

Supplemental Table 1: Inclusion and exclusion criteria

Inclusion criteria
<ul style="list-style-type: none">• Diagnosis of type 2 diabetes• Age ≥ 18 years*• Initiating a second-line therapy (add-on or switching) after a first-line oral treatment with monotherapy, dual therapy, or triple therapy†• Provision of written informed consent
Exclusion criteria
<ul style="list-style-type: none">• Type 1 diabetes• Pregnancy• Initiation of dual therapy after having previously received two different lines of monotherapy (eg, initiation of a combination of a sulphonylurea and a DPP-4 inhibitor after successive metformin monotherapy and sulphonylurea monotherapy)• Current treatment with chemotherapy or oral or intravenous steroids• Undergoing dialysis or has had a renal transplant• First-line treatment was insulin or an injectable agent‡• First-line treatment was herbal remedies/natural medicines alone• Participation in an interventional trial• Condition/circumstance which, in the opinion of the investigator, could significantly compromise the 3-year follow-up (eg, life-threatening comorbidities, tourist, non-native speaker or does not understand the local language where interpreter services are not reliably available, psychiatric disturbances, dementia, alcohol, or drug abuse)• Not willing to sign the informed consent form

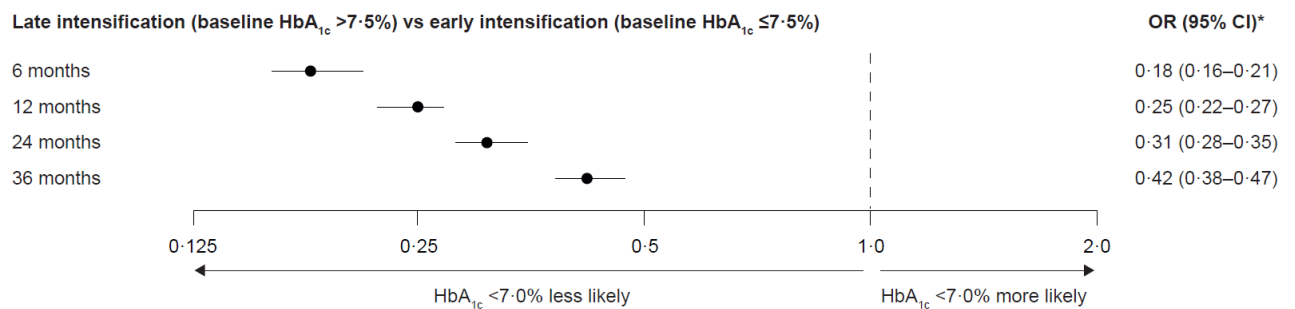
DDP-4=dipeptidyl peptidase-4. *Age ≥ 20 years in Japan. †In Japan, only patients using an oral monotherapy as first-line treatment were included. ‡Patients who received short-term initial treatment with insulin followed by oral therapy were eligible if the treatment with insulin lasted no more than 2 weeks and occurred at least 6 months before initiation of second-line therapy. In such patients, insulin was considered not as a first-line treatment, but as a short-term treatment to lower glycaemic levels quickly before starting regular treatment.

Supplemental Table 2: HbA_{1c} at baseline, by WHO region

	WHO region					
	Africa (n=416)	Americas (n=1345)	South-East Asia (n=1396)	Europe (n=2384)	Eastern Mediterranean (n=1712)	Western Pacific (n=2322)
HbA _{1c} at baseline, n (%)						
≤7.5%	128 (30.8)	429 (31.9)	349 (25.0)	844 (35.4)	381 (22.3)	1144 (49.3)
>7.5%	288 (69.2)	916 (68.1)	1047 (75.0)	1540 (64.6)	1331 (77.7)	1178 (50.7)

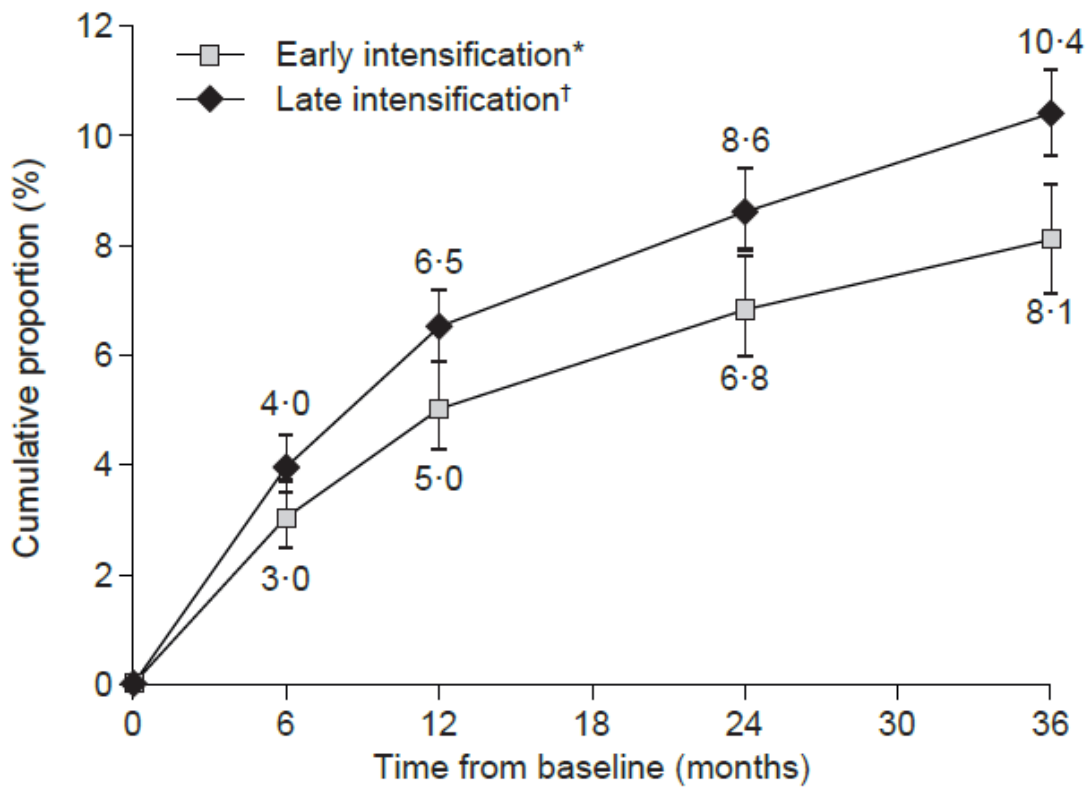
HbA_{1c}=glycated haemoglobin. WHO=World Health Organization.

Supplemental Figure 1: Likelihood of having HbA_{1c} <7.0% (53 mmol/mol) during follow-up in the late-intensification group (vs the early-intensification group)



CI=confidence interval. HbA_{1c}=glycated haemoglobin. OR=odds ratio. T2D=type 2 diabetes. *ORs and 95% CIs calculated using a repeated-measures model with country as a random factor, and adjusted for age, sex, time since T2D diagnosis, first-line therapy, second-line therapy, body mass index, history of hypoglycaemia requiring third-party assistance in the year before baseline, history of macrovascular complications (includes coronary artery disease, cerebrovascular disease, peripheral artery disease, heart failure, and implantable cardioverter defibrillator use), history of microvascular complications (includes nephropathy, retinopathy, and neuropathy), education level, smoking status, health insurance, type of centre, and World Health Organization region.

Supplemental Figure 2: Cumulative proportion of patients reporting at least one hypoglycaemic event during follow-up in patients who intensified treatment early (n=3275) versus those who intensified treatment late (n=6300)



Whiskers represent 95% confidence intervals. HbA_{1c} =glycated haemoglobin. *Early intensification defined as treatment intensification with baseline $HbA_{1c} \leq 7.5\%$ (59 mmol/mol). †Late intensification defined as treatment intensification with baseline $HbA_{1c} > 7.5\%$ (59 mmol/mol).