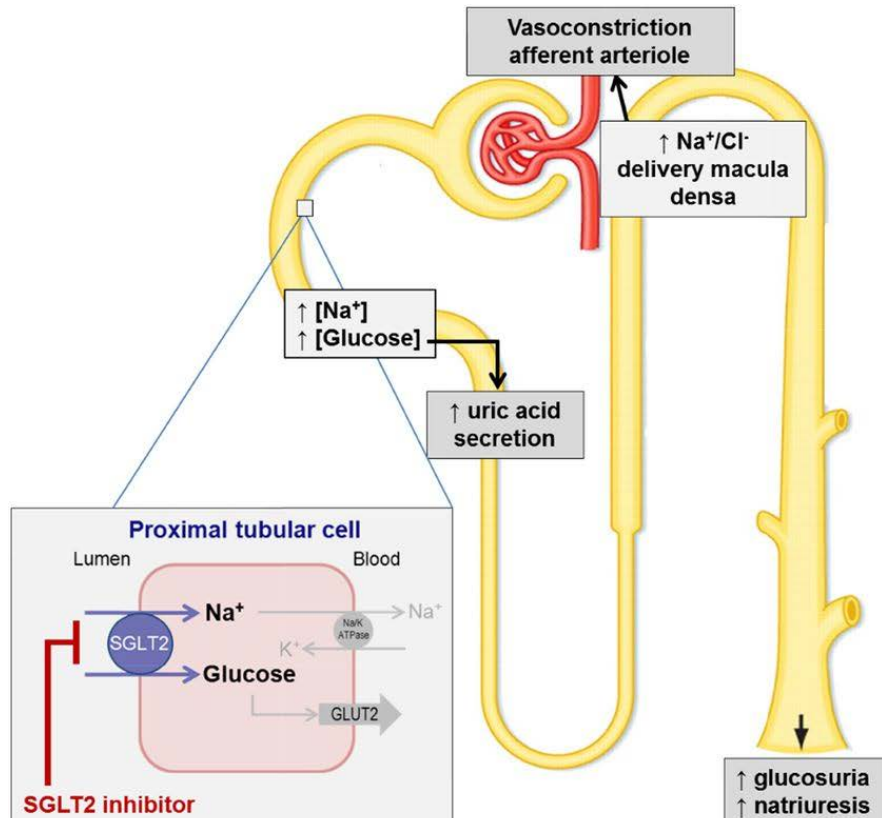


# Cost-Effectiveness Analysis of Amputation Risk and Cardiovascular (CV) Benefits with Canagliflozin in Patients with Type II Diabetes Mellitus

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# Background



## Canagliflozin Indications

- Pharmacological management of type 2 diabetes mellitus (T2DM)
- Risk reduction of end-stage renal disease (ESRD)
- **Risk reduction of major cardiovascular events in adults with type 2 diabetes (T2DM) and established cardiovascular disease**

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ORIGINAL ARTICLE

## Canagliflozin and Cardiovascular and Renal Events in Type 2 Diabetes

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### CONCLUSIONS

In two trials involving patients with type 2 diabetes and an elevated risk of cardiovascular disease, patients treated with canagliflozin had a lower risk of cardiovascular events than those who received placebo but a greater risk of amputation, primarily at the level of the toe or metatarsal. (Funded by Janssen Research and Development; CANVAS and CANVAS-R ClinicalTrials.gov numbers, NCT01032629 and NCT01989754, respectively.)

Safety outcomes.

### METHODS

The CANVAS Program integrated data from two trials involving a total of 10,142 participants with type 2 diabetes and high cardiovascular risk. Participants in each trial were randomly assigned to receive canagliflozin or placebo and were followed for a mean of 188.2 weeks. The primary outcome was a composite of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke.

# Objective

To evaluate the cost-effectiveness of canagliflozin plus background therapy considering both amputations risk and cardiovascular (CV) benefits compared to background therapy alone



# Methods



	Base-Case Model	Maximum Benefit Model
Number of Health States	6	6
Perspective	Payer	Payer
Time-Horizon	84 months	84 months
Willingness-to-Pay Threshold (WTP)	\$100,000	\$100,000
Costs	Events: average cost Canagliflozin: WAC	Events: first-year costs Canagliflozin: half of WAC
Utilities	Standard Value	Half Standard Value

# Methods



TABLE 1: Utility and Cost Inputs				
	Base Case Model		Maximum Benefit Model	
Event Measured	Utility Value	Costs <sup>3</sup>	Utility Value	Costs <sup>3</sup>
Month-Supply of Canagliflozin	---	\$518 <sup>10</sup>	---	\$259 <sup>10</sup>
Month-Supply of Baseline Medications	---	\$381.52 <sup>11</sup>	---	\$381.52 <sup>11</sup>
<b>Cardiac</b>				
Nonfatal MI or Stroke (Canagliflozin)	0.68 <sup>5</sup>	\$1295.07 <sup>12</sup>	0.34 <sup>5</sup>	\$4755.57 <sup>12</sup>
Nonfatal MI or Stroke (Placebo)	0.69 <sup>5</sup>	\$1276.22 <sup>12</sup>	0.345 <sup>5</sup>	\$4783.61 <sup>12</sup>
<b>Amputations</b>				
Amputation (Canagliflozin)	0.56 <sup>5</sup>	\$291.87 <sup>13</sup>	0.28 <sup>5</sup>	\$1898.81 <sup>13</sup>
Amputation (Placebo)		\$386.04 <sup>13</sup>		\$1836.57 <sup>13</sup>
Amputation + Nonfatal MI or Stroke(Canagliflozin)	0.48 <sup>5</sup>	\$1689.99 <sup>12,13</sup>	0.24 <sup>5</sup>	\$6654.38 <sup>12,13</sup>
Amputation + Nonfatal MI or Stroke(Placebo)	0.49 <sup>5</sup>	\$1397.90 <sup>12,13</sup>	0.245 <sup>5</sup>	\$5635.36 <sup>12,13</sup>
<b>Adverse Events (AE)**</b>				
Total AE for Canagliflozin	0.75 <sup>6-8</sup>	\$140.89 <sup>12,14</sup>	0.75 <sup>6-8</sup>	\$140.89 <sup>12,14</sup>
Total AE for Placebo	0.79 <sup>6-8</sup>	\$76.89 <sup>12,14</sup>	0.79 <sup>6-8</sup>	\$76.89 <sup>12,14</sup>
<b>Death</b>				
CV-Related	0	\$21021.73 <sup>15</sup>	0	\$21021.73 <sup>15</sup>
Non CV-Related	0	\$22475.64 <sup>16</sup>	0	\$22475.64 <sup>16</sup>

\*AE: UTI, vulvovaginal candidiasis, osmotic diuresis, and volume depletion

Event was defined as nonfatal myocardial infarction (MI) or stroke, amputation, or both amputation and nonfatal MI/stroke.

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# Results – Base Case Model



TABLE 2: Base Case Model - Incremental Cost, Incremental Effectiveness, and ICER/QALYs					
	Cost (2020 USD)	Incremental Cost (2020 USD)	Effectiveness (QALY)	Incremental Effectiveness (QALY)	ICER
BT alone	\$39,737.69	N/A	5.01	N/A	N/A
CANA + BT	\$81,022.30	\$41,284.61	5.04	0.03	\$1,294,370

TABLE 3: Base Case Model - Sensitivity Analyses on Amputation and CV Events in the Canagliflozin Group			
Variable	Reference Values	Range	Results
Probability of Nonfatal MI/Stroke	0.001227786	0 - 0.001534732	ICER > \$100,00 WTP threshold
Probability of Amputation	0.000525	0 - 0.00065625	ICER > \$100,00 WTP threshold

# Results – Maximum Benefit Model



TABLE 4: Maximum Benefit Model - Incremental Cost, Incremental Effectiveness, and ICER/QALYs					
	Cost (2020 USD)	Incremental Cost (2020 USD)	Effectiveness (QALY)	Incremental Effectiveness (QALY)	ICER
BT alone	\$57,764.44	N/A	4.86	N/A	\$524,220
CANA + BT	\$76,838.18	\$19,073.74	4.90	0.036	

TABLE 5: Maximum Benefit Model - Sensitivity Analyses on Amputation, CV Events, Costs of Canagliflozin in the Canagliflozin Group			
Variable	Reference Values	Range	Results
Probability of Nonfatal MI/Stroke	0.00093694	0 - < 0.000029	Cana dominant
		0.000029 - 0.00064	Cana more CE
		> 0.00064	ICER > \$100,00 WTP threshold
Probability of Amputation	0.000525	0 - 0.00065625	ICER > \$100,00 WTP threshold
Cost of Canagliflozin	\$259	0 - 20.23	Cana dominant
		>20.23 - 64.75	Cana more CE
		> 64.75	ICER > \$100,00 WTP threshold

# Discussion/Conclusion

- CV benefits awarded by canagliflozin did not translate to canagliflozin being cost-effective in the base case scenario or in the maximum benefit scenario
- Canagliflozin drug cost was a strong driver of cost-effectiveness in our models
- The models were not sensitive to the trade-offs in probability of amputation and CV risk
- Canagliflozin may still provide benefit to certain individuals with T2DM



# Questions?



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