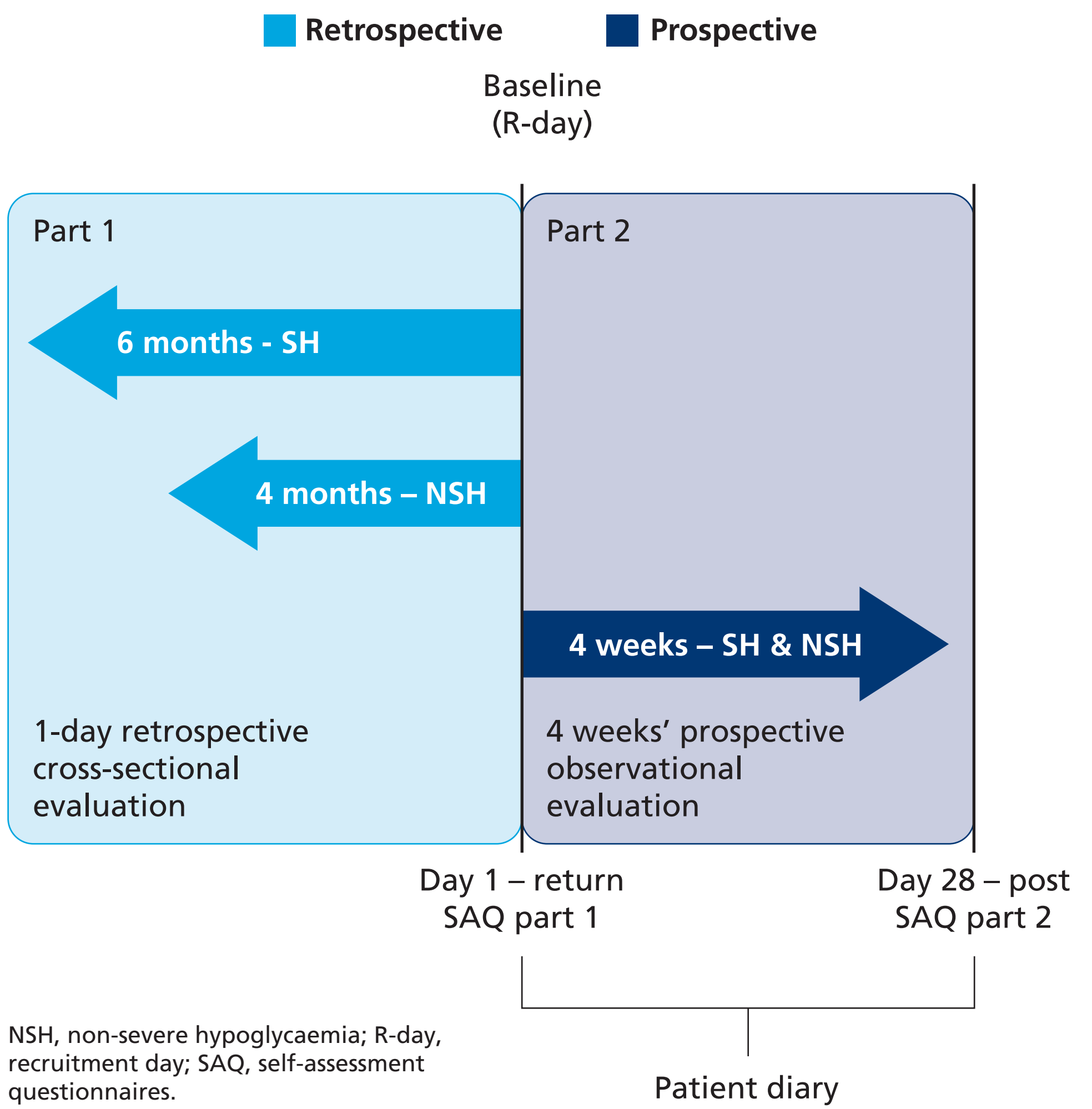


Hypoglycaemia among insulin-treated patients with diabetes: Indonesian cohort of International Operations Hypoglycaemia Assessment Tool (IO HAT) study

Introduction

- The incidence of diabetes is increasing in developing countries due to urbanisation leading to changes in lifestyle and diet.^{1,2}
- Indonesia is among the top 10 countries for number of people aged 20–79 years with diabetes, and is estimated to rise from rank 7 in 2010 to rank 6 in 2040.^{1,3}
- There were 10 million cases of diabetes reported in 2015 in Indonesia, a value that is estimated to increase to 16.2 million by 2040.³
- In Indonesia 36.75% of patients with diabetes are insulin users.⁴ Insulin therapy is associated with hypoglycaemia, and fear of hypoglycaemia often prevents or delays patients and healthcare providers in choosing to prescribe insulin.⁵
- Real-world data on the incidence of hypoglycaemia in Indonesia is limited.
- The International Operations Hypoglycaemia Assessment Tool (IO HAT) study was a non-interventional, real-world, observational 6-month retrospective and 4-week prospective study of self-reported hypoglycaemic events (Figure 1) in 7289 patients with insulin-treated type 1 (T1D) and type 2 diabetes (T2D) from nine countries (Bangladesh, Colombia, Egypt, Indonesia, Philippines, Singapore, South Africa, Turkey and UAE).

Figure 1. Study design.



Aim

- To assess the incidence of hypoglycaemia symptoms in insulin-treated patients from Indonesia included in the IO HAT study.

Methods

Study design

- Eligible patients had T1D or T2D treated with insulin for >12 months, were ≥18 years of age at baseline and had given consent to participate in the study.
- Study objectives:
 - The primary objective was the percentage of patients experiencing ≥1 hypoglycaemic event during the prospective period
 - Secondary objectives included the difference in retrospective and prospective rates of hypoglycaemia and hypoglycaemia unawareness.

Definition of hypoglycaemia

- Hypoglycaemia was defined by the following:
 - Confirmed hypoglycaemia – an event confirmed by plasma glucose levels <56 mg/dL (3.1 mmol/L);
 - Severe hypoglycaemia – based on the American Diabetes Association (ADA) definition (any hypoglycaemic event requiring third party assistance to administer carbohydrate, glucagon or other resuscitative actions);⁶
 - Non-severe hypoglycaemia – an event managed by the patient alone;
 - Any hypoglycaemia – the sum of severe and non-severe hypoglycaemia;
 - Nocturnal hypoglycaemia – an event occurring between 00:00 and 06:00.

Assessment of hypoglycaemia

- Incidence of hypoglycaemia based on symptoms or plasma glucose levels was recorded in the 6-month retrospective and 4-month prospective periods, using self-assessment questionnaires (SAQs) and patient diaries.
- The SAQs consisted of two parts:
 - Part 1: baseline demographic and treatment information, hypoglycaemia unawareness, perceptions of hypoglycaemia, history of severe hypoglycaemia over the previous 6 months, symptomatic hypoglycaemia over the previous 4 weeks
 - Part 2: history of both severe and symptomatic hypoglycaemia over the 4 weeks following baseline.
- Incidence of hypoglycaemia was compared in the retrospective and prospective periods.

Results

Patient characteristics

- There were 374 Indonesian patients enrolled in the IO HAT study, 17 patients with T1D and 357 patients with T2D (Table 1).

Table 1. Baseline characteristics.

	T1D (N=17)	T2D (N=357)
Age (years)	31.8 (13.9)	57.9 (10.1)
Median	27.0	59.0
Upper quartile, Lower quartile	34.0, 22.0	65.0, 52.0
Male/Female (%)	41.2/58.8	45.9/54.1
Duration of diabetes (years)	11.5 (9.3)	11.2 (7.7)
Median	10.0	10.0
Upper quartile, Lower quartile	19.0, 5.0	15.0, 5.0
Duration of insulin use (years)	8.7 (9.6)	4.0 (3.4)
Median	5.0	3.0
Upper quartile, Lower quartile	12.0, 2.0	5.0, 2.0
BMI (kg/m²)	22.4 (3.3)	26.2 (4.3)
Median	22.1	26.0
Upper quartile, Lower quartile	24.8, 20.6	28.3, 23.5
HbA _{1c} (%)	8.9% (2.1)	8.7% (2.0)
FBG (mg/dL)	155.0 (75.7)	165.8 (70.3)
PPG (mg/dL)	178.4 (79.3)	203.6 (77.5)

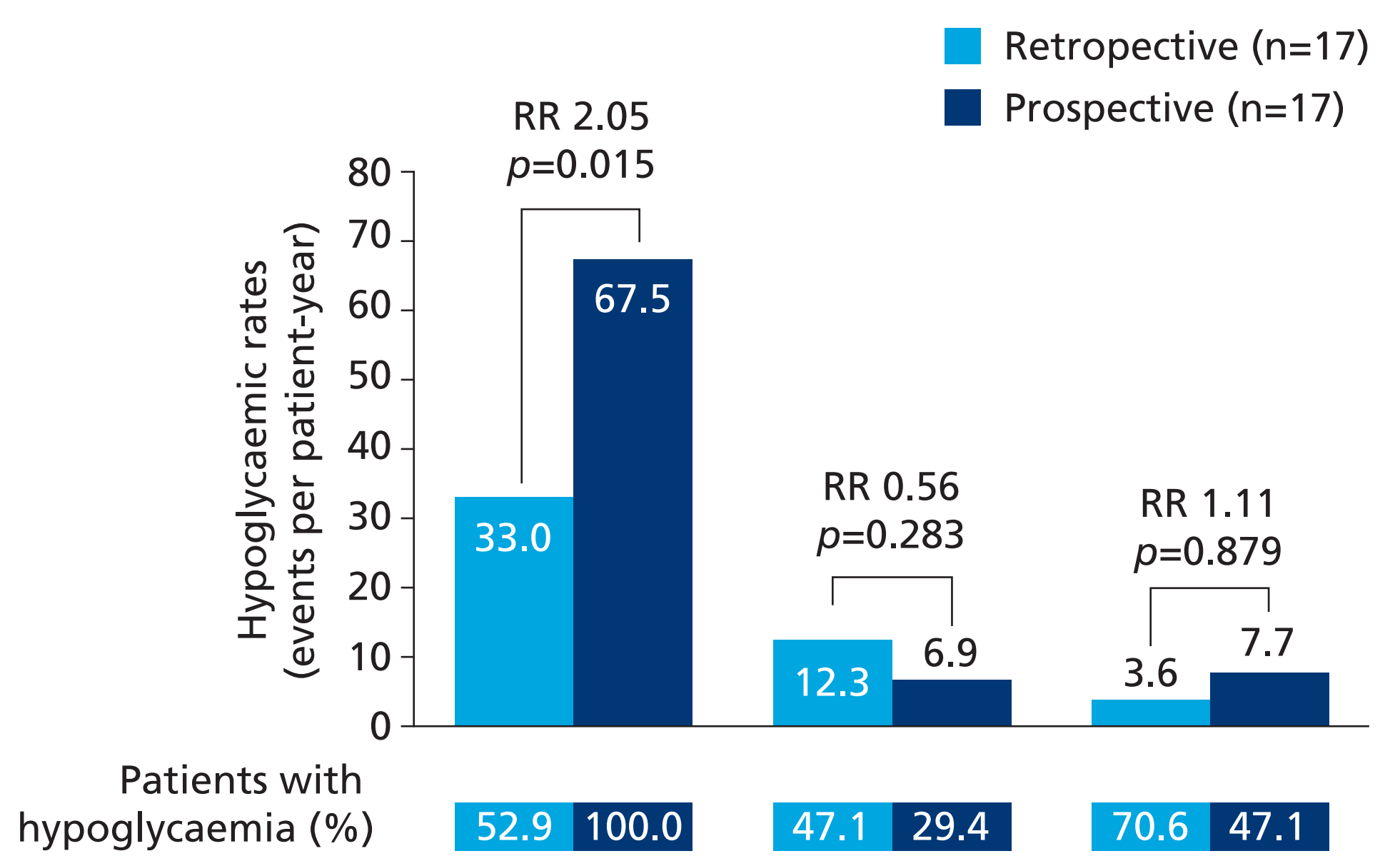
Data are presented as mean (SD) unless otherwise stated; SD, standard deviation; N, total number of subjects participating; HbA_{1c}, glycated haemoglobin; FBG, fasting blood glucose; PPG, postprandial glucose; T1D, type 1 diabetes; T2D, type 2 diabetes.

- Patient diaries and the Part 2 SAQ were completed by 364 patients (97.3%) in the 4-week prospective period of the study.
- At baseline, short/rapid plus long-acting insulin was the most used insulin treatment regimen by patients with T1D (n=13, 76.5%) and patients with T2D (n=164, 45.9%).

Hypoglycaemia frequency

- Figures 2 and 3 show the frequency of hypoglycaemia in the retrospective and prospective periods for patients with T1D and T2D, respectively.
- Incidence of any hypoglycaemia was reported at lower rates retrospectively than prospectively (T1D 33.0 vs. 67.5 events per patient-year [PPY], $p=0.015$; T2D 11.2 vs. 25.7 PPY, $p<0.001$).

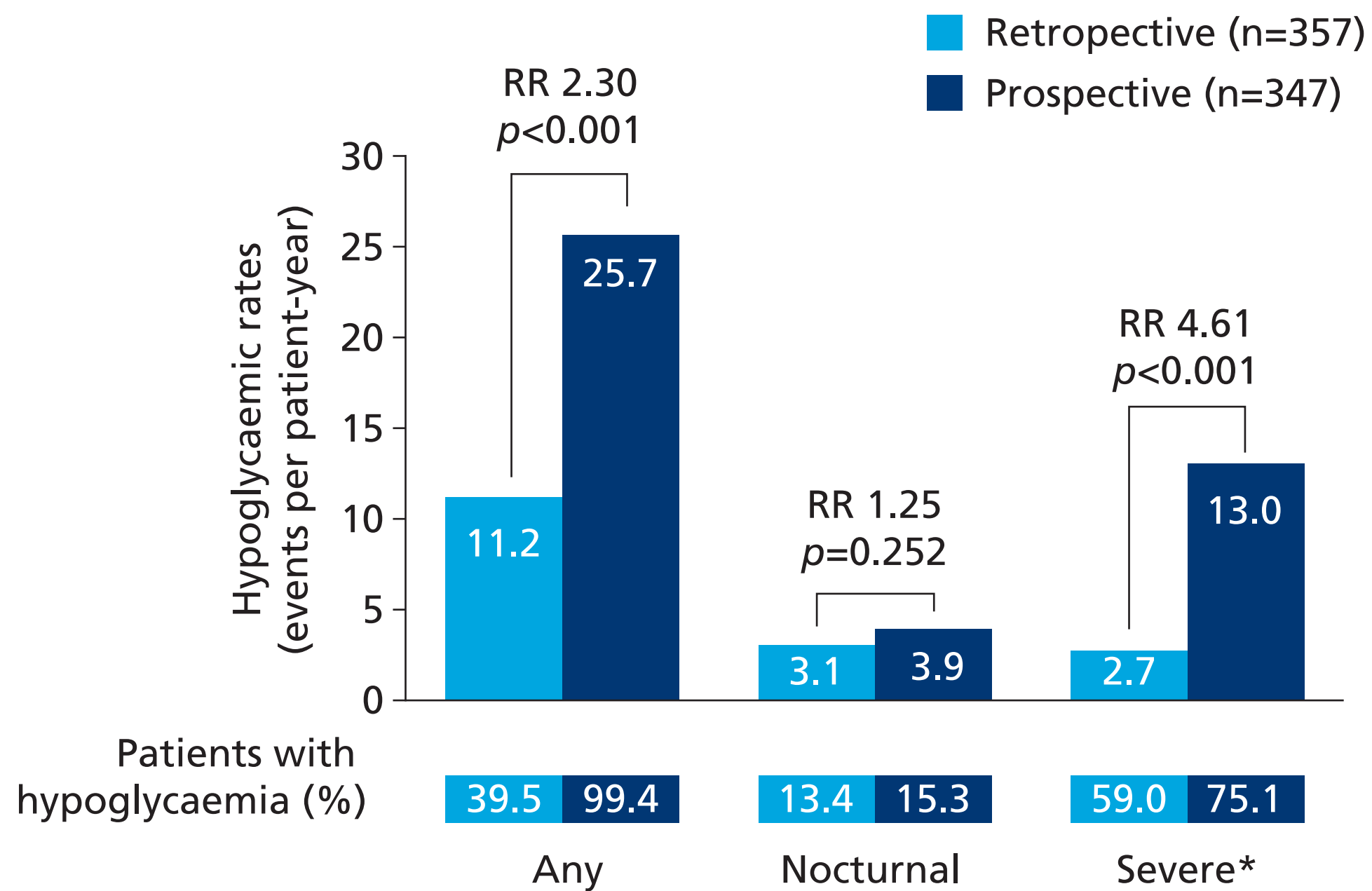
Figure 2. Retrospective and prospective hypoglycaemia rates in patients with type 1 diabetes in the IO HAT study Indonesian cohort.



*'Any' and 'Nocturnal' based on a 4-week period for both retrospective and prospective analyses. *Retrospective data based on 6-month period and prospective data based on 4-week period. RR, rate ratio.

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Figure 3. Retrospective and prospective hypoglycaemia rates in patients with type 2 diabetes in the IO HAT study Indonesian cohort.



*'Any' and 'Nocturnal' based on 4-week period for both retrospective and prospective analyses. *Retrospective data based on 6-month period and prospective data based on 4-week period. RR, rate ratio.

- Retrospectively, 52.9% of patients with T1D and 39.5% of patients with T2D reported any hypoglycaemia. In contrast, nearly all patients reported hypoglycaemia prospectively (T1D 100%, T2D 99.4%).
- Retrospective and prospective rates of severe hypoglycaemia in T1D were 3.6 and 7.7 events PPY, respectively ($p=0.879$), and in T2D were 2.7 and 13.0 events PPY, respectively ($p<0.001$).
- Rates of nocturnal hypoglycaemia were reported at higher rates retrospectively than prospectively in T1D (12.3 PPY vs. 6.9 PPY, $p=0.283$, respectively), but were lower retrospectively than prospectively in T2D (3.1 PPY vs. 3.9 PPY, $p=0.252$, respectively).

Hypoglycaemic events and insulin regimen

- Rates of any and nocturnal hypoglycaemia were highest in patients receiving short/rapid plus long-acting insulin regimens during the retrospective and prospective periods in patients with T1D.
 - The rate of any hypoglycaemia was 39.1 and 82.3 events PPY for the retrospective and prospective periods, respectively.
 - Rates of nocturnal hypoglycaemia were 14.1 PPY and 9.0 PPY, respectively.
- Rates of any hypoglycaemic event were highest in pre-mix insulin regimens in the retrospective period in patients with T2D (12.6 PPY) and in short/rapid plus long-acting regimens in the prospective period (28.3 PPY).
- Hypoglycaemic events were independent of HbA_{1c} in both T1D and T2D.

Patients and hypoglycaemia awareness

- Among patients with T1D and T2D, 5.9% and 36.4%, respectively, did not know what hypoglycaemia was at baseline.
- With respect to fear of hypoglycaemia, on a scale from 1 (not afraid) to 10 (absolutely terrified) mean scores were 5.1 in T1D and 4.1 in T2D.
- Most patients defined hypoglycaemia by symptoms only (T1D 35.3%, T2D 29.7%).
- A high proportion of patients (T1D 82.4%, T2D 67.2%) reported only occasionally having symptoms with low blood sugar measurement, indicating impaired hypoglycaemia awareness.
- Although 18.2% of all patients defined hypoglycaemia by symptoms and blood glucose measurements, 21.5% of patients measured their blood sugar but used values inconsistent with standard definitions.

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Conclusions

- These results are the first patient-reported dataset on hypoglycaemia in insulin-treated patients with diabetes in Indonesia.
- The high prospective incidence of hypoglycaemia, with almost all patients reporting events in the 4 weeks after baseline, may indicate hypoglycaemia underreporting during the retrospective period, and/or may be the influence of patient education during the study, leading to increased hypoglycaemia knowledge and therefore reporting, prospectively.