GLYCEMIC VARIABILITY AND COMPLICATIONS IN PATIENTS WITH DIABETES MELLITUS: EVIDENCE FROM A SYSTEMATIC REVIEW OF THE LITERATURE
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OBJECTIVES: Large prospective clinical studies in both type 1 Diabetes Mellitus (T1DM) and type 2 diabetes mellitus (T2DM) have shown that high HbA1c levels are a strong predictor of diabetic complications. New data suggest that variability in glucose values, specifically excursions in postprandial hyperglycemia, may also play a significant role in the risk of microvascular and macrovascular complications. The aim of this review was to assess the published evidence regarding an association between glycemic variability and diabetic complications in patients with DM. METHODS: A systematic review of studies published in English between 1990-November 2008 was undertaken. Studies in patients with T1DM or T2DM reporting a) measures of glycemic variability; and b) its impact on the development or progression of diabetic complications were assessed. RESULTS: Eighteen studies were identified. Seven and 11 studies focused on T1DM and T2DM patients, respectively. Studies in patients with T1DM revealed that glucose variability has little impact on the development of diabetic complications. Only in two T1DM studies did glucose variability have a significant association with prevalent peripheral neuropathy and presence of nephropathy, but not with other complications. Among T2DM studies, a significant positive association between glycemic variability and the development or progression of diabetic complications was reported in 10 of 11 studies. The risk of progression to diabetic retinopathy was significantly increased among patients in higher quartiles of glycemic variability (CV-FPG): 2nd quartile OR = 3.47 (95%CI:1.06–11.5); 3rd quartile OR = 3.66 (95%CI:1.12–12.0); and 4th quartile OR = 6.95 (95%CI:2.1–22.4). Similarly, the risk of all cause and cardiovascular mortality was significantly higher among patients in the 3rd and 4th quartiles of CV-FPG. CONCLUSION: Taken together, these data suggest that glycemic variability may be an independent predictor of complications regardless of HbA1c levels in patients with T2DM. Better control of blood glucose excursions may reduce the risk of these complications.

DIABETES/ENDOCRINE DISORDERS – Cost Studies

A BUDGET IMPACT MODEL (BIM) TO ASSESS THE IMPACT ON THE ITALIAN NATIONAL HEALTH SERVICE (INHS) BUDGET OF THE INTRODUCTION OF MIMIPARA (CINACALCET) IN THE NEW INDICATION PRIMARY HYPERPARATHYROIDISM (PHPT)
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OBJECTIVES: To evaluate the financial impact on the INHS following the introduction of cinacalcet for patients with intractable PHPT or in those whom parathyroidectomy (PTX) is contraindicated. METHODS: The number of patients expected to receive cinacalcet was estimated by literature and local demographic information. The BIM simulates the impact of PHPT management in patients with or without cinacalcet. Resources to manage patients not receiving cinacalcet included drugs for treatment of secondary osteoporosis, visits and diagnostics and a second PTX for patients refractory to their first PTX. Resources to manage patients receiving cinacalcet included 60 mg/day cinacalcet and all of the above except the re-surgery. The total cost was calculated by applying the resources used, the INHS tariffs for visits, diagnostics and surgery, and the reimbursed price for drugs. RESULTS: It was estimated that in the first three years following market introduction, just 113, 320 and 490 out of 1400 eligible patients with PHPT would be placed on cinacalcet therapy respectively. The baseline cost of PHPT management resulted in €794 per patient, per year (€256 for drugs, €314 for re-surgery, €224 for diagnostics). The introduction of cinacalcet resulted in a cost of €369 per patient per year with cinacalcet costing €4380, partially offset by savings due to less other drugs (-€256), avoiding PTX (-€114) and less diagnostics (-€112). The total incremental annual budget increase due to addition of cinacalcet was €147,864, €13,183,32 and €81,117,978 in the first three years, respectively. CONCLUSIONS: Because of the low prevalence of intractable PHPT, the incremental financial benefit on the INHS following the introduction of cinacalcet would be very small and partially offset by savings from less health care resource use. Based on these calculations, the INHS granted reimbursement for cinacalcet in this new indication in 2008.

ECONOMIC EVALUATION OF LONG TERM SOMATOSTATIN ANALOGS IN THE TREATMENT OF ACREMAGLY IN MEXICO: MONOTHERAPY VS SEQUENTIAL THERAPY
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OBJECTIVES: To compare cost and effectiveness between monotherapy with octreotide LR® vs. sequential therapy with lanreotide Autogel® and octreotide LR® or vice versa, for a temporary horizon of 18 months. The effectiveness measure was the percentage of patients achieving a reduction in IGF-1 and a growth hormone levels, obtained from clinical trials published in international literature. Only direct medical costs were considered in the analysis. Costs were estimated using prices of 2008 and are expressed in US dollars (exchange rate of 11.14 pesos 1 US dollar). RESULTS: Octreotide LR® monotherapy led to 30% of patients achieving a reduction in IGF-1 and growth hormone to safe levels, whereas sequential therapy achieved 37.8% patients with hormone reduction to safe levels. The treatment with lanreotide Autogel®/octreotide LR® showed the best average cost $24,792.3, per aperacemic patient treated, followed by the treatment with octreotide LR® from the Autogel® with a cost of $28,952.8 and finally octreotide LR® monotherapy with a cost of $29,514.0. According to incremental analysis, the treatment with lanreotide Autogel®/octreotide LR® is the dominant alternative. Univariate sensitivity and probability OBJECTIVES: The aim of this health economic analysis was to assess the cost-effectiveness of insulin detemir (IDet) + oral antidiabetics (OAD) versus OAD alone or neutral protamine Hagedorn (NPH) + OAD in patients with type 2 diabetes, based on the Czech sub-cohort type 2 patients of the large observational study PREDICTIVE METHODS: A published and validated Decision Model was used to project long-term economic and clinical outcomes in a cohort of type 2 diabetes patients treated with either IDet + OAD versus OAD alone or NPH + OAD, in the Czech setting. Probabilities of complications, management costs adjustments excluding complications and treatment costs were derived from Czech surveys from 2007. Future costs and clinical benefits were discounted at 3.5% per annum. RESULTS: IDet + OAD treatment was projected to improve life expectancy by approximately 0.33 years versus OAD (0.26 years more versus NPH + OAD (9.35,972) versus 8.249,910, and 9.35,972) and quality-adjusted life expectancy by 0.289,68 quality-adjusted life years (5,756,02 versus 5,465,34 QALYs). Treatment and complication costs associated with IDet treatment were higher over patient lifetime than with OAD with difference 76862 CZK (260862 CZK/QALY) and lower than with NPH + OAD with difference -151809 CZK (260862 CZK/QALY) dominant. CONCLUSIONS: CORE diabetes T2 patients sub-cohort simulation in 35 years perspective from PREDICTIVE study has demonstrated acceptable cost-effectiveness for patients with type 2 diabetes treated IDet+OAD. IDet + OAD treatment was projected to be associated with improvements in life expectancy, QALYs and acceptable or cost saving compared to OAD and NPH + OAD. Sensitivity analyses show cost-effectiveness result to be robust.

ECONOMIC EVALUATION OF RAPID-ACTING INSULIN ANALOGUES FOR THE TREATMENT OF PATIENTS WITH TYPE 1 AND TYPE 2 DIABETES MELLITUS IN CANADA
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OBJECTIVES: To estimate the cost-effectiveness of rapid-acting insulin analogues (RAIA) compared to regular human insulin (HI), for the treatment of diabetes mellitus (DM). This information may assist policy makers in making informed decisions on reimbursement of RAIA. METHODS: An economic evaluation, from the perspective of a third-party provincial payer, was conducted using the Center for Outcomes Research (CORE) Diabetes Model (CDM). Clinical outcomes (e.g., A1C and hypoglycemia) were derived from recent meta-analyses. Costs and utilities, both discounted at 5%, were obtained from published sources. Sensitivity analyses were performed to test the robustness of results. RESULTS: Type 1 DM (T1DM) – insulin aspart was more effective (0.055 quality-adjusted life years (QALYs)) and less costly (~$620) than regular HI. The incremental cost-utility ratio (ICUR) for insulin lispro relative to regular HI was $28,796 per QALY gained (change in A1C, $182; A QALYs, 0.006). Type 2 DM (T2DM) – the ICUR for insulin aspart compared to regular HI, was $22,488 per QALY gained (A1C cost, $333; A QALYs, 0.015). The ICUR for insulin lispro, relative to regular HI, was $130,845 per QALY gained (A1C cost, $784; A QALYs, 0.006). Results were sensitive to variations of parameters in sensitivity analyses. CONCLUSIONS: Compared with regular HI, the use of RAIA as treatment of DM was associated with relatively low ICURs, with the exception of insulin lispro in patients with Type 2 DM, which was associated with a relatively high ICUR.