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Four-year evolution of insulin regimens, glycaemic control, hypoglycaemia and body weight after starting insulin therapy in type 2 diabetes across three continents

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ABSTRACT

Aims: It is of interest to understand how insulin therapy currently evolves in clinical practice, in the years after starting insulin in people with type 2 diabetes. We aimed to describe this evolution prospectively over 4 years, to assist health care planning.
Methods: People who had started any insulin were identified from 12 countries on three continents. Baseline, then yearly follow-up, data were extracted from clinical records over 4 years.
Results: Of the 2999 eligible people, 2272 were followed over 4 years. When starting insulin, mean (SD) duration of diabetes was 10.6 (7.8) years, HbA1c 9.5 (2.0)% (80 [22] mmol/mol) and BMI 29.3 (6.3) kg/m^2. Initial insulin therapy was basal 52%, premix 23%, mealtime + basal 14%, mealtime 8% and other 3%; at 4 years, 30%, 25%, 33%, 2% and 5%, respectively, with 5% not on insulin. Insulin dose was 20.2 U/day at the start and 45.8 U/day at year 4. There were 1258 people (55%) on their original regimen at 4 years, and this percentage differed according to baseline insulin regimen. HbA1c change was −2.0 (2.2)% (−22 [24] mmol/mol) and was similar by final insulin regimen. Hypoglycaemia prevalence was <20% in years 1–4. Body weight change was mostly in year 1, and was very variable, mean +2.7 (7.5) kg at year 4.
Conclusion: Different insulin regimens were started in people with differing characteristics, and they evolved differently; insulin dose, hypoglycaemia and body weight change were diverse and largely independent of regimen.

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1. Introduction

When people with type 2 diabetes on metformin and other oral therapies can no longer attain the recommended glucose control targets, insulin therapy is generally started. Recommendations as to insulin type vary [1–3]. Some authorities endorse both basal and premix approaches, and others place more emphasis on basal insulin; mealtime insulin alone is used on occasion, or in a comprehensive mealtime + basal regimen even from the time of starting insulin [4]. Randomized clinical trials have provided evidence on the relative efficacy of insulin regimens [5,6], but these trials were conducted in people and clinical environments that may not be representative of those in routine clinical practice. Little is known of the impact of starting insulin for outcomes of importance to people with diabetes, such as change in insulin regimen, insulin dose, hypoglycaemia and weight change, with data available only for single countries [7–9], or in less or recently developed nations [4], or particular insulins [10,11], often with follow-up of 1 year or less [4,7,8].

Analyses based on non-interventional observational studies may overcome some of the challenges of generalizability inherent to randomized trials and such studies provide a bridge from randomized trials towards more routine settings [4]. The Cardiovascular Risk Evaluation in people with Type 2 Diabetes on Insulin Therapy (CREDIT) study, an international 4-year, non-interventional, longitudinal study, was designed to evaluate prospectively, in routine clinical practice in a large number of clinical centres, the relationship between blood glucose control and cardiovascular events in people beginning any insulin. Further, this study aimed to describe current medical practice in people with type 2 diabetes using insulin. Here we report the evolution of insulin use, associated blood glucose-related outcomes and effects on body weight and hypoglycaemia, over 4 years. Cardiovascular outcomes and the factors associated with them will be reported separately.

2. Methods

The CREDIT study design, site/participant selection process and participant baseline characteristics have been reported previously [12]. Briefly, the study was conducted in 314 centres in 12 countries – Canada, Japan and 10 in Europe – between December 2006 and May 2012. Ethical approval was obtained for all study sites. Conduct of the study adhered to standards of data collection for clinical trials, according to the Declaration of Helsinki. Prior written informed consent was obtained from all participants.

Men and women with type 2 diabetes, age >40 years, were eligible if they had started any insulin regimen >1 month and <12 months prior to study entry and had an HbA1c measurement within 3 months of beginning insulin. Data at the start of insulin were collected retrospectively from clinical records. As CREDIT was a non-interventional study, there was no fixed study visit schedule, and insulin choice, dosage, titration, funding and concomitant oral agent therapy were according to usual local practice. Data were gathered from routine clinical practice, with the physicians asked to report updated data every 6 months. Data at '4 years' represent that ascertained 42–54 months after beginning insulin, and data for 1, 2 or 3 years were for 9–18, 18–30 and 30–42 months, respectively.

Glucose control was assessed by HbA1c, fasting plasma glucose (FPG) and postprandial plasma glucose (PPPG). HbA1c is presented in both National Glycohemoglobin Standardization Program and International Federation of Clinical Chemistry units [13,14]. FPG and PPPG are reported as either laboratory or self-monitored glucose values. Documented symptomatic hypoglycaemia, nocturnal hypoglycaemia and severe hypoglycaemia were assessed over the 6 months prior to the follow-up date. Body weight change, other glucose-lowering medications and changes of insulin regimen were also assessed.

2.1. Statistical methods

Analyses were performed with SAS software, version 9.1 (Cary, NC, USA). All data are reported and analyzed using descriptive statistics. Data on insulin regimens, other glucose-lowering medications, blood glucose control and body weight are presented by insulin regimen when starting insulin. For 4-year and change from baseline data, data for insulin dose, blood glucose control, body weight and hypoglycaemia are presented by insulin regimen at 4 years. Initial and yearly data for insulin dose, HbA1c, FPG, PPPG and body weight change are presented for the entire population. Updated HbA1c, defined as the average of all values from 1 month after starting insulin to 4 years of follow-up, was used to report results by baseline insulin regimen; all other results for HbA1c are reported by year interval. Because of the likelihood of some degree of allocation bias, comparative statistical testing was not performed, avoiding the danger of spurious statistically significant findings with the large numbers of people studied.

3. Results

There were 3060 participants included, with 2999 having valid eligibility criteria (Supplementary, Fig. S1). When starting insulin, the eligible population was 49% female, with an average (standard deviation [SD]) age of 61 (10) years, body mass index of 29.3 (6.3) kg/m^2, duration of diabetes of 11 (8) years and HbA1c of 9.5 (2.0)% (80 [22] mmol/mol). Seventy percent had at least one microvascular disease, 34% had a macrovascular disease and 69% were previously diagnosed with hypertension. In the 4-year data interval, data were available for 2272 (75.8%) participants.

Supplementary Fig. S1 related to this article can be found, in the online version, at http://dx.doi.org/10.1016/j.diabres.2015.01.030.

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