Bifidobacterium animalis ssp. lactis 420
Outline

• The clinical problem
  o BMI in Canadian population
  o Weight gain/regain patterns
• Microbiome and body weight regulation
• Development pathway of B420
• B420 mechanisms of action
• Clinical data with B420
The clinical issue

26.7% of Canadians were obese (BMI >30kg/m$^2$) in 2015, an increase from 23.1% in 2004

The clinical issue

Clinical Statistics

Obesity is more prevalent in the 45-74 year range, 2007-2008 data from Statistics Canada

Obesity and the practitioner

Recent survey* results revealed that more than 50% of their patient population suffers from obesity

<table>
<thead>
<tr>
<th>What percent of your patient population has a BMI &gt; 30?</th>
<th>What percent of your patient population suffers from chronic conditions due to obesity?</th>
<th>How many of your patients have you assisted in losing between 10-20 lbs?</th>
<th>How many of your patients have you assisted in losing between 25-30 lbs?</th>
<th>How many of your patients have you assisted in losing between 25-30 lbs?</th>
<th>How many patients have you treated this year, in part or full, with a medically supervised weight loss program?</th>
<th>How many of your weight loss patients have you achieved success with?</th>
<th>Of the patients in question #7, how long did they maintain their weight loss goals?</th>
<th>Did you utilize Healthy Transformation for any of your weight loss patients?</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 stated 50% or more Of patients have BMI &gt; 30</td>
<td>4 stated 50% or more</td>
<td>6 stated 50% or more</td>
<td>4 stated 50% or more</td>
<td>4 stated 50% or more</td>
<td>All CC members have treated range 50- 250 patients</td>
<td>100% achieved success</td>
<td>8 stated that success lasted 1 year or more</td>
<td>7 stated they do not use HT</td>
</tr>
<tr>
<td>4 stated 20%</td>
<td>6 stated 20%</td>
<td>4 stated 20% between 20%- 40%</td>
<td>6 stated 20% between 15%- 40%</td>
<td>6 stated 20% between 10%- 40%</td>
<td>2 stated weight loss lasted between 1-3 months</td>
<td>3 stated they use HT</td>
<td>7 stated they use HT</td>
<td></td>
</tr>
</tbody>
</table>

*From a small internal survey of 10 practitioners
Clinically, waist circumference is a surrogate for disease risk

• Adipose tissue is an endocrine organ. Different depots have different metabolic activity

Visceral and subcutaneous abdominal adipose tissue

Clinical Measure
Waist Circumference

Inflammatory cytokines
Adiponectin

Associated with insulin resistance and atherogenic dyslipidemia.

Disease Risk
Type 2 Diabetes
Heart Disease
Hypertension

Bays H. Curr Opin Endocrinol Diabetes Obes. 2014;21(5):345–351
Canadian women have a higher prevalence of increased waist circumference, 2009-2011

Obesity is a driver of chronic disease—
Benefits of modest weight loss

<table>
<thead>
<tr>
<th>Obesity complication</th>
<th>Weight loss required for therapeutic benefit (%)</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes (prevention)</td>
<td>3-10</td>
<td>Maximum benefit at 10%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>5 to &gt;15</td>
<td>Blood pressure still decreasing at &gt;15%</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>3 to &gt;15</td>
<td>Triglycerides still decreasing at &gt;15%</td>
</tr>
<tr>
<td>Hyperglycemia (elevated HbA1c)</td>
<td>3 to &gt;15</td>
<td>HbA1c still decreasing at &gt;15%</td>
</tr>
<tr>
<td>NAFLD</td>
<td>10</td>
<td>Improves steatosis, inflammation and mild fibrosis</td>
</tr>
<tr>
<td>Sleep apnea</td>
<td>10</td>
<td>Little benefit at 5%</td>
</tr>
<tr>
<td>Osteoarthritis</td>
<td>5-10</td>
<td>Improves symptoms and joint stress mechanics</td>
</tr>
<tr>
<td>Stress incontinence</td>
<td>5-10</td>
<td></td>
</tr>
<tr>
<td>Gastroesophageal reflex disease</td>
<td>5-10 in women; 10 in men</td>
<td></td>
</tr>
<tr>
<td>Polycystic ovary syndrome</td>
<td>5-15 (&gt;10 optimal)</td>
<td>Lowers androgens, improves ovulation, increases insulin sensitivity</td>
</tr>
</tbody>
</table>

Weight maintenance is difficult to achieve

Only 1 in 6 overweight or obese US adults report ever having maintained weight loss of at least 10% for 1 year

Weight loss and maintenance are difficult to achieve over long term (UK data)

5% body weight loss over 9 year observation
- 1 in 12 men and 1 in 10 women with simple obesity (BMI 30-35kg/m²) lost 5% body weight.
- 1 in 8 men and 1 in 7 women with morbid obesity lost 5% body weight.

Odds of attaining normal body weight during 9-year follow-up
- 1 in 210 for men and 1 in 124 for women with simple obesity.
- 1 in 1290 for men and 1 in 677 for women with morbid obesity.

Weight regain
- In 9 years follow-up, only 14% of men and 15% of women showed reduction in BMI category without increases over the follow-up period.

Health records for 76704 obese men and 99791 obese women examined over 9 year period.
Helsinki Health Study—slow weight gain over time

30% of the normal middle-aged population gained at least 11 lbs (~5 kg) over the 5-7 year study period

<table>
<thead>
<tr>
<th>Age</th>
<th>Women</th>
<th></th>
<th>Men</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Weight gain ≥11lbs</td>
<td></td>
<td>Weight gain ≥11lbs</td>
</tr>
<tr>
<td></td>
<td>n</td>
<td>% [95% CI]</td>
<td>n</td>
<td>% [95% CI]</td>
</tr>
<tr>
<td>40</td>
<td>1075</td>
<td>34 [31.7-36.9]</td>
<td>208</td>
<td>32 [26.1-37.4]</td>
</tr>
<tr>
<td>45</td>
<td>1150</td>
<td>34 [31.0-36.1]</td>
<td>226</td>
<td>33 [27.3-38.2]</td>
</tr>
<tr>
<td>50</td>
<td>1198</td>
<td>26 [23.3-28.3]</td>
<td>252</td>
<td>28 [23.0-33.3]</td>
</tr>
<tr>
<td>55</td>
<td>1330</td>
<td>21 [18.1-22.8]</td>
<td>361</td>
<td>18 [13.7-22.3]</td>
</tr>
<tr>
<td>60</td>
<td>617</td>
<td>34 [10.5-17.4]</td>
<td>205</td>
<td>10 [4.0-15.5]</td>
</tr>
</tbody>
</table>

Microbiome and body mass regulation—what is the evidence?

Microbiome samples were taken from female twin pairs discordant for obesity (one lean, one with obesity).

When the human microbiome samples were transferred to mice, those receiving the obese microbiome sample gained significant body fat.

Microbiome and body mass regulation—differences between lean and obese

Microbiota commonly identified in samples from lean and obese individuals differ⁴

A less diverse microbial community has been identified in obesity⁴

Differences in microbial metabolism genes and microbial products affecting host metabolism have been shown in some studies to differ between lean and obese microbiome samples³,⁵,⁶

Summary of microbiome differences

There are three key differences between the microbiomes of lean and obese individuals:

1. **Composition**—Obese individuals tend to have more pathobionts (unwanted or potentially harmful bacteria)\(^1,2,4\)

2. **Diversity**—Obese individuals tend to have a less diverse microbiome\(^3\)

3. **Functionality**—Obese individuals tend to have altered gut-derived signals that impact satiety and fat deposition\(^1,5\)


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The complete genome of B420 has been characterized and was published in 2012\(^1\)

**Note:** The scientific name is *Bifidobacterium animalis* ssp. *lactis* 420, abbreviated form is B420

Development pathway of B420

**Cell culture studies:**
B420 contributes to epithelial barrier function

**Mouse studies:**
B420 improves metabolic health and gut barrier function

**Clinical study:**
B420 improves metabolic health

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B420 probiotic strain—Mechanisms of action

All of the actions below are supported by pre-clinical and/or clinical data with B420

- Increased SCFA production, which may increase production of satiety hormones
- Reduced food intake
- Decreased bacterial and LPS translocation
- Beneficial modifications in the gut microbiota
- Decrease in mucosal adherence of undesirable microbes
- Enhanced epithelial barrier function
- Increased in GLP-1
- Enhanced tight-junction integrity


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Summary of mechanisms of action

*Bifidobacterium animalis* ssp *lactis* 420 has three key potential mechanisms of action that may explain its effects of reducing energy intake in the clinical study:

1. **Animal studies demonstrate that B420 may increase levels of the anorectic (appetite-reducing) gut peptide GLP-1**

2. **The clinical study shows that B420 increases total intestinal short-chain fatty acid concentration**, which may promote the production of GLP-1

3. **In vitro** and animal studies demonstrate that B420 may improve gut barrier function, which may reduce LPS and bacterial translocation from the gut, which may lower LPS signaling in adipose tissue, reducing the signals associated with weight gain

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B420 clinical data\(^1\) —
Study design and study population

### STUDY POPULATION
- Age (average) ~50 yrs
- BMI (average) ~31 kg/m\(^2\)
- Otherwise healthy
- ~75% women

#### GROUP 1: PLACEBO
- Microcrystalline cellulose (MCC)

#### GROUP 2: B420
- B420 (10 billion CFUs) and MCC

#### OUTCOME MEASURES
- Body weight
- Total body fat (DXA)
- Trunk fat mass (DXA)
- Waist circumference
- Food intake

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B420 clinical data —

Body fat

*Bifidobacterium animalis ssp. lactis 420 helps control body fat*

*In a 6-month clinical study, of overweight individuals, those taking *Bifidobacterium animalis ssp. lactis 420 showed reduced body fat mass compared to placebo group.*

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**Total body fat (kg)**

<table>
<thead>
<tr>
<th>Baseline</th>
<th>6 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>36.4</td>
</tr>
<tr>
<td>B420</td>
<td>37.5</td>
</tr>
</tbody>
</table>

**Change in total fat mass (%)**

- Placebo: 0%
- B420: 4%

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* Indicates placebo vs. B420 groups significantly different at 6 months (p<0.05; per protocol post-hoc analysis)
B420 clinical data — Body weight

- *Bifidobacterium animalis* ssp. *lactis* 420 helps control body weight and body weight regulation
- Preliminary evidence shows that *Bifidobacterium animalis* ssp. *lactis* 420 may help contribute to long-term weight maintenance

<table>
<thead>
<tr>
<th></th>
<th>BASELINE</th>
<th>6 MONTHS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Placebo</strong></td>
<td>88.7</td>
<td>89.5</td>
</tr>
<tr>
<td><strong>B420</strong></td>
<td>88.5</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Change in body weight (kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Placebo</strong></td>
<td>1</td>
</tr>
<tr>
<td><strong>B420</strong></td>
<td>-0.2</td>
</tr>
</tbody>
</table>


* Indicates placebo vs. B420 groups significantly different at 6 months (p<0.05; per protocol post-hoc analysis)
B420 clinical data\textsuperscript{1} —
Waist circumference

*Bifidobacterium animalis ssp. lactis 420 helps reduce waist circumference*
*In a 6-month clinical study of overweight individuals, those taking Bifidobacterium animalis ssp. lactis 420 showed reduced waist circumference compared to placebo group

\begin{center}
\begin{tabular}{c}
\textbf{Change in waist circumference (\%)} \\
\hline
1 \hline
\hline
\textbf{Placebo} & \textbf{B420} \\
-1.4 \\
\end{tabular}
\end{center}


* Indicates placebo vs. B420 groups significantly different at 6 months (p<0.05; per protocol post-hoc analysis)
B420 clinical data\(^1\) — Abdominal fat

*Bifidobacterium animalis ssp. lactis 420 helps control abdominal fat*

*In a 6-month clinical study, of overweight individuals, those taking *Bifidobacterium animalis ssp. lactis 420 showed reduced abdominal fat compared to placebo group*


* Indicates placebo vs. B420 groups significantly different at 6 months (p<0.05; per protocol post-hoc analysis)
B420 clinical data\textsuperscript{1}—

**SCFA**

*Bifidobacterium animalis* ssp. *lactis* 420 promotes short chain fatty acid (SCFA) production

*In a 6-month study of overweight individuals, those taking *Bifidobacterium animalis* ssp. *lactis* 420 showed increased concentrations of short-chain fatty acids (SCFA)*

<table>
<thead>
<tr>
<th>Placebo</th>
<th>B420</th>
</tr>
</thead>
<tbody>
<tr>
<td>-10</td>
<td>4.6</td>
</tr>
</tbody>
</table>

*SCFA are produced by the microbiota*

*Change in SCFA concentration indicates altered metabolism and changes in the composition of the gut microbiota\textsuperscript{1}*

*SCFA have been shown to activate satiety signaling in the intestine*


* Indicates placebo vs. B420 groups significantly different at 6 months (p<0.05; per protocol post-hoc analysis)
B420 clinical data$^1$—

**Energy intake**

In a 6-month study of overweight individuals, those taking *Bifidobacterium animalis* ssp. *lactis* 420 showed reduced energy intake.

<table>
<thead>
<tr>
<th>Change in energy intake (kcal/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
</tr>
<tr>
<td>B420</td>
</tr>
<tr>
<td>-23</td>
</tr>
<tr>
<td>-320</td>
</tr>
</tbody>
</table>

* Indicates placebo vs. B420 groups significantly different at 6 months (p<0.05; per protocol post-hoc analysis)


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Conclusions

• Over the past decade, increasing evidence has linked the intestinal microbiome with regulation of body weight and body fat mass

• Pre-clinical work with the probiotic strain *Bifidobacterium animalis* ssp. *lactis* 420 improved the following:
  1. Intestinal barrier function
  2. Satiety signaling
  3. Body weight and body fat regulation

• A 6-month clinical study in obese men and women was published in 2016 and showed that *Bifidobacterium animalis* ssp. *lactis* 420 had the following benefits:
  - Helps control body fat
  - Helps control body weight and body weight regulation
  - Helps reduce waist circumference
  - Helps control abdominal fat
  - Promotes short chain fatty acid (SCFA) production
  - Reduces energy intake