**SHORT REPORT**

### Changes in diabetes prevalence and treatment in the last ten years in Luxembourg. A lesson from the United Kingdom prospective diabetes study?

M Perquin¹, G H Michel², C de Beaufort³, M Keipes⁴, R Wirion⁵, N Haas⁴

**SUMMARY**

**Objectives**: The aims of the study were to estimate the prevalence of diabetes in Luxembourg in 2002, to compare it to the prevalence reported in 1991 and to evaluate if prescription attitudes have changed since 1991.

**Methods**: The prevalence of diabetes was estimated using the drug sales data. The key parameters, total amount of antidiabetic drugs sold in one year and the average daily dose or Prescribed Daily Dose (PDD), have been obtained from the National Social Security Organization and by a standardized questionnaire sent to all general practitioners and all internists and endocrinologists of the country.

**Results**: The PDD was calculated on 2,402 questionnaires on individual diabetic patients. By this means, the proportion of patients only treated with appropriate diet could also be obtained. Compared to 1991, the total amount of antidiabetic drugs showed a four-fold increase in metformine tablet prescriptions. A high percentage of combined treatments was found. The prevalence of diabetes in Luxembourg was found to be 3.05% of the total population.

**Conclusions**: Compared to the status in 1991, prevalence of diabetes increased by 63%, which seems mainly due to type 2 diabetic patients as orally-treated diabetic patients almost doubled (2.11% vs 1.16%). A substantial change in prescriptions for diabetes has occurred, suggesting a positive influence of studies like the United Kingdom Prospective Diabetes Study (UKPDS).

**Key-words**: Epidemiology · Diabetes · Prevalence · Prescription attitudes · Pharmacology.

### Résumé

**Objectif** : Le but de cette étude a été d’estimer la prévalence du diabète au Luxembourg, de la comparer à celle rapportée en 1991 et d’évaluer les éventuels changements dans les conduites thérapeutiques.

**Méthodes** : La prévalence du diabète a été estimée grâce aux données sur les ventes de médicaments antidiabétiques. Les paramètres-clés, comme la quantité totale d’antidiabétiques vendus en un an et la dose quotidienne moyenne ou Dose Journalière Prescrite (DJP), ont été obtenus respectivement par l’Union des caisses de maladie (UCM) et par un questionnaire standardisé envoyé à tous les praticiens généralistes, internistes et endocrinologues du Grand-Duché.

**Résultats** : La DJP a été calculée à partir de 2402 questionnaires, chaque questionnaire correspondant à un patient diabétique différent. La procédure a également permis d’obtenir la proportion de patients exclusivement soignés par un régime alimentaire approprié. La quantité totale de metformine prescrite a augmenté de quatre fois par rapport aux données de 1991 et un pourcentage important de traitements combinés a été rapporté. La prévalence du diabète au Luxembourg a été estimée à 3.05 % de la population totale.

**Conclusions** : La prévalence du diabète a augmenté de 63 % par rapport à 1991, ce qui semble principalement résulter du nombre de patients diabétiques de type 2. En effet, les patients diabétiques sous traitement oral exclusif ont pratiquement doublé (de 1,16 % à 2,11 %). Un changement substantiel des prescriptions anti-diabétiques a pu être observé, ce qui suggère l’influence positive d’études telles que l’UKPDS (United Kingdom Prospective Diabetes Study).

**Mots-clés** : Épidémiologie · Diabète · Prévalence · Conduite de prescription · Pharmacologie.

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Prevalence of diabetes is rising in Western and developing countries [1, 2]. In the last 10 years, large prospective studies have been conducted on different therapeutic approaches and outcomes in diabetes [3, 4]. These studies, as well as the modification in diagnostic criteria proposed by the American Diabetes Association (ADA) in 1997 [5], may influence prevalence rates as well as prescription attitude. In 1991 [6, 7] the prevalence rate of diabetes in Luxembourg was estimated using drug sales data, an established method for estimating prevalence rates in chronic diseases [8, 9]. The same procedure was used to evaluate whether the prevalence rate had increased and/or prescription attitudes have changed in Luxembourg.

Methods

The methodology used to assess diabetes prevalence has been previously described [6, 10]. It was based on two key parameters considering a chronic disease, treated with specific drugs to be taken continuously.

Data required were the total amount of antidiabetic drugs sold in one year and the average daily intake or PDD.

Descriptive and non-parametric statistics (Wilcoxon, Mann-Whitney tests) were used to calculate differences between PDDs of general practitioners and specialists, especially for insulin.

Patients

All general practitioners (n = 373), internists and endocrinologists (n = 105) were invited to participate in the study. During 3 months, from September 15th to December 15th, 2002, they were asked to fill out a questionnaire for all diabetic patients seen during that time span in their outpatient clinics.

By using this questionnaire, demographic data, weight and height, duration of diabetes, prescribed medication and dosages as well as associated treatments, like antihypertensive and lipid lowering medications, were obtained. Individual PDD was calculated.

Statistical analysis

In this study, the prevalence and its subsequent 95% confidence interval (CI), computed from the estimated variance using the classical inference method [11], were determined following the method initially described by Fontbonne and Papoz [10] and generalised by Sartor and Walckiers [12]. Prevalence of drug-treated diabetes can be inferred from the knowledge of the amount of drugs sold, the average intake of these drugs i.e. the PDD, the proportion of patients treated with a combination of different classes of drugs, and the size of the total population. Four classes of drugs were included, namely insulin, metformine, sulfonylureas and glitazones.

Total amounts of drugs (T) prescribed for diabetes were obtained from the amount reimbursed by the “Union des Caisses de Maladie”, the association of all statutory health insurances in Luxembourg. The significance of this parameter is very high, because almost 100% of patients are covered by the statutory insurance in Luxembourg.

Results

Forty physicians (16 internists and endocrinologists, and 24 general practitioners) returned 2, 402 questionnaires with information on individual diabetic patients. Using these data, the average PDDs for the different antidiabetic medications were calculated and are summarized in table I. The average PDDs were almost identical to those found in 1991 [6, 7]. A combination with oral antidiabetic medication was prescribed to 26.5% of the insulin-treated patients. The combination treatments with insulin have more than doubled in eleven years (26.5% vs 11%). Finally, 6.83% of all diabetic patients were estimated to be treated only by diet.

The total amount of different antidiabetic drugs sold in 2002 is shown in table II. The most striking difference between the results of 1991 and 2002 is a four-fold increase in the number of metformine prescriptions [6, 7].

The prevalence of drug-treated diabetic patients was calculated from the data in tables I and II, adjusted to a total population of 448, 300 inhabitants on January 1st, 2003 (STATEC, 01012003).

Table I
Comparison between the PDD in 1991 and 2002.

<table>
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<tr>
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<tbody>
<tr>
<td>Insulin (IU/day)</td>
<td>47.0 15</td>
<td>49.9 26.7</td>
</tr>
<tr>
<td>(IU/kg/day)</td>
<td>-</td>
<td>0.65 0.32</td>
</tr>
<tr>
<td>Metformine (tablets/day)</td>
<td>1.7 0.7</td>
<td>1.93 0.69</td>
</tr>
<tr>
<td>Sulfonylureas (tablets/day)</td>
<td>1.9 0.9</td>
<td>1.99 0.93</td>
</tr>
<tr>
<td>Glitazones (tablets/day)</td>
<td>-</td>
<td>1.07 0.27</td>
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</tbody>
</table>

Table II
Total amount of different antidiabetic drugs.

<table>
<thead>
<tr>
<th></th>
<th>1991</th>
<th>2002</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin (IU)</td>
<td>34,524,400</td>
<td>59,697,500</td>
</tr>
<tr>
<td>Metformine (tablets)</td>
<td>965,250</td>
<td>4,018,040</td>
</tr>
<tr>
<td>Sulfonylureas (tablets)</td>
<td>2,812,630</td>
<td>5,992,610</td>
</tr>
<tr>
<td>Glitazones (tablets)</td>
<td>-</td>
<td>512,596</td>
</tr>
</tbody>
</table>
A combination of drugs belonging to two of the four different classes (sulfonylureas, metformin, glitazones, and insulin) was used by 30.8% of these patients, whereas a combination of drugs belonging to three of the four different classes was used by 7.1% of these patients, and a combination of drugs belonging to the four different classes was used by 0.2%.

Prevalence of drug-treated diabetes mellitus, Pdt, is estimated at 2.84% of the population in Luxembourg, i.e. 12,738 inhabitants. Because 6.83% of the diabetic patients are treated with diet only, which corresponds to 0.21% of the population, i.e. 934 patients, the overall prevalence of diabetes in Luxembourg, P (Pdt/0.93), is 3.05% of the population, i.e. 13,671 inhabitants (95 percent CI 1.91-3.77%, i.e. CI 8,600 - 17,000 inhabitants).

Discussion

Prevalence of diabetes in Luxembourg has increased by 63% over the last 11 years (from 1.87 to 3.05%). This increase is mainly due to orally-treated type-2 diabetes that rose by 82%. Nevertheless, the number of patients treated with insulin also increased by 38%.

The increase of diabetic patients could not result from a higher proportion of elderly compared to younger people from 1991 to 2002, because the percentage of patients older than 60 years is similar in the two surveys (19.1% vs 18.7%, data from STATEC).

With the methodology used, several biases must be considered. Other studies have described differences between prescribed and purchased medication. This may result in an underestimation of the number of patients, especially for oral antidiabetic drugs in type 2 diabetes. In insulin-treated patients, some units are lost with every vial or cartridge, and some vials are broken, leading to a possible overestimation of the number of insulin treated patients. Nevertheless, the observed increase in prevalence rates is very similar to those found in other European countries [13]. Selection bias due to the low response of the physicians must be considered also. However, the PDDs of the different drugs fit well with the internationally known PDDs and are very close to those of 1991 in Luxembourg. Furthermore, comparison between the PDDs of general practitioners and specialists, especially for insulin, did not show a significant difference (Mann-Whitney Wilcoxon, P > 0.6).

In 1997, a national screening campaign for diabetes was organized in Luxembourg, which may have led to higher awareness of diabetes and associated risks and thus to earlier diagnosis [14]. In this screening campaign, if we consider the new ADA diagnostic criteria [5], we found a difference of 7% more diabetic patients, which could not explain the increase in diabetic patients between 1991 and 2002.

A high combination rate of several antidiabetic drugs suggests an earlier and more intensive treatment of diabetic patients as recommended by UKPDS. The number of insulin-treated patients has increased, while incidence of type 1 diabetes did not rise in Luxembourg [15].

Finally, the total amount of metformin prescribed is more than four times higher than eleven years before. In the UKPDS, the benefit of metformin for obese type-2 diabetic persons has clearly been shown [16]. In conclusion, by using the same methodology as in 1991, we have demonstrated here an important increase in prevalence of diabetes in Luxembourg in 2002, mainly in the type 2 diabetes group. Over the last 11 years, a substantial change in prescription for diabetes has been observed, suggesting the helpful impact of studies like UKPDS. It remains to be evaluated whether this earlier diagnosis and intensification of therapy will lead to a reduction in complications.

Acknowledgments – This study was realized thanks to the help of the CRP-Santé, Luxembourg. The authors like to thank all the physicians having sent back the questionnaires allowing to calculate the PDD (S Adam-Becker, E Bauler, J Berg, M Besch, A Birget, C De Beaufort, F Engels, P Fernandes Lourenço, G Fischer, MA Goedert-Bové, N Haas, A Hanck-Conter, J Hensen, J Hoffelt, M Jacqué, P Jates, M Keipes, M Keti-Jungen, J Klees-Schumacher, J Kraus, F Leboutte-Adam, G Loos, M Mangen, J Mangeot, R Meyers, G Michel, S Mladinovic, F Modert, F Muller, R Nosbaum, S Rausch, A Ripp, I Rollinger-Holzinger, M Scholtes, I Spitters, C Steichen, R Stein, P Tabouring, C Weber, R Wirion).

References


Table III
Prevalence of diabetes in Luxembourg.

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<tbody>
<tr>
<td>(%)</td>
<td>(%)</td>
<td>(Patients)</td>
<td></td>
</tr>
<tr>
<td>Pd</td>
<td>0.18</td>
<td>0.21</td>
<td>934</td>
</tr>
<tr>
<td>Pdt</td>
<td>1.69</td>
<td>2.84</td>
<td>12,738</td>
</tr>
<tr>
<td>Pi</td>
<td>0.53</td>
<td>0.73</td>
<td>3,278</td>
</tr>
<tr>
<td>Po</td>
<td>1.16</td>
<td>2.11</td>
<td>9,460</td>
</tr>
<tr>
<td>P</td>
<td>1.87</td>
<td>3.05</td>
<td>13,672</td>
</tr>
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Pd = diet-treated; Pdt = drug-treated; Pi = insulin-treated; Po = oral drug-treated; P = total prevalence.
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