Supplementary Data

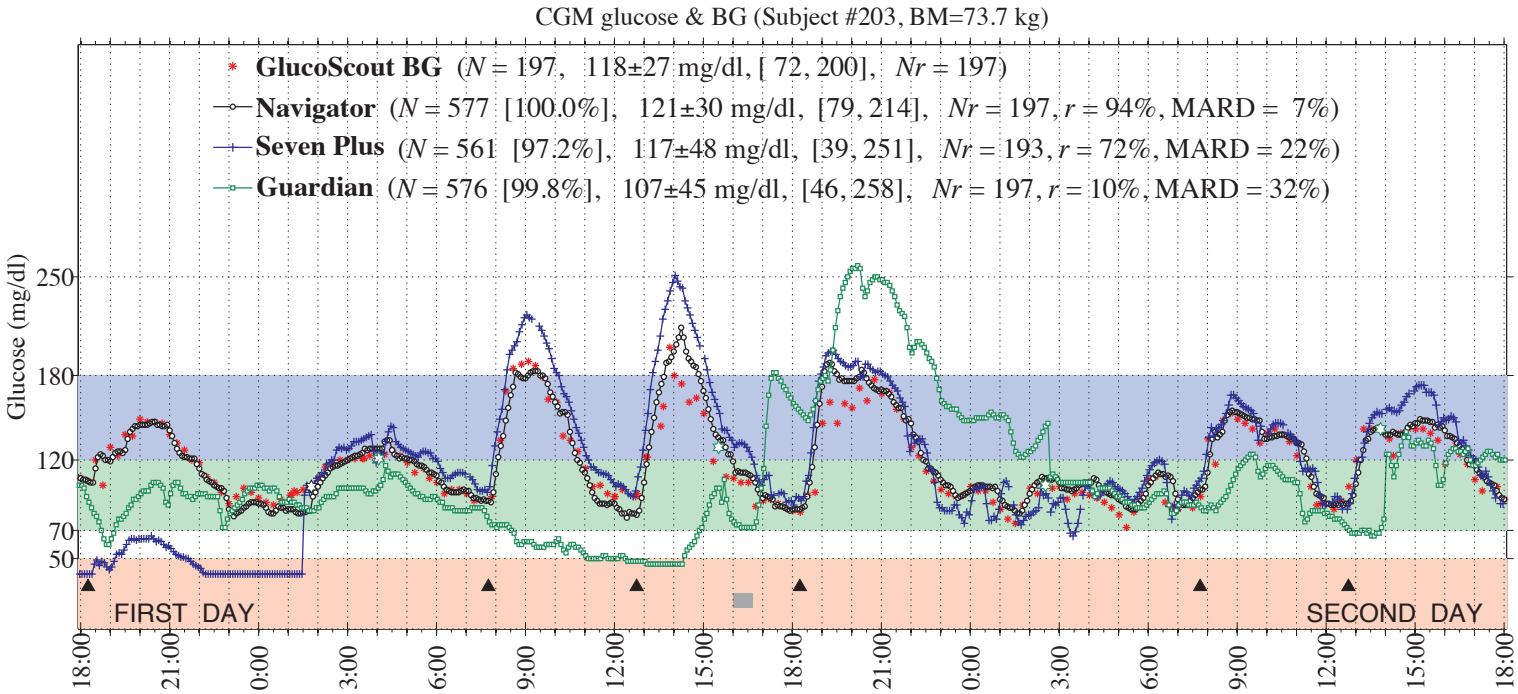
Damiano *et al.* – A comparative effectiveness analysis of three continuous glucose monitors in type 1 diabetes

1 CGM Calibrations

The manufacturer's calibration schedule for the Navigator requires calibrations at approximately 0, 2, 14, and 62 hours from the first calibration request, whereas the Seven Plus and Guardian require calibrations approximately every 12 hours from the first calibration. All three CGM devices were inserted the day before the experiment. The first two calibrations of the Navigator, and the first calibration of the Seven Plus and the Guardian were typically performed in the two to three hour period leading up to the experiment. Therefore, in each experiment, one scheduled calibration was requested by the Navigator and four scheduled calibrations were requested by the Seven Plus and the Guardian. Occasionally, a CGM device would request an additional calibrations beyond the usual scheduled calibrations; these were performed whenever requested. Additionally, there was a provision in the protocol to force a calibration of any of the three CGM devices at 6:00 daily if the glucose level displayed by a device was not within the International Organization for Standardization (ISO) standard compared with PG; namely within 20% of PG if the PG $>$ 75 mg/dl or within 15 mg/dl of PG if the PG $<$ 75 mg/dl. According to these criteria, of 24 possible occasions, this calibration was required and performed twice for the Guardian and once for the Seven Plus. There were two occasions when the Seven Plus was not reporting data at 6:00, and therefore these criteria could not be evaluated. There was one occasion when the Navigator and Seven Plus did not meet ISO standards at 6:00; according to protocol forced calibrations should have been performed at that time, but were omitted in error.

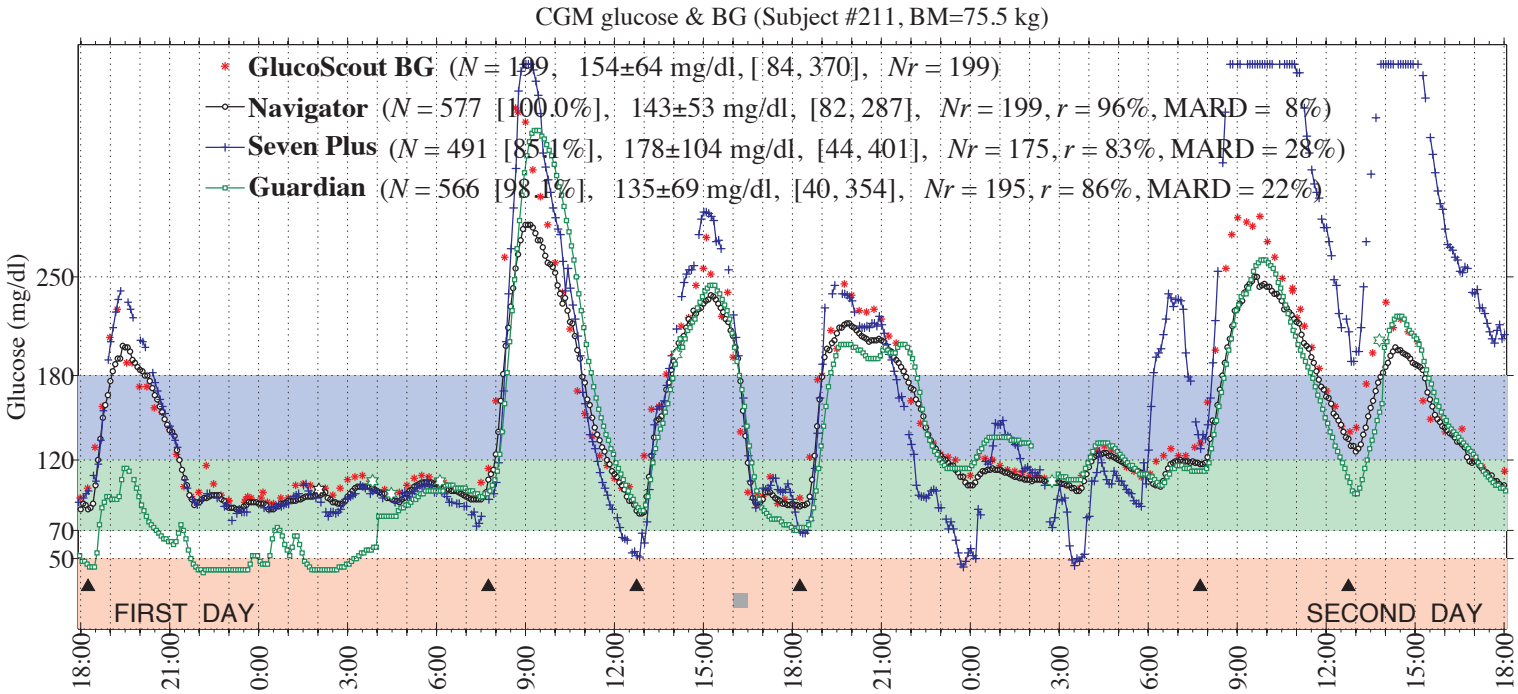
2 Boundedness of Device MARDs

The aggregate MARD of all paired points obtained for each CGM device (Fig. 2) is a quantity that is bounded from above and below. When the 2356 PG data points used to test the Navigator accuracy are randomly shuffled and then paired with the 2356 Navigator data points, the new paired data set is found to consistently produce an aggregate MARD of $\sim$ 41% through many random shuffling trials. This represents an upper bound on the aggregate MARD that the Navigator could achieve if there were no relationship between the Navigator CGMG and the reference PG. When a similar random shuffling is performed on the 1799 paired data points obtained for the Seven Plus and the 2328 paired data points obtained for the Guardian, the upper-bound aggregate MARDs for these data sets are found to be 54% and 47%, respectively. Note that the Clarke error grid for the GlucoScout (Fig. 2*A*) shows an aggregate MARD of 5.1%. Since the GlucoScout and YSI measured the glucose concentration of the same blood sample from the same IV, this MARD is arguably the best that can be achieved with reference-quality glucose monitors. Thus, the aggregate MARD of 11.8 $\pm$ 11.1% for the Navigator falls in the range of possible MARDs of between 5 and 41%, the aggregate MARD of 16.5 $\pm$ 17.8% for the Seven Plus falls in the range of possible MARDs of between 5 and 54%, and the aggregate MARD of 20.3 $\pm$ 18.0% for the Guardian falls in the range of possible MARDs of between 5 and 47%.



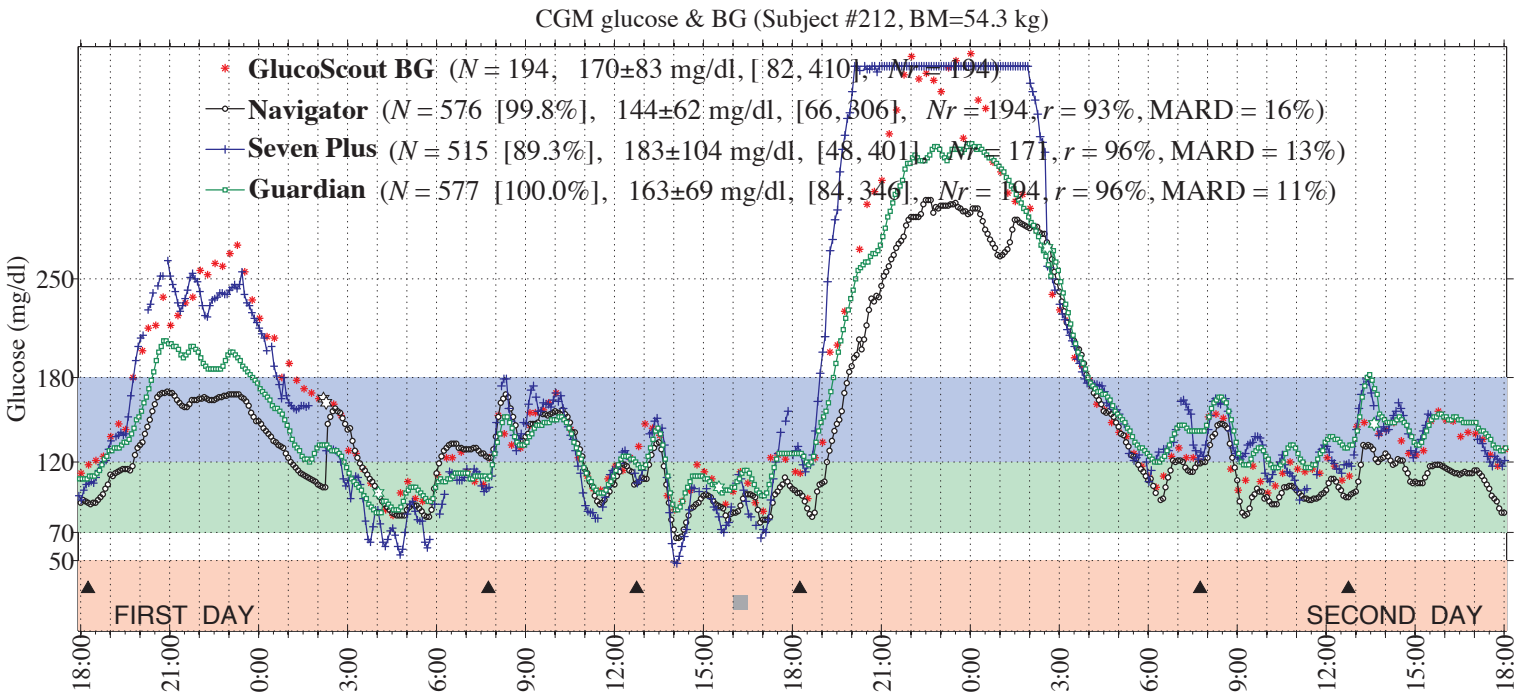
Supplementary Figure 1.

Results obtained during 48 hours of continuous closed-loop control in Subject #203 showing venous BG concentrations measured every 15 minutes with the GlucoScout (red symbols) and CGMG values measured with the Navigator (black symbols), Seven Plus (blue symbols), and Guardian (green symbols). Meals are indicated along the timeline by black triangles. A 30–40 minute period of structured exercise occurred at 16:00 hours at the end of the First Day and is indicated along the timeline by the grey rectangle. Note the 7.5-hour period from 18:00–1:30 hours in which the Seven Plus essentially missed the hyperglycemic excursion associated with the first meal, and falsely predicted severe hypoglycemia during most of this period. Note the 20-hour period from 7:30–3:00 hours in which the Guardian essentially missed the hyperglycemic excursions associated with the second and third meals, and the 7.5-hour period from 19:00–2:30 hours in which the Guardian severely over-estimated glucose during the fourth meal.



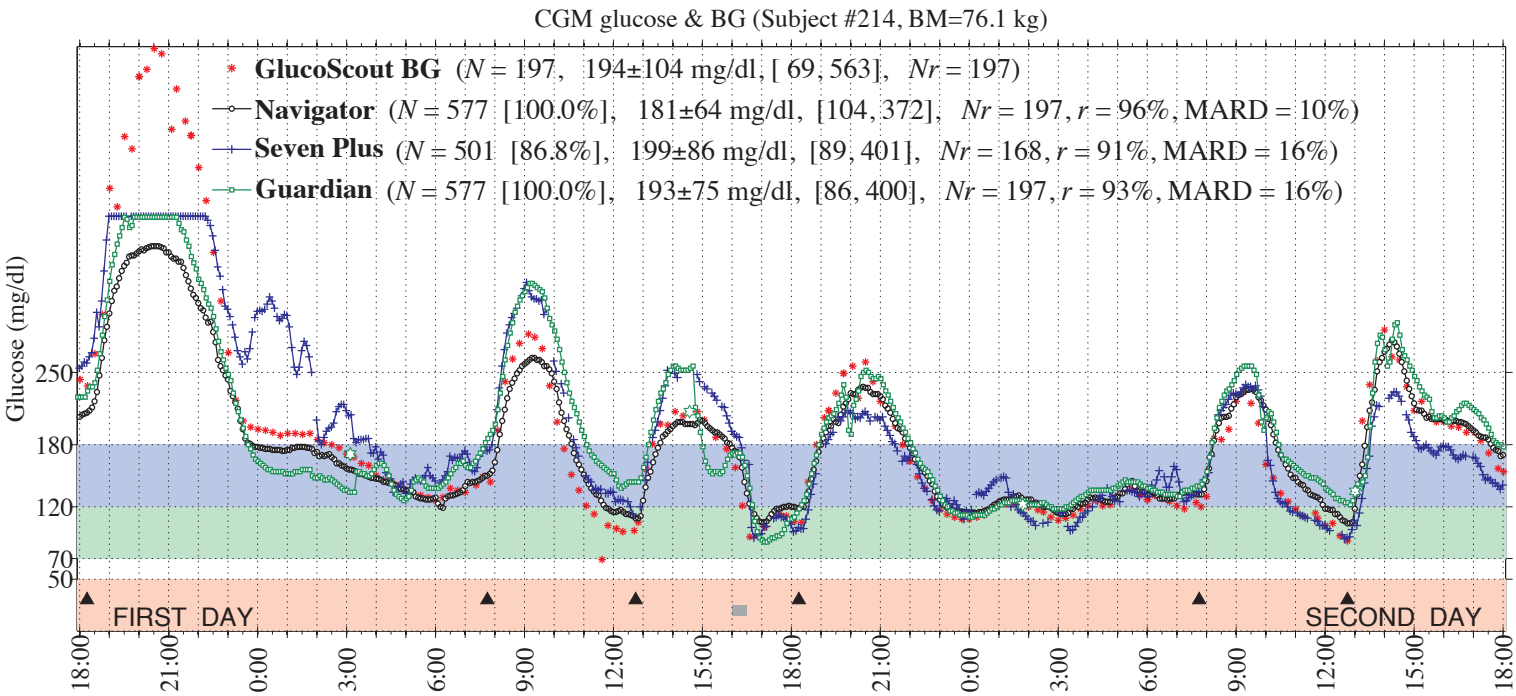
Supplementary Figure 2.

Results obtained during 48 hours of continuous closed-loop control in Subject #211. Note the 12-hour period from 6:00–18:00 hours in which the Seven Plus severely over-estimated glucose during the fifth and sixth meals. Note the 10-hour period from 18:00–4:00 hours in which the Guardian essentially missed the hyperglycemic excursion associated with the first meal, and falsely predicted severe hypoglycemia during some of this period.



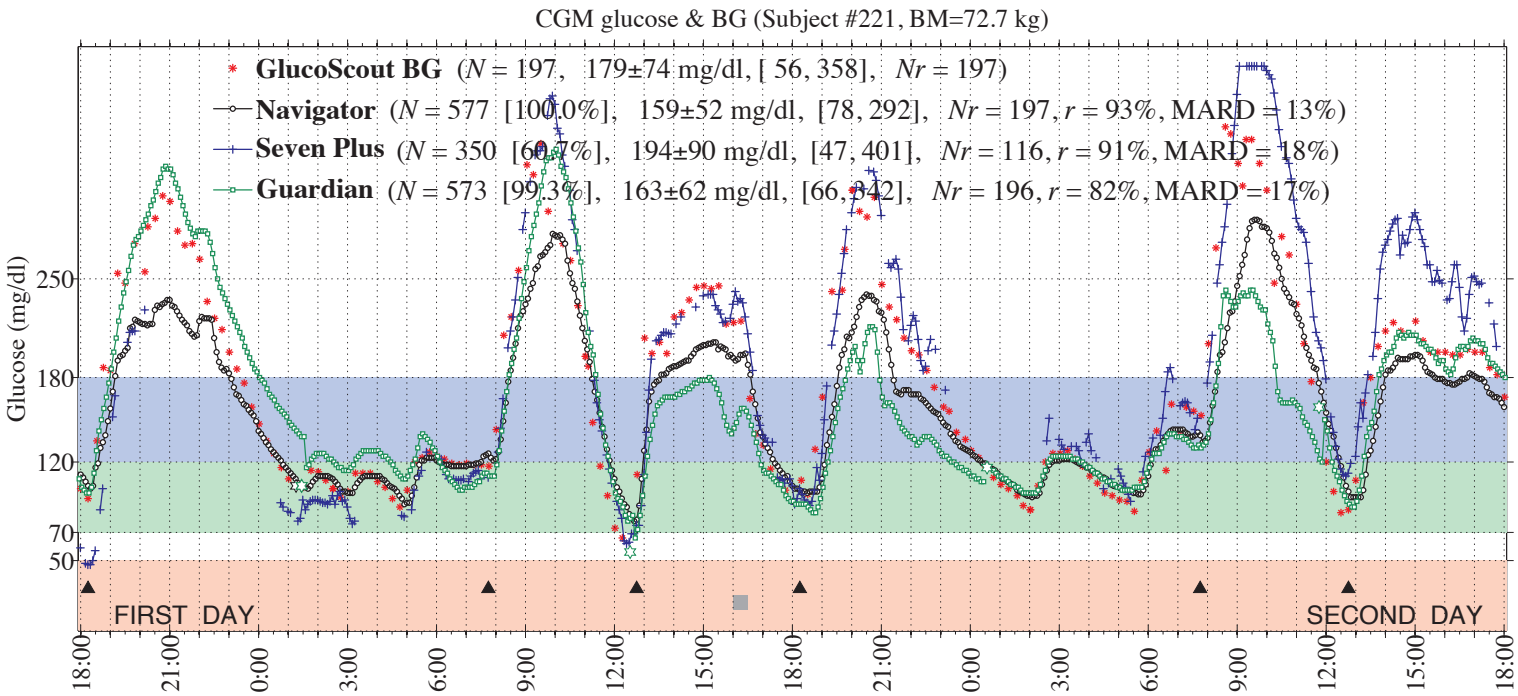
Supplementary Figure 3.

Results obtained during 48 hours of continuous closed-loop control in Subject #212.



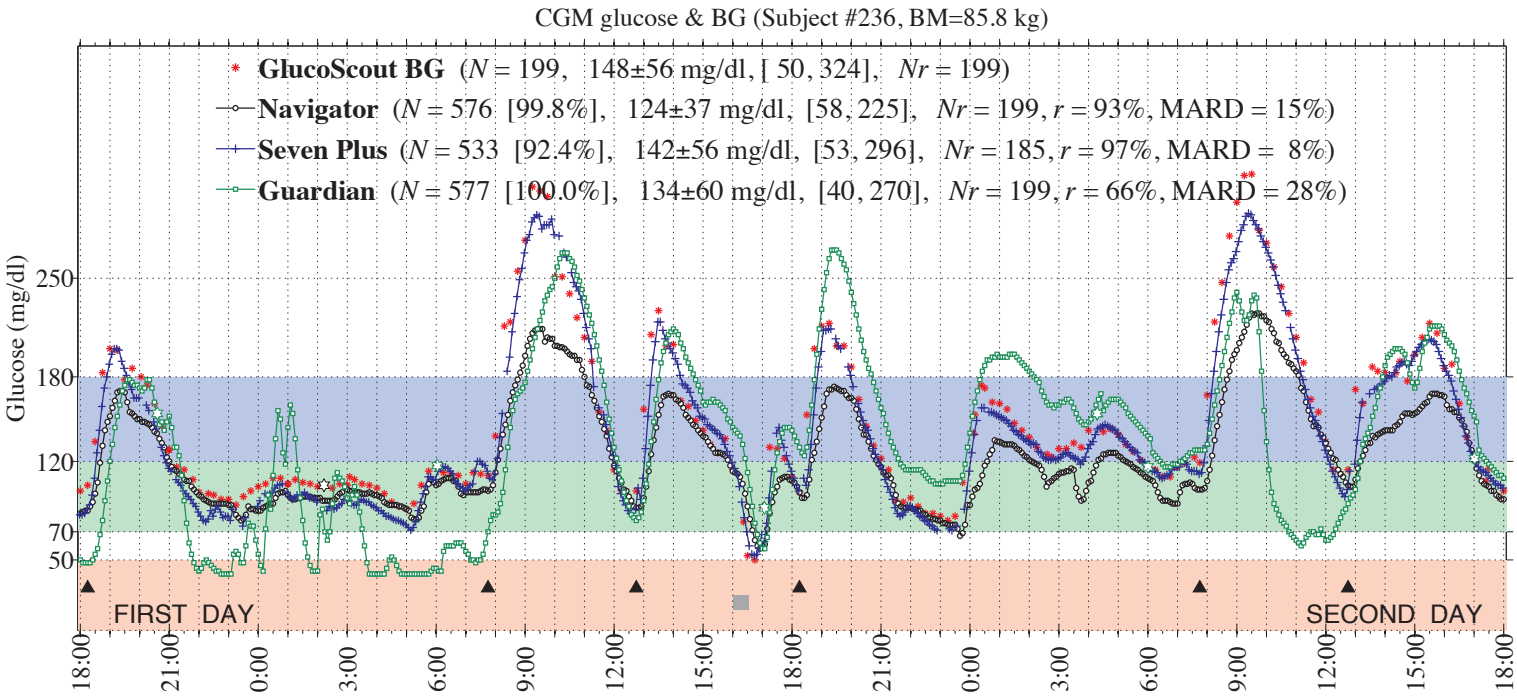
Supplementary Figure 4.

Results obtained during 48 hours of continuous closed-loop control in Subject #214.



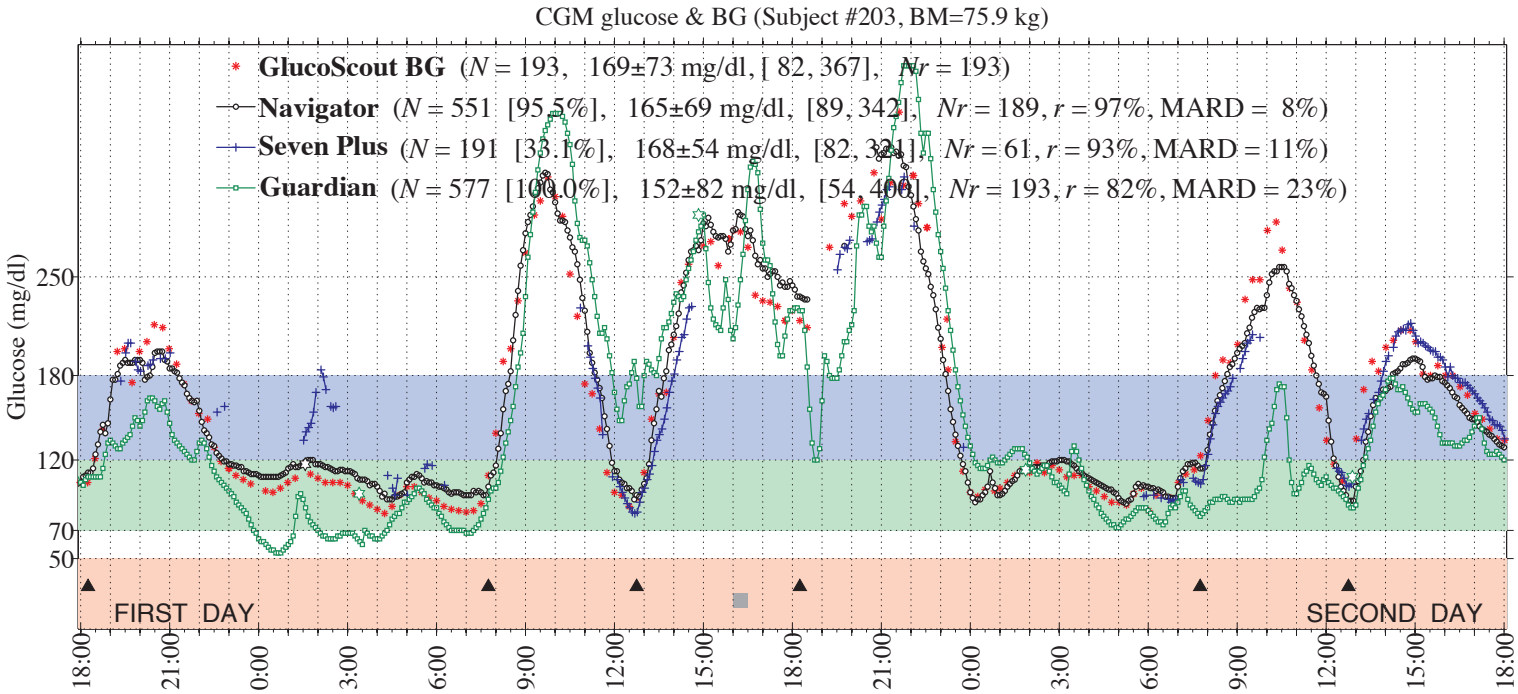
Supplementary Figure 5.

Results obtained during 48 hours of continuous closed-loop control in Subject #221.



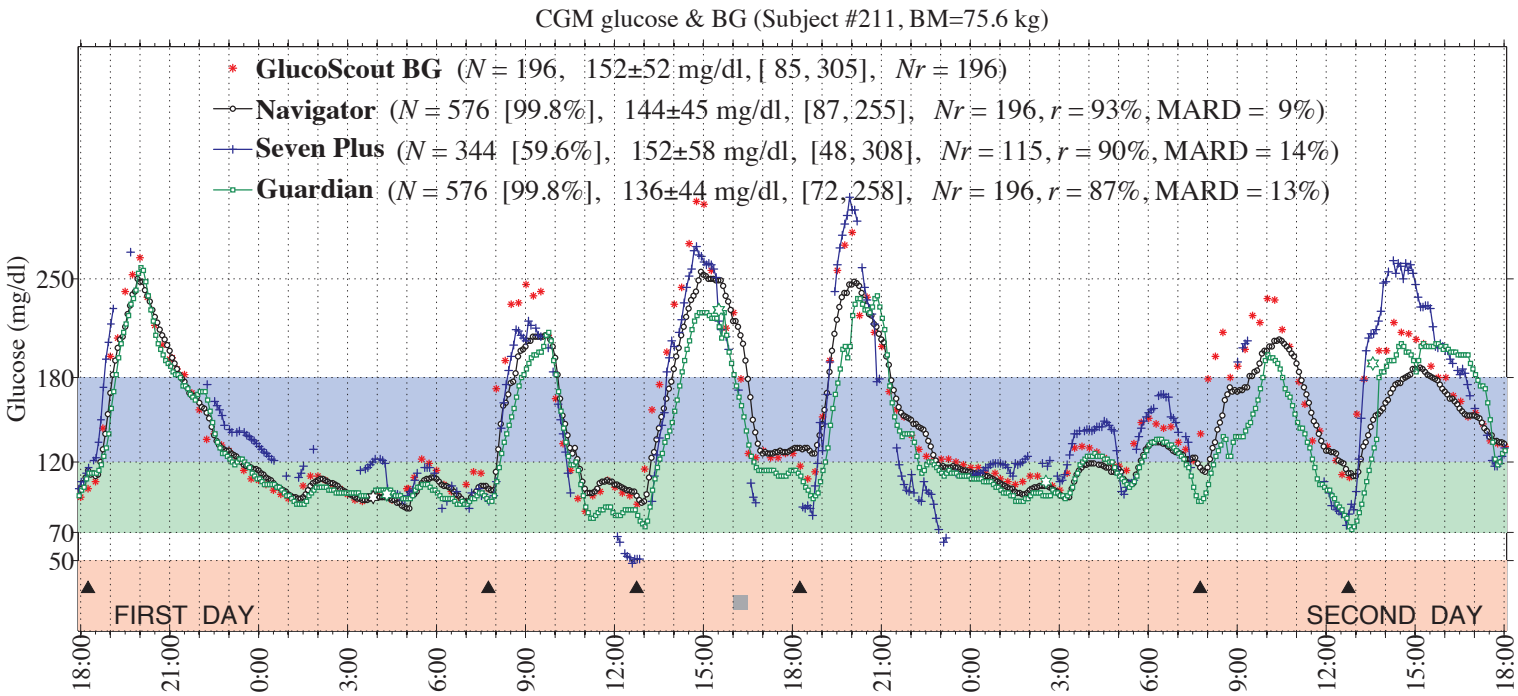
Supplementary Figure 6.

Results obtained during 48 hours of continuous closed-loop control in Subject #236. Note the 9-hour period of normoglycemia from 22:00–7:00 hours on the first night in which the Guardian falsely predicted severe hypoglycemia during most of this period.



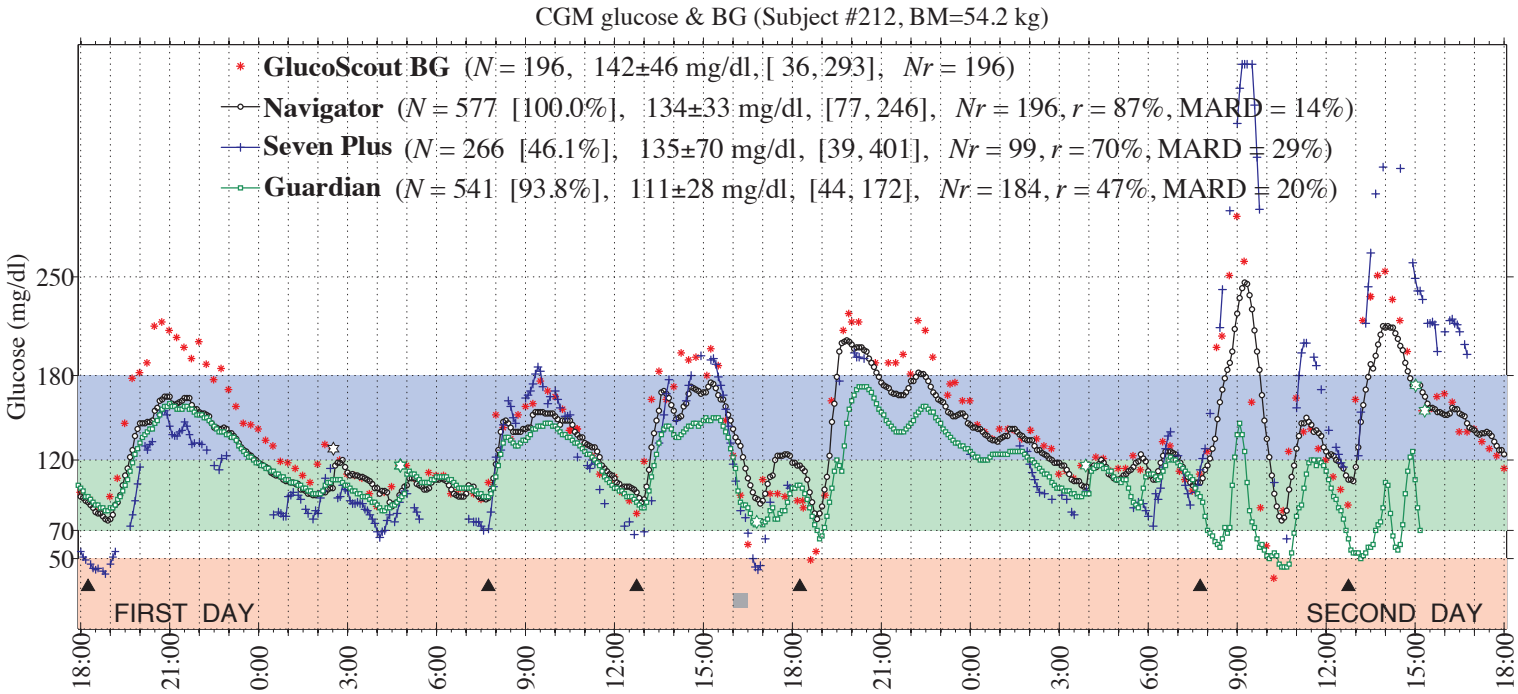
Supplementary Figure 7.

Results obtained during 48 hours of continuous closed-loop control in Subject #203. Note the 5-hour period from 7:00–12:00 hours in which the Guardian essentially missed the hyperglycemic excursion associated with the fifth meal. The closed-loop system had to be restarted between 18:30–20:45 as the fourth meal was ending. Because the Navigator data was streamed to the closed-loop system, it was not recorded during this interval. Consequently, the reporting percentage of the Navigator in this experiment is a lower-bound estimate.



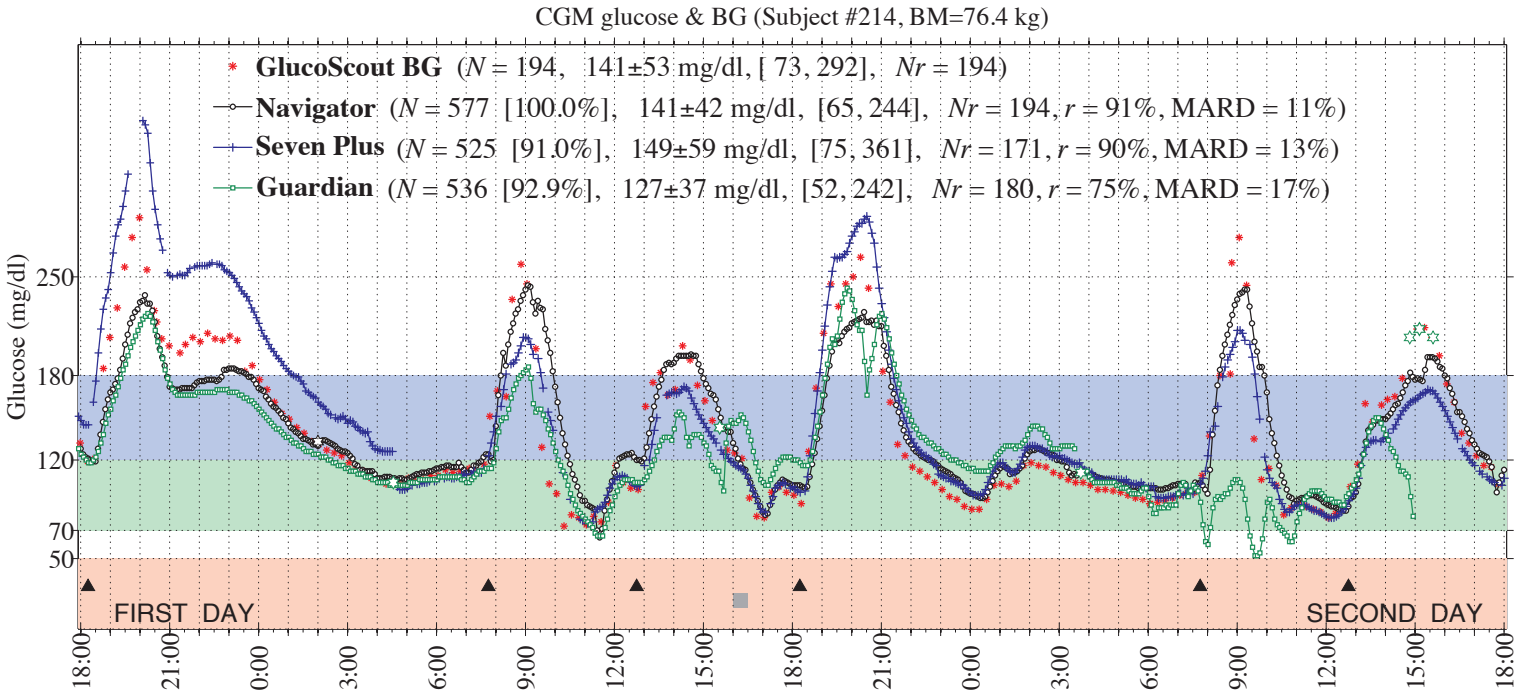
Supplementary Figure 8.

Results obtained during 48 hours of continuous closed-loop control in Subject #211.



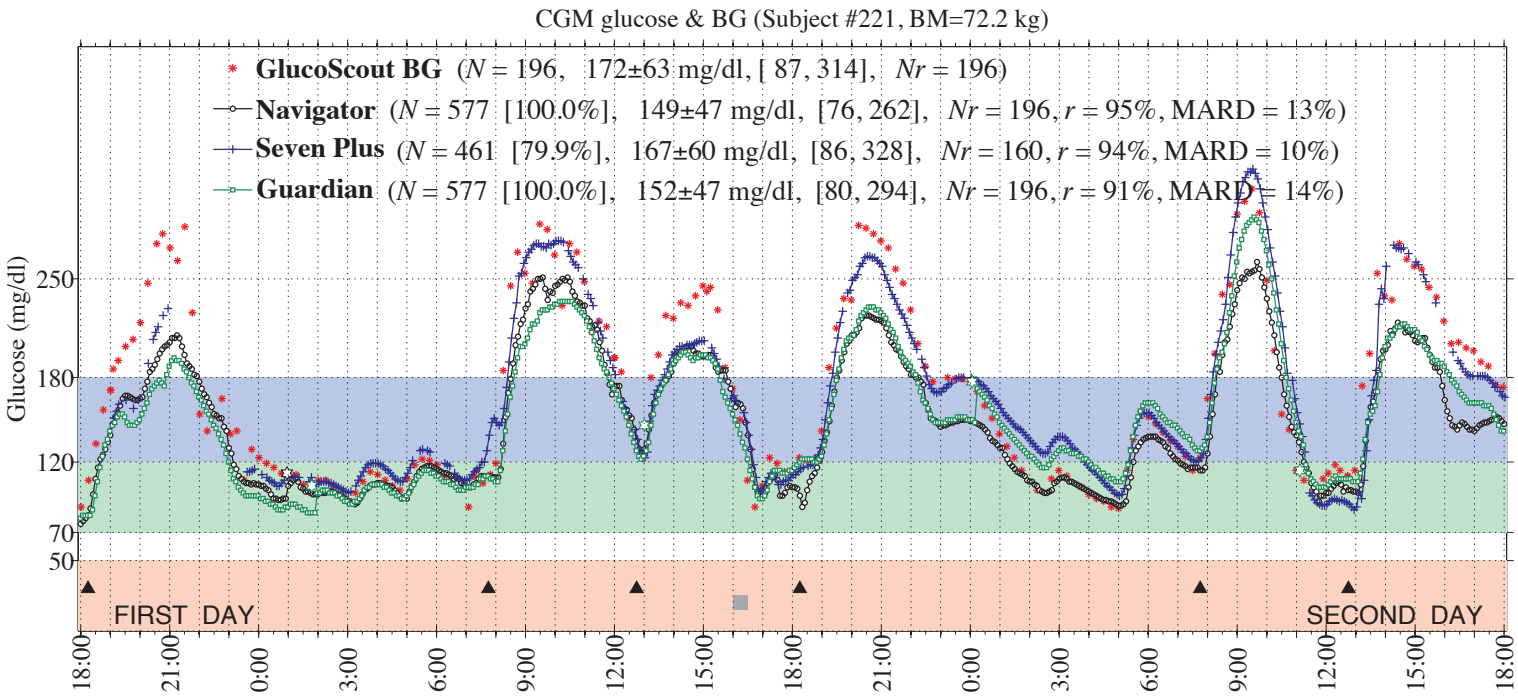
Supplementary Figure 9.

Results obtained during 48 hours of continuous closed-loop control in Subject #212. Note the 5-hour period from 13:00–18:00 hours in which the Guardian essentially missed the hyperglycemic excursion associated with the sixth meal.



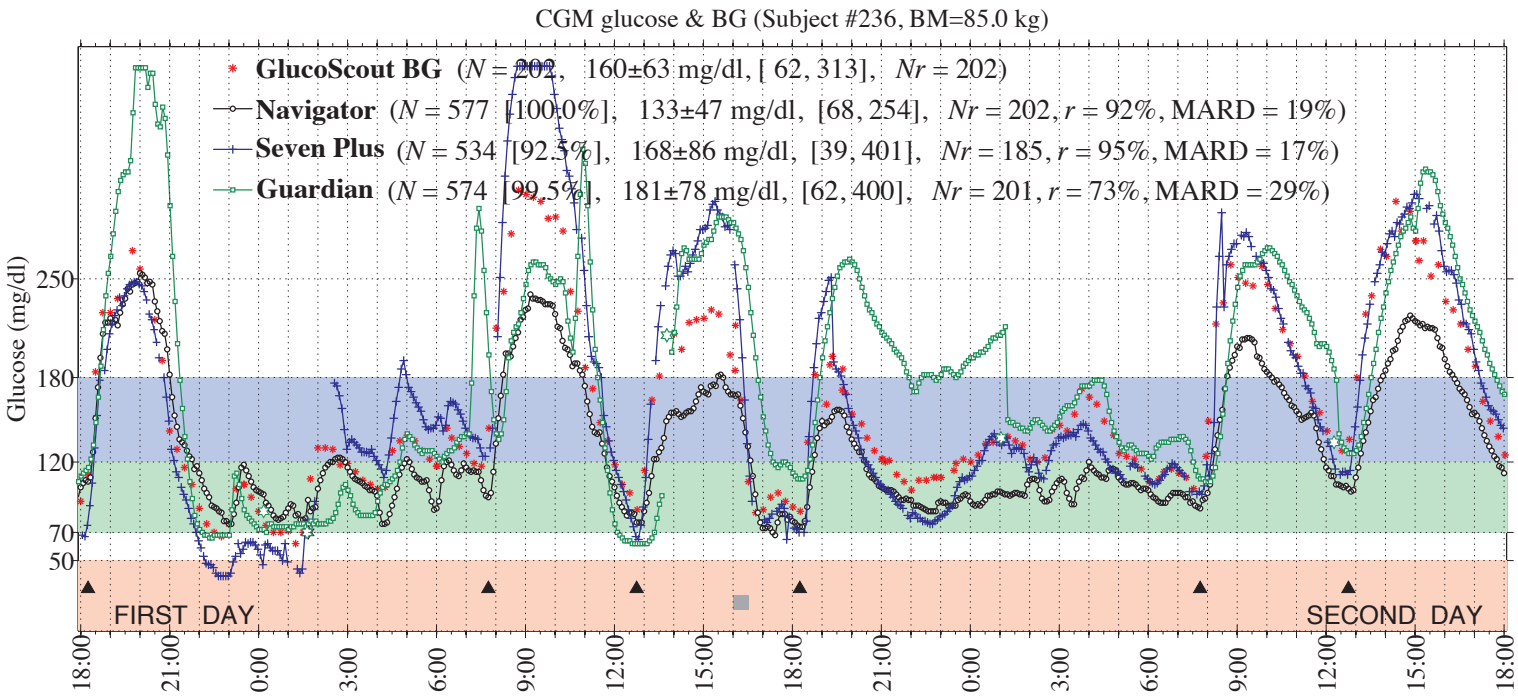
Supplementary Figure 10.

Results obtained during 48 hours of continuous closed-loop control in Subject #214. Note the 2-hour period from 8:00–10:00 hours and the 4-hour period from 14:00–18:00 hours in which the Guardian essentially missed the hyperglycemic excursions associated with the fifth and sixth meals, respectively.



Supplementary Figure 11.

Results obtained during 48 hours of continuous closed-loop control in Subject #221.



Supplementary Figure 12.

Results obtained during 48 hours of continuous closed-loop control in Subject #236. Note the 2-hour period from 8:30–10:30 hours in which the Seven Plus severely over-estimated glucose during the second meal. Note the 2-hour period from 19:00–21:00 hours and the 6-hour period from 19:00–1:00 hours in which the Guardian severely over-estimated glucose during the first and fourth meals, respectively.