

# Study confirms link between diabetes drug and increased risk of bladder cancer

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The diabetes drug pioglitazone is associated with an increased risk of bladder cancer, finds a study published by *The BMJ* today. The findings suggest that the risk increases with increasing duration of use and dose.

No [increased risk](#) was seen for a similar drug (rosiglitazone).

Pioglitazone and rosiglitazone belong to a class of drugs called thiazolidinediones that help to control [blood sugar levels](#) in patients with type 2 [diabetes](#). However, in 2005, a trial unexpectedly showed an imbalance in the number of [bladder cancer](#) cases with pioglitazone compared with placebo.

Since then, the association between the use of pioglitazone and bladder cancer has been controversial, with studies reporting contradictory findings.

So a team of Canadian-based researchers set out to determine whether the use of pioglitazone, when compared with other [anti-diabetic drugs](#), was associated with an increased risk of bladder cancer in patients with type 2 diabetes.

They analysed data for 145,806 patients from the UK Clinical Practice Research Database (CPRD), who were newly treated with diabetes drugs between 2000 and 2013. Potential influential factors such as age, sex, duration of diabetes, smoking status and alcohol-related disorders, were taken into account.

Compared with no thiazolidinedione use, the use of pioglitazone was associated with an overall 63% increased risk of bladder cancer (121 per 100,000 person years vs 89 per 100,000 person years), with the risk increasing with increasing duration of use and dose.

In contrast, the use of rosiglitazone was not associated with an increased risk of bladder cancer in any analysis, suggesting the risk is drug-specific and not a class effect.

These results remained largely unchanged after further sensitivity analyses.

The authors stress that, in absolute terms, the risk of bladder cancer remains low. But they suggest doctors and patients should be aware of this association when assessing the overall risks and benefits of this therapy.

A second study, also published by *The BMJ* today, compares diabetes drugs - particularly newer drugs (thiazolidinediones and gliptins) - in their potential ability to control [blood sugar](#) levels and prevent serious complications.

Professors Julia Hippisley-Cox and Carol Coupland at the University of Nottingham used another large UK primary care database (QResearch) to analyse data for 469,688 adult patients with type 2 diabetes between 2007 and 2015.

Again, potential influential factors such as age, sex, duration of diabetes, [smoking status](#) and deprivation, were taken into account.

They found clinically important differences between different drugs (alone and in combination) and risk of five key outcomes - blindness, amputation, severe kidney failure, high blood sugar (hyperglycaemia)

and low blood sugar (hypoglycaemia) events.

Both studies are observational so no firm conclusions can be drawn about cause and effect. However, the researchers say these results may have implications for prescribing, and suggest doctors and patients should be aware when assessing the overall risks and benefits of [diabetes drugs](#).

In an accompanying editorial, Victor Montori, Professor of Medicine at Mayo Clinic in the USA suggests that working closely with their clinicians, "[patients](#) can identify the agent that is best for them given their context, both clinical and personal."

He points out that observational evidence can help, but warns that "sometimes even large practice databases are too small and incomplete to provide reliable estimates." And he calls for broad collaboration and shared decision making "to compensate for imperfect and sometimes corrupt information, with a humble and generous commitment to understand fully what is best for each patient."

**More information:** Marco Tuccori et al. Pioglitazone use and risk of bladder cancer: population based cohort study, *BMJ* (2016). [DOI: 10.1136/bmj.i1541](#)

Julia Hippisley-Cox et al. Diabetes treatments and risk of amputation, blindness, severe kidney failure, hyperglycaemia, and hypoglycaemia: open cohort study in primary care, *BMJ* (2016). [DOI: 10.1136/bmj.i1450](#)

Victor M Montori. Selecting the right drug treatment for adults with type 2 diabetes, *BMJ* (2016). [DOI: 10.1136/bmj.i1663](#)

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