Canadian Agency for Drugs and Technologies in Health

Agence canadienne des médicaments et des technologies de la santé

# Insulin preparations: Which types for which patients?

## Examining the Evidence

**Presenter, Title, Affiliation**

*Month 2009*

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|---|---|

# Learning objectives

## Upon completion of this workshop the participant will:

- Understand the evidence base supporting the use of human insulin and insulin analogues in the treatment of diabetes
- Identify the appropriate use of insulin preparations in:
  - The general population with diabetes
  - Special cases where insulin analogues should be considered.

# Outline

## Context

- Diabetes in Canada
- Physiology and pathophysiology of diabetes
- Options for insulin therapy

## The evidence base for optimal therapy

- Scientific process
- Conclusions and recommendations

# Where did the evidence come from?

## Canadian Agency for Drugs and Technologies in Health (CADTH)

CADTH is an independent, not-for-profit agency funded by Canadian federal, provincial, and territorial governments to provide credible, impartial advice and evidence-based information about the effectiveness of drugs and other health technologies to Canadian health care decision makers.

# Diabetes in Canada
## (Types 1 and 2 combined)

### Prevalence

- In 2005-2006, approximately 1.9 million were diagnosed with diabetes
- One in 17 people had been diagnosed with diabetes
- The prevalence rate for both males and females was 5.9%

### Incidence

- In 2005-2006, 199,471 individuals were newly diagnosed with diabetes - 6.4 per 1,000 overall

PHAC. *Report from the National Diabetes Surveillance System: Diabetes in Canada*; 2008

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# Diabetes in Canada

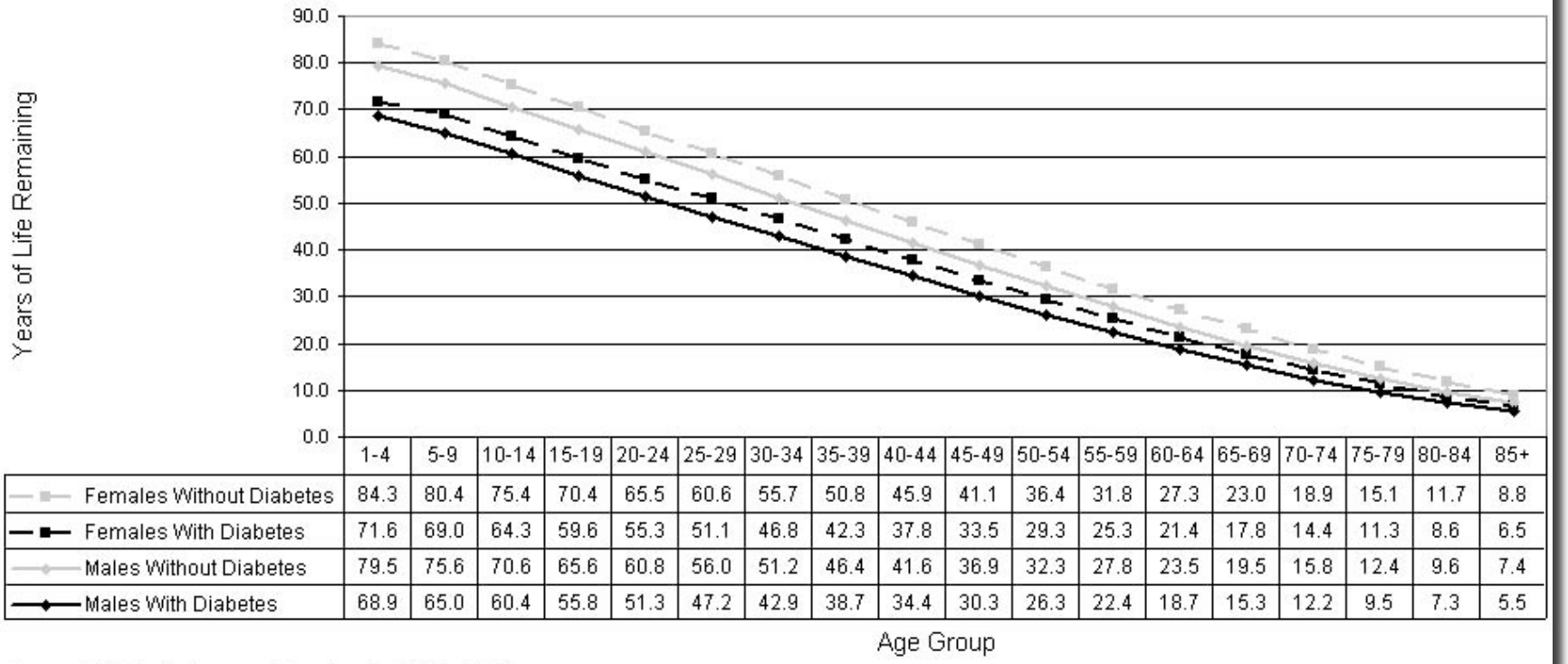
## Disease burden

- Diabetes shortens life expectancy for all ages.
  - For example, 25 to 39-year old people with diabetes had an approximate nine year reduction in life expectancy in 2005-2006.

PHAC. *Report from the National Diabetes Surveillance System: Diabetes in Canada;* 2008

# Years of life remaining

**Figure 7. Years of Life Remaining for People With Diagnosed Diabetes Compared to Those Without Diagnosed Diabetes, by Age Group, Canada, 2004-2005**




| | 1-4 | 5-9 | 10-14 | 15-19 | 20-24 | 25-29 | 30-34 | 35-39 | 40-44 | 45-49 | 50-54 | 55-59 | 60-64 | 65-69 | 70-74 | 75-79 | 80-84 | 85+ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Females Without Diabetes | 84.3 | 80.4 | 75.4 | 70.4 | 65.5 | 60.6 | 55.7 | 50.8 | 45.9 | 41.1 | 36.4 | 31.8 | 27.3 | 23.0 | 18.9 | 15.1 | 11.7 | 8.8 |
| Females With Diabetes | 71.6 | 69.0 | 64.3 | 59.6 | 55.3 | 51.1 | 46.8 | 42.3 | 37.8 | 33.5 | 29.3 | 25.3 | 21.4 | 17.8 | 14.4 | 11.3 | 8.6 | 6.5 |
| Males Without Diabetes | 79.5 | 75.6 | 70.6 | 65.6 | 60.8 | 56.0 | 51.2 | 46.4 | 41.6 | 36.9 | 32.3 | 27.8 | 23.5 | 19.5 | 15.8 | 12.4 | 9.6 | 7.4 |
| Males With Diabetes | 68.9 | 65.0 | 60.4 | 55.8 | 51.3 | 47.2 | 42.9 | 38.7 | 34.4 | 30.3 | 26.3 | 22.4 | 18.7 | 15.3 | 12.2 | 9.5 | 7.3 | 5.5 |

Source: Public Health Agency of Canada, using NDSS data files contributed by all provinces and territories, Life Table from Statistics Canada, August 2007

Source: PHAC, *Diabetes in Canada: highlights from the National Diabetes Surveillance System 2004-2005;* 2008. Reproduced with the permission of the Minister of Public Works and Government Services Canada; 2008.

# Diabetes in Canada: Disease burden

**Among adults aged 20 years and older, compared to adults without diabetes, adults with diabetes were hospitalized:**

- 23 times more often for lower limb amputations;
- seven times more often for chronic kidney disease;
- three times more often for hypertension or heart failure;
- three times more often for heart attack; and
- three times more often for stroke.

PHAC. *Report from the National Diabetes Surveillance System: Diabetes in Canada;* 2008

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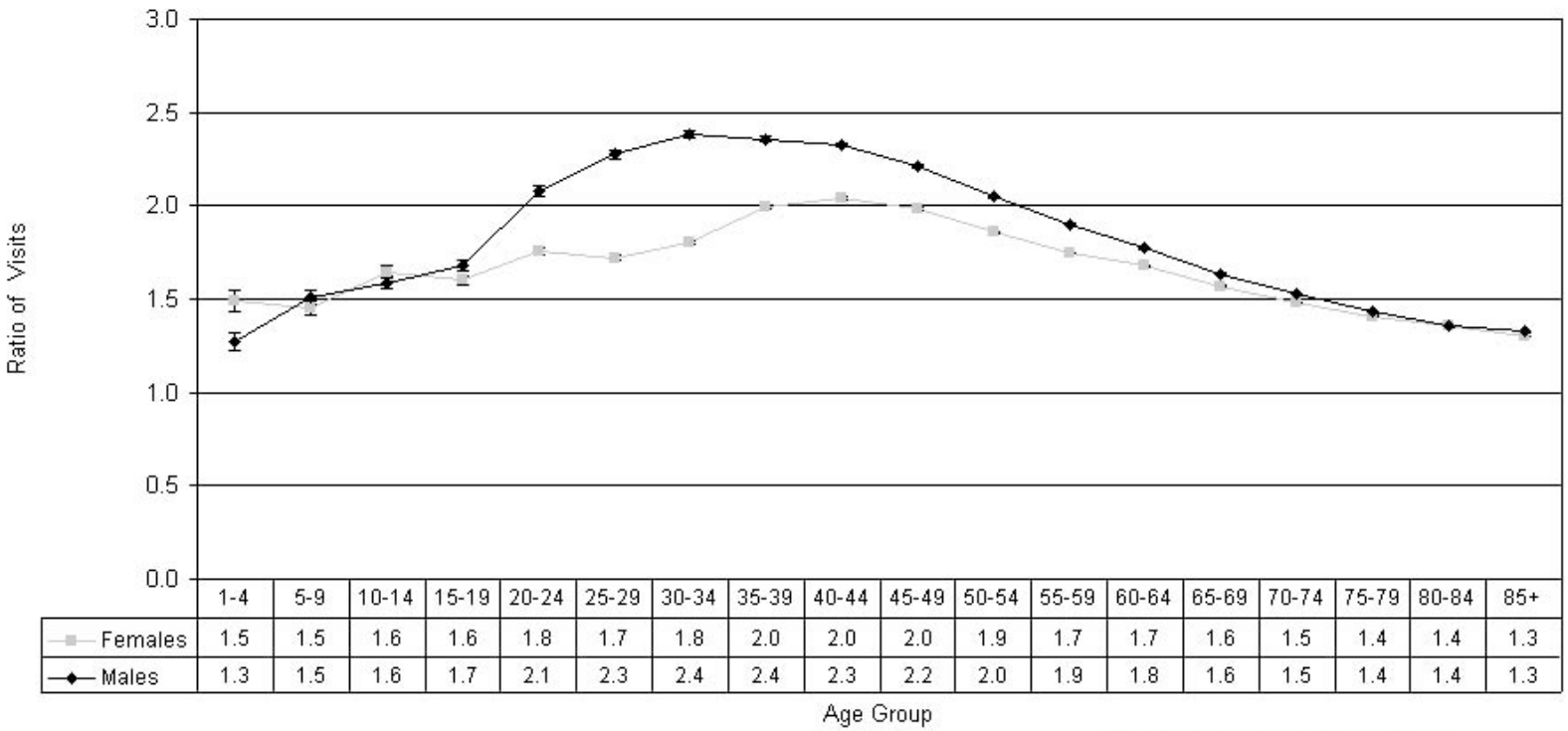
# Ratio of visits

**Figure 8. Ratio of Number of Visits to Family Physicians by People Aged 1 Year and Older With Diagnosed Diabetes Compared to Those Without Diagnosed Diabetes, Canada*, 2004-2005**




| | 1-4 | 5-9 | 10-14 | 15-19 | 20-24 | 25-29 | 30-34 | 35-39 | 40-44 | 45-49 | 50-54 | 55-59 | 60-64 | 65-69 | 70-74 | 75-79 | 80-84 | 85+ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Females | 1.5 | 1.5 | 1.6 | 1.6 | 1.8 | 1.7 | 1.8 | 2.0 | 2.0 | 2.0 | 1.9 | 1.7 | 1.7 | 1.6 | 1.5 | 1.4 | 1.4 | 1.3 |
| Males | 1.3 | 1.5 | 1.6 | 1.7 | 2.1 | 2.3 | 2.4 | 2.4 | 2.3 | 2.2 | 2.0 | 1.9 | 1.8 | 1.6 | 1.5 | 1.4 | 1.4 | 1.3 |

Age Group

Source: Public Health Agency of Canada, using NDSS data files contributed by all provinces and territories, as of October 31, 2007

‡The 95% Confidence Interval shows an estimated range of values which is likely to include the true rate ratio 19 times out of 20.

*Québec and Nunavut data not included In analysis

Source: PHAC. *Diabetes in Canada: highlights from the National Diabetes Surveillance System 2004-2005*; 2008. Reproduced with the permission of the Minister of Public Works and Government Services Canada; 2008.

# Physiology of insulin

## Basal insulin secretion

- Background low-level continuous secretion
- Prevents keto-acidosis

## Variable biphasic meal-stimulated secretion

- first phase rapid
- second phase lasts longer

## Insulin-receptor binding stimulates glucose uptake by target tissues


Eaton, et al. *J Clin Endocrinol Metab* 1990;71:1508-1518.
Polonsky, et al. *J Clin Invest* 1988;81:442-448.
Kruszynska, et al. *Diabetologia* 1987;30:16-21.
Polonsky, et al. *J Clin Invest* 1986;77:98-105.
Waldhaus, et al. *Diabetologia* 1979;17:221-227.

# Insulin secretion in a person without diabetes

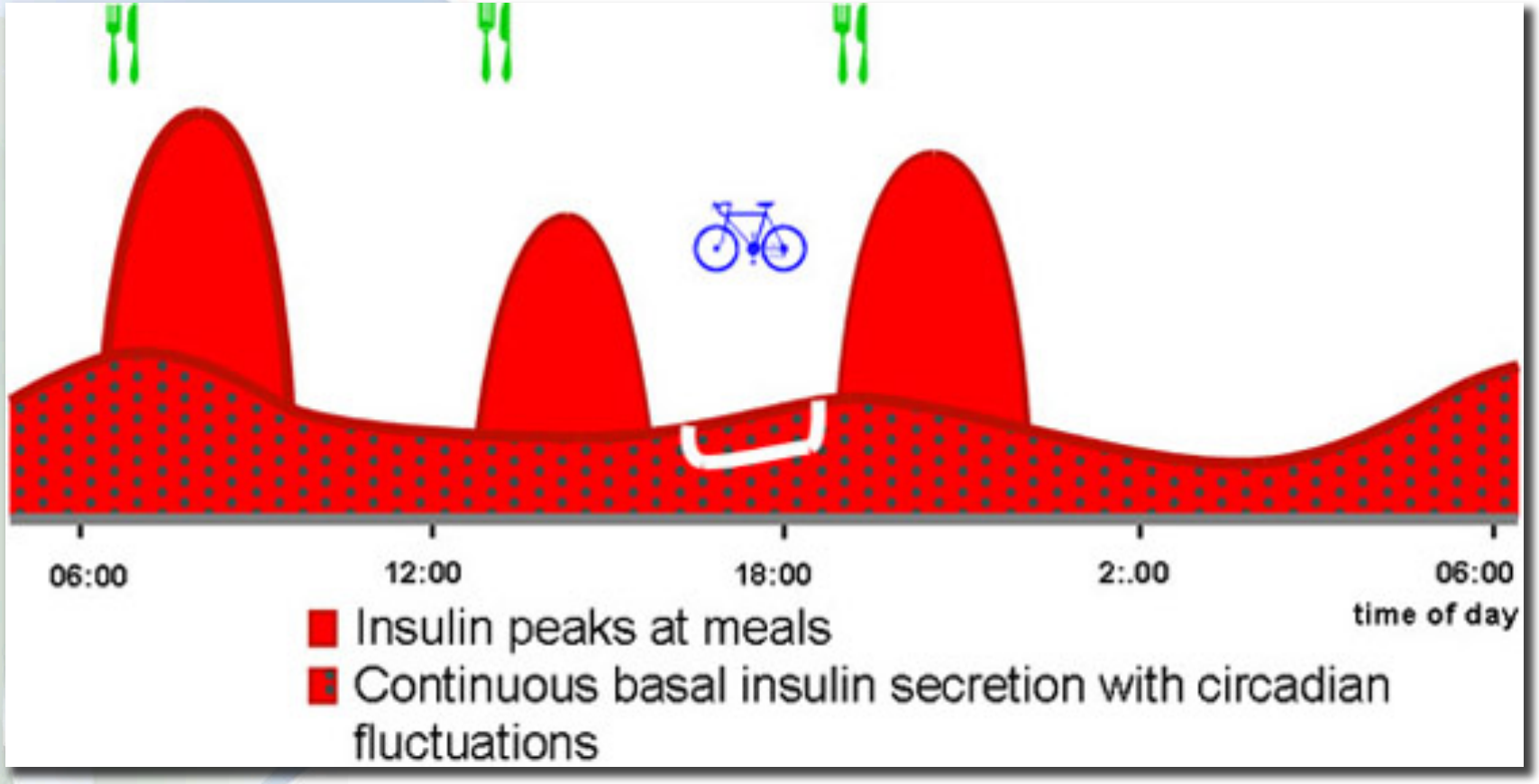



Image used with permission from*: Why use pump therapy?* Warwick (UK): Advanced Therapeutics (UK) Ltd; 2009.

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# Diabetes types: Insulin requirements

## Type 1: autoimmune. Complete insulin deficiency

- Always requires insulin treatment

## Type 2: insulin resistance and progressive loss of insulin secretory ability

- Initial pharmacologic treatment with oral agents for most patients
- Patients may require insulin at a later date

## Pregnancy

- Gestational Diabetes: similar to temporary type 2 diabetes; insulin therapy initiated if glycemic targets not achieved after 2 weeks from nutrition therapy alone
- Women with type 1 and type 2 diabetes have additional management issues when pregnant

WHO. *Definition, diagnosis and classification of diabetes mellitus and its complications;* 1999.
CDA. *Can J Diabetes* 2008;32(suppl 1):i-S201.

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# Human insulin

- **Genetically-engineered production from bacteria**
- **Different types have different pharmacokinetics due to solubility of diluent which affects absorption**
- **Brand names: “Humulin®, Novolin ®”**
- **“Prandial” or “Bolus” or Short-acting**
  - “R”, “Regular”, “Toronto”
  - Onset 30 minutes, peak 2-3 hours, duration 6.5 hours

CDA. *Can J Diabetes* 2008;32(suppl 1):i-S201.
CADTH. *Optimal Therapy Report - COMPUS* 2008;2(7).

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# Human insulin (cont'd)

- **"Basal" or Intermediate-acting**
  - "N", "NPH"
  - Onset 1-3 hours, peak 5-8 hours, duration up to 18 hours
- **Mixture of these two types:**
  - 30/70 (30%R and 70%N), 50/50

CDA. *Can J Diabetes* 2008;32(suppl 1):i-S201.
CADTH. *Optimal Therapy Report - COMPUS* 2008;2(7).

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# Insulin analogues

## Modified structures to change pharmacokinetics

- Switching sequences of amino acids (lispro, aspart)
- Addition of amino acids (glargine) or fatty acid moiety (detemir)

## Rapid-acting insulin analogues: ("Bolus" insulins)

- Lispro (Humalog®) and aspart (NovoRapid®)
- Onset 10-15 min, peak 1-2 hours, duration 3-5 hours

CDA. *Can J Diabetes* 2008;32(suppl 1):i-S201.
CADTH. *Optimal Therapy Report - COMPUS* 2008;2(7).

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# Insulin analogues (cont'd)

## Long-acting insulin analogues: ("Basal" insulins)

- Glargine (Lantus®) and detemir (Levemir®)
- Onset 90 minutes, no peak, duration glargine 24 hours, detemir 16-24 hours

## "Biphasic" mixtures containing short-acting analogues and intermediate acting insulins

- Humalog Mix 25® or Mix 50® and NovoMix 30®

CDA. *Can J Diabetes* 2008;32(suppl 1):i-S201.
CADTH. *Optimal Therapy Report - COMPUS* 2008;2(7).

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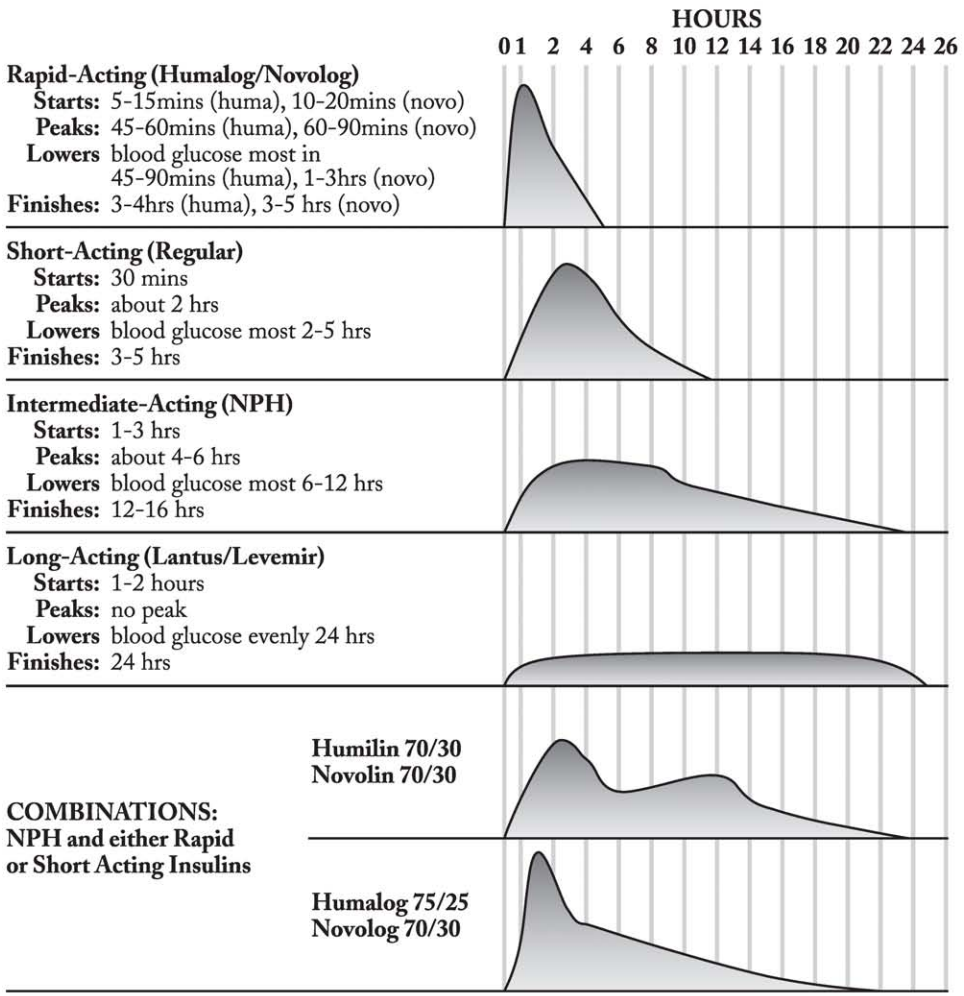
# Pharmacokinetics of insulins



# Approximate unit costs of basal insulins*

## Vial, 1x 10 mL, 100 units/mL:

- Lantus®=$56.80
- Humulin® N=$18.90
- Novolin® NPH=$19.40

## Cartridge, 5x3 mL, 100 units/mL

- Lantus®=$85.20
- Levemir®=$109.80
- Humulin® N=$36.90
- Novolin® NPH=$37.95

*Costs are current as of December, 2008 and may vary between regions and over time.

# Approximate unit costs of bolus insulins* (cont'd)

## Vial, 1x 10 mL, 100 units/mL:

- NovoRapid®=$26.90
- Humalog ®=$25.80
- Humulin ® R=$18.90
- Novolin ® ge Toronto=$19.40

## Cartridge, 5x3 mL, 100 units/mL:

- NovoRapid ®=$53.70
- Humalog ®=$51.60
- Humulin ®R=$37.95
- Novolin ® Toronto=$38.10

*Costs are current as of December, 2008 and may vary between regions and over time.

# Studying the evidence:
## COMPUS Expert Review Committee

| | | |
|---|---|---|
| BC | Dr. M. Dahl | Endocrinologist |
| BC | Dr. E. Ur | Endocrinologist |
| BC | Dr. A. Virani | Pharmacist |
| AB | Dr. S. Klarenbach | Nephrologist/Epidemiologist |
| AB | Dr. A. Colbourne | General Internist |
| SK | Dr. M. Caughlin | Family Physician |
| MB | Dr. H. Dean | Pediatric Endocrinologist |
| ON | Dr. L. Dolovich | Pharmacist/Health Economist |
| ON | Dr. M. Evans | Family Physician/Practice Support |
| ON | Panos Petrides | Public Member |
| NS | Dr. M. Allen | Family Physician/Health Education |
| NS | Cathy MacNutt | Public Member |

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# Scientific process:
## Selection of clinical outcomes

- **Surrogate outcomes:**
  - A1C
  - Fasting plasma glucose
  - Two hour post-prandial glucose
- **Short-term complications:**
  - Severe hypoglycemia
  - Nocturnal hypoglycemia
  - Overall hypoglycemia

CADTH. *Optimal Therapy Report - COMPUS* 2008;2(1).
CADTH. *Optimal Therapy Report - COMPUS* 2008;2(2).

# Scientific process:
## Selection of clinical outcomes (cont'd)

- Long-term complications/mortality
- Other surrogates: weight gain, BMI, blood pressure, LDL, % of patients A1C<7.0%
- Health-related quality of life and patient satisfaction
- Health care resource use

CADTH. *Optimal Therapy Report - COMPUS* 2008;2(1).
CADTH. *Optimal Therapy Report - COMPUS* 2008;2(2).

# Scientific process: Systematic review

## Systematic Review

- Search of world literature for studies of relevance
- Previous systematic reviews and meta-analyses
- Primary studies: Randomized-controlled (RCT), non-randomized controlled, and observational studies all considered
- Two independent researchers then rate studies for inclusion (e.g., excluded if target outcomes not obtainable)
- Quality of evidence depends on study design, conduct and analysis
- For this project:
  - 123 articles were included in the systematic review

CADTH. *Optimal Therapy Report - COMPUS* 2008;2(1).
CADTH. *Optimal Therapy Report - COMPUS* 2008;2(2).

# Considering the evidence

**Studies first analyzed for evidence of clinical benefit and harm**

- Safety, effectiveness and clinically-important differences (if any)

**Results then analyzed on the basis of cost for clinical benefit**

**Recommendations formulated**

- based on efficacy, safety and pharmacoeconomic data
- "GRADE" process ranks the quality of evidence and the strength of each recommendation

**Feedback sought from advocacy groups and industry**

# Information gaps

## Human insulins and insulin analogues:

- Most studies look at surrogate outcomes (lab tests, clinical measurements such as blood pressure, weight) and short-term complications (hypoglycemia)

## Virtually no studies on important long-term outcomes yet: diabetes related mortality, and microvascular and macrovascular disease

# Example of scientific process

**In patients with type 2 diabetes on oral antidiabetes drugs who also require a basal insulin:**

Are there advantages for either NPH or glargine?

# Glargine vs. NPH in patients with type 2 diabetes on oral antidiabetes drugs

## Clinical Outcomes:

- A1C
- Fasting plasma glucose
- Severe hypoglycemia
- Nocturnal hypoglycemia
- Overall hypoglycemia
- Long-term complications/mortality
- Surrogates: weight gain, BMI, blood pressure, LDL, % of patients A1C<7.0
- Health-related quality of life and patient satisfaction

## Cost-effectiveness

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# Glargine vs. NPH in patients with type 2 diabetes on oral antidiabetes agents: A1C

**Nine randomized-controlled studies**

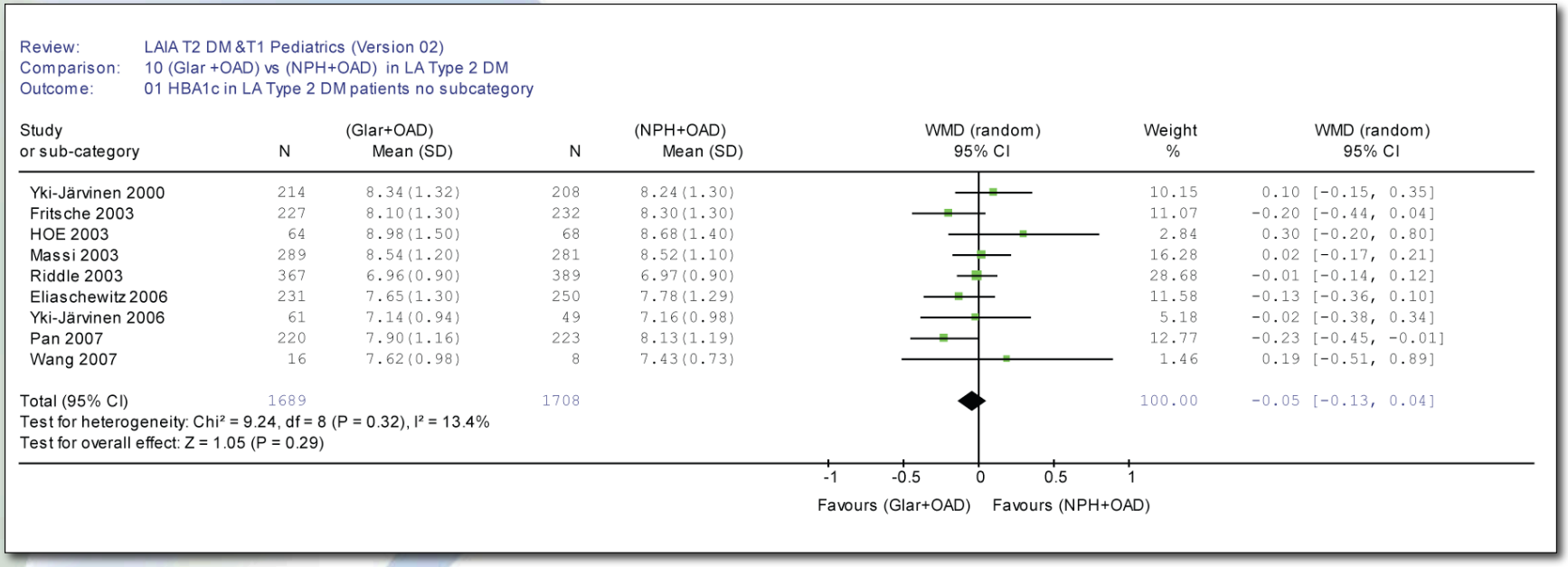
**N= 3,397 patients**

**No significant difference in A1C**

**Pooled estimates within each of the subgroups of oral antidiabetes drugs (sulfonylurea, metformin or various) showed slight but not clinically significant differences**

# Forest plot of A1C from all RCTs

## examining Glargine vs. NPH + in adult patients with type 2 diabetes on oral antidiabetes drugs – A1C, WMD




A1C=Glycosylated hemoglobin; CI=Confidence interval; Glar=Insulin glargine; NPH=Neutral protamine Hagedorn; OAD=Oral antidiabetes drug; RCT=Randomized controlled trial; SD=Standard deviation; WMD=Weighted mean difference

# Glargine vs. NPH in patients with type 2 diabetes on oral antidiabetes drugs

| Outcome | # RCTs (Total sample size) | Effect estimate (95% CI) |
|---|---|---|
| A1C | 9 (N=3,397) | -0.05 (-0.13 to 0.04) |
| Fasting Plasma Glucose | 6 (N=2,406) | -0.10 (-0.28 to 0.07) |
| Severe hypoglycemia (relative risk) | 7 (N=2,866) | 0.66 (0.29 to 1.48) |
| Nocturnal hypoglycemia (relative risk) | 7 (N=2,532) | **0.56 (0.47 to 0.68)** |
| Overall hypoglycemia (relative risk) | 8 (N=2,642) | **0.87 (0.81 to 0.93)** |
| Other surrogates | Weight, BMI, blood pressure, LDL | No difference |
| Long-term complications: Ischemic heart disease | | No difference |
| Long-term complications: other | | Insufficient data |
| Health-related Quality of Life/Patient Satisfaction | | Explanation: Next slides |
| Cost-effectiveness | | Explanation: Next slides |

A1C=Glycosylated hemoglobin; BMI=Body mass index; CI=Confidence interval; LDL=Low-density lipoprotein; RCT=Randomized controlled trial;

# Glargine vs. NPH in patients with type 2 diabetes on oral antidiabetes drugs (cont'd)

## Health-related quality of life and patient satisfaction

- Mean improvement score in treatment satisfaction significantly favoured glargine over NPH:
  - 1 RCT, N=481, moderate quality study

## Cost-effectiveness

- How is this determined?

CADTH. *Optimal Therapy Report - COMPUS* 2008;2(1).
Eliaschewitz, et al. *Arch Med Res* 2006;37(4):495-501.

# Cost-effectiveness

## Difference in treatment cost between strategies:

- $4,945 more expensive for glargine
- Difference in Quality-Adjusted Life Years (QALY): A commonly used measure of health and life-span
  - incremental benefit of 0.008 QALY with glargine

## Incremental cost-utility analysis

- Cost of glargine – cost of NPH/QALYs glargine-QALYs NPH
- There is no concrete cost-effectiveness threshold used in Canada
  - Published cost-effectiveness thresholds have ranged from $20,000/QALY - $100,000/QALY
- Glargine vs. NPH: $642,994/QALY gained

CADTH. *Optimal Therapy Report - COMPUS* 2008;2(1).
Culyer, et al. *J Health Serv Res Policy* 2007;12(1):56-8.
Hirth, et al. *Med Decis Making* 2000;20(3):332-42.
Laupacis, et al. *CMAJ* 1992;146(4):473-81.
McCabe, et al. *Pharmacoeconomics* 2008;26(9):733-44.
Rawlins, et al. *BMJ* 2004;329(7459):224-7.

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# Glargine vs. NPH in patients with type 2 diabetes on oral antidiabetes drugs

## Recommendation:

- NPH be used in preference to glargine in most adults with type 2 diabetes taking oral antidiabetes drugs who require a basal insulin

## Primary consideration:

- The incremental cost of glargine over insulin NPH outweighs its modest clinical benefit in this situation

## Strength of recommendation: “Strong”

## Quality of clinical evidence: “Moderate”

# Glargine vs. NPH: Type 1 diabetes (adults)*

| Outcome | RCTs (Total sample size) | Effect estimate (95% CI) |
|---|---|---|
| A1C | 8 (N=2,406) | **-0.12 (-0.25 to -0.01) reduction with glargine** |
| Severe hypoglycemia (relative risk) | 6 (N=2,113) | 0.81 (0.49 to 1.36) |
| Nocturnal Hypoglycemia (relative risk) | 5 (N=1,943) | 0.97 (0.87 to 1.09) |
| Overall Hypoglycemia (relative risk) | 5 (N=1,893) | 1.02 (0.97 to 1.07) |
| Weight | 3 (N=1,138) | **Favoured glargine** |
| Long-term complications/mortality | | Retinopathy no difference |
| HRQoL and Patient satisfaction | 1 (N=517) | No difference reported for HRQoL. **Patient satisfaction favoured glargine.** |
| Cost effectiveness | | $87,932 per QALY gained |

A1C=Glycosylated hemoglobin; CI=Confidence interval; HRQoL=Health-related quality of life; QALY=Quality-adjusted life year; RCT=Randomized controlled trial;

***Common pre-meal bolus insulin in both treatment study groups**

# Detemir vs. NPH: Type 1 diabetes (adults)*

| Outcome | RCTs (Total sample size) | Effect estimate (95% CI) |
|---|---|---|
| **A1C** | **7 (N=2,558)** | **-0.06 (-0.13, 0.02)** |
| | | **No statistical difference** |
| **Severe hypoglycemia (relative risk)** | **7 (N=2,442)** | Favoured detemir |
| **Nocturnal Hypoglycemia (relative risk)** | **6 (N=2,311)** | Favoured detemir |
| **Overall Hypoglycemia (relative risk)** | **6 (N=2,110)** | **No difference** |
| **Weight** | **6 (N=2,302)** | Favoured detemir |
| **Long-term complications/all cause mortality** | | **No difference** |
| **Patient satisfaction** | **No studies** | **Not applicable** |
| **Cost effectiveness** | | **$387,729 per QALY gained** |

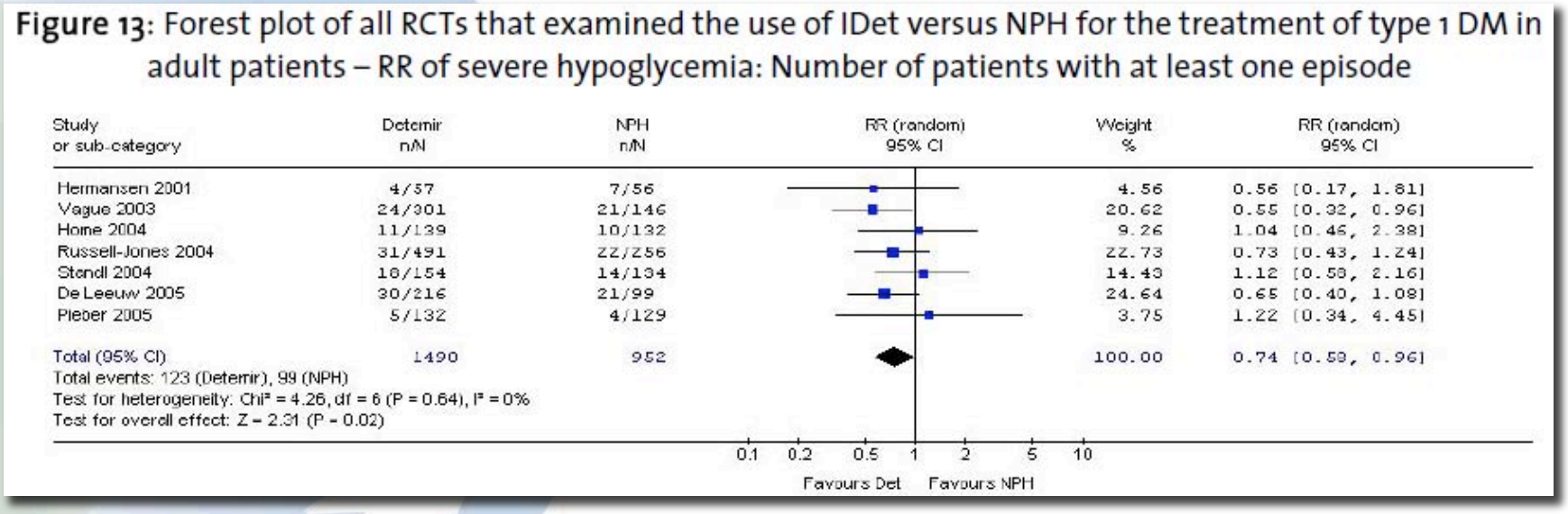
A1C=Glycosylated hemoglobin; CI=Confidence interval; QALY=Quality-adjusted life year; RCT=Randomized controlled trial;

*__Common pre-meal bolus insulin in both treatment study groups__

# Forest plot of the relative risk of severe hypoglycemia

## (number of patients with at least one episode) from all RCTs examining Detemir vs. NPH in adult patients with type 1 diabetes

**Figure 13**: Forest plot of all RCTs that examined the use of IDet versus NPH for the treatment of type 1 DM in adult patients – RR of severe hypoglycemia: Number of patients with at least one episode




DM=Diabetes mellitus; CI=Confidence interval; IDet=Insulin detemir; NPH=Neutral protamine Hagedorn; RCT=Randomized controlled trial; RR=Relative risk

# Long-acting insulin analogues and hypoglycemia

**Some comparative studies demonstrated a reduced risk/incidence of hypoglycemia with long-acting insulin analogues vs. NPH**

- Not observed consistently across studies
- Hypoglycemia not consistently defined

**Adults with type 1 diabetes with prior severe recurrent hypoglycemia actually excluded from seven of nine trials comparing detemir with NPH**

# Long-acting insulin analogues:
## Key message

**In patients with type 1 diabetes or type 2 diabetes requiring basal insulin, insulin NPH should be considered first.**

**Although the evidence is limited and inconsistent, patients experiencing significant hypoglycemia while using insulin NPH may benefit from long-acting insulin analogues.**

# Bolus insulin therapy (lispro or aspart) vs. regular insulin

## Type 1 diabetes: (Children, adolescents, adults and pregnancy)

- No clinically significant differences in A1C, however there was a marginal benefit
- Hypoglycemia: marginal benefits in some studies for pump users and adults and adolescents on multiple doses
- Significant increase patient satisfaction
- $673,041 per QALY gained is only for type 1 adults using MDI (lispro vs. human insulin);
- $104,598 per QALY gained is for type 1 adults using MDI (aspart vs. human insulin)

# Key message: Bolus insulin type 1 diabetes

**In patients with type 1 diabetes, either regular human insulin or rapid-acting insulin analogues can be considered as first-line therapy (except in adolescent patients).**

**In adolescent patients with type 1 diabetes, rapid-acting insulin analogues may be considered as first-line therapy.**

# Bolus insulin type 1 diabetes special considerations

## Regular human insulin may be preferred when

- Affordability is an important consideration

## Consider rapid-acting insulin analogues when:

- Flexibility of administration with meals is of primary importance
- Significant hypoglycemia is experienced while using regular human insulin, or in cases where hypoglycemia is a major concern

## Rapid-acting insulin analogues are preferred for adolescents using multiple daily injections

- Evidence for lispro
- A better fit for the unpredictable patterns of dietary intake and activity

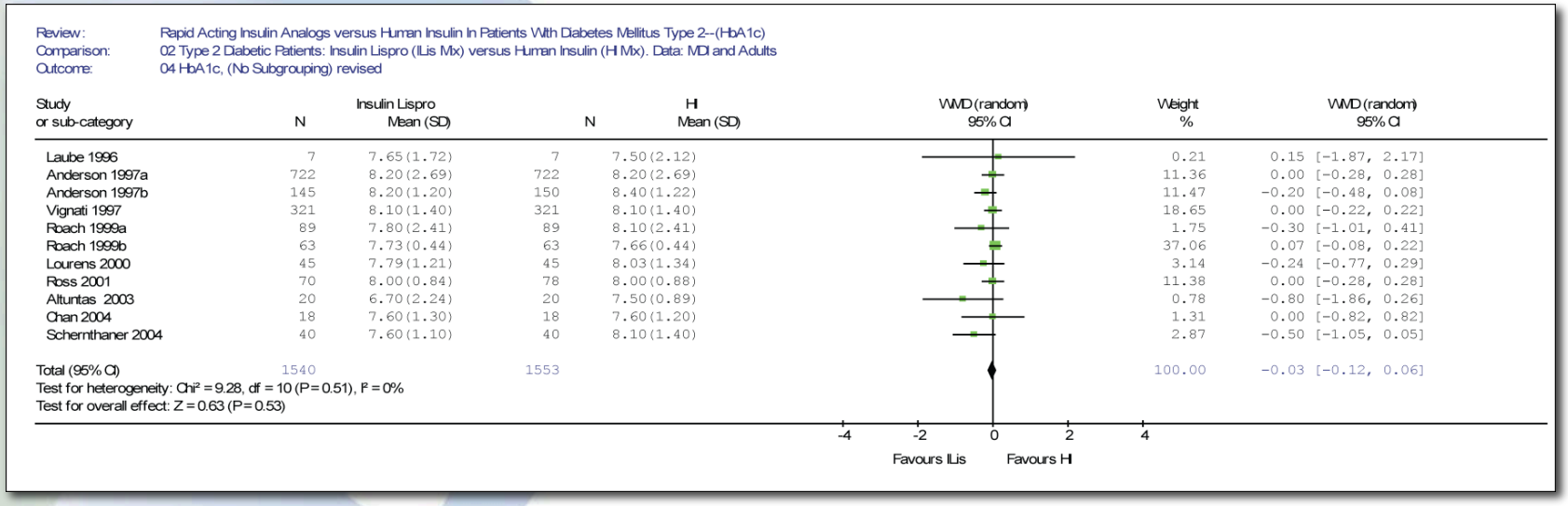
# Bolus insulin type 2 diabetes
# Lispro vs. regular insulin

| Outcome | RCTs (Total sample size) | Effect estimate (95% CI) |
|---|---|---|
| A1C | 11 (N=3,093) | No significant difference |
| Severe hypoglycemia (relative risk) | 2 (N=1,622) | No significant difference |
| Nocturnal Hypoglycemia (relative risk) | 1 (N=178) | No significant difference |
| Overall Hypoglycemia (relative risk) | 3 (N=384) | No significant difference |
| Weight | 3 (N=1,682) | No significant difference |
| All cause mortality | 1 (N=80) | No significant difference |
| Patient satisfaction | 1 (N=885) | No significant difference |
| Cost-effectiveness | | $130,865 per QALY gained |

A1C=Glycosylated hemoglobin; CI=Confidence interval; QALY=Quality-adjusted life year; RCT=Randomized controlled trial;

# Forest plot of A1C from all RCTs

## examining lispro or insulin lispro mix vs. human insulin in adult patients with type 2 diabetes – A1C, WMD




A1C=Glycosylated hemoglobin; CI=Confidence interval; DM=Diabetes mellitus; HI=Human insulin; ILis=Insulin lispro; QALY=Quality-adjusted life year; RCT=Randomized controlled trial; WMD=Weighted mean difference

# Type 2 diabetes
# A1C, hypoglycemia and weight

**No significant differences for lispro vs. human insulin as a single agent**

**No significant differences for A1C and overall hypoglycemia in insulin biphasic mixtures containing lispro vs. aspart**

# Other Evidence

## Other meta-analyses suggest no general advantage of analogues over human insulins

- Institute for Quality and Efficiency in Health Care [IQWiG] (Germany) 2007

IQWiG. *Rapid-acting insulin analogues in the treatment of diabetes mellitus type 1*; 2007.

# Key message: Bolus insulin

**In patients with type 2 diabetes requiring bolus insulin, regular human insulin may be considered first.**

- Although the evidence is limited and inconsistent, patients who are experiencing significant hypoglycemia while taking human insulin may benefit from rapid-acting insulin analogues.

# Cases where insulin analogues should be considered

## Adolescents with type 1 diabetes

- Insulin lispro is recommended as first line bolus insulin

## Although the evidence is limited and inconsistent, patients with type 2 diabetes who are experiencing significant hypoglycemia while taking human insulin may benefit from rapid-acting insulin analogues

## Other patient factors favoring analogue consideration:

- Flexibility of dose and meal timing for rapid-acting insulin analogues
- Increased patient satisfaction in some studies

# Pregnancy

## Type 1 diabetes in pregnancy

- Bolus insulin: either regular insulin or rapid-acting insulin analogues
- Basal insulin:
  - Long-acting insulin analogues not studied

## Gestational diabetes

- Bolus insulin: either regular insulin or rapid-acting insulin analogues (e.g., insulin aspart)
- Basal insulin
  - Long-acting insulin analogues not studied

# Learning objectives

**Understand the evidence-base which supports the use of human insulins and insulin analogues in the treatment of diabetes**

- Systematic review of world literature
- Pooled meta-analysis of peer-reviewed trials
- Recommendations based on clinical evidence with pharmacoeconomic analysis added afterwards

# Learning objectives (cont'd)

**Identify the appropriate use of insulin preparations in:**

- The general population with diabetes
  - First-line agents for bolus insulin:
    - Adults with type 1 diabetes: regular human insulin or rapid-acting insulin analogues
    - Adolescents with type 1 diabetes, insulin lispro or rapid-acting insulin analogues suggested over regular human insulin
    - Type 1 diabetes in pregnancy and gestational diabetes: regular human insulin or rapid-acting insulin analogues
    - Type 2 diabetes: regular human insulin
- First-line agents for basal insulin:
    - Type 1 and type 2 diabetes: NPH insulin

# Learning objectives (cont'd)

**Identify special cases where insulin analogues should be considered:**

- Adolescents with type 1 diabetes: lispro for bolus
- Hypoglycemia (severe episodes) in any patient: both rapid- and long-acting insulin analogues
- Patient convenience/meal flexibility: rapid-acting insulin analogue
- Patient preference

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