

Comparing Modeled Outcomes With Published Studies in the Japanese Setting: A Validation Analysis With the PRIME Type 2 Diabetes Model

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BACKGROUND

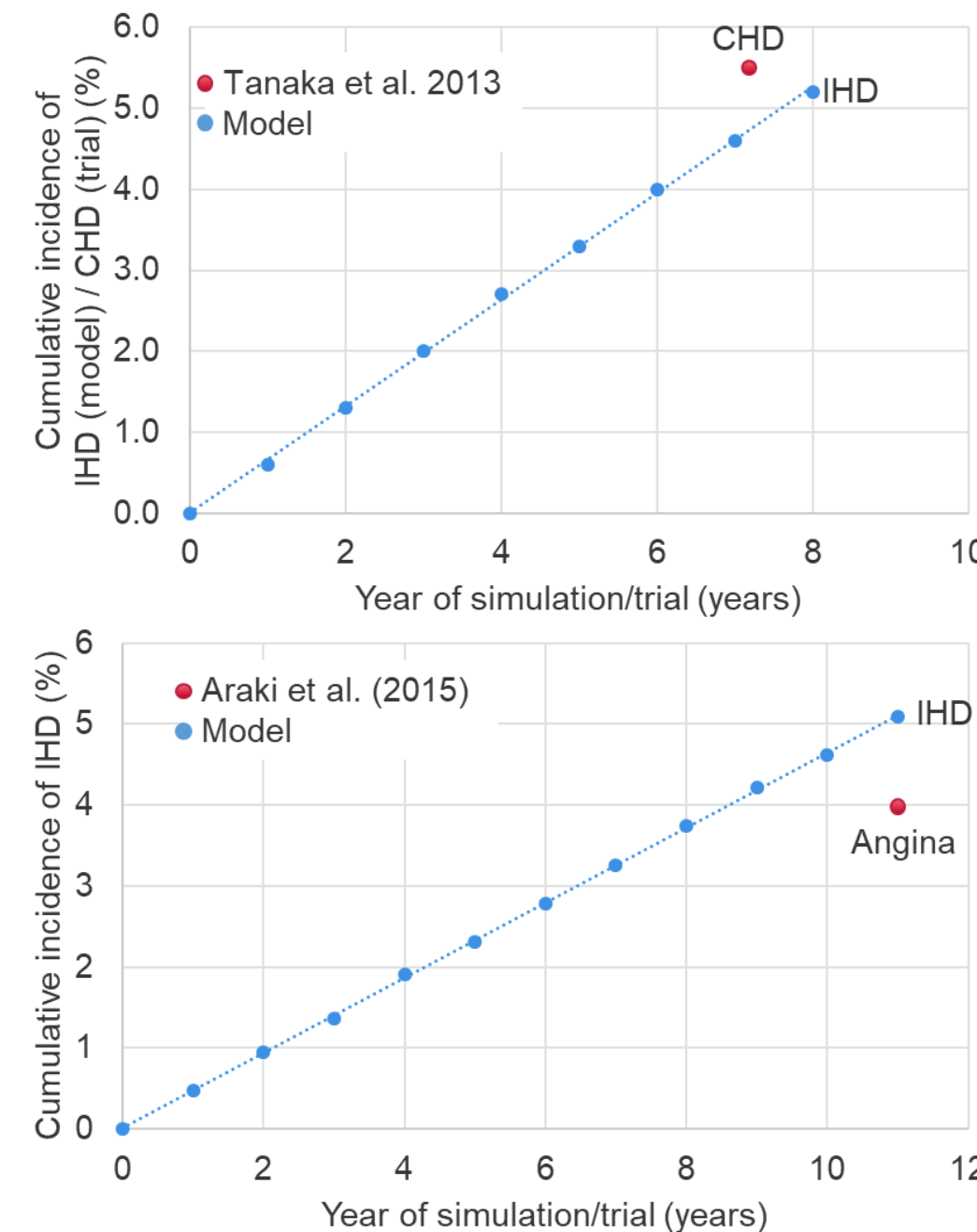
- In Japan, an estimated 19.7% of men and 10.8% of women are believed to have type 2 diabetes (T2D), with the prevalence of T2D expected to increase.¹
- The disease is already associated with a substantial economic burden, with estimates from 2015 indicating that the direct healthcare cost of diabetes exceeded USD 20 billion and accounted for 4.4% of total health expenditure in Japan.²
- The increasing burden of T2D in Japan requires the optimization of healthcare resource use, but little has been published on T2D models that could support economic evaluation of new diabetes interventions in this setting.
- The PRIME T2D Model is a new, product-independent, patient-level simulation model based on an extensive literature review, capable of projecting long-term clinical and cost outcomes for populations with T2D to support health economic evaluation.³

OBJECTIVE

- The aim of the present study was to perform a validation analysis using the PRIME T2D model to understand its potential validity for use in Japanese cost-effectiveness analyses.

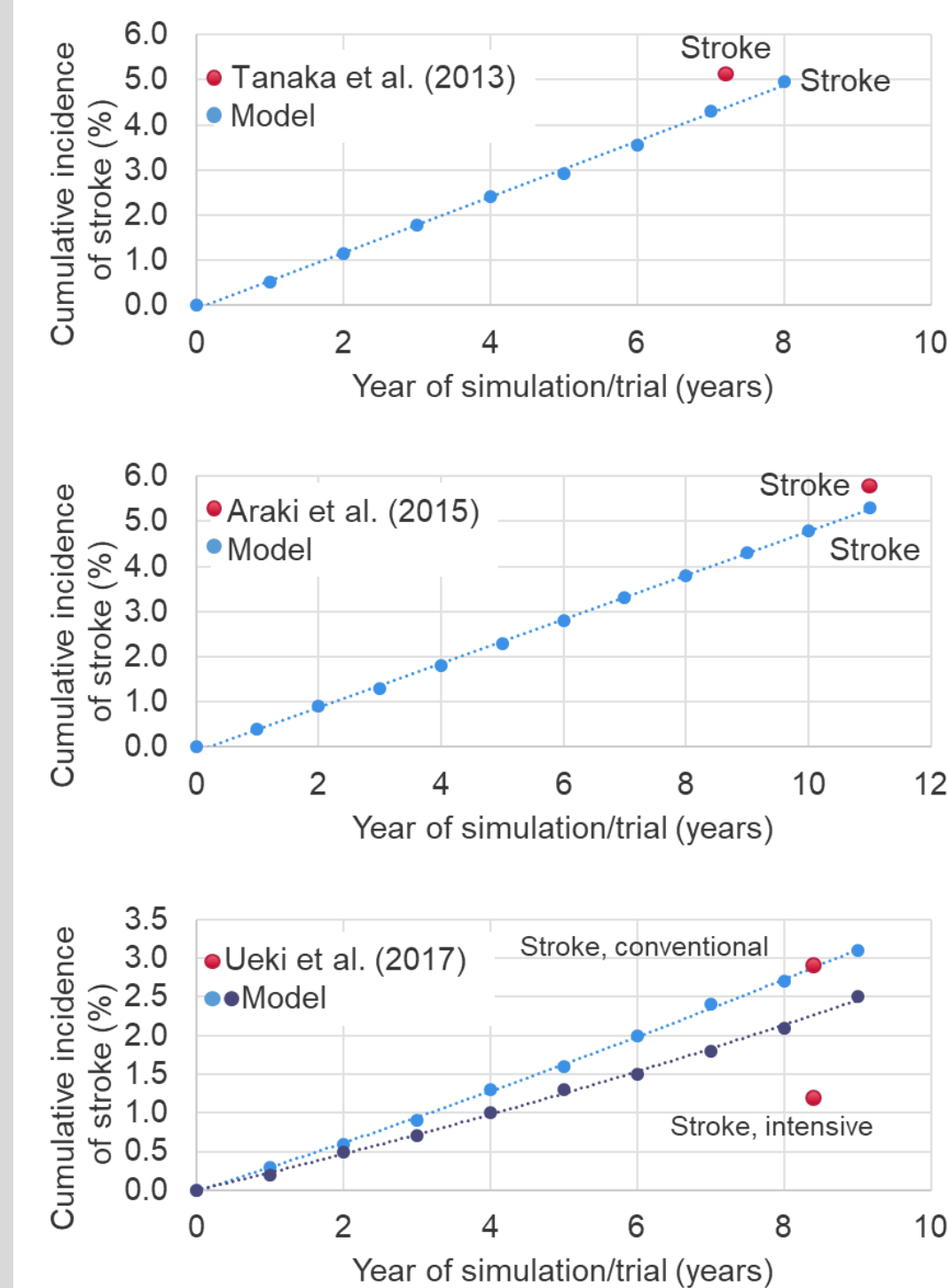
KEY RESULTS

Figure 1. Cumulative incidence of ischemic heart disease



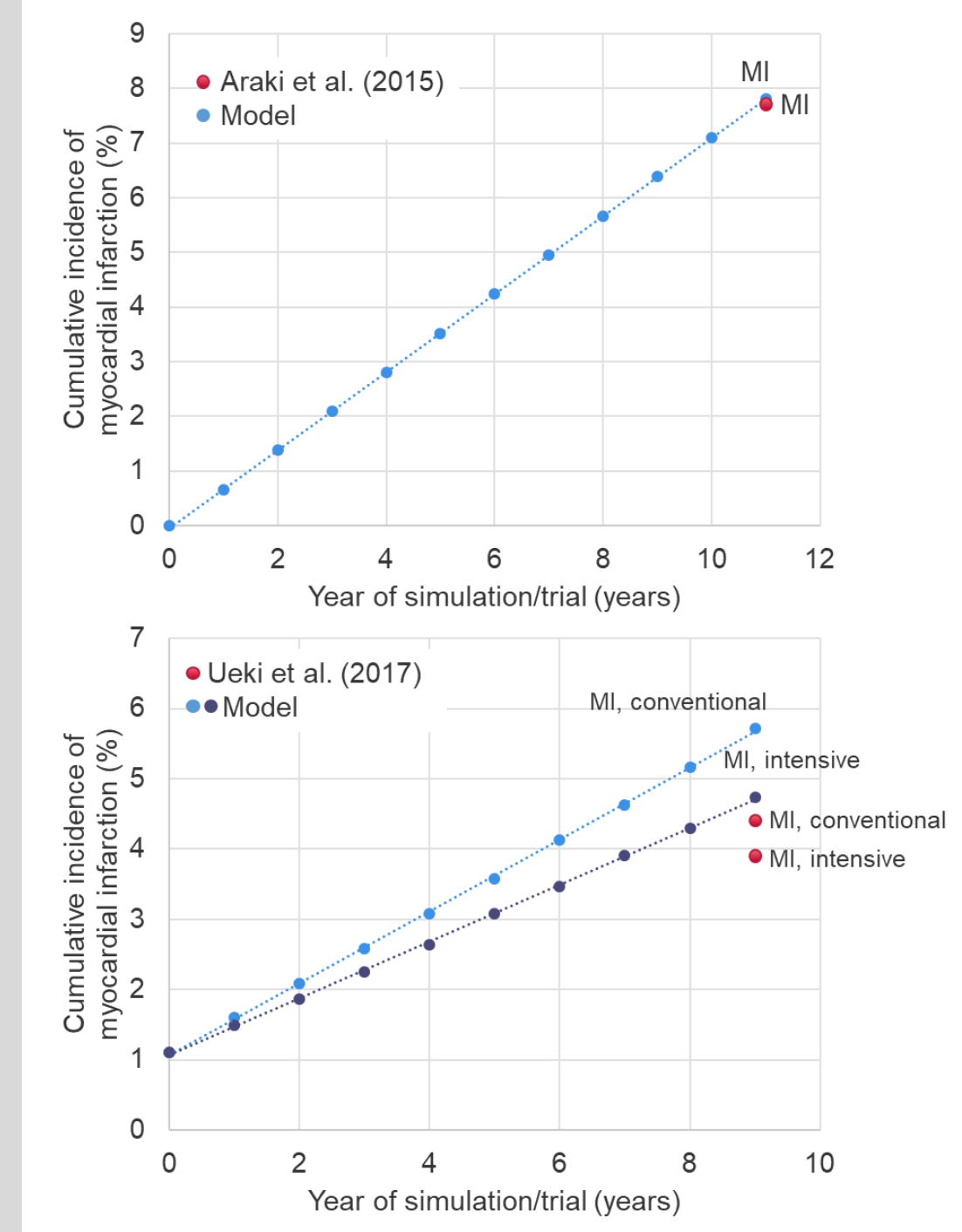
CI, cumulative incidence; CHD, coronary heart disease; IHD, ischemic heart disease. Modeled values are shown in blue. Published study values are shown in red.

Figure 2. Cumulative incidence of stroke



CI, cumulative incidence. Modeled values are shown in blue and purple. Published study values are shown in red.

Figure 3. Cumulative incidence of myocardial infarction



CI, cumulative incidence; MI, myocardial infarction; Modeled values are shown in blue and purple for conventional and intensive treatment arms respectively. Published study values are shown in red for the endpoint described as MI from Araki et al. (2015) and the endpoint of MI and/or revascularization from Ueki et al. (2017).

LIMITATIONS

- Mismatched endpoint definitions meant that certain outcomes could not be directly compared (IHD and ESRD) with the modeled endpoints.
- The literature review did not identify appropriate endpoint data to validate other outcomes reported by the model (e.g., heart failure, foot ulcer, amputation, blindness, macular edema and neuropathy).

CONCLUSIONS

- This analysis provides evidence that the PRIME T2D Model is capable of reproducing real-life cohort outcomes in the Japanese setting.
- Where endpoint definitions were well matched, the model produced results that were comparable with real-world data for MI and stroke (root mean squared difference 0.45%).
- The PRIME T2D Model is one of the few available diabetes models that utilizes risk data specific to Asian populations to evaluate long-term outcomes in patients with T2D and may offer an opportunity for more accurate projections of the outcomes in health economic evaluations in the Japanese setting.

METHODS

- A literature review was performed in September 2020 to identify recently published, long-term cohort studies with more than 3 years of follow-up in patients with T2D in Japan.
- Studies identified by literature search were screened to select those that reported long-term cumulative incidence of diabetes-related complications, with information on baseline characteristics and treatment regimens during follow up.
- Studies were excluded if they did not include a Japanese T2D population, enrolled fewer than 300 patients, had less than 3 years of median follow up time, or did not report relevant endpoint data.
- The PRIME T2D Model was used to run simulations designed to reproduce the outcomes of the published studies, by matching cohort characteristics, treatment effects/risk factor progression and running simulations over an equivalent time horizon.

- Model validation against real-life data from T2D populations was performed in line with best practice guidelines.⁴ Face validity of the model was established by review by clinical and diabetes modeling experts.
- Model predictions were compared with outcomes observed in the studies used to build the model and with outcomes observed in studies that were not used to build the model. To access compatibility, the root mean squared difference was calculated for each comparison.

RESULTS

- The literature search produced 234 hits, 207 of which were excluded at title and abstract screening, and 23 were excluded at full text review. Four studies were identified from the literature review that reported endpoint data suitable for validation.^{5,6,7,8}
- Validation analyses were performed for ischemic heart disease (IHD), myocardial infarction (MI), stroke and end-stage renal disease (ESRD).

Ischemic heart disease

- No published studies reported cumulative incidence of IHD, but Tanaka *et al.* and Araki *et al.* reported the cumulative incidence of coronary heart disease (CHD) and angina pectoris, respectively.
- The projected cumulative incidence of IHD in the PRIME T2D Model at 7 years was 4.6%, compared with the incidence of CHD reported by Tanaka *et al.* of 5.5% at 7.2 years follow up.
- The PRIME T2D Model projected a cumulative incidence of IHD at 11 years of approximately 5.1% versus 4% incidence of angina pectoris at 11 years as reported by Araki *et al.* (Figure 1).

Stroke

- Tanaka *et al.* reported a cumulative incidence of stroke of 4.3% at 7 years compared with 5.1% incidence at 7.2 years from the model. At 11 years follow-up, Araki *et al.* reported a cumulative incidence of 5.3% versus 5.8% incidence projected in the model.

- The cumulative incidence at 8.5 years follow up of patients receiving intensive and conventional therapy reported by Ueki *et al.* was 2.9% and 1.2% respectively, compared with the modeled incidence at 8 years of 2.7% and 2.1%, respectively (Figure 2).

Myocardial infarction

- Cumulative incidence of MI at 11 years was reported as 7.7% by Araki *et al.* compared with 7.8% projected in the simulation.
- Ueki *et al.* reported the cumulative incidence of MI at 8.5 years follow up when treated with intensive and conventional treatment as 0.4% and 0.9%, respectively, whilst the projected model incidence for MI was 3.5% and 4.5%, respectively.
- The values reported by Ueki *et al.* were low relative to other publications. When summed with the incidence of revascularization, patients on intensive and conventional therapy had a cumulative incidence of stroke of 3.9% and 4.4%, respectively (Figure 3).

End-stage renal disease

- Oshima *et al.* was the only study to report ESRD. Cumulative incidence was reported as 7.1% at 6.5 years follow up versus 0.93% at 6 years as projected in the model.
- This difference in incidence was likely due to disparate endpoint definitions, with Oshima *et al.* using a very broad definition of ESRD and as a result reporting cumulative incidence values higher than other cohort studies in comparable populations.^{9,10}

References:

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