Correlation between symptoms developed after the oral ingestion of 50 g lactose and results of hydrogen breath testing for lactose intolerance

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Abstract

BACKGROUND: Lactase deficiency is a common condition responsible for various abdominal symptoms. Lactose hydrogen breath test is currently the gold standard in diagnosing lactose intolerance.

AIM: To assess sensitivity and specificity of symptoms developed after oral lactose challenge.

METHODS: Intensity of nausea, abdominal pain, borborygmi, bloating and diarrhoea was recorded every 15 min up to 3 h after ingestion of 50 g lactose in patients with positive (i.e. breath H2-concentration > or =20 p.p.m. above baseline) and negative lactose hydrogen breath test.

RESULTS: Between July 1999 and December 2005, 1127 patients (72% females) underwent lactose hydrogen breath test. A positive result was found in 376 (33%). Sensitivity of individual symptoms ranged from 39% (diarrhoea) to 70% (bloating) while specificity ranged from 69% (bloating) to 90% (diarrhoea). A positive lactose hydrogen breath test was found in 21% of patients with one symptom, 40% of patients with two symptoms, 44% of patients with three symptoms, 67% of patients with four symptoms and 82% of patients with five symptoms. Symptom intensity was significantly higher for each symptom in the positive group.

CONCLUSION: Evaluating symptoms developed after ingestion of 50 g lactose can be used as a simple screening test to select patients who need to be referred for lactose intolerance testing.
Correlation between symptoms developed after the oral ingestion of 50g lactose and results of hydrogen breath testing for lactose intolerance

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Keywords:
- Lactose intolerance
- Lactose hydrogen breath testing
- Lactase deficiency

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Abstract (Word count 197)

**Background:** Lactase deficiency is a common condition responsible for various abdominal symptoms. Lactose hydrogen breath test (H2-BT) is currently the gold standard in diagnosing lactose intolerance.

**Aim:** Assessing sensitivity and specificity of symptoms developed after oral lactose challenge.

**Methods:** Intensity of nausea, abdominal pain, borborygmi, bloating and diarrhea was recorded every 15 minutes up to 3 hours after ingestion of 50g lactose in patients with positive (i.e. breath H2-concentration ≥20 ppm above baseline) and negative lactose H2-BT.

**Results:** Between July 1999 and December 2005 1127 patients (72% females) underwent lactose H2-BT A positive result was found in 376 (33%). Sensitivity of individual symptoms ranged from 39% (diarrhea) to 71% (bloating) while specificity ranged from 69% (bloating) and 90% (diarrhea). A positive H2-BT was found in 21% of patients with one symptom, 40% of patients with 2 symptoms, 44% of patients with 3 symptoms, 67% of patients with 4 symptoms and 82% of patients with 5 symptoms. Symptom intensity was significantly higher for each symptom in the positive group.

**Conclusion:** Evaluating symptoms developed after ingestion of 50g lactose can be used as a simple screening test to select patients that need to be referred for lactose intolerance testing.
Introduction

Lactose intolerance is a common condition affecting a large proportion of the world’s population\(^1\). The prevalence of lactose intolerance differs in various parts of the world ranging from 3-8\% in the Scandinavian and Northwest Europe population to 50-100\% of the Southeast Asian population\(^2,3,4\). In Europe the prevalence increases towards South and East reaching 70\% in southern Italy and Turkey\(^5\). The most common cause of lactose intolerance is lactase deficiency - a decreased production of the enzyme lactase in the small intestinal villi. Lactase deficient individuals are not able to cleave this disaccharide in glucose and galactose and may become symptomatic after the ingestion of lactose. As a consequence, lactose reaches the large intestine where it is metabolized by the colonic flora. The high osmotic load caused by lactose in the small intestine and the bacterial metabolites are considered to play an important role in the genesis of the classic symptoms of lactose intolerance such as diarrhea, bloating, nausea, borborygmi and abdominal pain.

Lactose hydrogen breath test (H2-BT) has been used for more than 30 years to diagnose lactase deficiency in clinical practice\(^6\). This test exploits the fact that normal colonic flora metabolizes lactose into hydrogen (H\(_2\)) and short chain fatty acids. Hydrogen reaches the splanchnic venous circulation by diffusion through the intestinal wall, is transported from here through the portal system to the liver and the systemic circulation and is eventually exhaled through the lungs. The sensitivity and specificity of an increase in H\(_2\) concentration in the exhaled air to diagnose lactose intolerance range from 76-94\% and 77-96\%, respectively\(^7\). While the H2-BT is considered the “gold standard” of the non-invasive tests to diagnose lactose intolerance there is limited information on the sensitivity and specificity of symptoms developed in response to the ingestion of a given amount of lactose\(^8\).

The aim of this study was to evaluate the sensitivity and specificity of symptoms developed after the ingestion of 50g of lactose for a positive H2-BT. We hypothesized an association between the number of symptoms developed after the ingestion of 50g of lactose and a positive hydrogen breath test.
Materials and methods

Data from all patients referred for H2-BT between 1999 and 2005 were collected prospectively. Demographic data included age, gender and country of origin (grouped by “Swiss” vs. “non-Swiss”). They included both the result of the test itself and information on symptom occurrence and severity after lactose ingestion as recorded in a structured questionnaire.

Breath H2 concentration was measured using a H2 breath test device (Stimotron Medizinische Geräte GmbH, Wendelstein, Germany) equipped with an electrochemically working hydrogen cell. The breath analyser is able to detect H2 concentrations in the range of 0-250 parts per million (ppm) with an accuracy of ± 2\% (1ppm at values below 50ppm). The instrument was calibrated using standardized compressed gas with a H2 concentration of 96.8 ppm (Calibration Gas, compressed gas, No. 5, BDL. A/R). Air samples (20 ml each) were insufflated in the H2 breath test device and the H2 concentration was read from a digital panel meter.

Patients underwent the H2-BT after fasting overnight at the Gastrointestinal Function Unit of the University Hospital of Zurich. Patients were asked to be fasting and refrain from smoking for at least 6 hours prior to the test. Furthermore patients were asked to discontinue possible use of antibiotics one week and laxatives one day before the H2BT. Prior to the beginning of the test, two samples of mixed end-expired air were aspirated into a 20ml plastic syringe (Injekt 20ml, Braun) fitted with a three-way stopcock. The sample with the higher amount of H2 was used as baseline value and the test was performed provided both values were below 20ppm. After determining the baseline H2 breath concentration, the subject ingested 50g of lactose dissolved in 300ml of water. Over a 2-3 hour period breath samples were collected as described above at 15 minutes intervals while the patient was in sitting position. At the time of breath sampling patients were asked to rate 5 symptoms (abdominal pain, nausea, bloating, borborygmi and diarrhea) using a 9-point scale (0 – no symptom to 9 – worst symptom severity).
For each patient we determined the maximal intensity of each of the 5 symptoms as the highest symptom intensity value recorded during the duration of the breath test.

The lactose H2-BT was considered positive if the H2 concentration in the exhaled air exceeded 20 ppm above baseline at least twice during the monitoring period. A symptom was considered positive if the patient reported a 2-point or more increase above baseline in the severity of the symptom at least twice.

The data analysis was approved by the ethical committee of the University Hospital of Zurich and of the Canton of Zurich, Switzerland.

**Statistical analysis**

The Chi-square test was utilized to analyze differences between proportions. Differences in the mean age of patients with positive and negative breath test were compared by using the unpaired Student t-test. Correlations between variables were quantified by calculating the Spearman-rank correlation coefficients. The significance level of all statistical analyses was set at alpha=0.05.

**Results**

Between July 1999 and December 2005, 1127 patients underwent a H2-lactose breath test. Their mean age was 39.8 years (range 7-87), 71.6% were women (n=807) and 28.4% men (n=320). Three hundred seventy-six (33.4%) patients had a positive H2-lactose breath test indicative of lactase deficiency. The mean age of patients with a positive (mean ± SD: 39.6 ± 15.6 years) and negative test (40.2 ± 15.3 years) did not differ significantly (p=0.51). Similarly, no statistically significant association was found between gender and the result of the H2-lactose breath test (p=0.086). Swiss patients were less likely (p<0.001) to have a positive H2-lactose breath test result (169/746; 22.7%) compared to non-Swiss individuals (207/381; 54.3%).
Sensitivity and specificity of individual symptoms

After the ingestion of 50g lactose, 370 (32.8%) patients reported nausea, 495 (43.9%) bloating, 220 (19.5%) diarrhea, 432 (38.3%) borborygmi and 419 (37.2%) abdominal pain. Bloating was the most sensitive (71%) and diarrhea the most specific (90%) symptom. At the present test positivity of 33.4%, diarrhea had the highest positive predictive value (66%) and bloating the highest negative predictive value (82%). The sensitivity, specificity and predictive values of the individual symptoms are presented in table 1. The table also lists the likelihood ratios for the different symptoms as this figure, contrary to predictive values, is independent of pre-test probability, i.e. disease prevalence.

Sensitivity and specificity of combinations of symptoms

Three hundred twenty six (28.9%) patients did not develop any symptoms during the monitoring period. In this group of patients, 288 (88%) had a negative H2-lactose breath test. The proportion of patients with a positive H2-lactose breath test increased with the number of symptoms developed after the ingestion of 50g lactose from 21% in those developing only one symptom to 82% in those developing all 5 symptoms (Figure 1a). There was a strong positive correlation between the number of symptoms and percentage of patients with a positive H2-lactose breath test (r=0.989; p<0.001).

Only a small proportion (20/241; 8.2%) of Swiss patients reporting no symptoms had a positive H2-breath test result whereas 31.8% (7/22) had a negative test despite 5 symptoms were present. Among non-Swiss, a larger proportion with no symptoms (18/85=21.2%) and of those reporting all 5 symptoms (31/34; 91.2%) had a positive H2-breath test result. The proportion of Swiss and non-Swiss patients with a positive H2-lactose breath test depending on the number of symptoms reported during the test are shown in figures 1b and 1c respectively. Sensitivity, specificity, PPV, NPV, positive and negative likelihood ratios of one, two, three, four and five symptoms to identify a positive lactose H2 breath test are detailed in table 2.
Intensity of symptoms in patients with positive vs. negative breath tests

Patients with a positive H2-lactose breath test reported higher symptom intensities compared to patients with a negative breath test. The differences in symptom intensity (Figure 2) were statistically significant for all 5 symptoms: abdominal pain (3.5 ± 0.1 vs. 2.1 ± 0.1; p<0.05), nausea (2.7 ± 0.1 vs 2.1± 0.1; p<0.05), bloating (4.3 ± 0.1 vs. 2.6 ± 0.1; p<0.05), diarrhea (2.6 ± 0.2 vs. 0.8 ± 0.1; p<0.05) and borborygmi (3.7 ± 0.1 vs. 1.8 ± 0.1; p<0.05). These differences were significantly different even when Swiss and Non-Swiss patients were analyzed separately.

Discussion

In the present study, we report the sensitivity and specificity of abdominal pain, nausea, bloating, borborygmi and diarrhea developed in response to the ingestion of 50g lactose to identify patients with lactase deficiency as shown by a positive H2-BT. This information is important since symptoms of lactose intolerance overlap with features of irritable bowel syndrome and, thus, discrimination between these two disease entities may result difficult. We found that bloating had the best sensitivity (71%) and negative predictive value (82%) while diarrhea had the best specificity (90%) and positive predictive value (66%) to identify patients with a positive H2-BT. Twenty-one percent of patients who developed one symptom after the ingestion of 50g lactose were found to have lactase deficiency based on the results of the lactose H2-BT. Eighty-one percent of patients who developed all 5 symptoms had a positive (abnormal) lactose H2-BT. These data indicate that evaluation of symptoms developed in response to the ingestion of a predefined amount of lactose could represent a simple screening test for lactose intolerance.

In a pragmatic approach we consider that patients who do not develop any symptoms after ingesting 50 grams of lactose do not need to be referred for hydrogen breath testing as (1) the likelihood of the test being positive is around 10% and (2) even in the case of a positive result it would be difficult to justify the clinical benefits of a lactose free diet in the absence of symptoms. At the other end of the spectrum, one might argue that a hydrogen breath testing would not be necessary in patients who
develop all 5 symptoms as the likelihood of them having a positive test is high (68-91% depending on demographic background). Recommending these patients to strictly adhere to a lactose-free diet and reevaluate of their symptom pattern after 4-6 weeks could be tried first. As lactose is used in various processed foods a consultation with a dietician might be necessary in some patients to ensure adherence to a lactose-free diet. Patients with persisting symptoms on a lactose free diet should be examined for other pathologies. In patients improving on a lactose-free diet formal documentation of low lactase activity would be required given the major lifestyle and diet changes implied by a life-long diagnosis of lactose intolerance.

Lactose intolerance testing should be recommended to patients who develop two or three symptoms after the ingestion of 50g lactose as the pretest probability of them having a positive or negative test is in the range of a coin toss. The same applies for patients who develop one or four symptoms after the ingestion of 50g lactose. Although patients developing one symptom are more likely to be negative and patients developing 4 symptoms are more likely to be positive, testing should be performed as this may have implications on lifestyle and diet. An important discussion point would be whether to perform a hydrogen breath test or a LCT gene test. Enattah et al reported adult-type hypolactasia in patients homozygote C/C to the C/T-13910 variant and in patients homozyote G/G to the G/A-22018 variant. Testing the single nucleotid polymorphism of the C/T-13910 base pair on the short arm of chromosome 2q.21-22 is commercially available in certain laboratories. In a recent study Högenauer et al documented an excellent agreement between CC genotype and positive H2-breath test (36/37 patients with CC genotype had a positive lactose H2-breath test). Therefore, if available, genetic testing (LCT 13910 test) in patients with symptoms developed after the ingestion of 50g lactose might be used instead of a standard lactose H2 breath test.

Data in Swiss vs. non-Swiss patients indicate that the utility of the clinical test depends on the prevalence of lactose intolerance in a given population. With overall 22.7% positive breath test results the Swiss population can be regarded as a population group with relative low prevalence of lactose intolerance. Conversely the group of non-Swiss patients with overall 54.3% positive breath test results can be considered as a population group with medium high prevalence of lactose
intolerance. The relationship between H2-breath test result and number of symptoms during the test in Swiss and non-Swiss patients indicate that clinical utility of the symptom analysis in response to the ingestion of 50g lactose is even higher when the prevalence of lactose intolerance in a tested population is known. By using the likelihood ratios, post-test probabilities, i.e. the probability that the H2-BT is positive or negative in presence or absence of symptoms, respectively, can be easily calculated for populations with different prevalence of lactose intolerance.

An additional rationale for a focused selection of patients referred for lactose intolerance testing is resource utilization. Although the lactose H2 breath test is not invasive and its direct costs are low, its performance requires a dedicated health-care person to collect breath samples over a period of 3-4 hours. From the patient perspective, the test is associated with a half to one day of missed work. Filling out only a symptom diary following the ingestion of 50g lactose offers the patient flexibility with regard to timing and place where to perform the test. Genetic testing involves a “simple blood draw” but the price of this test is high and not readily available everywhere. Using the symptom response to lactose challenge as an initial test would allow screening out patients who don’t develop symptoms (20-30% of patients referred for testing).

There are only few recent studies evaluating the relationship between symptoms and the result of the H2-BT. Hermans et al. evaluated the severity of bloating, flatulence, abdominal distension and diarrhea in 309 consecutive patients referred for lactose H2-BT as part of the work-up of unexplained abdominal complaints. Patients were asked to score their symptoms semi-quantitatively as 0 (no complaint), 1 (moderate complaint) or 2 (severe complaint). The total symptom score (TSS) was computed as the sum of these symptoms. In this group of patients, they noticed an abnormal H2-BT (i.e. raise of exhaled H2 concentration >20 ppm above baseline following the ingestion of 50g lactose) in 39.5% of patients. The mean TSS of patients with a positive H2-BT (TSS = 1.65) was significantly (p<0.001) higher than the mean score of patients with a negative H2-BT (TSS = 0.96). In addition, the authors noted that the peak H2-excretion was higher in patients with higher TSS compared to those with low TSS. Based on these data the authors concluded that gastrointestinal symptoms after 50g lactose challenge are strongly associated with the amount of breath H2
excretion. Unfortunately the authors did not provide an additional analysis of individual symptoms.

Suarez et al performed a randomized, double-blind, controlled study comparing symptoms in 30 patients with self-reported severe lactose intolerance. Each patient received 240ml of either 2% fat milk containing on average 12.1g lactose or 2% fat lactose-hydrolyzed milk for breakfast over a 2 week period and was asked to rate the occurrence and severity of bloating, abdominal pain / cramps and rectal gas distension during the 24-h period after each meal. The severity of symptoms was assessed on a 6-point scale (0-no symptoms, 1-trivial symptoms and up to 5-severe symptoms). Twenty-one (70%) patients were considered to have lactose malabsorption based on the results of lactose H2-BT (i.e. exhaled H2 concentration raise >10ppm following the ingestion of 15g lactose) while the others were classified as lactose-absorbers. Reviewing the diaries of these patients the authors noticed no difference in the severity of symptoms when patients consumed regular milk and lactose-hydrolyzed milk and no difference between the lactose-absorber and lactose-malabsorber group. Furthermore, although patients believed they were severely lactose intolerant the mean symptom scores recorded in their diaries were in trivial – mild range. These data suggest that even patients who consider themselves severely lactose intolerant can tolerate up to one glass (240ml) of milk a day.

The current study has some limitations. The positive and negative predictive values for individual symptoms and their combination depend on the prevalence of lactase deficiency in the examined population. Thus, these values should be interpreted with caution outside Central Europe. Nevertheless, in our study we calculated the respective likelihood ratio that allow to apply results to different prevalence scenarios. Although data were collected prospectively, we do not have clinical follow-up data to test the appropriateness of the proposed approach for patients who developed symptoms after the ingestion of lactose intolerance. A prospective trial to evaluate the validity and acceptance of the clinical lactose challenge needs to be performed.

Last but not least, since patients included in the present study were patients referred for H2 breath testing, a certain selection bias might be present. Thus, caution is advised when extrapolating present data to the general population but data would be applicable for patients suspected of having lactose intolerance.
In conclusion, the results of the present study offer the basis for developing a simple clinical lactose tolerance test aimed at screening patients who require further testing for hypolactasia.
Study highlights:
- Lactose intolerance is a prevalent condition causing diarrhea, bloating, nausea, borborygmi and abdominal pain
- The present study reports the sensitivity, specificity, PPV, NPV, pos. LR and neg. LR of each symptom developed after the ingestion of 50g lactose to identify patients with lactose intolerance
- The likelihood of an abnormal lactose hydrogen breath test increases parallel to the number of symptoms developed after the ingestion of 50g lactose
- Clinical evaluation of symptoms developed after the ingestion of 50g lactose could be used to screen patients who require further testing for lactose intolerance
Table 1: Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV), positive (LR+) and negative (LR-) likelihood ratios of individual symptoms in 1127 patients

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Total n=1127</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>LR+</th>
<th>LR-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>41%</td>
<td>71%</td>
<td>41%</td>
<td>71%</td>
<td>1.4</td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td>Bloating</td>
<td>71%</td>
<td>69%</td>
<td>54%</td>
<td>82%</td>
<td>2.3</td>
<td>0.4</td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>39%</td>
<td>90%</td>
<td>66%</td>
<td>75%</td>
<td>3.9</td>
<td>0.7</td>
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</tr>
<tr>
<td>Borborygmi</td>
<td>65%</td>
<td>75%</td>
<td>56%</td>
<td>81%</td>
<td>2.6</td>
<td>0.4</td>
<td></td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>55%</td>
<td>72%</td>
<td>49%</td>
<td>76%</td>
<td>2.0</td>
<td>0.6</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Swiss n=746</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>LR+</th>
<th>LR-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>39%</td>
<td>72%</td>
<td>28%</td>
<td>80%</td>
<td>1.4</td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td>Bloating</td>
<td>71%</td>
<td>69%</td>
<td>40%</td>
<td>89%</td>
<td>2.3</td>
<td>0.4</td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>31%</td>
<td>91%</td>
<td>50%</td>
<td>82%</td>
<td>3.4</td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td>Borborygmi</td>
<td>60%</td>
<td>76%</td>
<td>42%</td>
<td>87%</td>
<td>2.5</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>51%</td>
<td>71%</td>
<td>34%</td>
<td>83%</td>
<td>1.8</td>
<td>0.7</td>
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</table>

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Non-Swiss n=381</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>LR+</th>
<th>LR-</th>
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<tbody>
<tr>
<td>Nausea</td>
<td>42%</td>
<td>69%</td>
<td>62%</td>
<td>50%</td>
<td>1.4</td>
<td>0.8</td>
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<tr>
<td>Bloating</td>
<td>70%</td>
<td>72%</td>
<td>75%</td>
<td>67%</td>
<td>2.5</td>
<td>0.4</td>
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</tr>
<tr>
<td>Diarrhea</td>
<td>45%</td>
<td>87%</td>
<td>80%</td>
<td>57%</td>
<td>3.5</td>
<td>0.6</td>
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</tr>
<tr>
<td>Borborygmi</td>
<td>69%</td>
<td>71%</td>
<td>74%</td>
<td>66%</td>
<td>2.4</td>
<td>0.4</td>
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</tr>
<tr>
<td>Abdominal pain</td>
<td>58%</td>
<td>74%</td>
<td>72%</td>
<td>59%</td>
<td>2.2</td>
<td>0.6</td>
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Table 2: Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV), positive (LR+) and negative (LR-) likelihood ratios of 1, 2, 3, 4 and 5 symptoms developed after oral ingestion of 50 g lactose. Patients developing no symptoms (38 positive H2BT and 288 negative H2BT) were used as reference.

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>LR+</th>
<th>LR-</th>
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<tr>
<td>Total (N=1127)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 symptom (N=257)</td>
<td>58%</td>
<td>59%</td>
<td>21%</td>
<td>88%</td>
<td>1.4</td>
<td>0.7</td>
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<tr>
<td>2 symptoms (N=202)</td>
<td>68%</td>
<td>70%</td>
<td>40%</td>
<td>88%</td>
<td>2.3</td>
<td>0.5</td>
</tr>
<tr>
<td>3 symptoms (N=149)</td>
<td>63%</td>
<td>78%</td>
<td>44%</td>
<td>88%</td>
<td>2.8</td>
<td>0.5</td>
</tr>
<tr>
<td>4 symptoms (N=137)</td>
<td>71%</td>
<td>86%</td>
<td>67%</td>
<td>88%</td>
<td>5.2</td>
<td>0.5</td>
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<tr>
<td>5 symptoms (N=56)</td>
<td>55%</td>
<td>97%</td>
<td>82%</td>
<td>88%</td>
<td>16.3</td>
<td>0.5</td>
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<tr>
<td>Swiss (N=746)</td>
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<tr>
<td>1 symptom (N=184)</td>
<td>53%</td>
<td>58%</td>
<td>13%</td>
<td>92%</td>
<td>1.3</td>
<td>0.8</td>
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<tr>
<td>2 symptoms (N=136)</td>
<td>70%</td>
<td>71%</td>
<td>34%</td>
<td>92%</td>
<td>2.4</td>
<td>0.4</td>
</tr>
<tr>
<td>3 symptoms (N=90)</td>
<td>57%</td>
<td>78%</td>
<td>29%</td>
<td>92%</td>
<td>2.5</td>
<td>0.6</td>
</tr>
<tr>
<td>4 symptoms (N=73)</td>
<td>66%</td>
<td>87%</td>
<td>53%</td>
<td>92%</td>
<td>5.0</td>
<td>0.4</td>
</tr>
<tr>
<td>5 symptoms (N=34)</td>
<td>43%</td>
<td>97%</td>
<td>68%</td>
<td>92%</td>
<td>14.0</td>
<td>0.6</td>
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<tr>
<td>Non-Swiss (N=381)</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 symptom (N=73)</td>
<td>63%</td>
<td>61%</td>
<td>41%</td>
<td>79%</td>
<td>1.6</td>
<td>0.6</td>
</tr>
<tr>
<td>2 symptoms (N=66)</td>
<td>66%</td>
<td>68%</td>
<td>53%</td>
<td>79%</td>
<td>2.1</td>
<td>0.5</td>
</tr>
<tr>
<td>3 symptoms (N=59)</td>
<td>69%</td>
<td>78%</td>
<td>68%</td>
<td>79%</td>
<td>3.1</td>
<td>0.4</td>
</tr>
<tr>
<td>4 symptoms (N=64)</td>
<td>75%</td>
<td>86%</td>
<td>83%</td>
<td>79%</td>
<td>5.3</td>
<td>0.3</td>
</tr>
<tr>
<td>5 symptoms (N=34)</td>
<td>63%</td>
<td>96%</td>
<td>91%</td>
<td>79%</td>
<td>14.8</td>
<td>0.4</td>
</tr>
</tbody>
</table>
Figure 1: Number (values on the chart) and percentage (Y-axis) of patients with positive and negative breath tests based on the number of symptoms developed after the ingestion of 50g lactose in all patients (a), Swiss (b) and non-Swiss (c) subgroup.

Total

Swiss

- Number (values on the chart) and percentage (Y-axis) of patients with positive and negative breath tests based on the number of symptoms developed after the ingestion of 50g lactose in all patients (a), Swiss (b) and non-Swiss (c) subgroup.
- Total
- Swiss
Non-Swiss

Percentage of patients with different symptoms:

- No symptoms: 18%
- One symptom: 30%
- Two symptoms: 35%
- Three symptoms: 40%
- Four symptoms: 53%
- Five symptoms: 31%

The chart shows the distribution of symptoms among patients, with different symptoms indicated by bars and percentages.
Figure 2: Comparison of the mean maximal symptom intensity in patients with a positive and a negative hydrogen breath test. Patients with a positive H2-lactose breath test reported more intense symptoms compared to their lactose H2-breath test negative counterparts.
References


