An awareness tool
to recognize cow’s milk-related symptoms in infants and young children
Many infants present with symptoms that can be related to intake of cow’s milk.

Cow’s milk protein allergy (CMPA) however is often not considered as a diagnosis, mainly due to the lack of specific diagnostic marker.

There are two groups of patients:

1. those with obvious CMPA
2. those with unclear symptoms in different organ systems

The first group is easy to recognize:

- consists mainly of infants with immediate/rapid reactions
- most of the time IgE mediated

However, this group represents a minority of all the infants with suspected cow’s milk-related symptoms seen by primary healthcare providers.
In many cases, parents report some or all of these symptoms:

- Infant crying, having ‘colic’
- Difficult defecation or 2-3 loose stools per day
- Regurgitates 4 to 6 times a day
- Mild patches of atopic dermatitis

Due to the lack of diagnostic test for CMPA (other than the challenge test), an awareness tool to recognize cow’s milk-related symptoms for use by primary healthcare providers may increase the awareness and the recognition of symptoms possibly related to cow’s milk, leading to an accurate diagnosis at an earlier stage.

SYMPTOMS OF CMPA

The majority of affected children have one or more symptom involving one or more organ system, mainly the gastrointestinal tract or the skin.\(^1\)\(^2\)

The majority have at least two symptoms and symptoms in at least two organ systems.\(^2\)

About 50%-70% have cutaneous symptoms, 50-60% gastrointestinal symptoms, and about 20-30% respiratory symptoms.\(^3\)

WHAT IS CoMiSS®?

- The CoMiSS® awareness tool should be regarded as a tool to increase awareness of the most common symptoms of CMPA, that in turn can aid an earlier accurate diagnosis.

- The CoMiSS® should increase awareness and knowledge to minimize over- and under-diagnosis and to consider cow’s milk-related symptoms.

- The CoMiSS® is also a tool that can be used to evaluate and quantify the evolution of symptoms during a therapeutic intervention.

- Published data using the CoMiSS® in clinical trials show that the predictive value of the tool is 80% if the score is >12 at the start and decreases to <6 within 2 weeks under an elimination diet with an extensively hydrolysed formula.

CoMiSS® is not a diagnostic test for CMPA. It does not replace a food challenge and its usefulness will need to be evaluated by a prospective randomized study.

WHO IS CoMiSS® INTENDED FOR?

The CoMiSS® is intended for primary healthcare providers who are all too often very limited in time and therefore need a tool that is simple, fast and easy-to-use. It can be filled in by the healthcare provider or by the parents as preparation for the doctor’s visit.
Most patients with obvious CMPA, such as those with anaphylactic reactions or immediate IgE mediated reactions will not be picked-up by the CoMiSS®.

However, many infants present with non-IgE mediated reactions to cow’s milk protein. These infants are difficult to identify as they present with delayed reactions, often moderate to mild in severity and often in different organ systems.

Functional GI symptoms such as regurgitation and vomiting, constipation, crying and colic are considered as non-IgE mediated reactions. Atopic eczema is often not recognized as a possible consequence of ingestion of CMP.

Expert Consensus
How to use
THE CoMiSS® AWARENESS TOOL
IN CLINICAL PRACTICE

CoMiSS® quantifies the number and severity of symptoms.

Suspcion of ‘cow’s milk-related symptoms’ based on the presence of a combination of the following symptoms:

GENERAL DISCOMFORT
Persistent distress or colic (≥ 3 hours per day wailing/irritable) at least 3 days/week over a period of > 3 weeks.

GASTROINTESTINAL SYMPTOMS
Frequent regurgitation, vomiting, diarrhea, constipation (with/without perianal rash), blood in stool.

RESPIRATORY SYMPTOMS
Runny nose (otitis media), chronic cough, wheezing (unrelated to infection).

DERMATOLOGICAL SYMPTOMS
Atopic dermatitis, angioedema, urticaria unrelated to acute infections, drug intake manifestations.
CoMiSS®: Cow’s Milk-related Symptom Score

PURPOSE
The CoMiSS® is a simple, fast and easy-to-use awareness tool for cow’s milk-related symptoms. It increases awareness of the most common symptoms of cow’s milk protein allergy (CMPA) that in turn can aid an earlier diagnosis. CoMiSS® can also be used to evaluate and quantify the evolution of symptoms during a therapeutic intervention.

INSTRUCTIONS
If there is a suspicion of cow’s milk-related symptoms, rate the observed/reported symptoms by choosing the most appropriate score for each type of symptom. Once completed, add the scores together and put the total in the box at the bottom of the scoring form.

**SYMPTOM** | **SCORE**
--- | ---
Crying* | 0 ≤ 1 hour/day  
1 1 to 1.5 hours/day  
2 1.5 to 2 hours/day  
3 2 to 3 hours/day  
4 3 to 4 hours/day  
5 4 to 5 hours/day  
6 ≥ 5 hours/day
Regurgitation | 0 0 to 2 episodes/day  
1 ≥ 3 to ≤ 5 of small volume  
2 > 5 episodes of >1 coffee spoon  
3 > 5 episodes of ± half of the feeds in < half of the feeds  
4 Continuous regurgitations of small volumes >30 min after each feed  
5 Regurgitation of half to complete volume of a feed in at least half of the feeds  
6 Regurgitation of the complete feed after each feeding
Stools (Bristol scale) | 4 Type 1 and 2 (hard stools)  
0 Type 3 and 4 (normal stools)  
2 Type 5 (soft stool)  
6 Type 6 (liquid stool, if unrelated to infection)  
Type 7 (watery stools)
Skin symptoms | 0 to 6 Atopic eczema
| HEAD-NECK-TRUNK | ARMS-HANDS-LEGS-FEET |
| Absent | 0 | 0 |
| Mild | 1 | 1 |
| Moderate | 2 | 2 |
| Severe | 3 | 3 |
| 0 or 6 | Urticaria | NO | YES | 6 |
Respiratory symptoms | 0 No respiratory symptoms  
1 Slight symptoms  
2 Mild symptoms  
3 Severe symptoms

* Crying only considered if the child has been crying for 1 week or more, assessed by the parents, without any other obvious cause.

TOTAL SCORE

READING THE RESULT
The scoring ranges from 0 to 33. Each symptom has a maximal score of 6, except respiratory symptoms where the maximal score is 3.
If final score ≥ 12, the symptoms are likely cow’s milk related. This could potentially be CMPA.
If final score < 12, the symptoms are less likely related to cow’s milk. Look for other causes.

CMPA diagnosis can only be confirmed by an elimination diet followed by an oral food challenge.


Download the CoMiSS® scoring form at: NestleHealthScience.com/CoMiSS

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CRYING

- The duration of crying is evaluated. The longer the crying, the higher the score.
- At least > 3 days/week for 1 week or more, assessed by the parents, without any other obvious cause.
- Crying relates to colic. Colic is defined as > 3 hours crying/day for at least 3 days during 1 week and since at least 1 week.
- Up to 3 hours of crying/day accounts for a score of 3.

Crying*

**SCORE**

<table>
<thead>
<tr>
<th>Score</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≤ 1 hour/day</td>
<td>1 to 1.5 hours/day</td>
<td>1.5 to 2 hours/day</td>
<td>2 to 3 hours/day</td>
<td>3 to 4 hours/day</td>
<td>4 to 5 hours/day</td>
<td>≥ 5 hours/day</td>
</tr>
</tbody>
</table>

Age > 2 weeks, < 4 months

* Should only be considered if the child has been crying for 1 week or more, assessed by the parents and without any other obvious cause.

REGURGITATION

- Using the score for grading the regurgitation.¹
- Rates the regurgitated volume and severity of the regurgitation.

**Regurgitation**

**SCORE**

<table>
<thead>
<tr>
<th>Score</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 to 2 episodes/day</td>
<td>≥ 3 to ≤ 5 of small volume</td>
<td>&gt; 5 episodes of &gt;1 coffee spoon</td>
<td>&gt; 5 episodes of ± half of the feed in &lt; half of the feedings</td>
<td>Continuous regurgitations of small volumes &gt; 30 min after each feed</td>
<td>Regurgitation of half to complete volume of a feed in at least half of the feeds</td>
<td>Regurgitation of the complete feed after each feeding</td>
</tr>
</tbody>
</table>

Age > 2 weeks, < 6 months

Using the well established Bristol stool scale to evaluate the consistency of the stools:\(^2\)

- **Type 1 and 2** indicate constipation
- **Type 3 and 4** are ‘ideal consistencies’
- **Type 5** soft stools
- **Type 6** tends to indicate diarrhea
- **Type 7** indicates overt diarrhea

<table>
<thead>
<tr>
<th>Stools (Bristol scale)</th>
<th>SCORE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 1 (hard stools)</td>
<td>4</td>
</tr>
<tr>
<td>Type 2 (normal stools)</td>
<td>0</td>
</tr>
<tr>
<td>Type 3 (soft stool)</td>
<td>2</td>
</tr>
<tr>
<td>Type 4 (liquid stool, if unrelated to infection)</td>
<td>4</td>
</tr>
<tr>
<td>Type 5 (watery stools)</td>
<td>6</td>
</tr>
</tbody>
</table>

For at least one week

SKIN

- An easy to apply score based on an estimation of the surface covered by the dermatitis, using the surface estimation drawings from burns.

SKIN symptoms

<table>
<thead>
<tr>
<th>SCORE</th>
<th>Atopic eczema</th>
<th>HEAD-NECK</th>
<th>TRUNK</th>
<th>ARMS-HANDS</th>
<th>FEET</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-6</td>
<td></td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mild</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Severe</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

0 or 6 Urticaria NO YES 0 6

Estimated surface:
- 0 = 0
- < 1/3rd = 1
- 1/3-2/3rd = 2
- > 2/3rd = 3

RESPIRATORY

- Respiratory symptoms are considered in the CoMissa® although they have been given less importance (lower weighting) because most of the time chronic cough, runny nose and even wheezing are caused by viral infections.
- However, respiratory symptoms can be caused by cow’s milk.

Respiratory symptoms

<table>
<thead>
<tr>
<th>SCORE</th>
<th>No respiratory symptoms</th>
<th>Slight symptoms</th>
<th>Mild symptoms</th>
<th>Severe symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Chronic cough</td>
<td>Runny nose</td>
<td>Wheezing</td>
<td></td>
</tr>
</tbody>
</table>
The CoMiSS® score ranges from 0 to 33.

Each symptom has a maximal score of six, with the exception of respiratory symptoms (maximal score of three).

An arbitrary cut-off value of ≥12 was selected as the criterion to pick up infants at risk of CMPA. A score of 12 requires the presence of at least two severe symptoms and a score higher than 12 requires the presence of at least three symptoms and the involvement of two organ systems.

**USING THE SCORING FORM**

If there is a suspicion of cow’s milk-related symptoms, rate the observed/reported symptoms by choosing the most appropriate score for each type of symptom.

**Calculate the final score:**

- **Total ≥ 12:** This arbitrary cut-off value indicates that the symptoms are likely cow’s milk related. This could potentially be CMPA. However, a CMPA diagnosis can only be confirmed by an elimination diet followed by an oral food challenge.

- **Total < 12:** symptoms less likely related to cow’s milk. Look for other causes.