Congenital Hyperinsulinism International Collaborative Research Network

Continuous Glucose Monitoring

A Practical Guide for Families and Professionals Managing Hyperinsulinism

What is a continuous glucose monitor (CGM)?

A CGM is a wearable device that uses a small sensor, inserted under the skin, to measure interstitial glucose levels (the glucose in the fluid around the cells under the skin) at regular intervals. The CGM then shares this information via Bluetooth to a smartphone, receiver or smartwatch. Currently available sensors need to be replaced every 7–14 days.

How do CGM readings differ from manual glucometer checks?

Traditional blood glucose checks with a glucometer provide a snapshot of the glucose in the blood at an exact timepoint, whereas a CGM provides readings taken every 5 minutes – resulting in 288 measurements a day. Because a CGM measures interstitial glucose, there is a delay of about 10 minutes between the glucose level in the blood (measured by a glucometer) and the glucose level in the interstitial fluid. Therefore, when there are very rapid shifts in blood glucose, there will be differences between glucometer and CGM readings.

> ⚠ **Always confirm with a glucometer**
>
> In congenital hyperinsulinism (HI), CGM readings can be very helpful for identifying trends and potentially detecting hypoglycemia. However, all decisions regarding the treatment of hypoglycemia should be confirmed using blood glucose values from a glucometer, because these are comparatively more accurate.

If CGM readings cannot replace glucometer checks, what will they add?

A CGM helps families and specialist teams understand how an individual's glucose trends are affected by everyday life: feeds or meals, medicines, activities, illness and the environment. This extra layer of information – especially when supported through review and discussion with their team – can help families identify longer-term patterns that may lead to HI management changes by the specialist team, and help families make behavior changes to reduce vulnerability to episodes of low blood glucose.

CGM trends and alerts can act as a prompt when a person with HI is at risk of imminent hypoglycemia. This is particularly useful for individuals on either continuous medications or continuous glucose/feeds through a G-Button, where an equipment failure can lead to a rapid drop in blood glucose levels – the CGM can alert the family to a possible equipment problem. Families may also find these prompts helpful when managing the competing demands of everyday life, encouraging them to intervene early – for example, to perform a blood glucose check to confirm the CGM's reading, treat hypoglycemia according to your Emergency Hypo-plan, and ensure that all medication and feeds have been provided as per the treatment plan, while continuing to monitor carefully.

The ability to remotely monitor blood glucose levels provides reassurance to parents that these levels are being managed appropriately when a child is attending childcare or school. It also allows children with HI – who frequently report hypoglycemia unawareness – along with their parents and teachers, to feel informed of their blood glucose trends during the school day. This can be particularly helpful in reducing recurrent interruptions during activities that may

precipitate hypoglycemia, such as strenuous physical exercise during sports lessons and sitting examinations for older children. A CGM may also allow parents to demonstrate the need for adjustments to a child's school routine – for example, sport in the late morning leading to more frequent episodes of low blood glucose. The frequency of low blood glucose episodes during the school day can also be used as evidence of the impact of HI on education and the need for trained classroom support.

Research has shown that people with HI are particularly vulnerable to low blood glucose overnight, and that blood glucose checks with a glucometer overnight are less frequent. CGM data may enrich management discussions with your HI team by providing full 24-hour and weekly glucose profiles. A CGM may reveal overnight hypoglycemia, leading to adjustments to the treatment plan and highlighting the need for overnight checks. It is especially useful for children who depend on feeding pumps overnight to deliver continuous milk feeds or dextrose via feeding tubes in the home environment, where it may alert caregivers to problems with feed delivery.

Is CGM the right choice for this individual?

People with HI, families and clinicians should carefully consider the benefits and limitations, for the individual person with HI, of proceeding with or without this intensive monitoring.

For those who are vulnerable to frequent or severe hypoglycemia – for example, those with a short fasting tolerance (<6 hours), those who depend on medications, or those who require continuous overnight dextrose or feeds – the high number of daily interventions in their care increases the potential for technical and human errors. In this situation, CGM alerts can provide an extra layer of reassurance, which can be particularly helpful overnight.

For others, a short trial of CGM may be sufficient to demonstrate good blood glucose stability on their current treatment regimen. Trialling CGM must be a joint decision between the medical team and family. Both written information and regular virtual check-ins may help families feel supported in troubleshooting any issues and promote engagement.

Important considerations when using CGM

CGM is widely recommended for people living with diabetes, in whom it has been shown to improve blood glucose control and reduce hypoglycemia. However, research has not yet demonstrated that CGM use reduces hypoglycemia for people with HI. Studies of HI patient and family experiences and satisfaction with CGM have been positive, highlighting the benefits of remote monitoring, the reassurance it provides overnight and during activities, and improvements in sleep and overall quality of life.

Recently, regulatory authorities have used CGM to evaluate endpoints in clinical studies in HI, and CGM has been used in clinical trials to investigate the effectiveness of novel therapies for HI, demonstrating that CGM data is valuable. The large amounts of data generated from these studies will hopefully improve our understanding of the potential benefits of CGM use for people with HI. More research and development into sensors with high accuracy at low glucose levels, using algorithms specifically designed for hyperinsulinism, are needed.

Important limitations of using CGM

Because CGM has not been designed for use in low blood sugar conditions, the accuracy of CGM has not been demonstrated in the hypoglycemic range. Nor has the use of CGM, and its role in HI management in its current form, been thoroughly evaluated. There are a number of limitations of CGM that can cause distress to some users:

- **False alarms** – particularly at night when the user sleeps on the sensor.
- **Alarm fatigue** – a situation in which the CGM alarms so many times, and the user checks the glucose level with a glucometer and finds it to be normal so often, that they turn off the alarms.
- **Discomfort and skin issues** – some users find sensor insertion painful, and some experience skin irritation from the adhesive.

- **Staying in place** – there are reports of individuals who get very sweaty during sports having a hard time keeping the CGM in place.

Understanding your CGM

1 Getting started with CGM

- **Device familiarisation:** Your device will be supplied with detailed information to help you interpret glucose readings, including which apps you will need to install to allow remote viewing of real-time readings and trend data by parents or HI specialists. Availability of different devices varies by region, so we will not consider the advantages or disadvantages of specific devices in this leaflet.
- **Sensor placement:** Figure 1 shows the zones where wearable CGM devices are typically placed on children, but please consult the directions for your specific device. Many devices are not licensed for children under 2 years; if your infant with HI has been prescribed a CGM, please discuss device placement with your HI team. For adults, sensor placement is typically recommended on the back of the upper arm, but again, please consult the directions for your specific device.

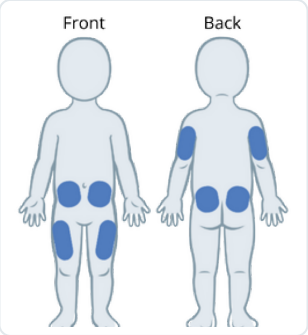


Figure 1. CGM placement zones in children.

- **Sensor insertion:** Follow the guidance that comes with your specific CGM device. Sensor applicators make a loud 'click' that may startle young children, and some individuals report that sensor insertion is painful.
- **Calibration:** If your device is consistently inaccurate (>1 mmol/L [>18 mg/dL] above or below a glucometer reading), calibration may help improve the accuracy of readings. Do not calibrate when glucose trends are changing rapidly (↑ or ↓). Not all CGM devices need to be calibrated.
- **Normal range:** Check your Hypo-plan or consult your HI specialist to confirm your acceptable blood glucose range. These values can be changed within the CGM receiver or smartphone app.
- **Over-patches and adhesives:** CGMs must be applied to clean, dry skin. It is recommended to wipe the skin with an alcohol wipe to remove any bacteria, oil or debris, and to allow the skin to dry fully before applying the CGM. The adhesive patch that holds the CGM to the skin continues to develop its bond over 24 hours, so consider this when choosing clothing and activities in the first 24 hours after a sensor change – for example, sun cream, sweating, bathing and swimming may reduce the effectiveness of the adhesive. Body hair may also need to be removed from the patch of skin where the sensor will be worn. Some individuals use additional adhesives and over-patches sourced from independent retailers; however, it is important to give feedback to your sensor provider and specialist team if you are having issues with sensor adhesives, as they may be able to provide troubleshooting advice and alternative solutions.
- **Removing the sensor:** As with removing a sticking plaster (band-aid), some people may find sensor changes distressing; therefore, adhesive remover is recommended. These are widely available as sprays, liquids and wipes. Follow the recommendations for the individual device.

2 Monitoring and interpretation

Regularly check the CGM data to monitor the blood glucose levels of the person with HI. Set up alerts for both high and low glucose values – acceptable normal-range limits should be detailed in your Emergency Hypo-plan, and CGM alert settings should also be confirmed with your specialist team. For children using CGM, ensure that all those caring for the child are trained on how to interpret alerts – for example, to double-check any alert reading with a blood glucose meter, and then follow your personal Emergency Hypo-plan if a low is confirmed.

↑↓ If CGM readings are within your normal range (e.g. 72–180 mg/dL or 4–10 mmol/L)

Continue to do blood glucose checks with a glucometer as advised by your HI team. Glucose levels should be checked with a glucometer if there are signs or symptoms of hypoglycemia (even if CGM readings are normal) or if the CGM alerts you to levels dropping quickly (↓).

A recent study found that when CGM readings are above 90 mg/dL (>5 mmol/L), approximately 1 in 100 readings may fail to detect a true low blood glucose level. When the CGM is displaying values closer to the hypoglycaemic range, it is more likely to miss hypoglycaemia. (Worth et al.)

↓ If CGM readings are low (e.g. <70 mg/dL or <3.9 mmol/L)

Check levels with your blood glucose meter before giving treatment, as the actual blood glucose level may be within the normal range. If blood glucose levels are consistent with hypoglycemia, treat according to your Emergency Hypo-plan, including performing a manual blood glucose check to ensure treatment was sufficient.

CGM accuracy is one of the main concerns of families with HI. The ability of CGM to detect hypoglycemia in HI is variable (around 50%). Some hypoglycemic episodes will be missed (around half), and sometimes normal glucose levels will be incorrectly identified as hypoglycemia by the CGM. Therefore, CGM alone should not be used as an acute hypoglycemia detector in HI.

↓↓ If trend arrows are pointing down (↓ or ↓↓)

Always check the level with a glucometer, particularly if CGM readings are coming down rapidly or are close to the hypoglycaemic range.

Pressure applied to the wearable sensor (e.g. when sleeping on it at night) can cause ‘compression lows’, where a sensor may indicate a sharp drop in glucose readings, display ‘LOW’ or ‘sensor error’, and the trend arrow may disappear. It is vital to perform a glucometer check to ensure blood glucose levels are in the safe range, then reposition the individual and wait for the sensor to recover from compression.

↑ If CGM readings are persistently high (>180 mg/dL or 10.0 mmol/L)

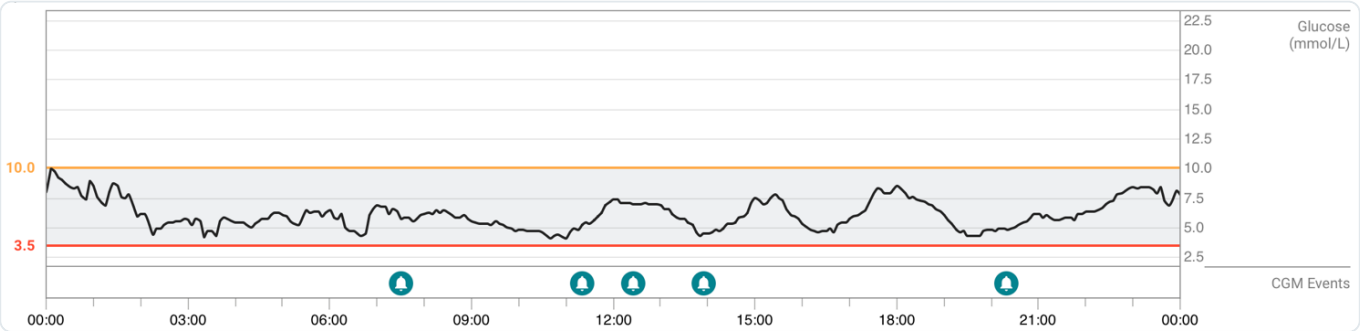
Confirm that CGM readings are accurate by checking levels on a glucometer, and if they are persistently high, contact your HI team for further advice. Some people with HI will have high levels when they are ill; others can have spikes of blood glucose due to stress or medication. Always seek urgent medical advice if the individual with HI is unwell. Each CGM user should have a plan in place, before starting CGM, with advice on when to call your doctor for high glucose levels.

3 Pattern recognition and trend analysis

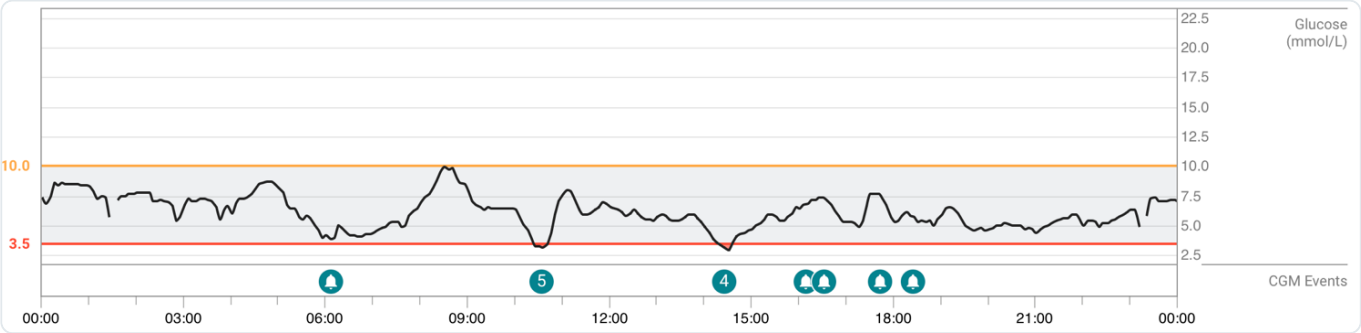
CGM is not reliable enough to replace regular blood glucose checks with a glucometer for people with HI. However, the information a CGM provides can enhance understanding of glucose trends throughout the day and help identify episodes of hypoglycemia. Families may identify recurring vulnerable times of day, specific weekdays or specific activities that require closer monitoring. This can allow families to anticipate and prevent recurring hypoglycemic episodes through small adjustments in routine or intake. Please note that it is important to always consult your HI specialist before making changes to the treatment regimen.

Please contact your HI team if there are recurrent hypo- or hyperglycemic episodes, or patterns, that you would like to discuss – they will not be reviewing your CGM glucose profiles in real time or be aware of low alerts.

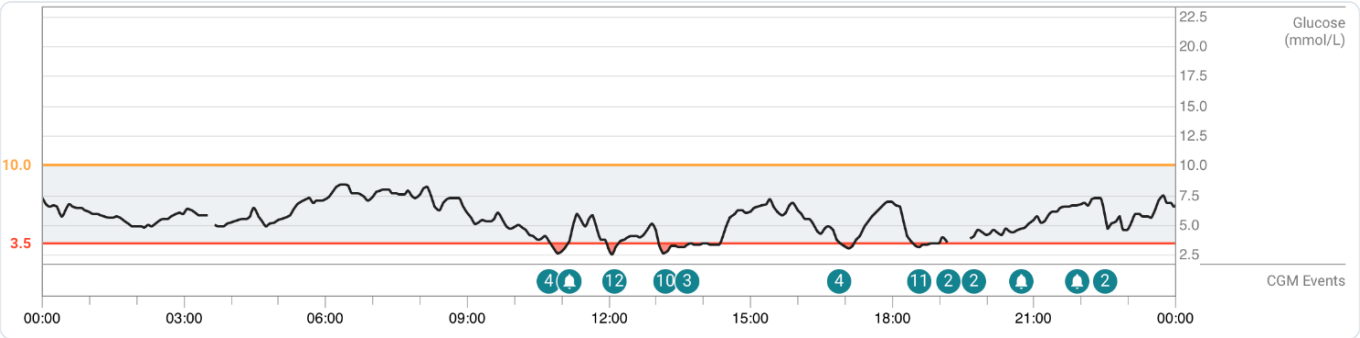
Case scenarios



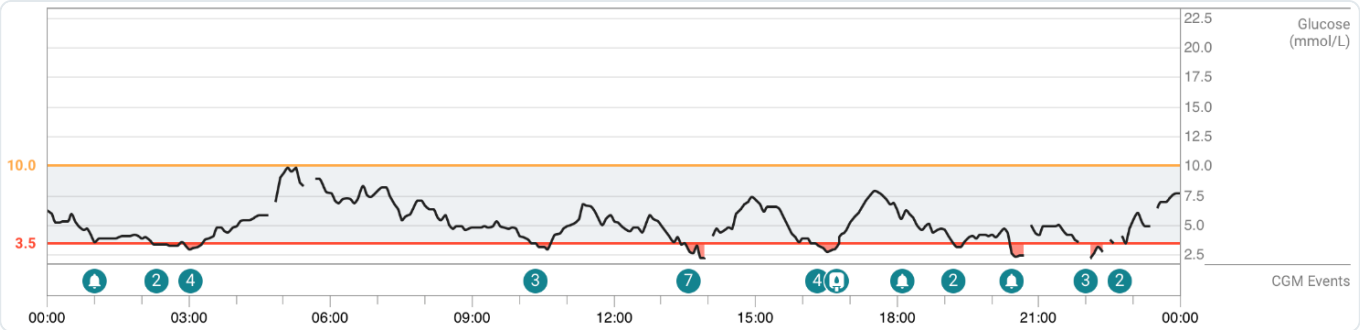
Case 1. A glucose profile for a person with HI. 100% of the day was in range 3.5–10 mmol/L (63–180 mg/dL), with 5 alerts ('CGM events'). Note the peak-and-trough pattern seen in response to slow bolus feeds given during the day at 11:00, 14:00 and 17:00.



Case 2. This individual had 2 brief hypoglycaemic events at 10:30 and 14:30, which were confirmed on a glucometer and treated promptly. Note how alerts are clustered around these times, or when there is a sharp change in the glucose trend (14 alerts in total).



Case 3. This CGM delivered a total of 53 alerts over 24 hours, alerting the family to 4 discrete hypoglycemic episodes, confirmed on a blood glucose meter (2.9–3.3 mmol/L) at 10:45, 12:00, 13:39 and 16:57. Without a CGM in place to prompt time-sensitive blood glucose meter checks and emergency treatment, these episodes may have been more severe and prolonged. The detection of this increase in the frequency of hypoglycemic episodes prompted discussion with the HI specialist center for advice.



Case 4. This daily review highlights both the role of CGM in alerting families to issues overnight and how small inaccuracies (in this case, the CGM was under-reading by ~0.5 mmol/L) can lead to alarm fatigue for families.

- **Overnight feed dependence:** At 00:30 the overnight continuous gastrostomy feed delivery was interrupted due to an 'air in line' alert on the feeding pump. The parents did not wake to the feeding pump alarm. The CGM began to alert at 01:00, eventually waking the parents with a series of 4 critical low alerts at around 03:00. The continuous feed was promptly restarted, and a potentially severe and prolonged episode of overnight hypoglycemia was avoided.
- **Sensor inaccuracies can lead to alarm fatigue:** During this 24-hour period the CGM provided 30 alerts; however, despite responsive glucometer checks and calibration (16:45), no hypoglycemic episodes were identified. Small variations from blood glucose meter values can dramatically increase alarm frequency for people with HI. Note also the missing data points at the end of the time window – an indicator that the sensor may be failing.

For more information on using CGM to support someone with HI, seek advice and support from their **HI Specialist team** or the HI community on the **CHI International Family Forums**.

CHI Collaborative Research Network

This guide, *Continuous Glucose Monitoring: A Practical Guide for Families and Professionals Managing Hyperinsulinism*, is prepared as part of Congenital Hyperinsulinism International's (CHI) Collaborative Research Network (CRN) initiative to improve the lives of children, young people and families experiencing a most challenging illness. The CHI CRN includes an international group of HI experts and patient advocates working together to solve the most important research questions that will lead to the best outcomes for people living with HI. The need for this statement arises from discussions with hundreds of parents, young people, doctors, nurses and other professionals from around the world.