LIRAGLUTIDE VS EXENATIDE IN COMBINATION WITH METFORMIN AND/OR SULFONYLUREA THERAPY IN TYPE 2 DIABETES MELLITUS THERAPY IN BULGARIA.

A MODELLING STUDY.

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Background

- Type 2 diabetes is a global health problem of alarming proportions.
- Diabetes is associated with microvascular and macrovascular disease.
- The cost of diabetes therapy and its complications is permanently increasing.

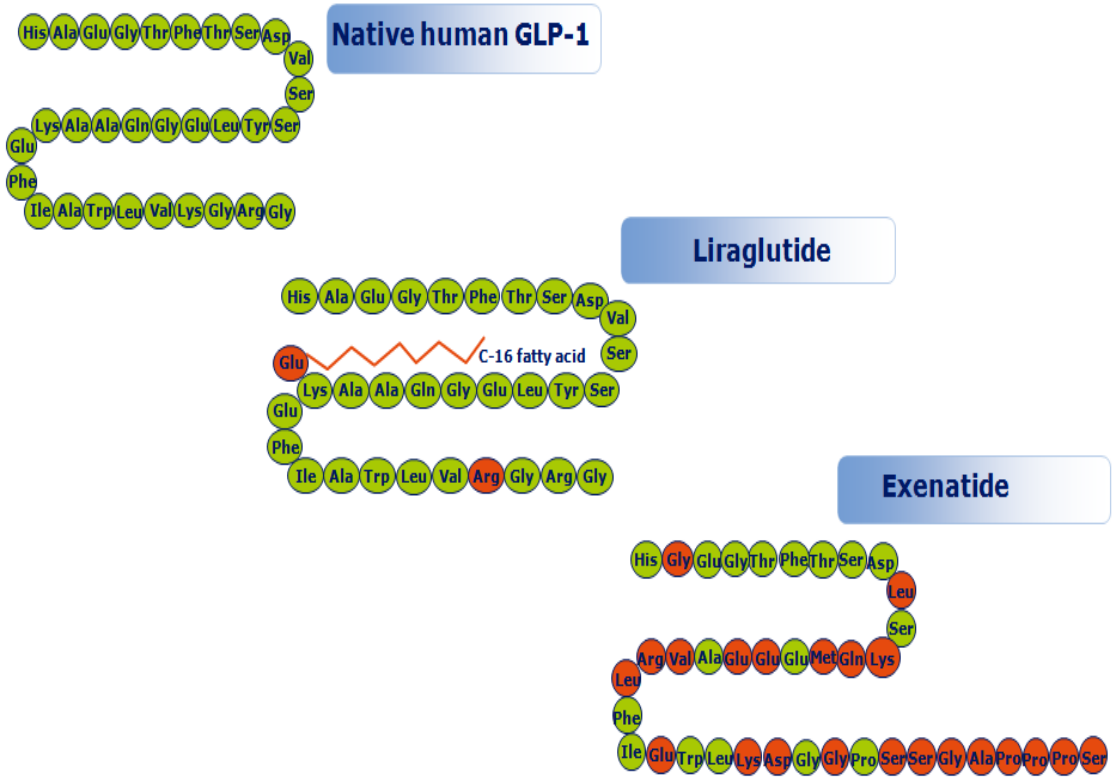
Background

- The “incretin effect” – insulinotropic activity of the gut hormones GIP and GLP-1 – is a critically important contributor to glucose metabolism
  - But is largely lost in type 2 diabetes
- Strategies that would prolong the half-life and/or introduce pharmacological (supraphysiological) levels of GLP-1 are logical targets in the treatment of type 2 diabetes

GLP-1 Has Multiple Desirable Effects

- Efficacious glucose lowering
  - Increased insulin secretion (glucose dependent)
  - Increased insulin biosynthesis
  - Increased ß-cell glucose sensitivity
  - Decreased glucagon secretion (glucose dependent)
  - Increased ß-cell mass (shown in animal models)

Structure of native GLP-1, liraglutide and exenatide



GOAL OF THE STUDY

- To conduct economic evaluation of liraglutide combined with metformin (MET) and/or sulfonylurea therapy (SU) in comparison to exenatide combined with MET and/or SU therapy in type 2 diabetes not adequately controlled.

- The study was conducted for the Bulgarian health care system.

- The analysis was performed from the health care services payer’s perspective including only direct medical costs and benefits.

MATERIALS AND METHODS

- The effects of the diabetes therapy with liraglutide 1,8 mg in combination with metformin and/or sulfonylurea were evaluated, and exenatide 10 µg twice daily in combination with metformin and/or sulfonylurea was chosen as a comparator.

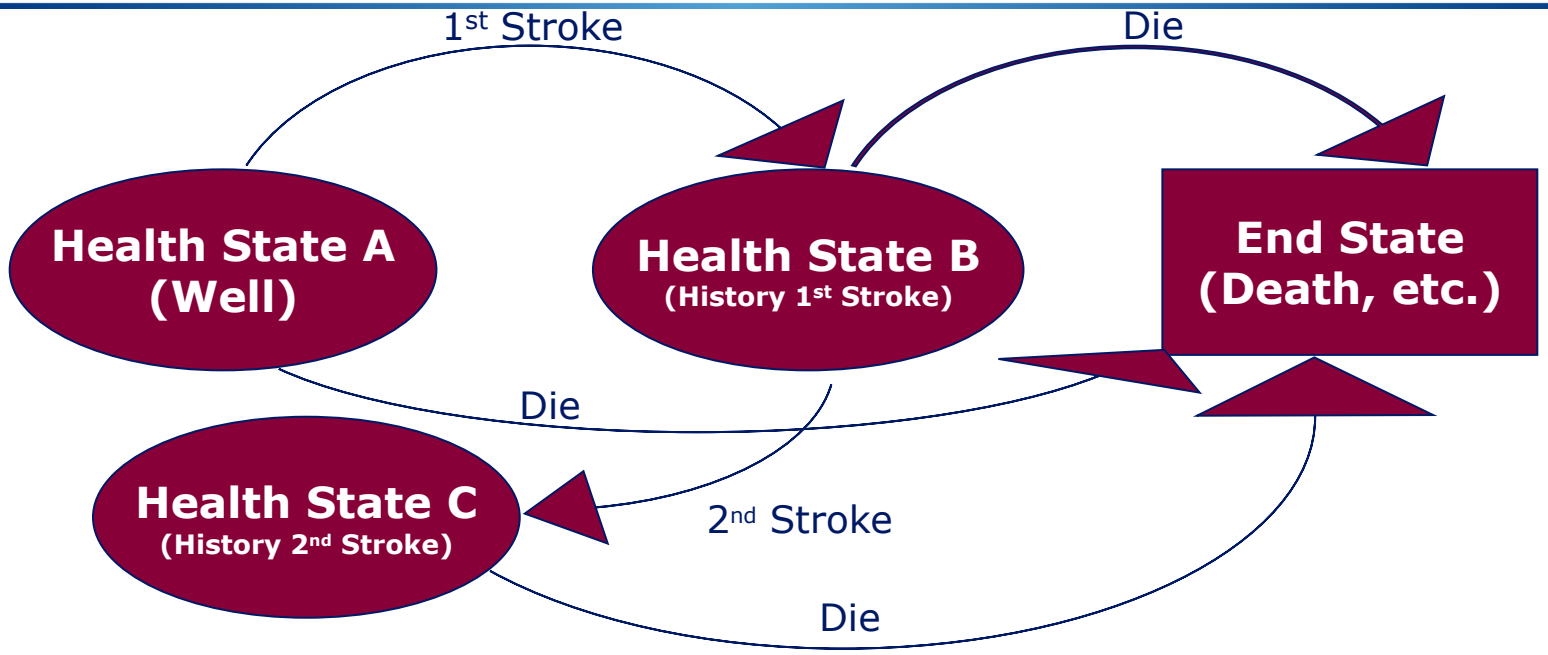
- Cost – effectiveness economic analysis was applied to calculate a cost per quality adjusted life year (cost/QALY) and cost per life year gained (cost/LYG), after modelling the cost of therapy and results from the clinical trial.

- CORE diabetes model have been used to model the clinical trials result for a life time period.

IMS Core Diabetes Model
Inter-dependent Markov-like sub-models

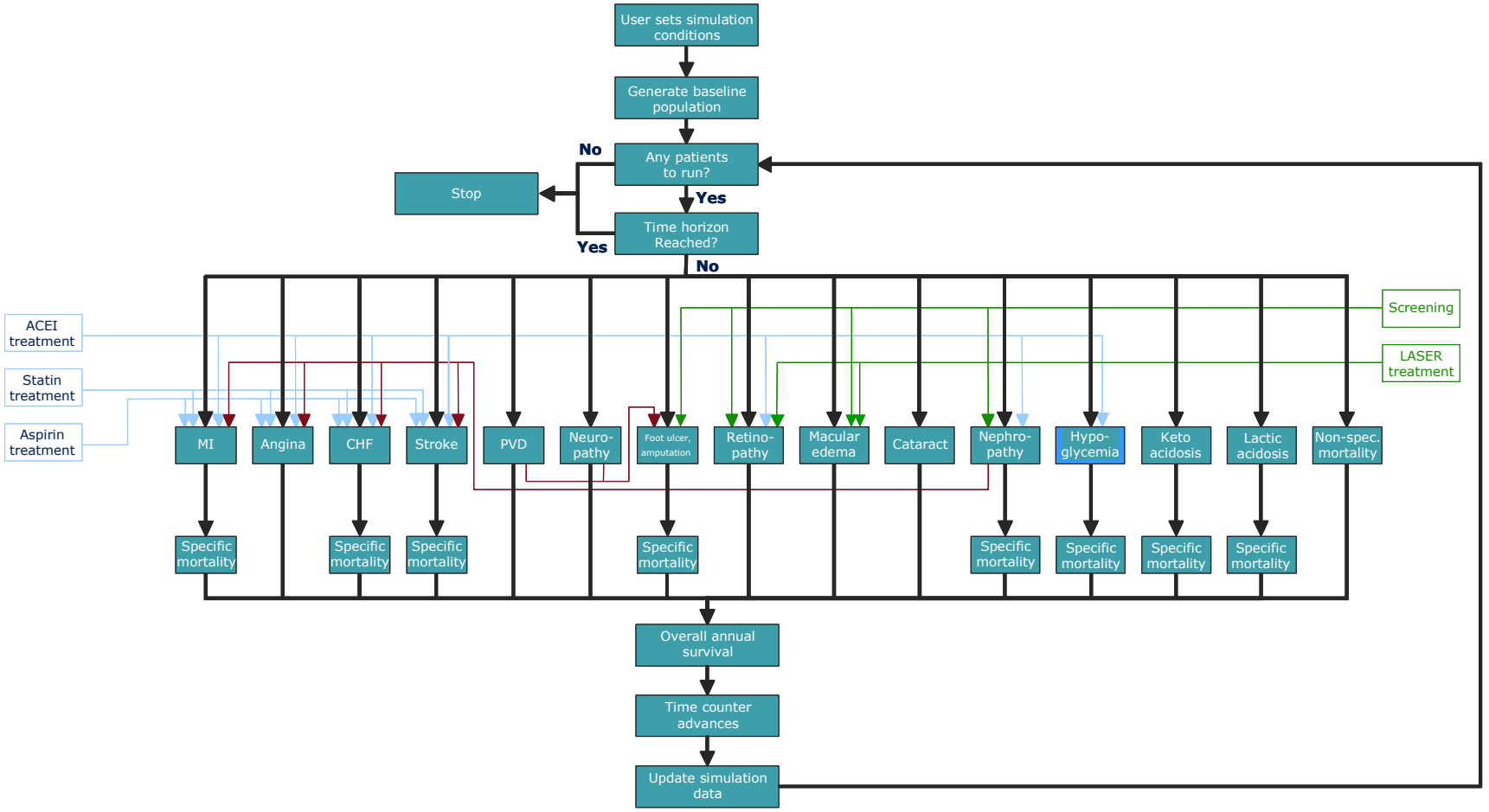
- Nephropathy
  - Microalbuminuria
  - Gross proteinuria
  - End-stage renal disease
- Retinopathy
  - BDR
  - PDR
  - Severe vision loss
- Macular oedema
- Cataract
- Cardiovascular disease
  - Myocardial infarction
  - Congestive heart failure
  - Stroke
  - Angina
  - Peripheral vascular disease
- Neuropathy
- Foot ulcer and amputation
- Hypoglycaemic events
- Ketoacidosis
- Lactic acidosis
- Peripheral oedema

Diabetes Modeling
Markov modeling



- Patients have different probabilities of moving from health state A, to B, to C or to the end/absorbing state (typically death)
- Patients cannot move back to A, B, or C from the end state
- The IMS Core Diabetes Model runs **16** of these models and many are inter-linked

IMS Core Diabetes Model
Flow diagram



LEAD-6 Endpoints

- Primary:
  - HbA_{1c} change after 26 weeks
- Key secondary:
  - fasting plasma glucose
  - seven-point plasma glucose profile
  - body weight change
  - beta-cell function
  - blood pressure
  - hypoglycaemia
  - adverse events

Buse *et al. Lancet* 2009;374:39–47 (LEAD-6)

Efficacy summary

Compared with exenatide 10 µg BID, liraglutide 1.8 mg OD was associated with:

- Significantly greater reductions in HbA_{1c} and FPG levels
- Significantly more patients achieving HbA_{1c} levels of <7.0% and ≤6.5%
- Comparable and clinically meaningful reduction in body weight

Buse *et al. Lancet* 2009;374:39–47 (LEAD-6)

Safety summary

Compared with exenatide 10 µg BID, liraglutide 1.8 mg OD was associated with:

- Significantly lower risk of minor hypoglycaemia despite lower HbA_{1c} at end of trial
- Fewer major hypoglycaemic episodes (none with liraglutide vs. two with exenatide)
- Less persistent nausea

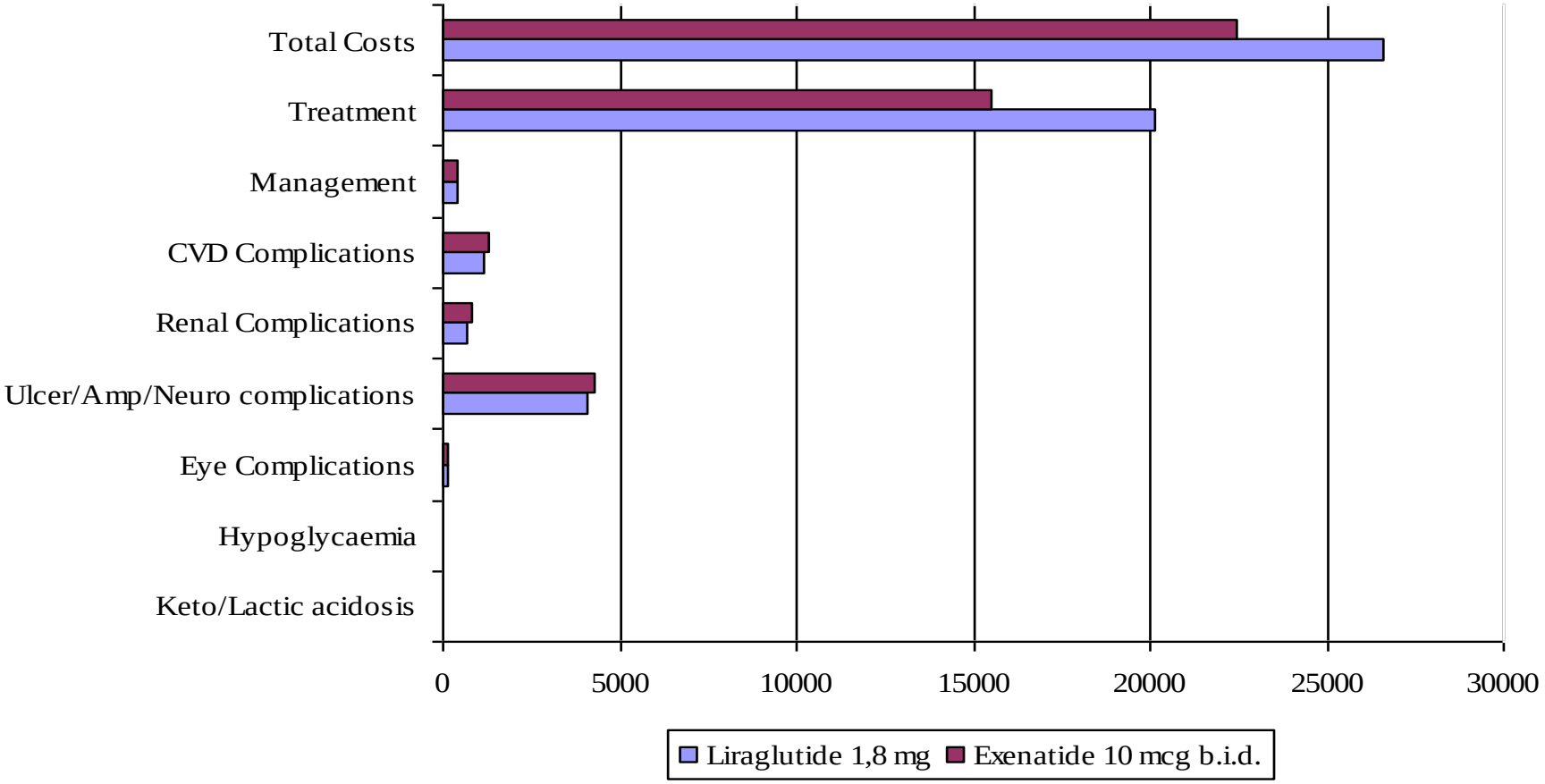
Buse *et al. Lancet* 2009;374:39–47 (LEAD-6)

COSTS & DISCOUNTING

- The sources of costs were official Bulgarian publication for medicines prices,[7] hospital charges,[8] and expert opinions. Costs are expressed in local currency BGN (BGN 1 = EUR0.51). Costs input for the model for treatment and complications were separately calculated.
- The discount rates were varied between 0% and 5% both future costs and outcomes.

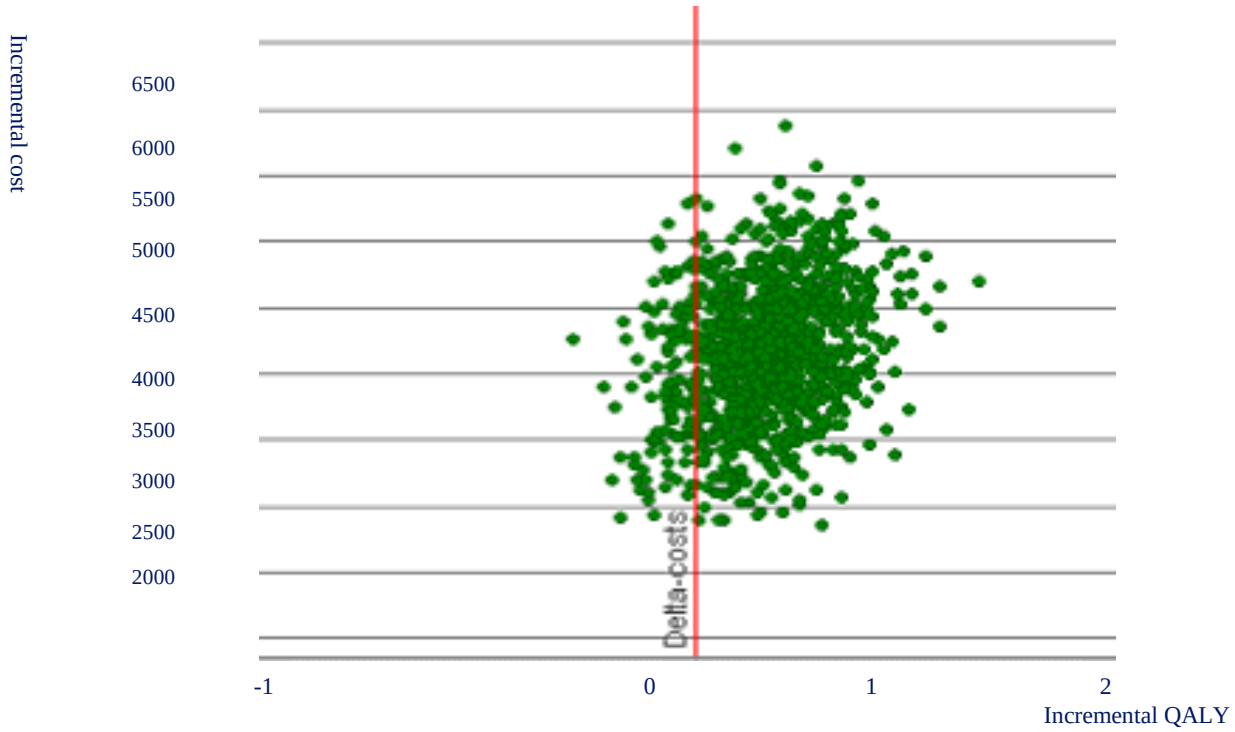
RESULTS: COST STRUCTURE

- Figure 1.



In the base case analysis the total cost of therapy with liraglutide is higher than that with exenatide, but the complications cost is lower that could be due to a better HbA1C control

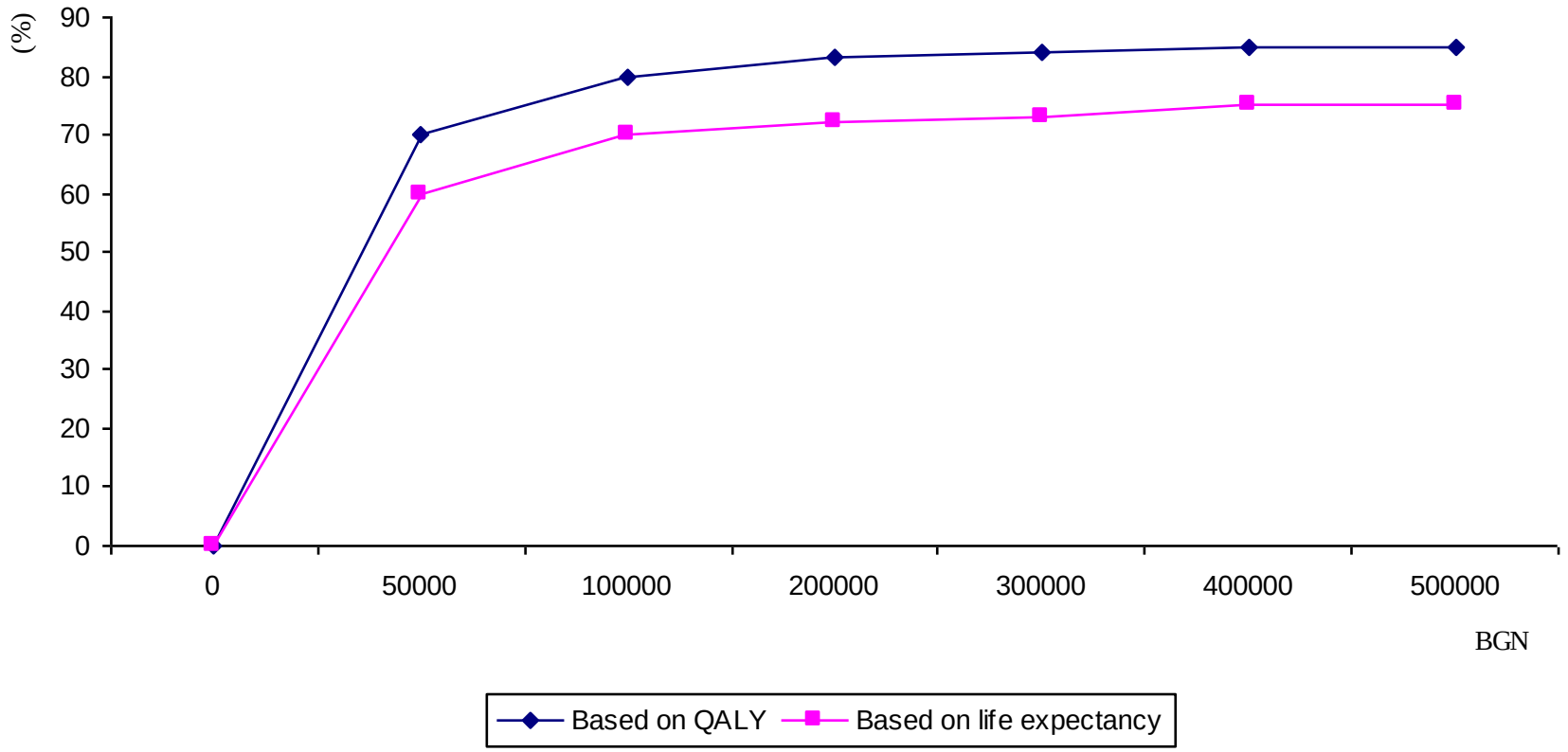
RESULTS: COST-EFFECTVENESS SCATTERPLOT



An incremental cost-effectiveness scatter plot (costs per additional QALY) for liraglutide 1,8 mg versus exenatide based therapy is shown in Figure 2.

The majority of the points on this scatterplot lie in the upper right hand quadrant, indicating increased costs and increased effectiveness.

RESULTS: COST-EFFECTIVENESS ACCEPTABILITY CURVE



The cost-effectiveness acceptability curves constructed from the scatterplot data (Figure 3) shows that liraglutide 1,8 mg can be considered a cost-effective treatment option compared to exenatide.

CONCLUSION

- QALYs increased with liraglutide 1,8 mg by 0,151 (SD 0,124) years. Total costs increased by BGN 4 151 resulting in an incremental cost per QALY gained of BGN 27 404.
- Life expectancy increased with liraglutide 1,8 mg by 0,129 (SD 0,175) years. Total costs increased by BGN 4 151 resulting in an incremental cost per LYG of BGN 32 082.
- The univariate sensitivity analyses revealed ICER for QALY from BGN 21 697 to BGN 82 538, for discount rates set to 5% and when no HbA1c reduction benefit was set, respectively.
- Liraglutide 1,8 mg has been shown to be cost effective when compared to exenatide for the treatment of type 2 diabetes if hypothetical willingness to pay threshold is around BGN 30 000 per QALY.

THANK YOU!

QUESTIONS?