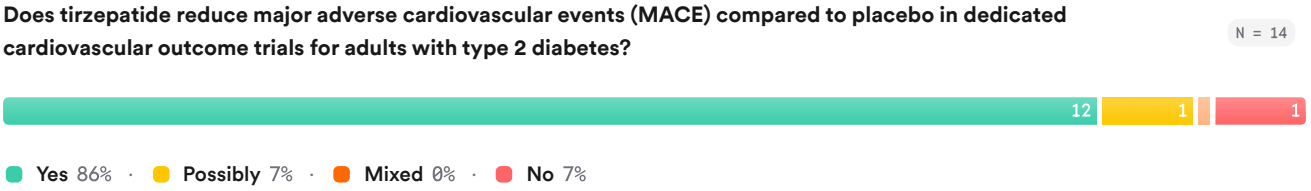

FIGURE 1 Consensus meter: Does tirzepatide reduce MACE vs placebo in dedicated CVOTs?

2. Methods

A comprehensive search was conducted across over 170 million research papers indexed by Consensus, including Semantic Scholar, PubMed, and other sources. A total of 10,064 papers were initially identified using targeted queries focused on tirzepatide, MACE, CVOTs, and related endpoints. After multi-phase filtering for relevance and quality—including screening for randomized controlled trials (RCTs), event-driven CVOTs, exploratory endpoint reporting, and reviews—50 papers were included in this review.

Search Strategy

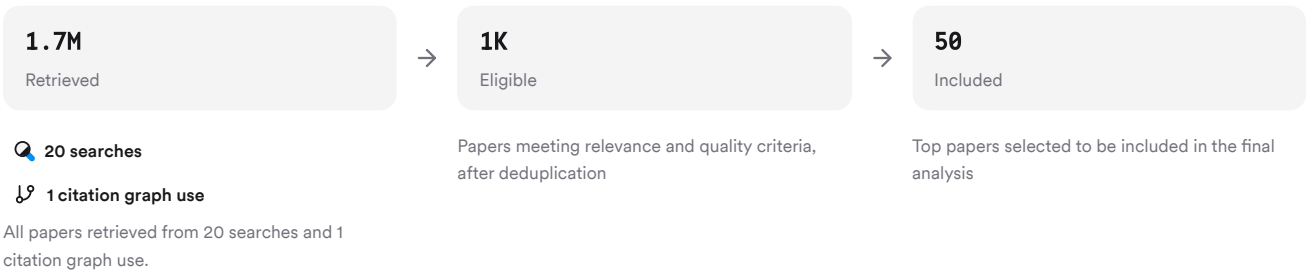

FIGURE 2 Flow diagram of search strategy from identification to inclusion.

Six unique search strategies were executed to capture foundational context, dedicated CVOT evidence, exploratory endpoints, comparator contrasts, alternate terminology, and limitations/gaps.

3. Results

3.1 Dedicated Cardiovascular Outcome Trials (CVOTs) with Tirzepatide

The SURPASS-CVOT is the first large-scale event-driven trial designed to assess the effect of tirzepatide on MACE as a primary endpoint in adults with type 2 diabetes and established atherosclerotic cardiovascular disease (Nicholls et al., 2025; Nicholls et al., 2023). This trial randomized over 13,000 participants to receive either tirzepatide or dulaglutide; the primary analysis demonstrated noninferiority of tirzepatide versus dulaglutide for time to first MACE (HR 0.92; 95.3% CI: 0.83–1.01; P=0.003 for noninferiority; P=0.09 for superiority), but did not show statistical superiority over dulaglutide or placebo (Nicholls et al., 2025). There was no direct comparison against placebo.

3.2 Exploratory Cardiovascular Endpoints from Glycemic Efficacy Trials

In phase 3 glycemic efficacy trials such as SURPASS-4 and SURPASS-AP-Combo—where MACE was an adjudicated secondary or exploratory endpoint—tirzepatide did not increase cardiovascular risk compared to insulin glargine or glargine-based regimens (HR ~0.74; CI includes unity) (Del Prato et al., 2021; Gao et al., 2023). However, these studies were not powered nor primarily designed to detect differences in MACE rates.

3.3 Biomarker Studies and Surrogate Endpoints

Post hoc analyses from phase 2b studies indicate that tirzepatide dose-dependently reduces several biomarkers associated with cardiovascular risk (e.g., hsCRP, ICAM-1), suggesting potential improvement in the overall risk profile (Wilson et al., 2021; Wilson et al., 2020; Bashir, 2021). However, these findings are hypothesis-generating rather than confirmatory.

3.4 Ongoing Trials and Future Directions

Ongoing studies such as SURMOUNT-MMO aim to evaluate morbidity/mortality outcomes—including composite CV endpoints—in broader populations (e.g., obesity without diabetes), but results are pending (Lam et al., 2025).

Results Timeline

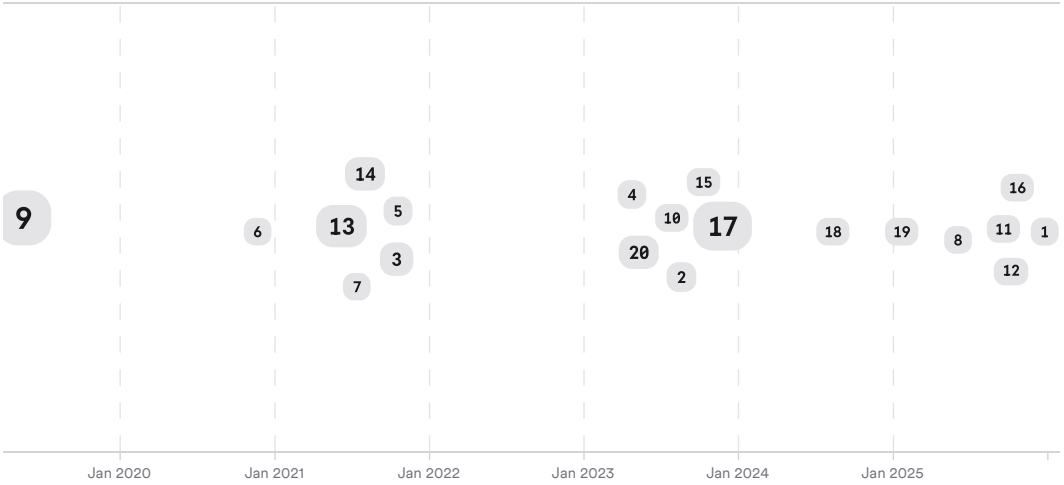

FIGURE 3 Timeline of key studies on tirzepatide's cardiovascular outcomes in T2D populations. Larger markers indicate more citations.

Top Contributors

Type	Name	Papers
Author	Stephen J. Nicholls	(Nicholls et al., 2025; Del Prato et al., 2021)
Author	S. Kahn	(Nicholls et al., 2025; Nicholls et al., 2023; Del Prato et al., 2021)
Author	G. Weerakkody	(Nicholls et al., 2025; Nicholls et al., 2023)

Type	Name	Papers
Journal	*Lancet*	(Nicholls et al., 2023; Soto et al., 2025)
Journal	*The New England journal of medicine*	(Del Prato et al., 2021)
Journal	*Diabetes*	(Frias et al., 2021)

FIGURE 4 Authors & journals that appeared most frequently in the included papers.

4. Discussion

Current evidence does not support a statistically significant reduction in MACE with tirzepatide versus placebo based on dedicated CVOTs; instead, available data are limited to noninferiority versus active comparators (dulaglutide) or exploratory endpoints from glycemic efficacy trials (Nicholls et al., 2023; Del Prato et al., 2021; Nicholls et al., 2025; Gao et al., 2023). The pivotal SURPASS-CVOT trial confirmed noninferiority but failed to demonstrate superiority over dulaglutide—a GLP-1 RA already proven superior to placebo for reducing MACE—thus leaving open the question of absolute benefit versus placebo (Nicholls et al., 2025; Gerstein et al., 2019). Exploratory analyses from glycemic trials consistently show no excess CV risk but lack statistical power for definitive conclusions (Del Prato et al., 2021; Gao et al., 2023).

Biomarker studies suggest improvements in inflammation and endothelial function markers with tirzepatide treatment (Wilson et al., 2021; Wilson et al., 2020), which may translate into long-term benefit but require confirmation through hard clinical outcomes (Bashir, 2021). The absence of direct head-to-head data against placebo means that any claim regarding superiority remains speculative until further results become available from ongoing or future event-driven outcome trials specifically designed with a placebo arm.

Overall research quality is high regarding study design (large RCTs), but limitations include lack of direct placebo-controlled CVOTs for tirzepatide and reliance on indirect comparisons or surrogate endpoints.

Claims & Evidence Table

Claim	Evidence Strength	Reasoning	Papers
Tirzepatide is noninferior to dulaglutide for reducing MACE	Strong	Large RCT shows HR=0.92 vs dulaglutide; upper CI < pre-specified margin; no direct comparison vs placebo	(Nicholls et al., 2025; Nicholls et al., 2023)
No statistically significant reduction in MACE vs placebo demonstrated	Moderate	No dedicated CVOT comparing tirzepatide directly against placebo; only indirect/comparator data available	(Nicholls et al., 2025; Gerstein et al., 2019)
Exploratory endpoints show no excess CV risk vs insulin glargine	Moderate	Secondary/exploratory analyses from glycemic efficacy RCTs	(Del Prato et al., 2021; Gao et al., 2023)
Tirzepatide improves biomarkers associated with CV risk	Moderate	Post hoc biomarker analyses show reductions in hsCRP/ICAM-1/leptin	(Wilson et al., 2021; Wilson et al., 2020; Bashir, 2021)
Superiority over dulaglutide or placebo not established	Moderate	Superiority p-value >0.05 vs dulaglutide; no direct comparison vs placebo	(Nicholls et al., 2025)

Claim	Evidence Strength	Reasoning	Papers
Data limited by lack of event-driven placebo-controlled CVOT	Strong	All current event-driven data use active comparators	(Nicholls et al., 2023; Gerstein et al., 2019)

FIGURE Key claims and support evidence identified in these papers.

5. Conclusion

In summary: In adults with type 2 diabetes at high cardiovascular risk, current evidence demonstrates that tirzepatide is noninferior—but not superior—to dulaglutide regarding major adverse cardiovascular events based on the completed SURPASS-CVOT trial; there is no direct evidence yet showing statistically significant reduction versus placebo from a dedicated event-driven outcome trial.

Research Gaps

Topic/Outcome	Placebo-controlled CVOTs	Active-comparator CVOTs	Exploratory Endpoints Glycemic Trials	Biomarker Studies
Hard MACE outcomes	GAP	1	5	GAP
Surrogate/bio-marker changes	GAP	GAP	GAP	4
Weight/glycemia improvement	GAP	5	8	GAP

FIGURE Matrix showing gaps: No published event-driven placebo-controlled CVOTs for tirzepatide's effect on hard MACE outcomes.

Open Research Questions

Future research should focus on clarifying whether tirzepatide provides incremental benefit over both active comparators and true placebos regarding hard cardiovascular outcomes.

Question	Why
Does tirzepatide reduce major adverse cardiovascular events compared to placebo in an event-driven outcome trial?	Only active-comparator data exist; direct evidence against placebo is needed for regulatory/clinical clarity.
What are the mechanisms underlying any potential cardioprotective effects of tirzepatide beyond weight loss?	Biomarker improvements suggest possible pleiotropic effects needing mechanistic elucidation via RCTs/biomarkers studies.
How does tirzepatide compare head-to-head against other GLP-1/GIP agonists or SGLT2 inhibitors for reducing hard CVD events?	Comparative effectiveness will inform optimal therapy selection among new incretin-based agents for T2D patients at high CVD risk.

FIGURE Open questions highlight need for direct event-driven comparisons versus placebo and mechanistic exploration.

In conclusion: While promising signals exist regarding safety and biomarker improvement with tirzepatide—and noninferiority has been shown versus an established GLP-1 RA—definitive evidence of statistically significant reduction in major adverse cardiovascular events compared to placebo awaits results from ongoing or future dedicated outcome trials.

References

Bashir, J. (2021). Review for "The Dual GIP and GLP -1 Receptor Agonist Tirzepatide Improves Cardiovascular Risk Biomarkers in Patients with Type 2 Diabetes: a Post-Hoc Analysis". *Diabetes, Obesity and Metabolism*. https://doi.org/10.1111/dom.14553/v1/review1

Del Prato, S., Kahn, S., Pávó, I., Weerakkody, G., Yang, Z., Doupis, J., Aizenberg, D., Wynne, A., Riesmeyer, J., Heine, R., & Wiese, R. (2021). Tirzepatide versus insulin glargine in type 2 diabetes and increased cardiovascular risk (SURPASS-4): a randomised, open-label, parallel-group, multicentre, phase 3 trial.. *Lancet*. https://doi.org/10.1016/s0140-6736(21)02188-7

Frias, J., Davies, M., Rosenstock, J., Manghi, F., Landó, F., Bergman, B., Liu, B., Cui, X., & Brown, K. (2021). Tirzepatide versus Semaglutide Once Weekly in Patients with Type 2 Diabetes.. *The New England journal of medicine*. https://doi.org/10.1056/nejmoa2107519

Gao, L., Lee, B., Chawla, M., Kim, J., Huo, L., Du, L., Huang, Y., & Ji, L. (2023). Tirzepatide versus insulin glargine as second-line or third-line therapy in type 2 diabetes in the Asia-Pacific region: the SURPASS-AP-Combo trial. *Nature Medicine, 29*, 1500-1510. https://doi.org/10.1038/s41591-023-02344-1

Gerstein, H., Colhoun, H., Dagenais, G., Diaz, R., Lakshmanan, M., Pais, P., Probstfield, J., Riesmeyer, J., Riddle, M., Rydén, L., Xavier, D., Atisso, C., Dyal, L., Hall, S., Rao-Melacini, P., Wong, G., Avezum, Á., Basile, J., Chung, N., Conget, I., Cushman, W., Franek, E., Hancu, N., Hanefeld, M., Holt, S., Janský, P., Keltai, M., Lanas, F., Leiter, L., López-Jaramillo, P., Munoz, E., Pirags, V., Pogosova, N., Raubenheimer, P., Shaw, J., Sheu, W., Temelkova-Kurktschiev, T., Abella, M., Alebuena, A., Almagro, S., Amoroso, E., Anadon, P., Andreu, E., Aristimuño, G., Arzadun, M., Barbieri, M., Barcudi, R., Bartolacci, I., Bolobanich, G., Bordonava, A., Labarta, M., Bustos, B., Caccavo, A., Camino, A., Cantero, M., Carignano, M., Cartasegna, L., Cipullo, M., Commendatore, V., Conosciuto, V., Costamagna, O., Crespo, C., Cuello, J., Cuneo, C., Cusimano, S., Dean, S., Dituro, C., Domínguez, A., Farah, M., Fernández, A., Fernández, F., Ferrari, A., Flammia, P., Fuentealba, J., Gallardo, K., Garcia, C., Duran, R., Garrido, M., Gavícola, R., Gerbaudo, C., Gilli, G., Giotto, A., Bolzán, P., Vilamajó, O., Guerlloy, F., Guridi, C., Garrido, N., Hasbani, E., Hermida, S., Hominal, M., Hrabar, A., Ingaramo, A., Izzicupo, A., Krynski, M., Lagrutta, M., Lanchiotti, P., Langhe, M., Leonard, V., Llanos, J., Santi, R., Lowenstein, J., Luquez, C., Mackinnon, I., Mana, M., Manzur, S., Marino, J., Martella, C., Martinez, R., Matias, R., Matkovich, J., Meritano, M., Montaña, O., Mulazzi, M., Ochoa, J., Paterlini, G., Pelagagge, M., Lopez, M., Prado, A., Pruyas, L., Racca, M., Ricotti, C., Rodriguez, C., Vidomlansky, M., Ronderos, R., Sadowski, A., Sala, J., Sánchez, A., Santoro, A., Schiavi, L., Sein, M., Sernia, V., Serra, L., Sicer, M., Smith, T., Soso, L., Sposetti, G., Steinacher, A., Stival, J., Tedesco, J., Tonin, H., Tortolo, M., Ulla, M., Vallejos, J., Vico, M., Virgillito, L., Visco, V., Vogel, D., Waisman, F., Zaidman, C., Zucchiatti, N., Badshah, I., Cohen, N., Colman, P., Colquhoun, D., Davis, T., Fourlanos, S., Fulcher, G., Hamlyn, J., Haywood, C., Hocking, S., Huchinson, M., Jeffries, W., Kyl, M., Lo, C., Mah, P., Makepeace, A., Marope, D., Nanayakkar, N., Nankervis, A., Palmer, N., Palolus, B., Pillai, S., Price, S., Proietto, J., Reutens, A., Rodrigo, N., Sheikh, A., Smith, G., So, M., Soldatos, G., Stuckey, B., Sumithran, P., Teede, H., Vora, P., Williams, L., Abib, E., Poço, C., Alves, É., Barea, J., Oliveira, L., Castro, D., Cruz, I., Costa, M., Cruz, I., Cunha, S., Da Silva, M., Bona, R., Paula, B., Eliaschewitz, F., Fazolli, G., Filho, C., Fortes, J., França, C., Franco, D., Genestreti, P., Giorgeto, F., Gonçalves, R., Grossman, M., Marcelino, A., Hernandes, M., Horta, A., Jaeger, C., Kaneblai, M., Rutenberg, C., Saraiva, J., Lemos, M., Maia, L., Manenti, E., Marques, M., Valério, C., Moreira, R., Mothé, F., Mouco, O., Moura, P., Jorge, J., Nakashima, C., Nakazone, M., Napoli, T., Nunes, C., Salles, J., Oliveira, K., Oliveira, M., De Souza Pantano, G., Petri, F., Piazza, L., Pires, A., Pizzato, P., Prata, S., Précoma, D., Rech, R., Reis, G., Reis, H., Resende, E., Fortes, J., Rodovalho, S., Santos, F., Salles, J., Sampaio, C., Santos, T., Santos, V., Quadros, T., Silveira, D., Siqueira, K., Teireira, M., Uehara, M., Valerio, C., Vianna, H., Vidotti, M., Visconti, G., Zanella, M., Andreeva, V., Borisov, R., Botushanov, N., Dimitrov, G., Dimova, K., Dragoychev, T., Grigorova, V., Gushterova, V., Ivanov, I., Kocelova, T., Kurktschiev, D., Miletieva, M., Nenkova-Gugusheva, N., Pancheva, R., Pavlova, M., Raev, D., Spasova, V., Stoikov, A., Troev, D., Yanev, T., Yoncheva-Mihaylova, M., Abitbol, A., Ajala, B., Alguwaihes, A., Ardilouze, J., Aris-Jilwan, N., Arnaout, A., Aronson, R., Aslam, N., Babin, S., Bailargeon, J., Bailey, A., Bajaj, H., Beauchesne, C., Beca, S., Bélanger, A., Bell, A., Bellabarba, D., Berard, L., Berenbaum, B., Bergeron, V., Berlingieri, J., Bernier, F., Bishara, P., Blank, D., Blumer, I., Brault, S., Breton, D., Carpentier, A., Cha, J., Chandra, P., Chiasson, J., Conway, J., Couture, G., Couture, N., Dagenais, G., Datta, D., D'Ignazio, G., Dumas, R., Fay, D., Fréchette, A., Frenette, L., Fung, D., Gagnon, N., Galter, M., Garon, J., Gauthier, J., Geadah, C., Gilbert, J., Girard, R., Goldenberg, R., Grossman, L., Gupta, N., Hallé, J., Hivert, M., Houde, G., Houlden, R., Hramiak, I., Jablonski, T., Jain, A., Khandwala, H., Khosla, M., Lachance, C., Laflamme, E., Langlois, M., Larivée, L., Liutkus, J., Lochnan, H., Malik, S., McDonald, C., Mehta, P., Mihailidis, J., Milot, A., Narula, P., Nault, P., Nayar, A., Nisker, W., Ouellet, G., Palardy, J., Patel, M., Paul, T., Pedersen, S., Perron, P., Pesant, M., Poirier, P., Poulin, M., Punthakee, Z., Rehman, W., Ross, S., Sagar, P., Saliba, N., Sandler, S., Schiffrin, A., Schlosser, R., Seth-Sharma, A., Sherman, M., Sionit, D., Sivakumar, T., Soto, J., St-Amour, E., Steen, O., Sussman, J., Telner, A., Tobe, S., Twum-Barima, D., Zanten, A., VanRossum, N., Vecchiarelli, J., Ward, R., Wessengel, J., Weisnagel, S., Wilderman, I., Woo, V., Yakubovich, N., Yale, J., Yared, Z., Acevedo, M., Aguirre, M., Aizman, A., Barroso, M., Cobos, L., Vargas, A., Descalzi, B., Godoy, G., Grumberg, E., Lahsen, R., Larenas, G., Ortiz, E., Paredes, J., Potthoff, S., Retamal, E., Rojas, L., Salgado, M., Santibáñez, C., Solis, C., Stokins, B., Accini, J., Acebedo, J., Baena, L., Alarcon, S., Angel, J., Arcos, E., Martinez, M., Atuesta, L., Balaguera, J., Ballestas, D., Barrera, S., Reyes, R., Bayona, A., Bermúdez, A., Bernal, D., Blanquicett, M., Bravo, V., Bueno, W., Delgado, A., Cadena, A., Cadena, A., Caicedo, S., Celemin, C., Consuegra, R., Pimienta, C., Corredor, K., Cure, C., De La Hoz Rueda, L., Delgado, E., Díaz, S., Diego, M., Donado, A., Sanabria, W., Escobar, J., Escorcia, G., Forero, L., Fuentes, L., García, M., Lozada, H., Ortiz, L., Giraldo, Á., Gonzalez, L., Granada, J., Gutierrez, C., Henao, N., Hernandez, E., Uejbe, O., Cobos, J., Gómez, J., Jaimes, E., Jaramillo, M., Jaramillo, N., Gomez, C., Sanchez, M., Durán, I., Ceballos, C., Madrid, C., Amastha, E., Mercado, J., Molina, D., Soto, J., Montoya, C., Morales, A., Muñoz, C., Orozco, L., Osorio, O., Sanchez, J., Peña, A., Perez, J., Agudelo, J., Amador, G., Pertuz, C., Posada, I., Puerta, C., Quintero, A., Quiroz, D., Rendon, C., Reyes, A., Reyes, Á., Ripoll, D., Rivera, C., Rocha, M., Rodriguez, J., Villanueva, K., Zabala, J., Rojas, S., Romero, M., Rosero, R., Cardenas, A., Rueda, L., Sánchez, G., Sanchez, T., Herazo, A., Suárez, M., Torres, M., Trujillo, F., Urina, M., Van Strahlen, L., Velandia, C., Guzman, C., Velazquez, E., Prada, T., Alvaran, J., Zarate, D., Andelova, J., Benešová, R., Buzová, B., Čech, V., Chodova, I., Choura, M., Dufka, A., Gamova, A., Gorgol, J., Hála, T., Havlová, H., Hlávková, D., Horanska, P., Ilcisin-Valova, J., Jenickova, P., Jeřábek, O., Kantorová, I., Kolomaznikova, K., Kopeckova, I., Kopeckova, M., Linhart, K., Linhart, T., Malecha, J., Malicherova, E., Neubauerova, D., Oznerova, M., Partys, R., Pederzoliova, E., Petrušová, M., Prymkova, V., Račická, E., Reissova, I., Roderova, E., Staněk, L., Striova, A., Svarcova, D., Svoboda, P., Malicharova, E., Urge, J., Vesely, L., Wasserburger, B., Wasserburgerova, H., Zahumensky, E., Zamrazil, V., Alawi, H., Anastasiadis, E., Axthelm, E., Bieler, T., Buhrig, C., Degtyareva, E., Dellanna, F., Derwahl, K., Diessel, S., Dogiami, B., Dorn-Weitzel, K., Ernst, M., Faulmann, G., Fetscher, B., Forst, T., Freyer-Lahres, G., Funke, K., Ganz, X., Gleixner, C., Hanefeld, C., Heinrichs, S., Helleberg, S., Henkel, E., Hetzel, G., Hoffmann, C., Jacob, F., Jacob, S., John, F., Jonczyk, A., Kamke, W., Klein, C., Kleinhardt, M., Kleophas, W., Kosch, C., Kreutzmann, K., Kühn, A.,

Lee-Barkey, Y., Lier, A., Maatouk, S., Minnich, J., Mitry, M., Muessig, I., Nicula, D., Niemann, M., Nothroff, J., Ott, P., Pfuetzner, A., Pfützner, A., Pistrosch, F., Pohl, W., Procházková, Z., Retkowska, M., Rosin, H., Sachsenheimer, D., Samer, H., Sanuri, M., Schaefer, A., Schaper, F., Schulze, E., Schulze, M., Schumann, M., Segiet, T., Sowa, V., Stahl, H., Steinfeldt, F., Teige, M., Trieb, B., Tschoepe, D., Uebel, P., Warken, B., Weigmann, I., Weyland, K., Wilhelm, K., Baló, T., Balsay, M., Bende, I., Bezzegh, K., Birkus, Z., Buday, B., Csomai, M., Deák, L., Dezso, E., Faludi, P., Faluvegi, M., Fazekas, I., Feher, A., Fejér, C., Finta, E., Fulcz, Á., Gaál, Z., Gurzó, M., Hati, K., Herczeg, G., Jozsef, I., Juhász, M., Keltai, K., Koranyi, L., Kulcsár, E., Kun, K., Laczko, A., Literáti-Nagy, B., Mező, I., Miléder, M., Móricz, I., Nagy, K., Nagybaczoni, B., Németh, C., Őze, Á., Pauer, J., Péterfai, É., Polocsanyi, B., Poor, F., Reiber, I., Salamon, C., Sebestyen, J., Torok, I., Tuu, M., Varga, A., Vass, V., Ahn, C., Ahn, C., ByungWon, P., Chang, H., Chang, K., Choi, E., Choi, H., Chung, J., Hong, B., Hong, Y., Hyon, M., Jeong, M., Kang, S., Kim, B., Kim, J., Kim, J., Kim, K., Kim, M., Kim, P., Kim, S., Kim, Y., Kim, Y., Koh, Y., Kwon, H., Lee, B., Lee, B., Lee, J., Lee, M., Lim, Y., Min, P., Park, J., Park, J., Park, K., Park, S., Pyun, W., Rim, S., Ryu, D., Seo, H., Seung, K., Shin, D., Sim, D., Yoon, Y., Andersone, I., Babicka, K., Balcere, I., Barons, R., Capkovska, I., Geldnere, K., Grigane, I., Jegere, B., Lagzdina, I., Mora, L., Pastare, S., Ritenberga, R., Romanova, J., Saknite, I., Sidlovska, N., Sokolova, J., Steina, S., Strizko, I., Teterovska, D., Vizina, B., Barsienė, L., Belozariene, G., Daugintyte-Petrusiene, L., Drungiliene, N., Garsviene, N., Grigiene, A., Grižas, V., Jociene, V., Kalvaitiene, D., Kaupiene, J., Kavaliauskienė, J., Kozloviene, D., Lapteva, I., Maneikiene, B., Marcinkeviciene, J., Markauskiene, V., Meiluniene, S., Norkus, A., Norviliene, R., Petrenko, V., Radzeviciene, R., Šakalytė, G., Urbonas, G., Urbutiene, S., Vasiliauskas, D., Veličkienė, D., Aguilar, C., Alcocer, M., Avalos-Ramirez, J., Banda-Elizondo, R., Bricio-Ramirez, R., Mejia, K., Cavazos, F., Chapa, J., Cienfuegos, E., Peña, A., De La Peña Topete, G., Ibarra, M., Elias, D., Flores-Moreno, C., Hernandez, P., González, L., Moya, R., Guerra-López, A., Baylon, R., Colorado, C., Herrera-Marmolejo, M., Islas-Palacios, N., Lopez, E., López, F., Alvarado, A., Ceballos, R., Villegas, E., Moreno-Virgen, G., Perez, R., González, S., Peralta-Cantu, I., Previn, R., Ramirez, R., Ramirez, R., Zavala, M., Rodríguez, M., Salgado-Sedano, R., Sánchez-Aguilar, A., Franco, E., Sauque-Reyna, L., Otero, R., Torres, I., Velarde-Harnandez, E., Villagordoa, J., Villeda-Espinoza, E., Vital-Lopez, J., Bello, C., Baker, J., Barrington-Ward, E., Brownless, T., Carroll, R., Carson, S., Choe, M., Corin, A., Corley, B., Cutfield, R., Dalaman, N., Dixon, P., Drury, P., Dyson, K., Florkowski, C., Ford, M., Frengley, W., Helm, C., Katzen, C., Kerr, J., Khanolkar, M., Kim, D., Koops, R., Krebs, J., Leikis, R., Low, K., Luckey, A., Luke, R., Macaulay, S., Marks, R., McNamara, C., Millar-Coote, D., Miller, S., Mottershead, N., Reid, J., Robertson, N., Rosen, I., Rowe, D., Schmiedel, O., Scott, R., Sebastian, J., Sheahan, D., Stiebel, V., Ternouth, I., Tofield, C., Venter, D., Williams, M., Williams, M., Wu, F., Young, S., Arciszewska, M., Bochenek, A., Borkowski, P., Borowy, P., Chrzanowski, T., Czerwiński, E., Dwojak, M., Grodzicka, A., Janiec, I., Jaruga, J., Jaźwińska-Tarnawska, E., Jedynasty, K., Juzwiak-Czapiewska, D., Karczewicz-Janowska, J., Konieczny, J., Konieczny, M., Korol, M., Kozina, M., Krzyżagórska, E., Kucharczyk-Petryka, E., Laz, R., Majchrzak, A., Mrozowska, Z., Mularczyk, M., Nowacka, E., Peczyńska, J., Petryka, R., Pietrzak, R., Pisarczyk-Wiza, D., Różańska, A., Ruzga, Z., Rzeszotarska, E., Sacha, M., Sekulska, M., Sidorowicz-Białynicka, A., Stasińska, T., Strzelecka-Sosik, A., Swierszcz, T., Szymkowiak, K., Turowska, O., Wiśniewska, K., Wiza, M., Woźniak, I., Żelazowska, K., Ziolkowska-Gawron, B., Zytkiewicz-Jaruga, D., Albota, A., Alexandru, C., Avram, R., Bala, C., Barbonta, D., Barbu, R., Braicu, D., Calutiu, N., Catrinoiu, D., Cerghizan, A., Ciorba, A., Crăciun, A., Doros, R., Duma, L., Dumitrache, A., Ferariu, I., Moza, A., Ghergan, A., Ghişe, G., Graur, M., Gribovschi, M., Mihai, B., Mihalache, L., Mihalcea, M., Mîndrescu, N., Morosanu, M., Morosoanu, A., Moţa, M., Moza, A., Nafornita, V., Natea, N., Nicodim, S., Niţă, C., Onaca, A., Onaca, M., Pop, C., Pop, L., Popa, A., Popescu, A., Prună, L., Roman, G., Roşu, M., Sima, A., Sipciu, D., Sitterli-Natea, C., Szilagyi, I., Tapurica, M., Tase, A., Tutescu, A., Vanghelie, L., Verde, I., Vlad, A., Zarnescu, M., Akhmetov, R., Allenova, I., Avdeeva, I., Baturina, O., Biserova, I., Bokovin, N., Bondar, I., Burova, N., Chufeneva, G., Chumachek, E., Demidova, M., Demin, A., Drobysheva, V., Egorova, I., Esenyan, L., Gelig, E., Gilyarevsky, S., Golshmid, M., Goncharov, A., Gorbunova, A., Gordeev, I., Gorelysheva, V., Goryunova, T., Grebenshchikova, I., Ilchenko, R., Ivannikova, M., Karabalieva, S., Karpeeva, J., Khaykina, E., Kobalava, Z., Kononenko, I., Korolik, O., Korshunova, A., Kostenko, V., Krasnopevtseva, I., Krylova, L., Kulkova, P., Kuzmina, I., Ledyaeva, A., Levashov, S., Lokhovinina, N., Lvov, V., Martirosyan, N., Nedogoda, S., Nilk, R., Osmolovskaya, Y., Panov, A., Paramonova, O., Pavlova, E., Pekareva, E., Petunina, N., Ponamareva, S., Reshedko, G., Salasyuk, A., Sepkhanyan, M., Serebrov, A., Shabelnikova, O., Skvortsov, A., Smirnova, O., Spiridonova, O., Strogova, S., Taratukhin, E., Tereschenko, S., Trukhina, L., Tsarkova, O., Tsoma, V., Tumarov, F., Tyan, N., Tyurina, T., Villevalde, S., Yankovaya, E., Zarutskaya, L., Zenkova, E., Badat, A., Bester, F., Blignaut, S., Blom, D., Booysen, S., Boyd, W., Brice, B., Brown, S., Burgess, L., Cawood, R., Coetzee, K., Conradie, H., Cronje, T., De Jong, D., Ellis, G., Emanuel, S., Engelbrecht, I., Foulkes, S., Fourie, D., Gibson, G., Govender, T., Hansa, S., Hemus, A., Hendricks, F., Heradien, M., Holmgren, C., Hoosain, Z., Horak, E., Howard, J., Immink, I., Janari, E., Jivan, D., Klusmann, K., Labuschagne, W., Lai, Y., Latiff, G., Lombaard, J., Lottering, H., Meeding, R., Middlemost, S., Mitha, H., Mitha, I., Mkhwanazi, S., Moodley, R., Murray, A., Musungaie, D., Osman, Y., Peacey, K., Pillay-Ramaya, L., Pretorius, C., Prozesky, H., Sarvan, M., Scholtz, E., Sebesteny, A., Skinner, B., Skriker, M., Smit, M., Stapelberg, A., Swanepoel, N., Urbach, D., Aswegen, D., Zyl, F., Zyl, L., Venter, E., Wadvalla, S., Wing, J., Wolmarans, K., Abreu, C., Águila, P., Aguilera, E., Alonso, N., Alvarez, C., Cajas, P., Castro, J., Codinachs, R., Contreras, J., Coves, M., Fajardo, C., Ferrer, J., Font, N., Garcia, M., Gil, M., Gómez, F., Gomez, L., Gonzálbez, J., Griera, J., Masmiquel, L., Mauricio, D., Perez, S., Nicolau, J., Contreras, O., Oliván, J., Olivares, J., Ortega, E., Pellitero, S., Pertusa, S., Rius, F., Rodríguez, I., Sánchez-Juan, C., Santos, D., Soldevila, B., Subías, D., Terns, M., Trescolí, C., Vilaplana, J., Villanueva, A., Albo, J., Antus, K., Axelsson, M., Bergström, L., Binsell-Gerdin, E., Boman, K., Botond, F., Dotevall, A., Graipe, A., Jarnet, C., Kaminska, J., Kempe, A., Korhonen, M., Linderfalk, C., Liu, B., Ljungstroem, K., Ljungström, K., Malmqvist, L., Mellbin, L., Mooe, T., Nicol, P., Norrby, A., Ohlsson, Å., Rosengren, A., Saaf, J., Salmonsson, S., Strandberg, O., Svensson, K., Tengmark, B., Tsatsaris, G., Ulvenstam, A., Vaško, P., Chang, C., Chang, H., Chen, J.,

Chen, T., Chung, M., Fu, C., Hsia, T., Hua, S., Kuo, M., Lee, C., Lee, I., Liang, K., Lin, S., Lu, C., , W., Pei, D., Shen, F., Su, C., Su, S., Tai, T., Tsai, W., Tsai, Y., Tung, S., Wang, J., Yu, H., Al-Qaissi, A., Arutchelvam, V., Atkin, S., Au, S., Aye, M., Bain, S., Bejnariu, C., Bell, P., Bhatnagar, D., Bilous, R., Black, N., Brennan, U., Brett, B., Bujanova, J., Chow, E., Collier, A., Combe, A., Courtney, C., Courtney, H., Crothers, J., Eavis, P., Elliott, J., Febbraro, S., Finlayson, J., Gandhi, R., Gillings, S., Hamling, J., Harper, R., Harris, T., Hassan, K., Heller, S., Jane, A., Javed, Z., Johnson, T., Jones, S., Kennedy, A., Kerr, D., Kilgallon, B., Konya, J., Lindsay, J., Lomova-Williams, L., Looker, H., Macfarlane, D., MacRury, S., Malik, I., McCrimmon, R., McKeith, D., McKnight, J., Mishra, B., Mukhtar, R., Mulligan, C., O'Kane, M., Olateju, T., Orpen, I., Richardson, T., Rooney, D., Ross, S., Sathyapalan, T., Siddaramaiah, N., Sit, L., Stephens, J., Turtle, F., Wakil, A., Walkinshaw, E., Ali, A., Anderson, R., Arakaki, R., Aref, O., Ariani, M., Arkin, D., Banarer, S., Barchini, G., Bhan, A., Branch, K., Brautigam, D., Brietzke, S., Brinas, M., Brito, Y., Carter, C., Casagni, K., Casula, S., Chakko, S., Charatz, S., Childress, D., Chow, L., Chustecka, M., Clarke, S., Cohen, L., Collins, B., Vega, G., Comulada-Rivera, A., Cortes-Maisonet, G., Davis, M., De Souza, J., Desouza, C., Dinnan, M., Duffy-Hidalgo, B., Dunn, B., Dunn, J., Elman, M., Felicetta, J., Finkelstein, S., Fitz-Patrick, D., Flórez, H., Forker, A., Fowler, W., Fredrickson, S., Freedman, Z., Narron, B., Gainey-Ferree, K., Gardner, M., Gastelum, C., Giddings, S., Gillespie, E., Gimness, M., Goldstein, G., Gomes, M., Gomez, N., Gorman, T., Goswami, K., Graves, A., Hacking, S., Hall, C., Hanson, L., Harman, S., Heber, D., Henry, R., Hiner, J., Hirsch, I., Hollander, P., Hooker, T., Horowitz, B., Hoste, L., Huang, L., Huynh, M., Hyman, D., Idriss, S., Iranmanesh, A., Karounos, D., Kashyap, M., Katz, L., Kaye, W., Khaiton, Y., Khardori, R., Kitchen, T., Klein, A., Knffem, W., Kosiborod, M., Kreglinger, N., Kruger, D., Kumar, A., Laboy, I., Larrabee, P., Larrick, L., Lawson, D., Ledet, M., Lenhard, J., Levy, J., Li, G., Li, Z., Lieb, D., Limcolioc, A., Lions-Patterson, J., Lorber, D., Lorch, D., Lorrello, M., Lu, P., Lucas, K., , S., Macadams, M., Magee, M., Magno, A., Mahakala, A., Marks, J., McCall, A., McClanahan, W., McClary, C., Melendez, L., Melish, J., Michaud, D., Miller, C., Miller, N., Mora, P., Moten, M., Mudaliar, S., Myrick, G., Narayan, P., Nassif, M., Neri, K., Newton, T., Niblack, P., Nicol, P., Nyenwe, E., Odugbesan, A., Okorocha, Y., Carrasquillo, R., Osei, K., Palermo, C., Patel, H., Patel, K., Pau, C., Perley, M., Plevin, S., Plummer, E., Powell, R., Qintar, M., Rawls, R., Reyes-Castano, J., Reynolds, L., Richards, R., Rosenstock, J., Rowe, C., Saleh, J., Sam, S., Sanchez, A., Sander, D., Sanderson, B., Savin, V., Seaquist, E., Shah, J., Shi, S., Shivaswamy, V., Shlotzhauer, T., Shore, D., Skukowski, B., Soe, K., Solheim, V., Soufer, J., Steinberg, H., Steinsapir, J., Tarkington, P., Thayer, D., Thomson, S., Thrasher, J., Tibaldi, J., Tjaden, J., Tores, O., Trence, D., Trikudanathan, S., Ullal, J., Uwaifo, G., Vo, A., Vu, K., Walia, D., Weiland, K., Whitehouse, F., Wiegmann, T., Wyne, K., Wynne, A., Yuen, K., Zaretzky, J., Zebrack, J., Zieve, F., & Zigrang, W. (2019). Dulaglutide and cardiovascular outcomes in type 2 diabetes (REWIND): a double-blind, randomised placebo-controlled trial.. *Lancet*. https://doi.org/10.1016/s0140-6736(19)31149-3

Lam, C., Rodríguez, A., Aminian, A., Ferrannini, E., Heerspink, H., Jastreboff, A., Laffin, L., Pandey, A., Ray, K., Ridker, P., Sanyal, A., Yki-Jarvinen, H., Mason, D., Strzelecki, M., Bartee, A., Cui, C., Hurt, K., Linetzky, B., Bunck, M., & Nissen, S. (2025). Tirzepatide for reduction of morbidity and mortality in adults with obesity: rationale and design of the SURMOUNT-MMO trial. *Obesity, 33*, 1645 - 1656. https://doi.org/10.1002/oby.24332

Nicholls, S., Pavo, I., Bhatt, D., Buse, J., Del Prato, S., Kahn, S., Lincoff, A., Mcguire, D., Miller, D., Nauck, M., Nishiyama, H., Nissen, S., Sattar, N., Weerakkody, G., Wiese, R., Zinman, B., Zoungas, S., Basile, J., Davies, M., Giorgino, F., Kellerer, M., Ji, L., Várkonyi, T., Menon, V., Broder, J., Herschtal, A., & D'Alessio, D. (2025). Cardiovascular Outcomes with Tirzepatide versus Dulaglutide in Type 2 Diabetes.. *The New England journal of medicine, 393 24*, 2409-2420. https://doi.org/10.1056/nejmoa2505928

Nicholls, S., Bhatt, D., Buse, J., Prato, S., Kahn, S., Lincoff, A., Mcguire, D., Nauck, M., Nissen, S., Sattar, N., Zinman, B., Zoungas, S., Basile, J., Bartee, A., Miller, D., Nishiyama, H., Pavo, I., Weerakkody, G., Wiese, R., & D'Alessio, D. (2023). Comparison of Tirzepatide and Dulaglutide on Major Adverse Cardiovascular Events in Participants with Type 2 Diabetes and Atherosclerotic Cardiovascular Disease: SURPASS-CVOT Design and Baseline Characteristics.. *American heart journal*. https://doi.org/10.1016/j.ahj.2023.09.007

Soto, E., Gómez-Luján, M., Espinal, J., Fajardo, I., Mariscal, H., García, M., López, E., & Echeona, K. (2025). The Role of GLP-1 Receptor Agonists (Ozempic and Mounjaro) as Secondary Therapy in Chronic Kidney Disease. *Revista Científica Multidisciplinar SAGA*. https://doi.org/10.63415/saga.v2i3.257

Wilson, J., Lin, Y., Luo, M., Considine, G., Cox, A., Bowsman, L., Robins, D., Haupt, A., Duffin, K., & Ruotolo, G. (2021). The dual glucose-dependent insulinotropic polypeptide and glucagon-like peptide-1 receptor agonist tirzepatide improves cardiovascular risk biomarkers in patients with type 2 diabetes: A post hoc analysis. *Diabetes, Obesity & Metabolism, 24*, 148 - 153. https://doi.org/10.1111/dom.14553

Wilson, J., Lin, Y., Considine, G., Cox, A., Bowsman, L., Robins, D., Riesmeyer, J., Haupt, A., Duffin, K., & Ruotolo, G. (2020). Abstract 13426: The Dual GIP/GLP-1 Receptor Agonist Tirzepatide Improves Cardiovascular Risk Protein Biomarkers in Patients With Type 2 Diabetes. *Circulation*. https://doi.org/10.1161/circ.142.suppl_3.13426