CamAPS FX

User Manual

1 IMPORTANT SAFETY INFORMATION

Indications for Use

CamAPS FX is an Android app intended for managing glucose levels in people with type 1 diabetes, aged 1 year and over, using a hybrid closed loop approach (automated basal insulin delivery with manual bolusing for meals). Additional age restrictions may apply depending on the chosen continuous glucose monitor and insulin pump.

CamAPS FX requires an insulin pump and a continuous glucose monitor (CGM) to fulfil its intended use. The list of supported insulin pumps and CGMs is provided in this User Manual.

CamAPS FX is intended for use with rapid or ultra-rapid insulin analogues including diluted analogues.

Warnings

- Please review the product instructions before using the CamAPS FX app. The instructions contain important information on the performance characteristics of the app.

- Parents/guardians of young children utilizing the CamAPS FX app are advised to become familiar with the operation of the app, and ensure the status of the system is regularly reviewed.

- Failure to use the CamAPS FX app and the required devices according to the instructions for use and all indications, contraindications, warnings, precautions and cautions may result in hypoglycaemia (low blood glucose) or hyperglycaemia (high blood glucose) occurrence. Seek medical advice when appropriate.

- In general, sensor accuracy is less studied in infants, pregnant women and those on renal dialysis treatment or with critical illness and therefore greater caution may be required in these user groups.

- Do not use the CamAPS FX app if sensor glucose reading is unreliable especially when the sensor is over-reading. If your sensor reading does not match your symptoms or expectations, use a capillary blood glucose value to assess the sensor accuracy and to calibrate the sensor, as appropriate. Sensor over-reading could result in over delivery of insulin, which may lead to hypoglycaemia.

- Prior to using Auto mode, confirm if the glucose sensor you are using requires calibration in accordance with the manufacturer recommended calibration procedure.

- Ensure that the insulin pump is correctly configured by a healthcare professional prior to using with the CamAPS FX app.

- When using the CamAPS FX app it is important that all boluses and meals are recorded within system, as to ensure these are taken into consideration by the Control Algorithm. Failure to record all meal/boluses could result in under/over delivery of insulin during Auto mode.

- Automatic updates of the app or your device operating system can change settings or shut down the app. Always update manually and verify correct device settings afterward.

- Do not install the app on a rooted device. These devices have modified security features, which makes them less secure. The CamAPS FX app will not operate on a rooted smart device.

- If using an incompatible smart device or operating system, a reliable communication with the insulin pump and the CGM cannot be guaranteed.

- CamAPS FX account holders are advised to create strong passwords and to change their password at regular intervals.

- Ensure your smart device is locked using a PIN or a more secure method such as a password or your fingerprint. Without a secure lock, you will not be able to use the bolus calculator.

- Ensure display settings of your smart device, such as brightness or screen resolution, are appropriate for the level of ambient light and quality of your sight. Adjust display settings accordingly.

- If the display of the smart device malfunctions to the extent that you are unable to determine status of the CamAPS FX app, or your smart device is damaged, it is advised not to use the app until device is repaired and performance verified. If it is not possible to deactivate the CamAPS FX app, depower the phone and revert to manual control of pump.

- It is advised that users of the CamAPS FX app regular verify alerts (sound/vibration) are working effectively on your smart device, as to ensure the user is aware of any system status changes during Auto mode. It is also advised not to silence alerts on the smart device during use of the CamAPS FX app, unless essential.

- When using/charging your smart device that hosts an active CamAPS FX app, good housekeeping is advised to mitigate against trip hazards from trailing cables. The smart device should also be easily accessible to the user during the night, and positioned to avoid accidental user initiated input.

- Users are advised to set correct time on the smart device hosting CamAPS FX app. All graphs displayed on the CamAPS FX app shall display all activity using the time of occurrence on the smart device hosting the app.

- When using the CamAPS FX app for glucose control, it is very important that users comply with national driving standards and recommendations to avoid hypoglycaemia when driving.

- For earlier versions of Dana Diabecare RS insulin pump, the ‘Decreasing ratio’ has to be set on the CamAPS FX app. Incorrect selection of the

Decreasing ratio will result in an incorrect reporting of active insulin values by the app which may result in incorrect correction insulin boluses.

- Although the CamAPS FX app is a medical device, the smart device on which it is hosted is not, and as such is not built to the same electrical safety standards as a medical device.
- To use CamAPS FX in Auto mode during a flight, switch to ‘flight mode’ then turn Bluetooth on. Follow any additional advice related to the connected devices. Contact your airline for their policy.

- Before you decide to stop using the CamAPS FX app, it is important that you consult your health care professional who may review your insulin pump settings.

- Do not share your CamAPS FX account login details with anyone as a safety precaution and to prevent misuse of your data.

- You are responsible for securing your smart device and using it safely. If you suspect a cybersecurity incident involving CamAPS FX, contact customer support.

- Do not use applications which could compromise cybersecurity of your smart device.

- When linked to mylife YpsoPump: You will be required to enter your bolus calculator settings on the CamAPS FX app. These settings determine how the bolus calculator calculates your suggested bolus. It is therefore very important that these settings are correct. Do not make any settings without discussing these previously with your physician or diabetes counsellor. Please make sure that a trained healthcare professional with experience in diabetes management supervises the initiation and programming of the bolus calculator.

- When using Companion: not all CamAPS FX features are available. Data cannot be shared, data entry and control of the actual insulin pump is not possible.

Note: Any serious incident that has occurred in relation to CamAPS FX should be reported to CamDiab or CamDiab Distributor, and to the relevant authority in the country of residence.

2 GETTING ACQUAINTED

Definitions

Term	Meaning
Android	Operating system used in smart devices
App or Application	Software installed on a smart or mobile device
Auto mode	Mode of operation where insulin infusion is modulated by Control Algorithm; consists of repeated closed loop cycles
Basal (insulin) profile	A sequence of basal insulin rates over 24 hours pre-programmed on an insulin pump
Basal (insulin) rate	The insulin infusion rate pre-programmed to be delivered by insulin pump at a given time
Bluetooth	A technology that allows devices to communicate wirelessly with each other
Boost	Mode of operation when an increase in insulin needs is assumed
CamAPS	Cambridge Artificial Pancreas System
CGM	Continuous Glucose Monitor
Closed Loop (CL)	Mode of operation where the insulin infusion is modulated by Control Algorithm; consists of repeated closed loop cycles; also known as Auto mode
Closed loop cycle (CLC)	A periodically repeated sequence of events comprising: (i) running the Control Algorithm and (ii) initiating the recommended insulin delivery on the insulin pump
Confirmatory message	A message that is displayed on the smart device to confirm execution of a desired command
Control algorithm (CA)	Software running on the smart device calculating insulin delivery
Default	A manufacturer's preset option for a device setting
Ease-off	Mode of operation when a reduction in insulin needs is assumed
Hybrid closed loop	An approach where closed loop modulates basal insulin and the user is required to bolus for meals manually
Open loop (OL)	Mode of operation where insulin infusion is delivered at a pre-programmed basal rate or temporary rate set by the user
Temporary basal rate	Insulin infusion rate of limited duration overriding pre-programmed basal rate
Terminating condition	Condition which causes Auto mode to turn off
Total daily dose (TDD)	Insulin amounts administered from 00:00 to 24:00 over a given day
Warning message	A message that is displayed on a smart device when a potential problem is detected

Resources

Guides

This User Manual gives you the most comprehensive overview of the CamAPS FX app, covering the features, important safety information and more. You can view the manual from inside the app by tapping **Main Menu > Help > User Manual**.

Printed copy of the IFU can be requested by contacting CamDiab representative or distributor.

In-App Help

You will find an information icon in the top right corner of many of the CamAPS FX screens. Tapping on the icon brings up a pop-up window with additional information related to the screen. Frequently asked questions are accessible by tapping **Main Menu > Help > Frequently Asked Questions**.

Introduction to Closed Loop

A healthy pancreas releases insulin according to the body's needs. As a result a normal, narrow range of blood glucose is maintained. In type 1 diabetes this function of the pancreas is lost, leading to the need to inject insulin to control blood glucose. By inserting a very thin catheter under the skin we can mimic the action of the pancreas by using an insulin pump to infuse the correct dosage of insulin for the body's needs. A continuous glucose sensor, also known as continuous glucose monitor (CGM), measures glucose in the subcutaneous tissue allowing the calculation and delivery of insulin required in a continuous and uninterrupted fashion.

The continuous glucose sensor and the insulin pump are two of the three necessary components of a closed loop system also known as an artificial pancreas. The remaining component is a closed loop algorithm housed on a compatible smart device that calculates the insulin dose based on the glucose sensor readings. Those three interlinked components form what we call a "closed loop" (see Figure 1).

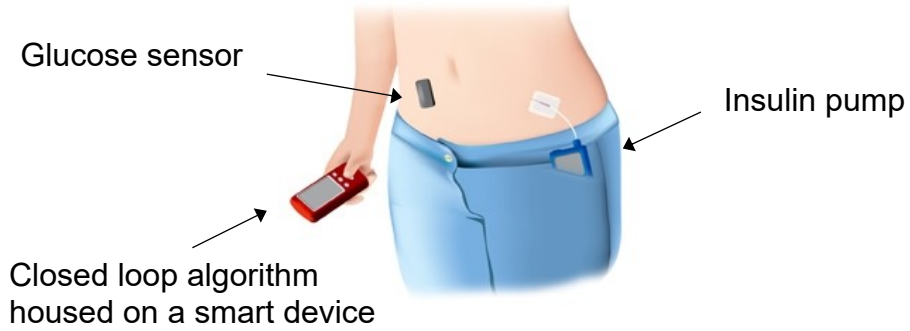


Figure 1: The components of a closed loop system.

What is CamAPS FX?

CamAPS FX is an app that runs on an android smart device. The app is designed to work with a pre-defined selection of commercially available insulin pumps and continuous glucose monitors. Please refer to Appendix A for the list of supported pumps and for pump specific information; refer to Appendix B for the list supported CGM devices and for CGM specific information.

The app also allows data upload to the cloud for data visualisation and remote monitoring. See Figure 2 for an example configuration of a closed loop system with CamAPS FX app.

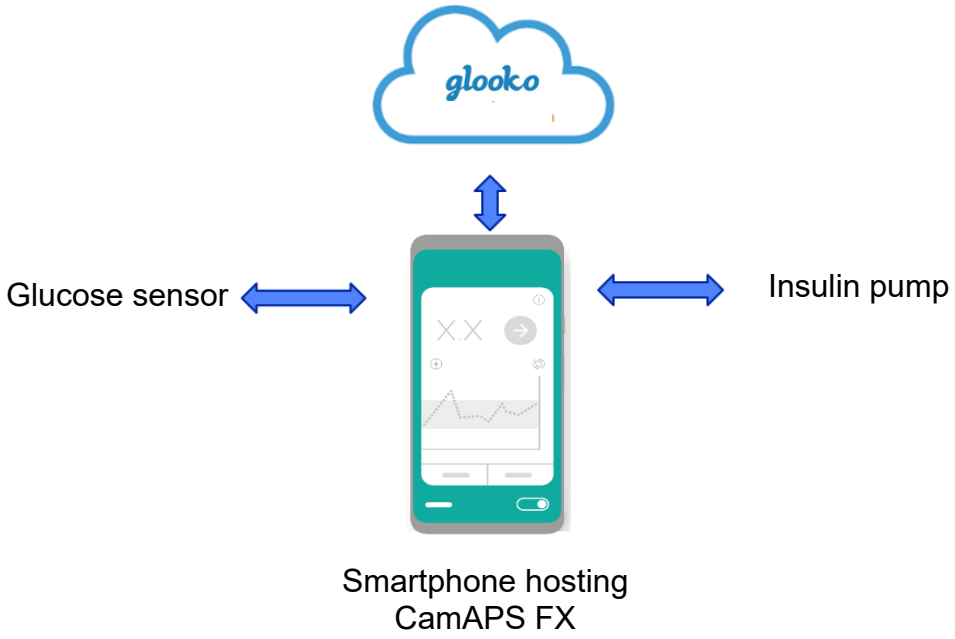


Figure 2: Example configuration of the closed loop system with the CamAPS FX app residing on an Android smartphone.

For a list of smart devices and operating systems compatible with CamAPS FX see the 'System Specifications' section of this User Manual.

Modes of Operation

The CamAPS FX app operates in one of the following modes:

Auto mode 'Off' (open loop)

Auto mode Off is the mode of operation most familiar to current pump users. In this mode of operation, the pump operates at the pre-programmed basal profile, or as instructed by the user. The communication with the CGM is maintained and the sensor glucose information is displayed.

Auto mode Off is the default mode of operation on system start-up.

Auto mode 'On' (closed loop)

Auto mode or closed loop mode is a mode of operation where insulin delivery is directed by the app replacing pre-programmed basal insulin delivery.

Auto mode 'Attempting'

Auto mode 'Attempting' is a mode of operation when the app is attempting to enter Auto mode but a condition is preventing it from doing so. The reasons leading to 'Attempting' auto mode include:

- Sensor glucose data unavailable (includes sensor warmup)
- Loss of communication with insulin pump
- Pump insulin delivery suspended
- Total daily insulin dose exceeded (Dana pump)
- Bluetooth turned off (pump or smartphone)
- Extended bolus disallowed on the pump (Dana pump)

The 'attempting' mode continues until the condition preventing the start of Auto mode is resolved. When in 'attempting' mode, insulin infusion will revert to the pre-programmed basal rate after approximately 30 minutes.

Note: Information on the condition preventing Auto mode operation can be found by tapping the 'i' icon in the bottom left corner of the screen.

Once Auto mode On is activated by the user, the system will stay in this mode until the user deactivates it.

'Fail safe' mode

In the event of an unrecoverable error or your smart device depowering, your insulin pump will revert to the pre-programmed basal profile within 30 minutes.

CamAPS FX Availability, Installation and Updates

The CamAPS FX app is available to download from designated app portal(s). Follow the portal installation procedure and verify that the installation was successful. Once the app is installed, please check the online portal for updates at regular intervals and update the app when an update becomes available.

You are advised to turn off Auto mode prior to an update and to re-start Auto mode after the update completed.

3 YOUR CamAPS FX ACCOUNT

When running the app the first time, you will need to create a CamAPS FX account by providing an email address and setting up a password. You can also use an existing CamAPS FX account if you already have one.

4 SCOPE OF THE USER MANUAL

This user manual relates to the set up and operation of the CamAPS FX app **ONLY**. Please refer to the manufacturers' documentation for all issues relating to:

- Insulin pump
- CGM transmitter
- CGM receiver (optional)
- Cloud data upload system
- Smart device

5 GETTING STARTED

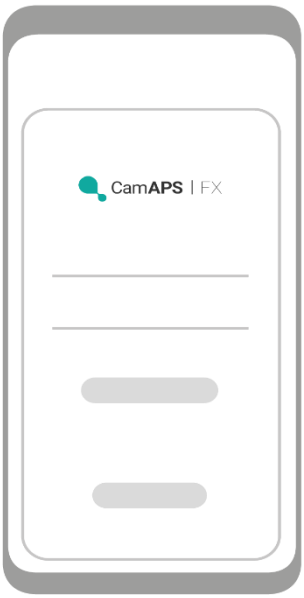
In this section you will learn how to:

- Setup your CamAPS FX account
- Link your insulin pump and your continuous glucose monitor (CGM)
- Start a new sensor

Setting up your CamAPS FX Account

Open the CamAPS FX app and you will see the login screen. If you already have a CamAPS FX account, simply login with your credentials.

If you don't have an account, tap on the 'Sign up' button at the bottom of the screen to register. You must give a valid email address, a confirmation code will be sent to this address. Enter the code to confirm your account.



Once you have logged in to your account the Welcome screen will appear. You are now ready to start setting up your closed loop system. Read the information on the screen, have your pump and CGM device ready and tap 'Start' to proceed. If you wish to access the user manual, you can do it via the link at the bottom of the Welcome screen.

Using Existing CamAPS FX Account

Once you login into an existing CamAPS FX account, such as when you re-install CamAPS FX app or when you install CamAPS FX app on a different smart device, you may receive a notification that CamAPS FX settings have been restored.

The following CamAPS FX settings are restored from cloud CamAPS FX repository:

- Alarm/alert settings
- CGM transmitter details (if using Dexcom, Dexcom G6 transmitter serial number)
- Followers settings
- Cloud data upload settings
- Hidden messages
- Personal glucose target
- Personalised meal sizes
- Carbohydrate units
- Bolus increment
- Bolus calculator settings (when linked to mylife YpsoPump only)

You will be able to review these settings after you completed the remaining login steps.

Linking your Pump and CGM to CamAPS FX

The app needs to link with an insulin pump and a glucose sensor. You may need to refer to your pump and CGM system User Guides for pairing instructions.

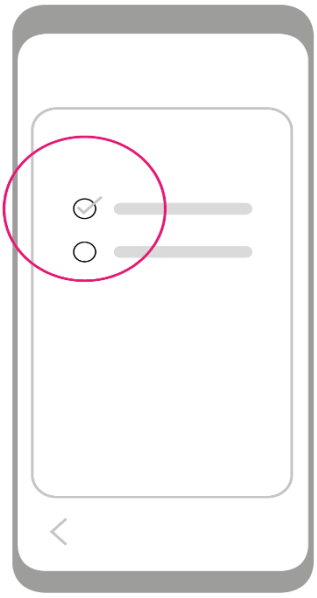
To link your pump to the app, begin by tapping ‘Start’ on the Welcome screen. ‘Select pump’ screen appears: Please allow CamAPS FX to access your location, should the pop-up window appear.

Note: Linking instructions for insulin pumps differ slightly. Please refer to the relevant section below depending on the type of pump you wish to link.

Linking to mylife YpsoPump

- Select ‘mylife YpsoPump’ from the list

- Read the information on the Help screens then tap ‘Continue’
- Select your country of residence
- Wait until serial number of your pump appears on the ‘Scanning’ screen, select it and tap ‘Continue’

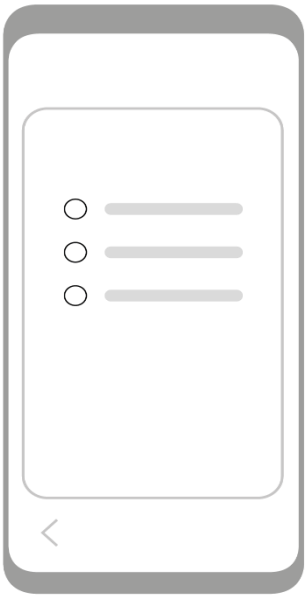


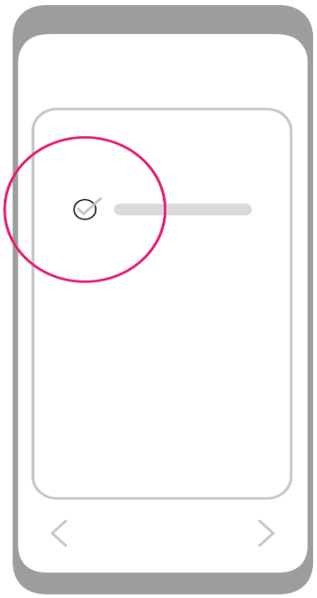
- **Activate pairing on your pump**
- Pop-up window appears: confirm the pump serial number
- When prompted enter pairing code displayed on your pump
- A confirmation message appears that the pump is now linked
- You will be required to set up your bolus calculator settings, see details in section Bolus Calculator Settings

Linking to Dana Diabecare RS

- Select ‘Dana Diabecare RS’ from the list

- Read the information on the Help screens then tap ‘Continue’
- Wait until serial number of your pump appears on the ‘Scanning’ screen, select it and tap ‘Continue’





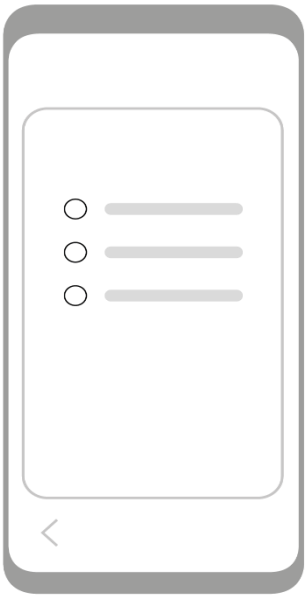
- Pop-up window appears: confirm the pump serial number
- When prompted confirm pairing by pressing ‘OK’ **on your pump**

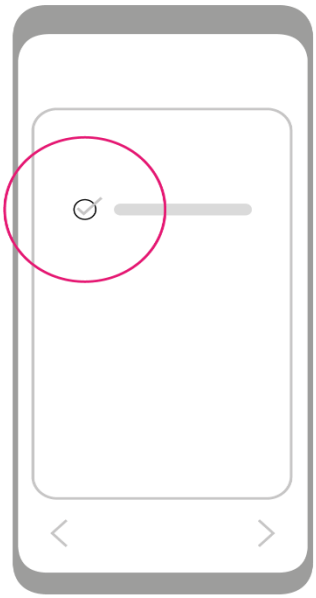
- For the earlier version of Dana Diabecare RS pump
  - A confirmation message appears that the pump is now linked

- For the recent version of Dana Diabecare RS pump
  - You are requested to enter Pairing key 1 and Pairing key 2 as shown on the pump

Linking to DANA-i

- Select ‘DANA-i’ from the list
- Read the information on the Help screens then tap ‘Continue’
- Wait until serial number of your pump appears on the ‘Scanning’ screen, select it and tap ‘Continue’

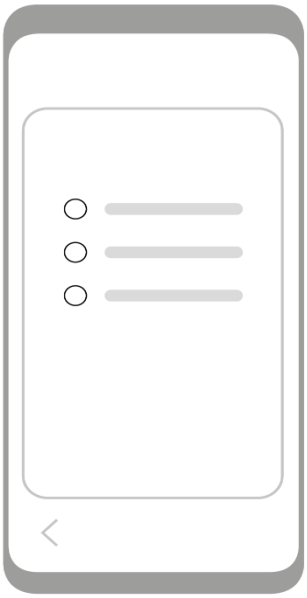


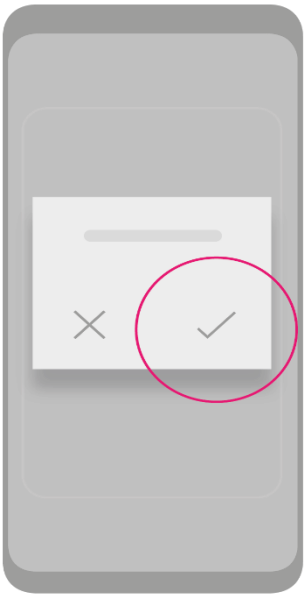


- Pop-up window appears: confirm the pump serial number
- When prompted, start pairing by pressing ‘OK’ on your smartphone and then **on your pump**
- You are requested to enter pairing PIN shown on the pump

Linking to virtual pump

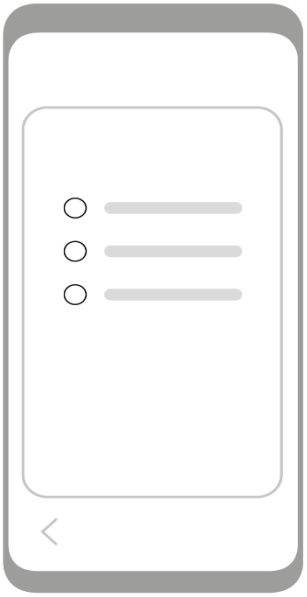
- Select ‘Virtual pump’ from the list
- Read the information on the Help screens then tap ‘Continue’
- Select the suggested serial number of virtual pump and tap ‘Continue’
- Pop-up window appears: confirm the virtual pump serial number





Note: Virtual pump should be used for **training and demonstration purposes** only. Not all CamAPS FX features are available when using virtual pump. No insulin is actually administered.

Linking to Companion



- Select ‘Companion ’ from the list
- Read the information on the Help screen, then tap ‘Continue’
- Select your invitation from the list of invitations and tap ‘Continue’
- Pop-up window appears: confirm the invitation

Note: Companion is used to receive and display data from a pump and glucose sensor worn by another person. Not all CamAPS FX features are available when using Companion.

Trainer identification

After you link CamAPS FX app to an insulin pump, you may be asked to enter identification of a certified trainer who will be training you on CamAPS FX app. Please ask your trainer for his/her identification code or add your own training code.

Identification of trainer and the training code are only required the first time you are using CamAPS FX app.

Linking to your Continuous Glucose Monitor

***Note*:** Linking instructions for CGM monitor differ slightly. Please refer to the relevant section below depending on the type of CGM Monitor you wish to link.

Linking to Dexcom G6

Note: Before linking, insert a sensor and attach the transmitter.

- Select CGM device screen appears: select Dexcom G6 from the list
- Enter your CGM transmitter Serial Number and tap ‘Continue’
- Confirm the serial number of your CGM transmitter

Linking to the FreeStyle Libre 3

- Select CGM device screen appears: select the FreeStyle Libre 3 from the list

Linking to virtual CGM

- Select CGM device screen appears: select your device from the list
- Confirm the suggested serial number of your CGM transmitter

Note: A virtual CGM is available for use with virtual pump only. It cannot be used in combination with a real pump.

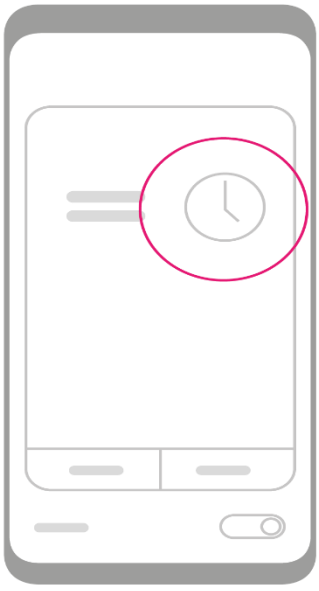
Note: A virtual CGM should be used for **demonstration and training purposes** only. No alerts and alarms will be sounded. Not all CGM features will be available. For example, you will not be able to start and stop sensor.

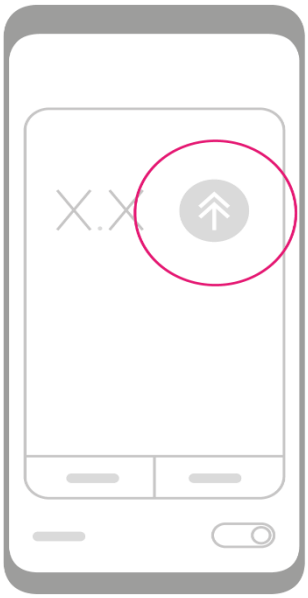
Entering Weight and Total Daily Insulin Dose

- Weight screen appears
- Tap in the field to enter body weight in kg (*allowed range 10 to 300kg in 1kg increments*) then tap 'Continue'
- Confirmation screen appears – check the entered value and tap 'Confirm' or tap 'Cancel' if you wish to make a correction
- Total daily insulin dose (TDD) screen appears
- **Enter an average of TDD over the past 5 days** (*allowed range 5 to 350 Units in 1U increments*) and press 'Continue'
- Confirmation screen appears – check the entered value and tap 'Confirm' or tap 'Cancel' if you wish to make a correction

When using Dexcom G6, the following applies

- Message appears 'Now connecting to transmitter': make sure the sensor is inserted and the transmitter is attached and ready for pairing
- Screen appears 'Now connecting to transmitter': note the time delay and the timer at the top right of the screen





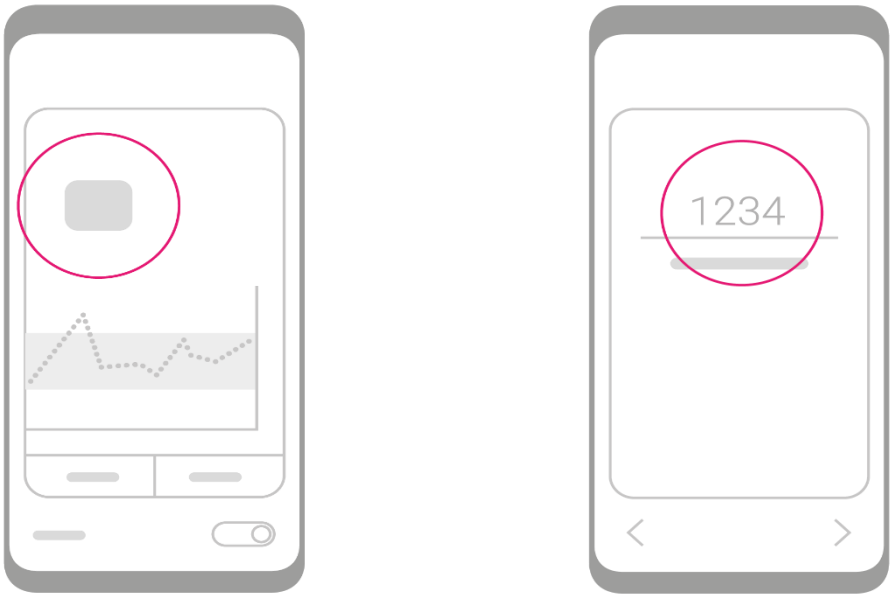
- The home screen appears. If your sensor had already been started, you should see sensor glucose displayed on the screen and the set-up is complete.

Starting a New Sensor

If your sensor had not been started yet, or the current sensor session has ended, you will see a ‘Start Sensor’ button on the screen.

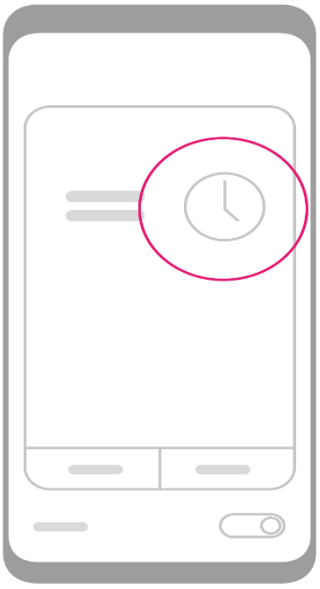
To initiate a new sensor:

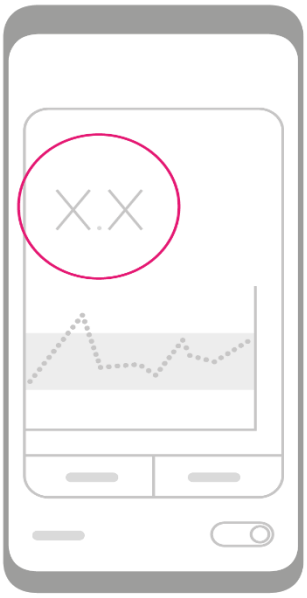
- **When using Dexcom G6**
  - Tap on the ‘Start Sensor’ button; sensor code entry screen appears
  - Tap in the entry field and enter the sensor code, then tap ‘Continue’
  - Confirmation screen appears, tap ‘Confirm’



  - Pop-up window appears informing you that a 2-hour long sensor warmup has started; read then dismiss
  - Message ‘Sensor warmup. Wait 120 minutes’ appears on the screen; timer to the right of the message shows how much time is left until the end of warmup
  - After 120 minutes, your sensor glucose value will appear on the screen

- **When using the FreeStyle Libre 3**





  - Tap on the ‘Start Sensor’ button
  - Follow instructions how to insert and start sensor
  - After starting sensor, message ‘Sensor warmup. Wait 60 minutes’ appears on the screen; timer to the right of the message shows how much time is left until the end of warmup
  - After 60 minutes, your sensor glucose value will appear on the screen

The set-up is now complete and the closed loop system is ready to use.

Note: Before you turn Auto mode on, familiarise yourself with the information on the home screen (The ‘Home Screen’ section), learn how to navigate between the different screens and access additional information (‘Status and Navigation’ section) and how to personalise the system settings (‘Settings’).

Replacing CGM Transmitter when using Dexcom G6

To replace a transmitter that has expired or needs to be changed:

- Go to the Main Menu and tap on the current transmitter Serial Number
- ‘Select CGM device’ screen appears; select CGM type and press ‘Continue’
- Follow linking instructions for the selected CGM device.

Replacing or Re-linking Insulin Pump

To replace or re-link the insulin pump:

- Go to the Main Menu and tap on the current pump Serial Number
- ‘Select pump’ screen appears; select the pump type and press ‘Continue’
- Follow linking instructions for the selected pump type.

6 THE BASICS

This section includes:

- An overview of the Home Screen and the Main Menu
- Instructions on how to access additional information
- Information about alarms and alerts and how to personalise them
- Instructions on how to start and stop closed loop

The Home Screen

The Home Screen consists of three main sections:

- The top section shows the phone status and displays the navigation icons
- The middle section displays closed loop and sensor glucose information, your sensor glucose profile, and has the ‘Boost’ and the ‘Ease off’ tabs at the bottom
- The bottom section shows closed loop status and the Auto mode On/Off button

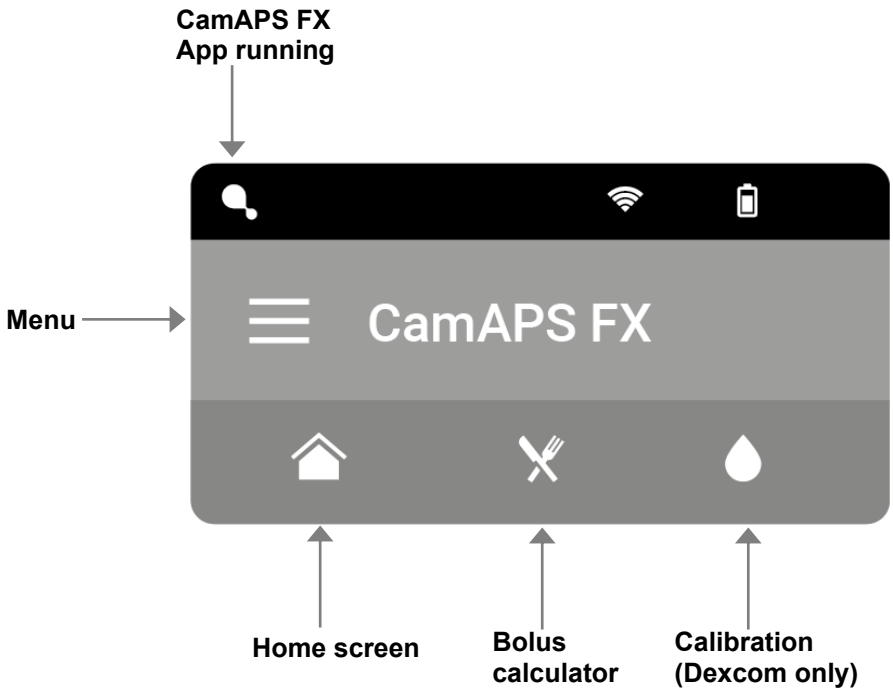
Note: The accuracy of the sensor glucose measurement is determined by the manufacturer of your CGM device. Please refer to the manufacturer's documentation.

The colour of the home screen background changes depending on the status of the Auto mode:

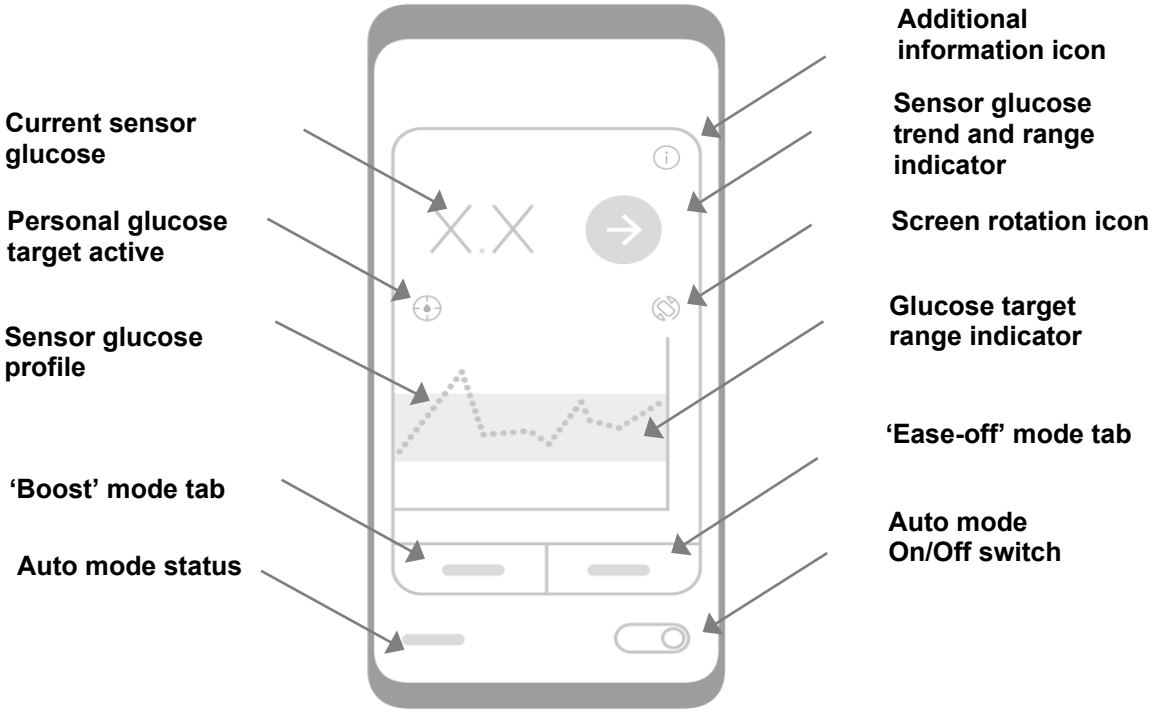
- Auto mode ‘Off’ (**Dark grey**)
- Auto mode ‘Attempting’ (**Orange**)
- Auto mode ‘On’ (**Green**)

Home Screen Overview

The navigation icons and other symbols shown at the top of the home screen:

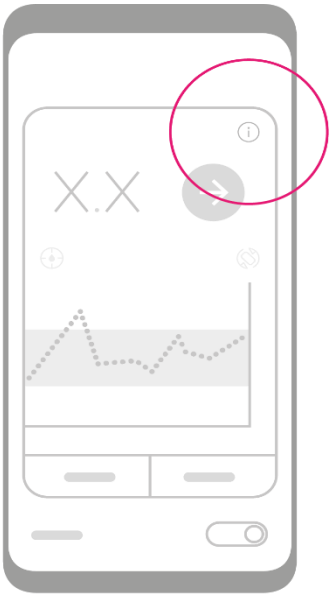


Other Home Screen information is shown below.



Tap on the ‘Additional information icon’ at the top right corner of the home screen to view additional useful information:

- Active insulin (also known as insulin on board)
- Current insulin infusion rate
- Amount of insulin remaining in the pump reservoir
- Pump battery level
- Last time connected to pump
- Last time sensor glucose received
- Average glucose today
- Average glucose yesterday
- Insulin today
- Insulin yesterday



Sensor Glucose Trend and Range

The sensor glucose trend and range indicator is represented by a large coloured circle at the top right corner of the main section of the home screen.

The background colour of the circle indicates sensor glucose status:

- Above high glucose alert level (**yellow**)
- Below low glucose alert level or will be below within 20 minutes in urgent low soon alert state (**red**)
- Within target range (**grey**)

The white arrow inside the circle shows the speed and direction of your glucose trend based on recent readings. A double arrow head indicates a rapid glucose rise or fall.

Glucose within target range and steady

Glucose within target range and falling

Glucose within target range and rising

Glucose within target range and falling fast

Glucose within target range and rising fast

Glucose below low glucose alert range and falling slowly

Glucose above high glucose alert range and steady

Status and Navigation

This section includes:

- How to get around the app
- How to take a quick view of the closed loop and the glucose sensor status

The Navigation Icons

Tapping on one of the four icons at the top of the Home Screen will take you to the following relevant screen:

- Tap on the ‘Bolus Calculator’ icon to open the Bolus Calculator screen where you will be able to initiate your meal bolus
- Tap on the ‘Calibration’ icon to open the calibration screen where you will be able to calibrate your glucose sensor
- Tap on the ‘Home’ icon to return to the Home Screen
- Tap on the ‘Menu’ icon at the top left of the screen to open the main menu

The Menu Overview

Tapping on the ‘Menu’ icon at the top left of the screen, or swiping from left to right, opens up the main menu. From the main menu, you can access the following:

- Add a meal
- Your pump and sensor information
- Personalise your settings
- Add followers to share your data
- Setup cloud data upload account
- View your account details
- Access the help screen
- Stop sensor when using Dexcom G6 sensor
- Start sensor when using FreeStyle Libre 3 sensor

Scroll down the list to view all items. Tap on an item to move to the selected item.
The middle sections provide information about your insulin pump and the continuous glucose monitor. In these two sections, only fields in blue can be edited.

Quick Status Check

Sensor glucose and closed loop status information, including alerts and alarm information, is displayed on the locked screen for quick viewing. To access this information on an unlocked screen on your device, just swipe the screen from the top down to bring it to view.

Starting Auto mode

To start Auto mode, tap the ‘Auto mode On/Off’ button at the bottom right of the screen or slide the button to the right. The confirmation screen will appear, tap ‘Confirm’ or ‘Cancel’.

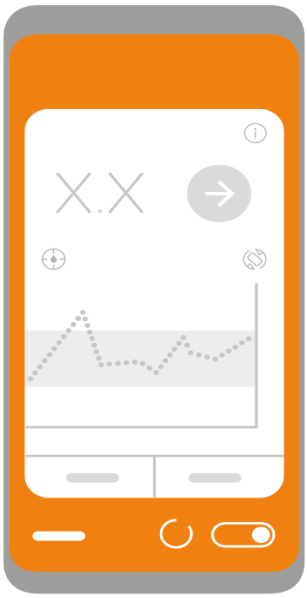
Once confirmed the following changes will be observed:

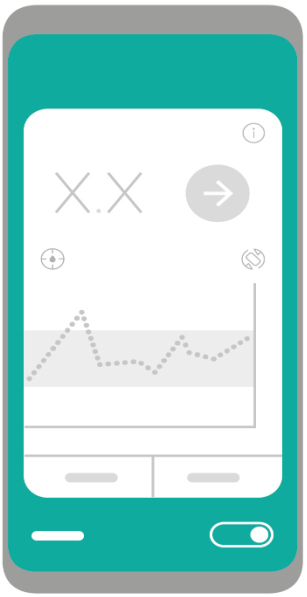
- Information screen appears: review the provided information
- The screen background turns orange indicating that Auto mode is attempting to start – the initialisation may take a few minutes
- Auto mode status at the bottom of the screen changes to ‘starting’

If sensor glucose data are available and after a short while, Auto mode should be successfully started.

The following changes will be observed on the screen:

- The screen background turns green
- Auto mode status changes to ‘On’





Stopping Auto mode

To stop Auto mode, tap the ‘Auto mode On/Off’ button at the bottom right of the screen or slide it to the left. The confirmation screen will appear, tap ‘Confirm’ or ‘Cancel’.
Once confirmed:

- The screen background turns orange
- Auto mode status changes to ‘stopping’

After a short while, the screen background will turn dark grey and the Auto mode status will change to ‘Off’.

Note: Turning Auto mode On and Off is disallowed when the ‘Block’ feature is turned On.

7 THE NEXT STEPS

In this section you will learn how to:

- Access and interpret the detailed graph
- View summary statistics
- Use the Boost/Ease-off modes
- Use the Bolus Calculator
- Add a meal
- Calibrate your sensor (Dexcom G6 sensor only)

Detailed Graph

To view the detailed graph, featuring sensor glucose values and insulin delivery, turn the Home Screen to a landscape position or tap on the ‘rotate screen’ icon.

As well as your sensor glucose and insulin delivery, the graph displays usual (pre-programmed) basal rate, meals, insulin boluses, target glucose range, high and low glucose range and the closed loop status with a resolution as obtained during data acquisition.

The Auto mode status is indicated by a black horizontal bar at the top of the graph (‘closed loop status bar’)

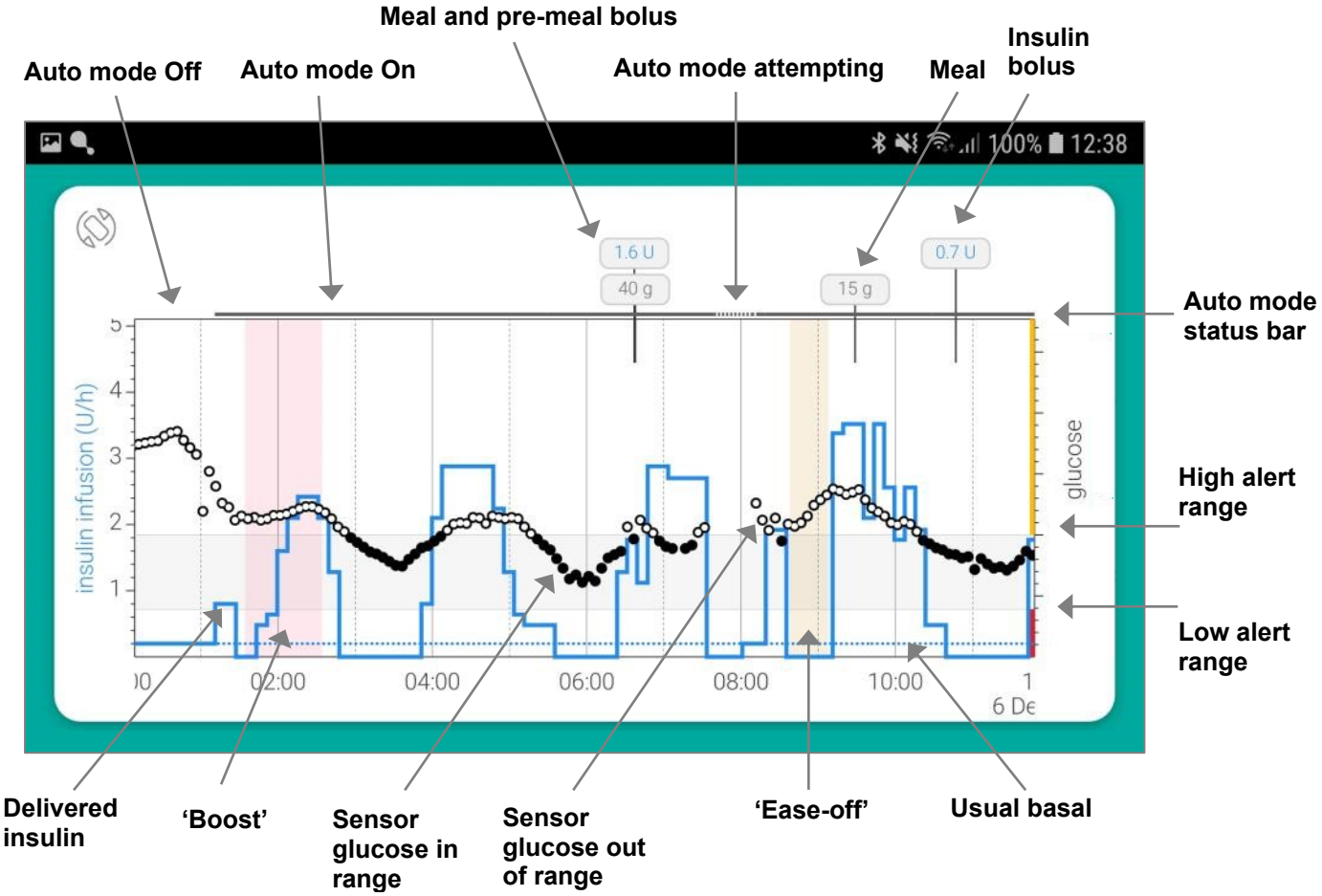
- The solid bar indicates Auto mode ‘On’
- The dashed bar indicates Auto mode ‘Attempting’
- No line indicates Auto mode ‘Off’

The glucose range is shown on the right side of the graph. The yellow line represents the high glucose range (if high glucose alert is on) and the red line represents the low glucose range (if low glucose alert is activated).

The horizontal grey shaded area represents the target glucose range used for visual display and to calculate statistics.

The vertical pink shaded area represents the period when ‘Boost’ was active.

The vertical yellow shaded area represents the period when ‘Ease-off’ was active.



Pinch the time axis to extend or to shrink it, swipe the screen to move the graph back and forth in time. The maximum time-period that can be displayed on the graph is about 15 days. The data are retained when your smart device is depowered or its battery is depleted.

Summary Statistics

To view summary statistics over a chosen period, go to the main menu and tap on ‘Statistics’. You will be able to choose between daily, weekly and monthly summaries, and a summary of the past three months (the maximum period). Once on the daily/weekly/monthly summary screen swipe left and right to move back and forth. Scroll down to view more data.

You can change the threshold values used to calculate the time when glucose was in, above and below target by going to ‘Statistics’ in the ‘Settings’ menu.

It is possible to generate a two-week summary statistics and detailed data review as a PDF file by selecting the relevant option in the ‘Statistics’ screen.

Note: Daily, weekly, monthly, and three months summaries are calculated using data stored on your smart device. Data used to generate the PDF report are retrieved from CamAPS service cloud.

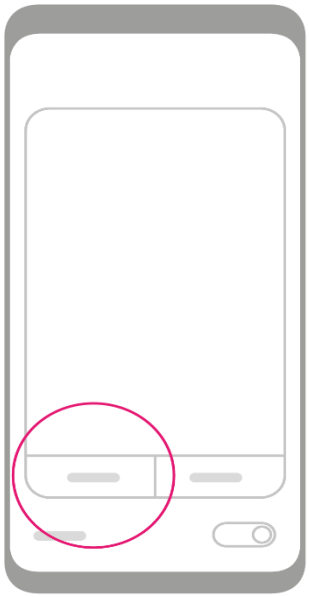
Note: PDF reader is required to generate the report.

Boost

‘Boost’ is a mode of operation that can be used when more insulin is needed. This could be at times of inactivity, increased food intake or during illness or stress. You will be able to set up the duration (from 0 to 13 hours) and the time you want the Boost mode to start.

To start ‘Boost’:

- Tap on the ‘Boost’ tab located on the home screen
- Help screen appears; read and dismiss
- ‘Boost duration’ window appears; tap in the Hrs/Mins entry fields to enter duration



- Tap ‘Next’
- ‘Boost start’ window appears; tap ‘Confirm’ if you want Boost to start immediately
- Blue ‘Boost’ status tab appears below the graph showing that the Boost mode is now active; note the timer on the left of the tab indicating how much time is left before Boost expires
- Should you wish ‘Boost’ to start at a later time, select the desired duration as before and tap ‘Next’; then in the ‘Boost start’ window select ‘Later’
- Clock dial appears; select time to start ‘Boost’ then tap ‘Confirm’
- ‘Planned Boost’ status tab appears below the graph showing that the Boost mode is due to start at a set time; note the clock symbol and the time on the left of the tab indicating the planned time of ‘Boost’

***Note**:* 'Boost' and 'Planned Boost' can be cancelled at any time by tapping on 'Cancel' icon on the right. When cancelled, the 'Confirmation' screen appears; tap 'Confirm' to proceed.

Note: It is strongly recommended that the user closely monitors CGM during periods when 'boost' is active, as to ensure setting is correct.

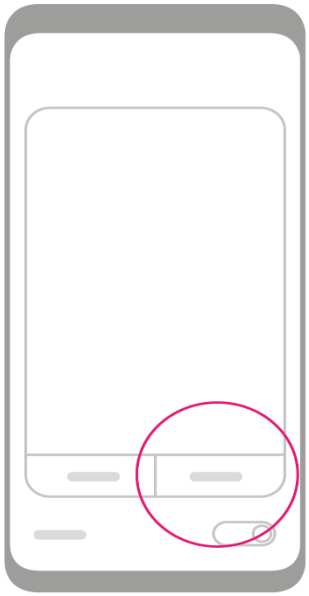
Ease-off

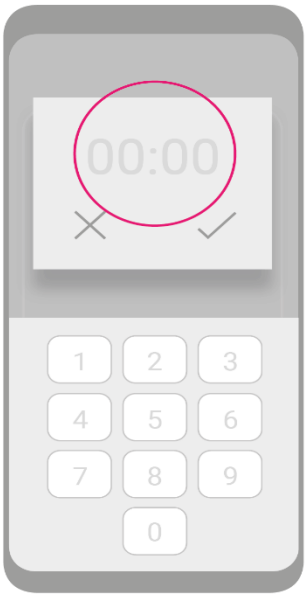
'Ease-off' can be used when less insulin is needed. This could be during exercise or when glucose tends to be low. You will be able to set up the duration (from 0 to 24 hours) and the time you want the 'Ease-off' to start.

The steps for setting up and activating 'Ease-off' are similar to the steps to set up and activate 'Boost'.

To start 'Ease off':

- Tap on the 'Ease-off' tab on the home screen
- Help screen appears, read then dismiss
- 'Ease-off duration' window appears; tap in the Hrs/Mins entry fields to enter duration



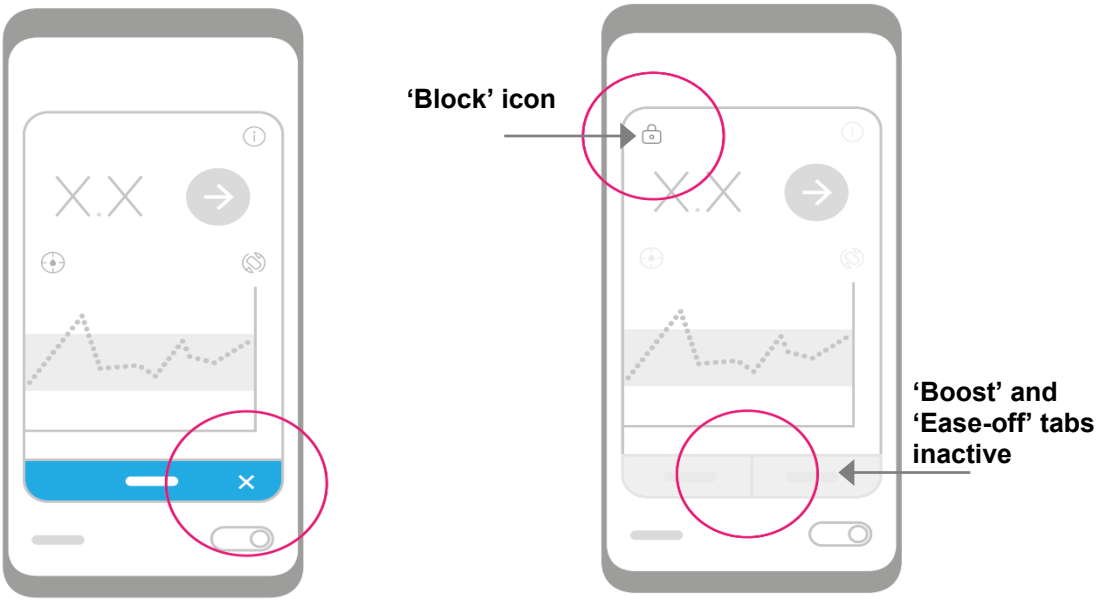


- Tap 'Next'
- 'Ease-off start' window appears; tap 'Confirm' if you want 'Ease-off' to start immediately

- Blue ‘Ease-off’ status tab appears below the graph showing that ‘Ease-off’ is now active; note the timer on the left of the tab indicating how much time is left before ‘Ease-off’ expires

If you wish to start ‘Ease-off’ at a later time, select the desired duration as before and tap ‘Next’; then in ‘Ease-off start’ window select ‘Later’

- Clock dial appears; select the time to start ‘Ease-off’ then tap ‘Confirm’
- Blue ‘Planned Ease-off’ status tab appears below the graph showing that the ‘Ease-off’ is due to start at a set time; note the clock symbol and the time on the left of the tab indicating the planned time of start



***Note**:* ‘Ease-off’ and ‘Planned Ease-off’ can be cancelled at any time by tapping on the ‘Cancel’ icon on the right. When cancelled, the ‘Confirmation’ screen appears; tap ‘Confirm’ to proceed.

***Note**:* ‘Boost’ and ‘Ease-off’ cannot be activated when the ‘Block’ setting is On.

Note: It is strongly recommended that the user closely monitors CGM during periods when ‘Ease-off’ is active, as to ensure setting is correct.

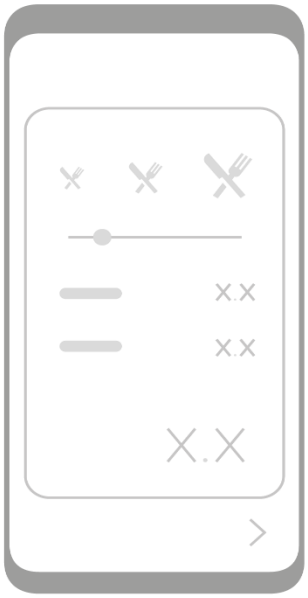
Bolus Calculator

The Bolus Calculator allows you to bolus for meals and snacks, or to calculate and deliver a correction bolus. You are able to initiate a bolus when the Auto mode is On or Off. Only a standard bolus can be administered via the Bolus calculator. An extended bolus or combination bolus (standard bolus combined with an extended bolus) cannot be delivered. The bolus step size, 0.1 unit or 0.05 unit, can be selected in 'Settings'. This option is not available for mylife YpsoPump as the bolus step size is set at 0.1 unit.

Note: You will not be able to start the bolus calculator if your smart device is not secure, e.g. not protected by a PIN.

To start a correction bolus:

- Tap on the Bolus Calculator icon at the top of the screen and wait for a connection to the pump to be established; this may take a short while
- Bolus Calculator set-up screen appears
- Tap in the 'Glucose' entry field; the current sensor glucose level appears; you can change it by tapping on the value in blue; tap 'Confirm' when ready
- Bolus amount based on your insulin sensitivity factor appears to the right of the glucose level; below in brackets is the active insulin on board (this amount will be subtracted) Total amount of insulin to be delivered as bolus is shown at the bottom
- For a correction bolus, leave the Carbs field empty and tap 'Next' to start the delivery



- Bolus delivery screen appears; tap on 'Deliver' to proceed or tap on the amount in blue to edit and change the amount

- Delivery screen appears and the countdown begins;
- Once the insulin has been delivered a confirmation screen appears

To start a meal bolus:

- Tap the ‘Carbs’ entry field and enter the size of meal in the units shown; alternatively, tap on one of the pre-defined meal size icons along the selection line at the top to select a small, medium, large or a very large meal (these can be personalised via ‘Meal size’ in ‘Settings’); tap ‘Confirm’ when ready
- While in Auto mode it is advised not to enter the glucose level when bolusing for a meal, current sensor glucose is greyed out in the ‘Glucose’ entry field and will not be used in the bolus calculation; if Auto mode is off or you wish the glucose level to be taken into account just tap in the Glucose entry field and change or confirm the sensor glucose value; then tap ‘Confirm’
- Bolus amount based on your pump insulin-to-carb ratio appears to the right of the ‘Carbs’ amount;
- Total amount of insulin to be delivered as bolus is shown at the bottom; tap ‘Next’ to start the delivery
- Bolus delivery screen appears; tap on ‘Deliver’ to proceed or tap on the amount in blue to edit and change the amount
- Delivery screen appears and the countdown begins;
- Once the insulin has been delivered a confirmation screen appears

Note: You can stop the delivery at any time by tapping on the ‘Cancel’ icon at the bottom of the screen.

Note: Glucose and carbs can be entered when Auto mode is Off.

Note: When using Dana pump, settings of your bolus calculator, i.e. insulin-to-carbohydrate ratio and correction factor, are read from your pump.

Note: Bolus Calculator is disallowed when ‘Block’ feature is turned On.

Add a meal

To add a meal/snack outside of the Bolus Calculator, go to main menu:

- Select ‘Add meal’
- Tap the ‘Amount’ field to enter the size of the meal
- You may indicate that this is
    - a *meal or snack*, or
    - a *hypoglycaemia treatment*, or
    - a *slowly absorbed meal*
- Tap ‘Continue’
- ‘Meal’ confirmation screen appears; confirm the amount to return to the home screen

Note: When hypoglycaemia treatment is selected, the meal is shown on the detailed graph. However, the control algorithm is prevented from delivering insulin to cover the meal. This reduces the risk of follow up hypoglycaemia.

Note: When slowly absorbed meal is selected, insulin for these carbohydrates will be delivered gradually over the following three (3) to four (4) hours in response to rising glucose levels. Auto mode must be turned on to receive this additional insulin.

Calibrate (Dexcom G6 sensor only)

When calibration of your CGM is required a red blood drop symbol appears on the ‘Calibration’ icon at the top right of the screen. To calibrate your glucose sensor:

- Perform a fingerstick test
  - Wash and dry your hands
  - Take fingerstick with your meter
- Tap on the ‘Calibration’ icon; ‘BG value’ screen appears
- Enter glucose value and tap ‘Confirm’

8 SETTINGS

In this section, you will learn how to:

- Setup alarms and alerts
- Change weight
- Personalise meal sizes
- Change carbohydrate unit
- Setup a personal glucose target
- Bolus calculator settings (applies to mylife YpsoPump only)
- Use the Block feature

Go to the CamAPS FX menu and scroll down the list to below the CGM section to access the ‘Settings’. From the ‘Settings’ menu you can also access Statistics settings, select the bolus step size (when using Dana pump only), select the bolus speed (when using Dana pump only), restore hidden messages and personalise notifications.

Alarm and Alerts

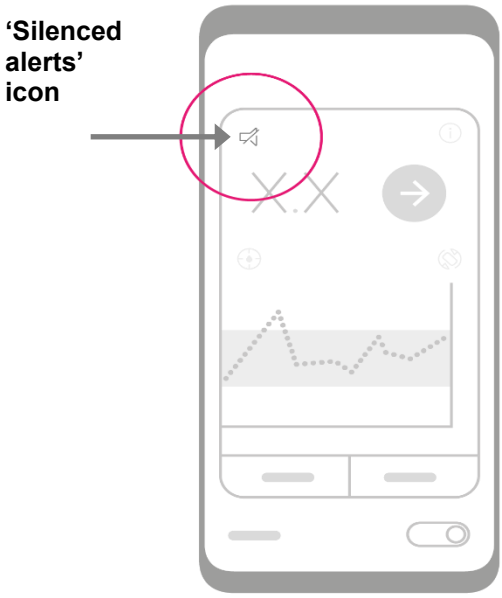
When your glucose level exceeds the set alarm or alert threshold a message accompanied by an audio sound or vibration is displayed on the screen.
The alarm or alert threshold, repeat time and the type of sound can be personalised. Tap on ‘Alerts’ at the top of the main dropdown menu to open the submenu with all available alarms and alerts. Alarms and alerts are specific to the CGM device you are using. Please refer to your CGM user guide for more detailed information about the alarm and alerts.

Menu items from top down (may differ depending on CGM device):

- **Urgent low alarm**: alarms when glucose falls below the set level (cannot be turned off)
- **Urgent low soon:** alerts when glucose is falling fast and will be at Urgent low level in < 20mins
- **Low:** alerts when glucose falls below the set level
- **High:** alerts when glucose rises above the set level
- **Rise rate:** alerts when glucose is rising at or above the set rate
- **Fall rate:** alerts when glucose is falling at or below the set rate
- **Sensor signal loss:** alerts when the app stops receiving glucose readings from your sensor

Pump refill: when it is time to refill your pump with insulin
All alerts can be turned off using the On and Off toggle at the top of the Alerts menu.

Note: The ‘Urgent low’ glucose alarm cannot be turned off.
***Note*:** If the smart device sound setting is on the most restrictive **Do Not Disturb** setting, alarm/alerts may not sound. While the smart device is on a telephone call, alarm/alerts may not sound.



It is also possible to ‘Snooze’ alerts for between 10 and 120 minutes.

Tap on the alarm or alert name to change the settings such as the alarm threshold, repeat time and the type of sound, or to turn the individual alert on or off.

The Alert Schedule lets you pick how your alarm/alerts notify you at different times and on different days. For example, you may choose loud alarm/alerts when you are not at work, but have them only vibrate during work hours.

Alert Schedule lets you add one schedule.
When you turn on the Alert Schedule for the first time, your glucose alert settings are copied into your schedule. The Alert Schedule guides you through creating the name, start time and end time of an additional schedule. You can then change glucose alert settings and select days of the week when Alert Schedule should be used to fit your needs.

Change Weight

During Auto mode, body weight is used to approximate glucose and insulin concentrations within the body. It is advisable to update weight when it has increased or reduced significantly.

To change weight:

- Tap ‘Settings’ and then ‘Change weight’
- ‘Enter body weight’ screen appears showing your current weight
- Tap in the entry field to update the weight and tap ‘Continue’
- Confirmation window appears; tap to confirm the change
- Confirmation message appears

Personalise Meal Size

The meal size icons at the top of the Bolus Calculator represent a small, medium, large and a very large meal. These categories can be personalised.

To personalise meal sizes:

- Tap on ‘Meal size’ in the ‘Settings’ menu; ‘Meal size’ screen appears
- Select each of the categories to update the corresponding meal size
- When updating the ‘Small meal’ size, tap on the icon at the top
- ‘Meal size’ entry screen appears; dial to the desired amount and tap ‘Confirm’
- Note the updated meal size corresponding to the ‘Small meal’

Change Carbohydrate Unit

It is possible to change the carbohydrate unit from grams of carbs (default) to one of the ‘Exchange units’ commonly used in some countries.

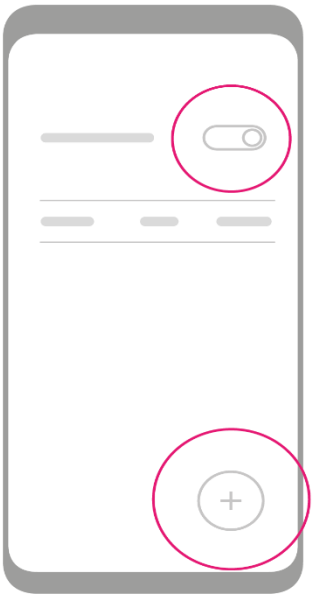
To change the carbohydrate unit:

- Tap on ‘Carbohydrate unit’ in the ‘Settings’ menu; ‘Carbohydrate unit’ screen appears
- Select the required unit from the list and go back to the main ‘Settings’ menu
- The new unit will now be used; select ‘Meal size’ option to view the meal sizes expressed in the newly selected units

Setting up a Personal Glucose Target

The default glucose target of 5.8 mmol/L used during Auto mode can be personalised. You can set your own target in 30min steps via the 'Personal glucose target' option in 'Settings'. Before activating, please read the help information about personal targets by tapping the information icon at the top right of the 'Personal target' screen.

To activate your personal target:



- Tap on 'Personal glucose target' in 'Settings'
- 'Personal glucose target' screen appears; tap on the information icon to familiarise yourself with the personal target feature
- Tap the toggle at the top right of the screen to turn the personal target feature on
- To add new target tap on the green '+' button at the bottom right of the screen

Example: In order to have a glucose target of 6.5mmol/L between midnight and 08:00 followed by the default target of 5.8mmol/L for the rest of the day, complete the following steps:

- Tap the green '+' icon
- In the 'Target glucose' entry screen add 00:00 as the time and 6.5 as the glucose value, then tap 'Confirm'

- Personal target value of 6.5mmol/L over 24hrs is now shown on the screen
- Tap the green '+' icon again to make another entry
- When the 'Target glucose' entry window appears enter 08:00 for time and 5.8 (104) for the glucose value, then tap 'Confirm'
- Your personal glucose target is now set at 6.5mmol/L from midnight to 08:00 and 5.8mmol/L from 08:00 in the morning until midnight.

Once activated, the personal target icon will be shown on the home screen (see Home Screen overview). To deactivate, slide or tap the toggle in the top part of the Personal glucose target screen. The nominal (i.e. default) glucose target will then apply and the personal target icon will disappear from the home screen.

Bolus Calculator Settings (mylife YpsoPump only)

Bolus calculator settings must be setup on the CamAPS FX app when the app is linked to mylife YpsoPump.

Bolus calculator settings are not available on the CamAPS FX app when linked to other insulin pumps. In such a case, bolus calculator settings stored on the insulin pump are used by the CamAPS FX bolus calculator.

The bolus calculator settings determine how the bolus calculator calculates your suggested bolus. It is therefore very important that these settings are correct. Do not make any settings without discussing these previously with your physician or diabetes counsellor. Please make sure that a trained healthcare professional with experience in diabetes management supervises the initiation and programming of the bolus calculator.

Note: Refer to mylife App user instructions about further details and meaning of the bolus calculator settings.

Note: The bolus calculator settings do not affect how Auto mode operates.

Note: Refer to section Setting Up a Personal Glucose Target for information how to set up personal glucose target during Auto mode.

Bolus calculator settings include the following items:

- Minimum glucose value for calculation
- Maximum bolus suggestion
- Glucose target value
- Correction factor
- Insulin-to-carb ratio
- Duration of insulin action

Minimum Glucose Value for Calculation

Here you can define the minimum limit of the glucose value for bolus calculation. If you enter a lower current glucose value, the bolus calculator will alert you that your current glucose value is too low to calculate a bolus suggestion.

Maximum Bolus Suggestion

Here you can define how high the maximum bolus suggestion of the calculation may be in insulin units.

Glucose Target Value

The bolus calculator will correct high or low blood glucose measurements to this value. Blood glucose measurements above this value result in a (positive) correction dose. A blood glucose measurement below the target value results in a negative correction dose which will always be used to reduce the suggested dose.

If you have different glucose target throughout the day, you can define those in the corresponding time segments in 30 min increments.

Example: In order to have the default target of 5.5mmol/L between midnight and 08:00 and a glucose target of 6.5mmol/L for the rest of the day, complete the following steps:

- Tap the green '+' icon
- In the 'Target glucose' entry screen add 08:00 as the time and 6.5 as the glucose value, then tap 'Confirm'

Correction Factor

Enter your correction factor here (example: if 1 unit of insulin lowers your blood glucose by 2 mmol/L, your correction factor is 2).

If you have different correction factors throughout the day, you can define those in the corresponding time segments in 30 min increments. The process of entering correction factor throughout the day is identical to that when entering glucose target value.

Insulin-to-Carb Ratio

The insulin-to-carb ratio describes the number of grams of carbohydrates (or bread units) covered by one unit of insulin.

If you have different insulin-to-carb ratios over the course of the day, you can define those in the corresponding time segments in 30 min increments. The process of entering insulin-to-carb ratio throughout the day is identical to that when entering glucose target value.

Duration of Insulin Action

This setting defines how long your injected insulin remains active in your body to lower your blood glucose. This setting is used for insulin on board calculation.

Note: Information about handling of insulin on board by the bolus calculator:

- Insulin on board is subtracted only from the correction bolus
- Insulin on board is never subtracted from the meal bolus

Using Block Feature

The Block feature is used to prevent the use of certain app functionality in order to prevent unauthorised or unintended entry. This may be helpful when the app is used by children. When the Block feature is activated, certain app functionality will not be allowed including:

- Stopping or starting Auto mode
- Bolus calculator
- Sensor calibration
- ‘Boost’ and ‘Ease-off’

Deactivate the Block feature in the Settings menu to be able to use these functions again.

9 DATA UPLOAD AND REMOTE MONITORING

Data upload to the cloud

The CamAPS FX app supports data upload to the cloud. Data including glucose, insulin, meal intake, Auto mode, Boost and Ease-off status, will be uploaded every 5 to 10 minutes during Auto mode and when Auto mode is off.

Supported cloud upload portals are listed in Appendix C. You may need to register with the cloud upload system provider in advance and provide your account details to the app.

You can link to up to two cloud upload accounts via the 'Share' option in the main menu:

- Tap on the 'User 1' or 'User 2' field to open the account details entry screen
- Enter your account details including email address and password
- Tap on 'Link' to link the account to the app

To stop uploading data to this account, turn the toggle to 'off'. To unlink the account, tap on the active user then tap 'Unlink'.

Please refer to the cloud upload provider user guide for detailed instructions regarding the account setup and data viewing.

***Note**:* Prior to taking any action in response to analysis of CamAPS FX data on the Cloud, it is advised that user/guardian or clinician validates the information by speaking to the user or reviewing graphs on the active system.

Companion Remote Monitoring

The CamAPS FX app allows glucose levels, insulin delivery and other data to be shared with "Companions".

Companion setup is located in 'Share' option of the main menu:

- For each Companion, provide a nickname and a valid email address
- An invitation email is sent to Companion's email address
- The Companion must **install the CamAPS FX app, create personal CamAPS** account using the same email address**,** and select '**Companion**' when initialising the CamAPS FX app
- Data are sent to the Companion using end-to-end encryption

Data shared with Companions include:

- Sensor and blood glucose levels
- Insulin delivery
- Meal intake
- Auto mode status
- Ease-off and Boost
- Amount of insulin remaining in the pump reservoir
- Pump battery level

Note: Internet connectivity is required to receive data by Companions; possible delays in receiving data may be caused by unreliable internet connectivity, delays in cloud data processing or inappropriate smart device settings.

Note: It is not possible to share data with Companion while using virtual pump.

SMS-based Remote Monitoring

The CamAPS FX app supports SMS-based remote monitoring during Auto mode On and Off. All app generated alarms and alerts will be sent via SMS message to active ‘Followers’. Follower setup is located in the ‘Share’ option of the main menu:

- For each Follower, provide a nickname and a valid mobile number; an authentication code will be sent to that mobile number for verification purposes
- Once verified, the Follower nickname will be shown on the ‘Share’ screen

To stop sending messages to a Follower, turn off the toggle next to the Follower’s nickname.

To remove a Follower, tap on the Follower’s nickname and tap ‘Unlink’.

To test sending an alert, tap on ‘Send test SMS’. A SMS message will be send to all active Followers.

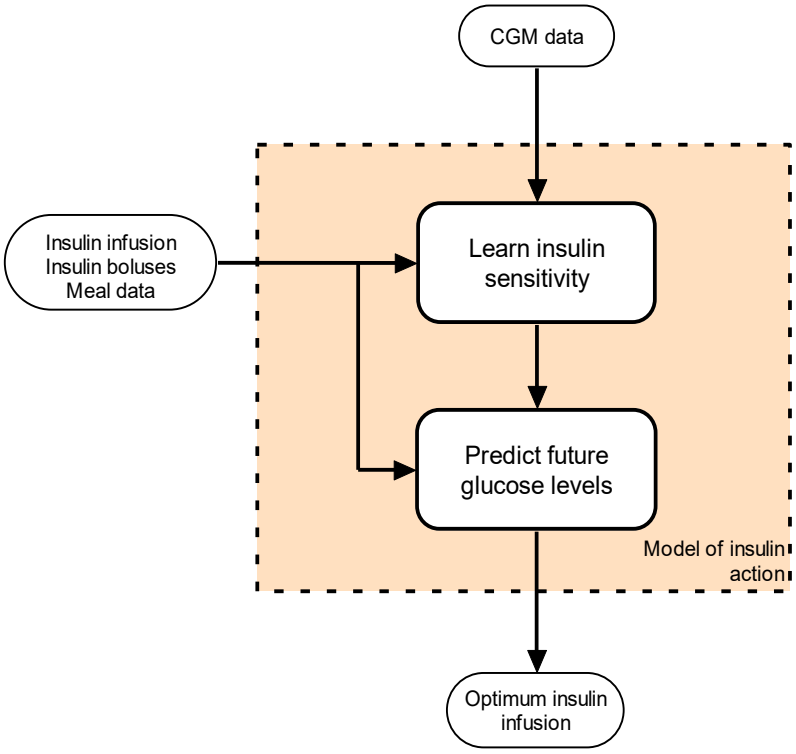
Note: SMS messages are sent directly from the smartphone to the Follower(s) and a SIM card has to be inserted in the smartphone to send the SMS messages.

10 TECHNICAL INFORMATION

How does it work?

The CamAPS FX app uses a mathematical model of insulin action to determine insulin infusion leading to a target glucose of around 5.8mmol/L.

For the model of insulin action to operate correctly, information is needed at setup and then during the system operation. The **body weight** is used to approximate glucose and insulin concentrations within the body. The **total daily dose** of insulin is an initial indicator of **insulin sensitivity**, which is further refined by analysing continuous glucose monitor (CGM) data, previously administered insulin infusion and boluses, and meal intake.



Previous insulin infusion and boluses, together with CGM and meal data are used to update insulin sensitivity and other subject specific characteristics. The mathematical model then uses these characteristics together with information about active insulin and active meals to predict future glucose concentrations and to determine the optimum insulin infusion leading to the target glucose level. The maximum of insulin infusion rate is determined on individual basis and is limited to reduce the risk of hypoglycaemia. In certain situations such as when CGM glucose is low or is decreasing fast, the control algorithm may further reduce insulin to reduce the risk of hypoglycaemia.

11 SPECIFICATION AND PERFORMANCE CHARACTERISTICS

Medical Indication

Type 1 diabetes (including type 1 diabetes pregnancy)

Target Population

Age	1 year and older
Sex	Male/Female
Weight	10kg – 300kg
Total daily insulin	5 U/day – 350 U/day
Condition	Adequate hearing to hear alarms
	Adequate vision to view display

User Profile

People with type 1 diabetes and their guardians

User Training Requirements

Training is carried out by certified healthcare professional or by completing certified online training

Operating Environment

As defined by the manufacturer of your smart device

Supported Devices

Insulin pumps

Compatible insulin pumps must have the following characteristics:

- Receive regulatory approval in the territory where used including regulatory approval of secure Bluetooth communication protocol for remote pump control
- Allow Auto mode to be carried out using (i) 15 to 60 minute long temporary basal insulin rates, or (ii) 15 to 60 minute long extended boluses, or (iii) a combination of (i) and (ii)
- Have delivery accuracy for basal rate ±5% [±0.05U/h for rates < 1.0U/h] or better
- Have delivery accuracy for bolus ±5% [±0.05U for boluses < 1.0U] or better

- Enable maximum delivery of at least 10 U per 5 to 15 minute long closed loop cycle during Auto mode
- Enable resolution of insulin delivery of at least 0.05 U per 5 to 15 minute long closed loop cycle during Auto mode
- Communicate via Bluetooth over a range of at least 1.5 meters
- Provide downloadable time-stamped history of insulin delivery
- Provide status information including time, pre-programmed basal settings, ongoing bolus, ongoing temporary basal rate, suspended state, and error status

A complete list of insulin pumps that can be presently used with the CamAPS FX app is provided in **Appendix A.** Additional pumps may be added in the future.

Continuous Glucose Monitoring Devices

Compatible continuous glucose monitoring devices must have the following characteristics:

- Receive regulatory approval in the territory where used including regulatory approval of secure Bluetooth communication protocol
- Have mean absolute relative deviation $\leq$14% or be approved for insulin dosing
- Provide sensor glucose readings with a resolution of at least 0.1mmol/L / 1mg/dL
- Provide nominally glucose reading at least once every 5 minutes
- Communicate via Bluetooth over a range of at least 1.5 meters
- Provide downloadable time-stamped history of sensor glucose readings
- Provide status information including calibration state, sensor expiry, and error status

A complete list of continuous glucose monitoring devices that can be presently used with the CamAPS FX app is provided in **Appendix B.** Additional continuous glucose monitoring devices may be added in the future.

Cloud Upload Portals

Compatible cloud upload portals must have the following characteristics:

- Receive regulatory approval in the territory where used including approval of secure communication protocol
- Allow secure authentication for individual users
- Enable upload of relevant diabetes therapy related information

A complete list of cloud upload portals that can be used with the CamAPS FX app is provided in **Appendix C.** Additional cloud upload portals may be added in the future.

Compatible Smart Devices

The minimum requirements for CamAPS FX app is a smart device running Android 8.0 OS or above.

If using a Dexcom sensor see Dexcom Mobile App recommended smart devices on http://www.dexcom.com/compatibility

If using a FreeStyle Libre 3 Sensor, please ensure you have an Android smart device with NFC (near field communication). A list of smart devices that have been shown to be compatible with the FreeStyle Libre 3 Sensor and the FreeStyle Libre 3 app can be found at https://www.diabetescare.abbott/support/manuals.html in the “Mobile Device & OS Compatibility” guide.

Communication Protocols

Secure communication protocols are used by the CamAPS FX app for communicating with your insulin pump, your continuous glucose monitoring device, and cloud portals.

Insulin

All rapid or ultra-rapid insulin analogues including diluted insulin analogues.

12 FAILURE MODES AND TROUBLESHOOTING

Introduction

This section will help you figure out what to do if you encounter problems. The next section describes typical failure modes and their possible causes. The following subsections provide troubleshooting advice categorised by components, i.e. the CamAPS FX app, insulin pump, CGM, and the cloud upload portal.

Failure modes

The table below depicts common failure modes, how they appear on the screen, and what you should do to resolve them.

Failure mode	Screen appearance	Cause and resolution
Unable to use bolus calculator	*Information* *Unable to start bolus calculator as your device is not **secure**.* ***Set PIN or similar** on your mobile device to be able to use bolus calculator.*	This information screen appears when your smart device does not have a secure lock. Please set up a PIN or other secure method such as a password, fingerprint or face recognition.
Unable to connect to pump during bolus delivery attempt	*Alert* *Unable to start **step** bolus.* *Please try again.*	This alert screen appears when the CamAPS FX App is unable to connect to the pump to start bolus delivery. Try moving smart device closer to the pump. Ensure pump is not in an 'airplane mode' and Bluetooth on your smart device is turned on.
Unable to reconnect to Ypsopump	*"Your pump cannot be accessed as key exchange failed. Please connect to the internet. If the issue does not resolve in 10 to 20 minutes, then re-link your pump to be able to connect to it."*	The App must be connected to the internet at least once every 28 days in order to exchange the pairing keys
Transmitter not found (Dexcom G6 only)	*Transmitter not found.*	This screen indicates that the transmitter could not be linked. To resolve, follow the troubleshooting steps in 'Dexcom G6' section below.

Lost connection to transmitter/sensor	*Signal loss.*	This screen indicates that the connection to transmitter/sensor has been lost. To resolve, follow the troubleshooting steps in the relevant CGM device section below.
Transmitter/sensor not providing sensor data	*Sensor error. Wait up to 3 hours.*	The screen indicates that the transmitter/sensor and smart device are communicating but there is a problem with the data arriving from the sensor. The issue could be due to (i) a sensor error or (ii) disrupted communication between the sensor and transmitter. As applicable, please check if the transmitter is snapped in properly.
'Boost' and 'Ease-Off' features disabled	*Boost / Ease-off* *Auto mode* *Off*	The screen shows that 'Boost' and 'Ease-off' features have been disabled. This could be due to (i) 'Block' feature being turned on, (ii) insecure lock on your smart device. To resolve, disable the 'Block' feature or secure your smart device with a PIN, a password or a more secure method.
Unable to link to FreeStyle Libre 3 sensor	*Unable to proceed to link with Freestyle Libre 3 sensor. Please connect to the internet and restart the CamAPS app.* *You can also try later but you should maintain connectivity to the internet*	Disconnect and reconnect to the internet. On occasion this message can occur due to the phone not passing the integrity test. For App version 1.4(170) and above, please go to the "Help" Menu and touch "*phone integrity*

		check" to find out if your phone is not failing this test.

CamAPS FX App

Unable to login to CamAPS FX account

Likely cause

- No internet connection
- Unregistered account
- Incorrect login details

Solution

- Make sure your smart device is connected to the internet; confirm the connection by opening a popular website
- If not already registered, open CamAPS FX app and click on 'Register' to create your CamAPS FX account
- Make sure your login details, i.e. the username and password are correct; request the password reminder to be sent to the email address linked with your account

Unable to setup a SMS follower

Likely cause

- Unable to send SMS from the smart device hosting the CamAPS FX app
- No phone signal or no data on the SIM. Incorrect mobile number of the follower

Solution

- Make sure mobile number of the follower is correct
- Confirm the phone hosting the CamAPS FX app has an active SIM card with sufficient funds available to send SMS
- Attempt to send SMS or make a call using the phone
- Check balance on the SIM account
- If in doubt, use another SIM card to setup a follower
- Check mobile network reception on the smartphone

Cannot hear alarm/alerts

Likely cause

- Your smartphone volume is turned off

- The sound setting on your smartphone is on *Do Not Disturb*
- Alerts are turned off in the app
- Individual pre-selected alerts are turned off or set to 'vibration only'
- Selected ring tone is not easily heard

Solution

- Make sure the volume on your smart device is turned on and sufficiently high
- Make sure *Do Not Disturb* setting on your smart device is turned off
- Make sure all alerts are turned on in *Main Menu > Alerts*
- Check individual alerts settings to ensure your selected alert is turned on and 'vibration only' option is turned off; if desirable, change the ring tone and make sure you can hear it well

Alarm/alerts repeat too often

Likely cause

- Alarm/Alert not acknowledged on the smart device
- 'Repeat' option in Alarm/Alert settings is set too short

Solution

- Acknowledge every alarm/alert message on the smart device
- Set the 'Repeat' option in alarm/alert settings to a longer period

CamAPS FX app stops working/crashes

Likely cause

- Internal error, e.g. error message *"CamAPS stopping. Update info or close app*"

Solution

- Turn off your smart device
- Wait for 1 minute and turn your smart device back on
- If CamAPS FX app is still not working uninstall, re-install the app (follow steps below 'Having to re-install the CamAPS FX app')

Having to re-install the CamAPS FX app (using Dana pump or mylife YpsoPpump pump)

Before Uninstalling

- Make sure you have your CamAPS FX account details at hand

- Make a note of the average total daily insulin dose (TDD) from your insulin pump or from the app: *Main Menu* > *Statistics* > *Week* > *TDD*
- Make a note of your weight from the app: *Main Menu* > *Settings* > *Change weight*
- Although the rest of settings will be restored such as alarm settings, meal sizes, personal target settings, share/followers settings, and Dexcom G6 transmitter serial number (if using Dexcom G6 sensor), you may want to take note of these settings

After Uninstalling

- Install the CamAPS FX app from app store
- Open the app and log in with your CamAPS FX username and password
- Proceed with linking the pump
- Enter weight and TDD when prompted
- In the rare case your settings were not restored and before initiating the Auto mode please remember to set the following settings (in any case, you may want to review these settings after they were restored):
- Reset your alarm/alerts settings and other personal settings
- Link your Glooko account with the app: *Main Menu* > *Share* > *User 1 account details*
- Add any followers: *Main Menu* > *Share* > *Follower*

Dexcom G6

General guidelines and troubleshooting about Dexcom G6 system are provided in Dexcom user manual. The following section covers issues related to the use of Dexcom G6 from within the CamAPS FX app.

Unable to link the app with Dexcom G6 transmitter

Likely cause

- Dexcom G6 transmitter already linked to another app, i.e. Dexcom app
- Incorrect Dexcom G6 transmitter serial number
- Electronic background noise interference, e.g. the use of a mobile phone signal booster or a close proximity of WiFi router may affect connectivity

Solution

- Check Bluetooth is turned on in your smart device settings
- Turn Bluetooth off and on
- Check ‘Location‘ is set to ‘On‘ in your smart device privacy/security settings
- Restart your smart device

- If linking for the first time, check transmitter not already linked to Dexcom app; unlink and try again

Transmitter already linked with CamAPS FX

- Unpair the transmitter in Bluetooth settings on the phone: *Settings* > *Connections*> *Bluetooth* > *Paired devices* > *Dexcom device Settings* > *Unpair*
- Enter correct Dexcom serial number into CamAPS FX app: *Main Menu* > *Dexcom G6;* wait a while
- If the above fails after several tries, link **Dexcom G6 receiver** or **Dexcom app** to the transmitter to check that it works

***Note**:* Only one app, Dexcom app or CamAPS FX app, can connect to the Dexcom transmitter at any one time, while Dexcom G6 receiver and CamAPS FX app can be connected at the same time

The app losing communication with G6 transmitter

Likely Cause

- Use of unapproved Android smart device/phone
- High level of electronic background noise interferes with connection

Solution

- **Use Android smart device/phone approved for use with Dexcom G6** (Visit http://www.dexcom.com/compatibility for list of approved devices)
- Keep your transmitter and the smart device within 20 feet / 6 meters of each other; if you are showering or swimming keep them closer as the Bluetooth range is reduced in water; wait 30 minutes
- Reduce the level of electronic background noise – it may be helpful to restart the smart device every few days to improve connectivity
- Follow solutions in 'Unable to link the app with Dexcom G6 transmitter'

No G6 readings for the last 20 minutes: 'No Readings' alert

Likely cause

- Sensor error or sensor failure
- G6 transmitter not providing sensor signal

Solution

- Tap on the information icon in the message alert window to get more information

- Make sure your sensor is secure and G6 transmitter is snapped flat in its holder

No G6 readings for the last 20 minutes: 'Signal Loss' alert

Likely cause

- G6 transmitter not communicating with your smart device

Solution

- Keep your transmitter and your smart device within 20 feet / 6 meters of each other; wait 30 minutes
- Turn Bluetooth on and off on your smart device; wait 10 minutes
- Restart your smart device and reopen CamAPS FX app
- Follow solutions in 'The app losing communication with G6 transmitter'

New sensor not starting

Likely cause

- Previous sensor not stopped in the CamAPS FX app
- Sensor ended prematurely or fell out

Solution

- Stop previous sensor in the app: *Main Menu* > *Stop sensor*
- Wait for 'Start Warm up' message to appear on the home screen

FreeStyle Libre 3

General guidelines and troubleshooting about the FreeStyle Libre 3 system are provided in the FreeStyle Libre 3 user manual. The following section covers issues related to the use of the FreeStyle Libre 3 from within the CamAPS FX app.

Unable to start the FreeStyle Libre 3 sensor

Likely cause

- The FreeStyle Libre 3 sensor started by another app, i.e. the FreeStyle Libre 3 app
- Incorrect positioning of NFC reader on your smart device
- NFC turned off on your smart device

Solution

- Turn NFC off and on
- Tap **Main Menu > Start new sensor** and follow the instructions

- Scan a new sensor with the back of your smart device. Each smart device is different. You may need to touch the sensor with your smart device or move your smart device slowly until you learn how to scan your smart device settings

  ***Note**:* If sensor is started by the FreeStyle Libre 3 app, CamAPS FX is unable to receive sensor data and vice versa.

The app is not receiving data from the FreeStyle Libre 3 sensor

Likely Cause

- Use of unapproved smart device/phone
- High level of electronic background noise interferes with connection

Solution

- **Use smart device/phone with Android 8.0 OS and above approved for use with FreeStyle Libre 3** (Visit https://www.diabetescare.abbott/support/manuals.html for list of approved devices)
- Keep your sensor and the smart device within 33 feet / 10 meters of each other; if you are showering or swimming keep them closer as the Bluetooth range is reduced in water; wait 30 minutes
- Reduce the level of electronic background noise – it may be helpful to restart the smart device every few days to improve connectivity
- Follow solutions in 'Unable to start FreeStyle Libre 3'

No sensor readings for the last 20 minutes: 'Sensor Error' message

Likely cause

- Temporary sensor error or sensor failure

Solution

- Wait until the issue resolves
- Follow solutions in 'Unable to start FreeStyle Libre 3'

No sensor readings for the last 20 minutes: 'Signal Loss' alert

Likely cause

- Sensor not communicating with your smart device

Solution

- Keep your sensor and your smart device within 33 feet / 10 meters of each other; wait 30 minutes
- Turn Bluetooth on and off on your smart device; wait 10 minutes
- Follow solutions in ‘Unable to start FreeStyle Libre 3’
- Restart your smart device and reopen CamAPS FX app

No sensor readings: ‘Sensor too cold’ or ‘Sensor too hot’ message

Likely cause

- Sensor temperature too low / too high

Solution

- Slowly warm up / cool down skin in the area where senor is placed

mylife YpsoPump, Dana Diabecare RS and DANA-i

General guidelines and troubleshooting about mylife YpsoPump, Dana Diabecare RS and DANA-i insulin pumps are provided in the pump's user manual. The following section covers issues related to the use of the pump from within the CamAPS FX app.

Unable to link the insulin pump to the CamAPS FX app

Likely cause

- Bluetooth communication issues:
    - Your smart device Bluetooth not working
    - Pump Bluetooth not working
    - High level of electronic background noise interferes with connection
- Internet connection issues:
    - Your smart device lost connection to the internet and is unable to confirm if your pump is registered
- Other issues:
    - Privacy/security settings of your smart device
    - Unregistered pump used

Solution

- Update the CamAPS FX app to the latest version; check for updates on app store
- Check Bluetooth is turned on in your smart device settings; turn Bluetooth off and on again
- Check your smart device is connected to the internet by opening a known website in browser
- Check Bluetooth is turned on in the pump, i.e. the pump is not in flight mode
- Check 'Location' is turned on in the privacy/security settings on your smart device
- Initiate bolus calculator using the CamAPS FX app and observe if pump connection is established
- Try re-linking the pump; make sure to confirm the linking on the pump screen
- If still unsuccessful, restart your smart device and try again
- If still unsuccessful, remove pump battery and reinsert after a few minutes; then try again

App losing communication with the insulin pump

Likely cause

- Bluetooth communication between the pump and your smart device interrupted
- Internet connection is required at least once every 28 days in order to stay connected.
- Pump too far away from your smart device

Solution

- Check Bluetooth is turned on your smart device; turn it off and on
- Check your smart device is connected to the internet by opening a known website in browser
- Initiate bolus calculator on the CamAPS FX app and observe if pump connection is established
- Restart your smart device and reopen the app
- Try re-linking the pump: make sure to confirm the linking on the pump screen
- Remove pump battery and reinsert after a few minutes

Glooko

Unable to link Glooko account to CamAPS FX app

Likely cause

- No internet connection
- Incorrect login details
- Unregistered Glooko account

Solution

- Make sure your smart device is connected to the internet; confirm the connection by opening a known website
- If not already registered, create a personal account on Glooko website
- Log in to Glooko website with your personal account

13 APPENDIX A SUPPORTED INSULIN PUMPS

The following insulin pumps are supported:

- mylife YpsoPump (Ypsomed, Switzerland)
- Dana Diabecare RS (Sooil, South Korea)
- DANA-i (Sooil, South Korea)
- Virtual pump
- Companion

mylife YpsoPump specific instructions

- Use mylife YpsoPump compatible with CamAPS FX (consult insulin pump instructions for use).
- Bolus calculator settings must be entered on the CamAPS FX app.
- mylife YpsoPump pump will become unlinked from the app if the pump is linked to another app such as mylife App. If you want to continue to use the pump, you must reinitiate linking the pump by tapping **Main Menu > mylife YpsoPump**.
- During Auto mode, delayed bolus initiated manually by the user will be stopped. When in Auto mode, apply standard boluses to bolus for meals and snacks.
- The maximum recommended distance between the smart device hosting CamAPS FX app and the pump is 5 to 10 meters or 16 to 30 feet.
- Internet connection is required at least once every 28 days in order to stay connected.

Dana Diabecare RS specific instructions

- Ensure ‘Extended bolus’ is enabled and the ‘Beep’ sound is turned off on the pump. Refer to pump user manual for specific instructions.
- Ensure ‘Bolus increment’ on the pump is set to 0.05U.
- For an earlier version of Dana Diabecare RS pump, ensure correct value of ‘Decreasing ratio’ is entered on the app by tapping **Main Menu > Settings > Decreasing ratio**. In such a case, the app disregards ‘Decreasing ratio’ entered on the pump.
- Dana Diabecare RS pump will become unlinked from the app if the pump is linked to another app such as the ANYDANA mobile app, or password is changed on the

pump. If you want to continue to use the pump, you must reinitiate linking the pump by tapping **Main Menu > Dana Diabecare RS**.

- During Auto mode, extended bolus initiated manually by the user will be stopped. When in Auto mode, apply step boluses to bolus for meals and snacks.
- The maximum recommended distance between the smart device hosting CamAPS FX app and the pump is 5 to 10 meters or 16 to 30 feet.
- Internet connection is required at least once every 30 days in order to stay connected.

DANA-i specific instructions

- Ensure 'Extended bolus' is enabled and the 'Beep' sound is turned off on the pump. Refer to pump user manual for specific instructions.
- Ensure 'Bolus increment' on the pump is set to 0.05U.
- DANA-i pump will become unlinked from the app if the pump is linked to another app such as the ANYDANA mobile app, or password is changed on the pump. If you want to continue to use the pump, you must reinitiate linking the pump by tapping **Main Menu > DANA-i**.
- During Auto mode, extended bolus initiated manually by the user will be stopped. When in Auto mode, apply step boluses to bolus for meals and snacks.
- The maximum recommended distance between the smart device hosting CamAPS FX app and the pump is 5 meters or 16 feet.
- Internet connection is required at least once every 30 days in order to stay connected.

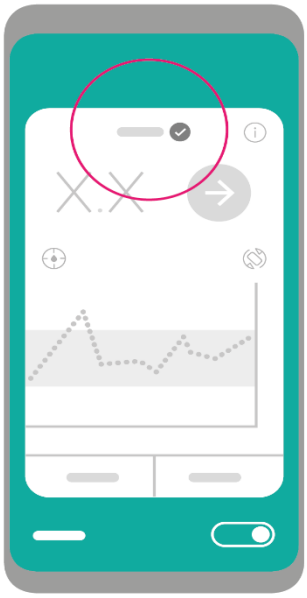
Virtual pump specific instructions

- Virtual pump should be used for **training and demonstration purposes** only.
- Not all CamAPS features are available when using virtual pump.
- No insulin is actually administered.

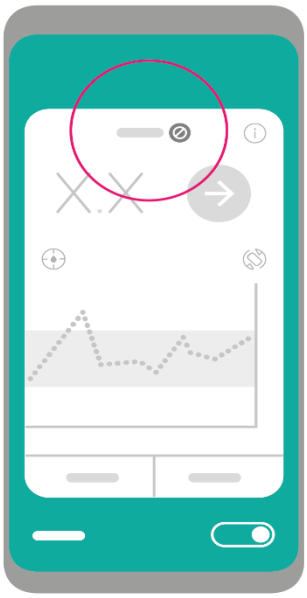
Companion specific instructions

- Companion is used to display data from a pump and glucose sensor worn by another person.
- The other person must invite you to view his/her data, see 'Companion Remote Monitoring' section of this User Manual.

- Not all CamAPS FX features are available when using Companion.
- You can set up your own alarms and alerts.
- Data are received using end-to-end encryption.
- Internet connectivity is required to receive the data.
- The top of the home screen shows the name of the person whose data are being displayed.



- When no data are received for more than 12 minutes, a disconnect icon is shown next to the name of the person whose data are being followed. Tapping on the icon shows the last time data have been received.



14 APPENDIX B SUPPORTED CGM SYSTEMS

The following CGM systems are supported:

- Dexcom G6 (Dexcom, San Diego, CA, USA)
- FreeStyle Libre 3 (Abbott Diabetes Care, CA, USA)
- Virtual CGM

Dexcom G6 specific instructions/information

- The maximum recommended distance between the smart device hosting CamAPS FX app and the Dexcom G6 transmitter is 6 meters or 20 feet.
- When starting a new sensor, you must enter the sensor code into your smart device to use G6 sensor without fingerstick calibrations; if you do not enter the sensor code you will be expected to calibrate the sensor every 12 hours.
- When calibrating the sensor, calibrations must be entered within 5 minutes of taking fingerstick glucose measurement.
- G6 sensor reading updates every 5 minutes.

Note: The Dexcom G6 app cannot be used while using the CamAPS FX app. This is due to the restriction of the Dexcom G6 transmitter being connected to a single app/smart device.

FreeStyle Libre 3 specific instructions/information

- The maximum recommended distance between the smart device hosting CamAPS FX app and FreeStyle Libre 3 sensor is 10 meters or 33 feet.
- It is not possible to calibrate FreeStyle Libre 3 sensor.
- FreeStyle Libre 3 sensor reading updates every 1 minute.

Note: If sensor is started by the FreeStyle Libre 3 app, CamAPS FX is unable to receive sensor data and vice versa.

Virtual CGM specific instructions/information

- A virtual CGM should be used for **demonstration and training purposes** only.
- No alerts and alarms will be sounded.
- Not all CGM features will be available. For example, you will not be able to start and stop sensor.

15 APPENDIX C SUPPORTED CLOUD UPLOAD PORTALS

The following cloud upload portals are supported:

- Glooko

16 APPENDIX D CLINICAL BENEFITS

Summary

The CamAPS FX app uses a control algorithm which has been evaluated in a series of randomised clinical studies to assess its safety and efficacy [1]. Early clinical studies focused on iterative enhancements and optimisation of algorithm performance. This was followed by longer clinical studies demonstrating improved glucose control and reduced burden of diabetes [2-4]. The use of the control algorithm led to increased time when sensor glucose was in the target range, reduced glycated haemoglobin, reduced mean sensor glucose and reduced time when glucose was in the hypoglycaemia range. These benefits were particularly pronounced overnight.

Key Clinical Study - APCam11 study

The APCam11 study was a multinational study evaluating day-and-night closed-loop insulin delivery in the home setting in youth and adults, aged 6 years and above with sub-optimally controlled type 1 diabetes [3].

Study participants

All participants had type 1 diabetes for at least one year, were on insulin pump therapy for at least three months, and had glycated haemoglobin between 7.5% and 10% (58 to 86 mmol/mol). Participants were at least six years old with an equal proportion of youths between six and 21 years, and adults aged 22 years and older. Key exclusion criteria included regular use of real-time continuous glucose monitoring in preceding three months, history of one or more episodes of severe hypoglycaemia in preceding six months, and significantly reduced hypoglycaemia awareness in subjects aged 18 years and older defined by Gold score of greater than four.

Eligible adults were identified from diabetes clinics attending Addenbrooke's Hospital (Cambridge, UK), Manchester Royal Infirmary (Manchester, UK), International Diabetes Center at Park Nicollet (Minneapolis, USA), and Barbara Davis Center for Childhood Diabetes (Aurora, USA). Children and adolescents were recruited from paediatric diabetes centres at Addenbrooke's Hospital (Cambridge, UK), Royal Hospital for Sick Children (Edinburgh, UK), Leeds Teaching Hospital (Leeds, UK), and the International Diabetes Center at Park Nicollet, (Minneapolis, USA).

Study design and procedures

The study had an open-label, multi-centre, multi-national (UK, USA), randomised, one-period, parallel design contrasting day-and-night hybrid closed-loop (closed-loop group) and sensor-augmented pump therapy (control group) during free-living over 12 weeks.

Participants in both study groups used modified 640G insulin pump (Medtronic, Northridge, CA, USA), Enlite 3 glucose sensor (Medtronic), and Contour Next Link 2.4 glucometer (Ascensia Diabetes Care, Basel, Switzerland). Participants were not remotely monitored or supervised. They were free to consume any meals of their choice and were allowed to choose any indoor or outdoor physical activity. Blood samples were drawn for glycated haemoglobin measurements at enrolment, before and after each treatment period.

On enrolment following training on the study pump and continuous glucose monitoring, participants underwent at least a 4-week run-in period. Eligible subjects were randomised using randomisation software to the use of day-and-night hybrid closed-loop or sensor-augmented pump therapy.

Participants randomised to the closed-loop group attended the clinical research facility for a two- to three-hour visit. Training was provided on initiation and discontinuation of the hybrid closed-loop system which comprised the CamAPS FX control algorithm running on a lockdown Android smartphone, switching between closed-loop and standard insulin pump therapy, meal bolus procedure, and the use of study devices during exercise. After discharge, participants applied the closed-loop system for the following 12 weeks.

Participants randomised to the control group (sensor-augmented insulin pump therapy), received additional training on the effective use of real-time continuous glucose monitoring for optimisation of insulin therapy. Participants were instructed not to activate pump’s threshold suspend or predictive low-glucose features. Participants were free to optimise their treatment independently or on advice from health care professionals.

Table. Baseline characteristics of study participants.

	Closed-loop (N=46)	Control (N=40)
Sex no.(%)		
Female	22 (48)	22 (55)
Male	24 (52)	18 (45)
Age (years)	22 (13 to 36)	21 (11 to 36)
Age subgroup no.(%)		
6-<13 yr	11(24)	12(30)
13-<22 yr	11(24)	8(20)
22-<40 yr	18(39)	14(35)
>40yr	6(13)	6(15)
BMI (for age>20)	28 ± 4 (N=24)	27 ± 3 (N=21)
BMI* Z Score (for age≤20)	0.70±0.92 (N=22)	0.69±0.86 (N=19)
Duration of diabetes (years)	13 (7 to 20)	10 (7 to 19)
Total daily insulin dose (U/kg/day)	0.62±0.15	0.89±0.24
Glycated haemoglobin at screening		
(mmol/mol)	67±7	66±6
(%)	8.3±0.6	8.2±0.5

Data are mean (SD) or median (IQR), unless otherwise stated
*BMI z-score adjusted for age and gender based on 2000 CDC growth charts

Results

86 eligible participants were randomised, 46 participants assigned to the closed-loop group and 40 participants to the control group. Of those, 43 participants were 22 years and older, 19 were 13 to 21 years old, and 33 were 6 to 12 years old. Baseline characteristics are shown below.

The proportion of time when sensor glucose was in the target range between 3.9 and 10.0 mmol/L, was 10.8 percentage points higher (95% CI 8.2 to 13.5 percentage points, p<0.001) in the closed-loop group (65±8%, mean±SD) than in the control group (54±9%). Improvements in time in range did not differ among the three age groups (< 13 years, 13 to 22 years, ≥22 years). All participants in the closed-loop group experienced an improvement in percentage time spent with glucose levels in target range compared to run-in period.

In both groups, glycated haemoglobin reduced from a screening value (closed-loop: 8.3 ± 0.6%; control: 8.2 ± 0.5%) to post run-in assessment (closed-loop: 8.0±0.6%; control: 7.8 ± 0.6%). Glycated haemoglobin levels were significantly lower post closed-loop intervention (7.4 ± 0.6%) compared to control intervention (7.7 ± 0.5%) with a mean difference between groups favouring the closed-loop group by 0.36% (95% CI, 0.19% to 0.53%; p<0.001). Glycated haemoglobin improvements were not different among children, adolescents and adults.

Day-and-night closed-loop significantly reduced mean glucose ($p<0.001$) and time spent above target ($p<0.001$) compared to the control group. Glucose variability measured as the standard deviation of sensor glucose was lower in the closed-loop group ($p<0.001$). The coefficient of variation of sensor glucose was not different between groups ($p=0.5$).

Closed-loop significantly reduced the percentage of time sensor glucose was below 3.9 mmol/L ($p=0.008$). The percentage of time spent with sensor readings below 3.5 mmol/L and below 2.8 mmol/L were low and not different between interventions.

Increased time when glucose was in target range, reduced mean glucose, reduced time when glucose was below target, and a reduction in glycated haemoglobin was brought about by closed-loop without significantly increasing total daily insulin ($p=0.09$). Higher basal insulin delivery during closed-loop ($p<0.001$) was offset by lower bolus delivery ($p<0.001$) presumably due to lower glucose levels resulting in a reduced amount of insulin delivered as correction boluses. There was no significant between-group difference in the change of body weight from the screening value (2.2 ± 2.3 vs. 1.4 ± 2.6, closed-loop vs. control; $p=0.19$).

Adverse events

After randomisation, no severe hypoglycaemia occurred in either study group. One diabetic ketoacidosis presented in closed-loop group due to infusion set failure and was not closed-loop related. Two participants in each study group experienced significant hyperglycaemia with capillary glucose greater than 16.7 mmol/L and elevated plasma ketones (>0.6 mmol/L). There were other 13 adverse events in the closed-loop group and 3 in the control group. All participants recovered fully without clinical sequelae.

Table. Comparison of day-and-night glucose control during closed-loop and control periods.

	Baseline		12 weeks			
	Closed-loop (N=46)	**Control (N=40)**	**Closed-loop (N=46)**	**Control (N=40)**	**Difference (95% Confidence Interval)***	**P value***
Time spent at glucose level in range (%)						
3.9 to 10.0 mmol/L	**62 ± 10**	**52 ± 9**	**65 ± 8**	**54 ± 9**	**+10.8 (+8.2 to +13.5)**	**<0.0001**
< 3.9 mmol/L	3.5 (2.0 to 5.4)	3.3 (1.2 to 5.5)	2.6 (1.9 to 3.6)	3.9 (1.7 to 5.3)	-0.83 (-1.40 to -0.16)‡	0.0130
< 3.5 mmol/L	1.8 (0.8 to 3.2)	1.9 (0.6 to 3.3)	1.4 (0.9 to 1.9)	2.0 (0.9 to 3.0)	-0.33 (-0.81 to +0.04)‡	0.08
<2.8 mmol/L	0.4 (0.1 to 1.0)	0.5 (0.1 to 1.0)	0.3 (0.2 to 0.6)	0.5 (0.2 to 0.9)	-0.09 (-0.24 to +0.01)‡	0.11
>10.0 mmol/L	44 ± 11	44 ± 11	32 ± 8	42 ± 10	-10.3 (-13.2 to +7.5)	<0.0001
>16.7 mmol/L	5.5 (3.3 to 8.3)	4.9 (2.7 to 7.3)	3.5 (1.9 to 4.6)	4.4 (2.9 to 6.5)	-1.42 (-2.20 to -0.69)‡	<0.0001
Glycated haemoglobin (%)	8.0 ± 0.6	7.8 ± 0.6	7.4 ± 0.6	7.7 ± 0.5	-0.36 (-0.53 to -0.19)	<0.0001
Glycated haemoglobin (mmol/mol)	63 ± 7	62 ± 6	57 ± 7	60 ± 6	-4.0 (-5.8 to -2.2)	<0.0001
Mean glucose (mmol/L)	9.8 ± 1.1	9.8 ± 1.1	8.9 ± 0.7	9.7 ± 1.0	-0.82 (-1.06 to -0.57)	<0.0001
Glucose SD (mmol/L)	3.9 ± 0.5	3.8 ± 0.5	3.5 ± 0.5	3.8 ± 0.5	-0.35 (-0.48 to -0.22)	<0.0001
Glucose CV (%)	40 ± 5	39 ± 5	40 ± 4	40 ± 4	-0.4 (-1.4 to +0.7)	0.5
Total daily insulin (U/kg/day)	0.75 ± 0.22	0.70 ± 0.18	0.81 ± 0.25	0.71 ± 0.19	+0.031 (-0.005 to +0.067)	0.09
Total daily basal insulin (U/kg/day)	0.32 ± 0.07	0.31 ± 0.08	0.46 ± 0.13	0.32 ± 0.10	+0.124 (+0.099 to +0.150)	<0.0001
Total daily bolus insulin (U/kg/day)	0.43 ± 0.19	0.39 ± 0.14	0.34 ± 0.17	0.39 ± 0.13	-0.087 (-0.114 to -0.060)	<0.0001
Body weight change from screening (kg)			2.2 ± 2.3	1.4 ± 2.6	+0.68 (-0.34 to +1.69)	0.19

Data are mean (SD) or median (IQR)
* Difference is “Closed-loop minus Control”

Conclusions

This multinational, multi-centre, open-label, randomised trial demonstrated that 12-week use of a day-and-night hybrid closed-loop insulin delivery system compared to sensor-augmented insulin pump therapy was associated with an improvement in overall glucose control and a reduction in hypoglycaemia risk in sub-optimally controlled type 1 diabetes including children, adolescents and adults. The hybrid closed-loop system was used safely during daily living without supervision or remote monitoring.

The study reports a 10.8 percentage point increase in time with glucose levels in target glucose range across all age groups. This improvement resulted from a reduction of time spent in hyperglycaemia without change in total insulin delivery. The study observed a lower amount of bolus insulin and a higher amount of basal insulin in the closed-loop group compared to the control group. Lower bolus insulin requirements could be explained by lower glucose levels during closed-loop use lessening the need for correction boluses. Insulin to carbohydrate ratio did not need to be increased. Benefits of closed-loop appeared greater overnight as daytime control is confounded by meals and physical activity even with the use of a closed-loop system. These improvements are attributable to the use of the closed-loop system alone as no regular health-care professional driven adjustments of insulin pump therapy took place.

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17 APPENDIX E EXPLANATION OF UNIVERSAL SYMBOLS

	Refer to Instruction Manual/Booklet
	Warning
	Manufacturer
	Date of manufacture
	CE Mark
	EU Authorised Representative

CamDiab Ltd
Level 4, Institute of Metabolic Science
Box 289, Addenbrooke's Hospital, Hills Rd
Cambridge CB2 0QQ
United Kingdom
support@camdiab.com

CE
2797

EC REP

CEpartner4U BV
Esdoornlaan 13
3951 DB Maarn
The Netherlands

Sponsor in Australia

Ypsomed Australia Pty Ltd
602/20 Bungan St
NSW 2103 Mona Vale
Australia
info@ypsomed.cam.au
Free Call: 1800 447042