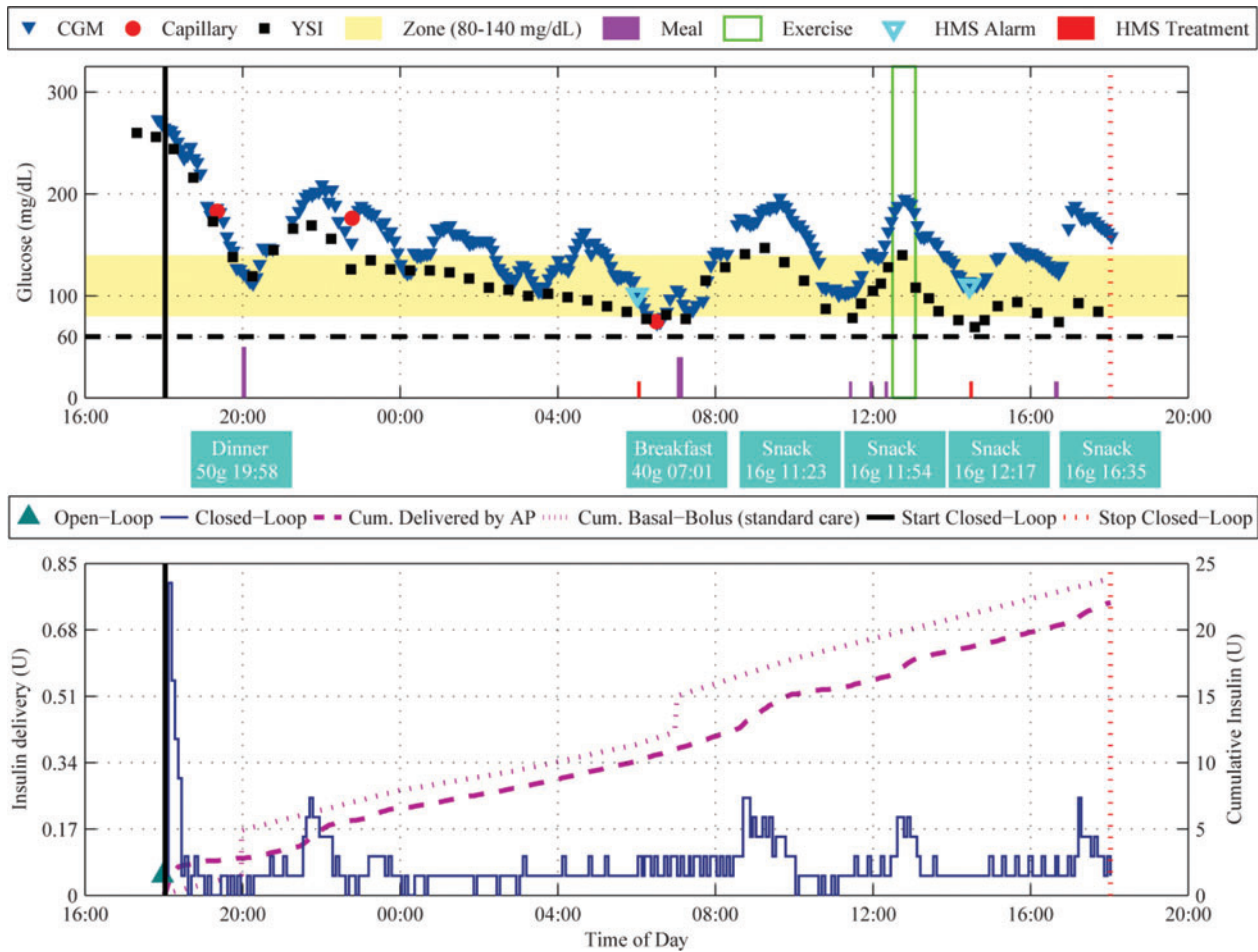
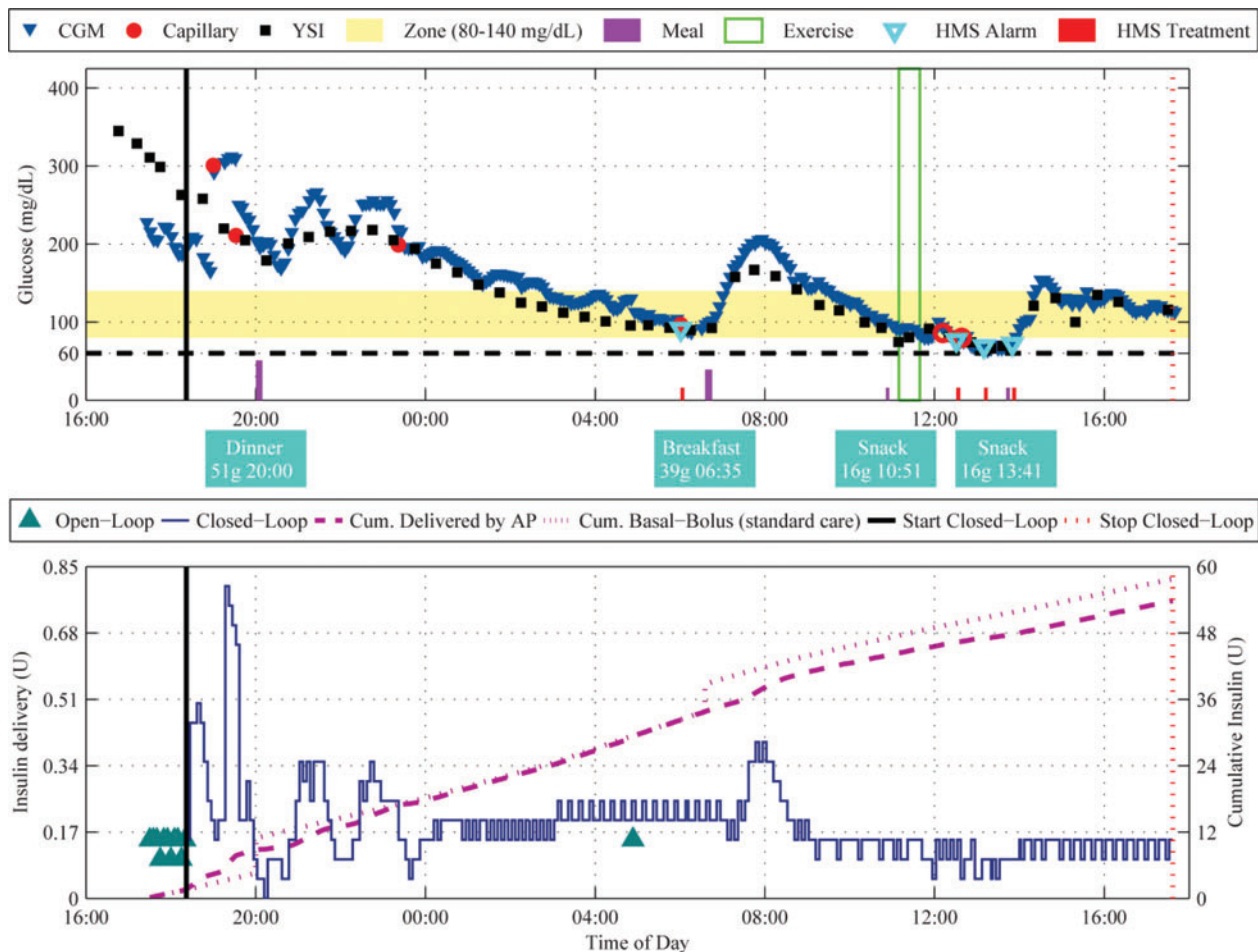


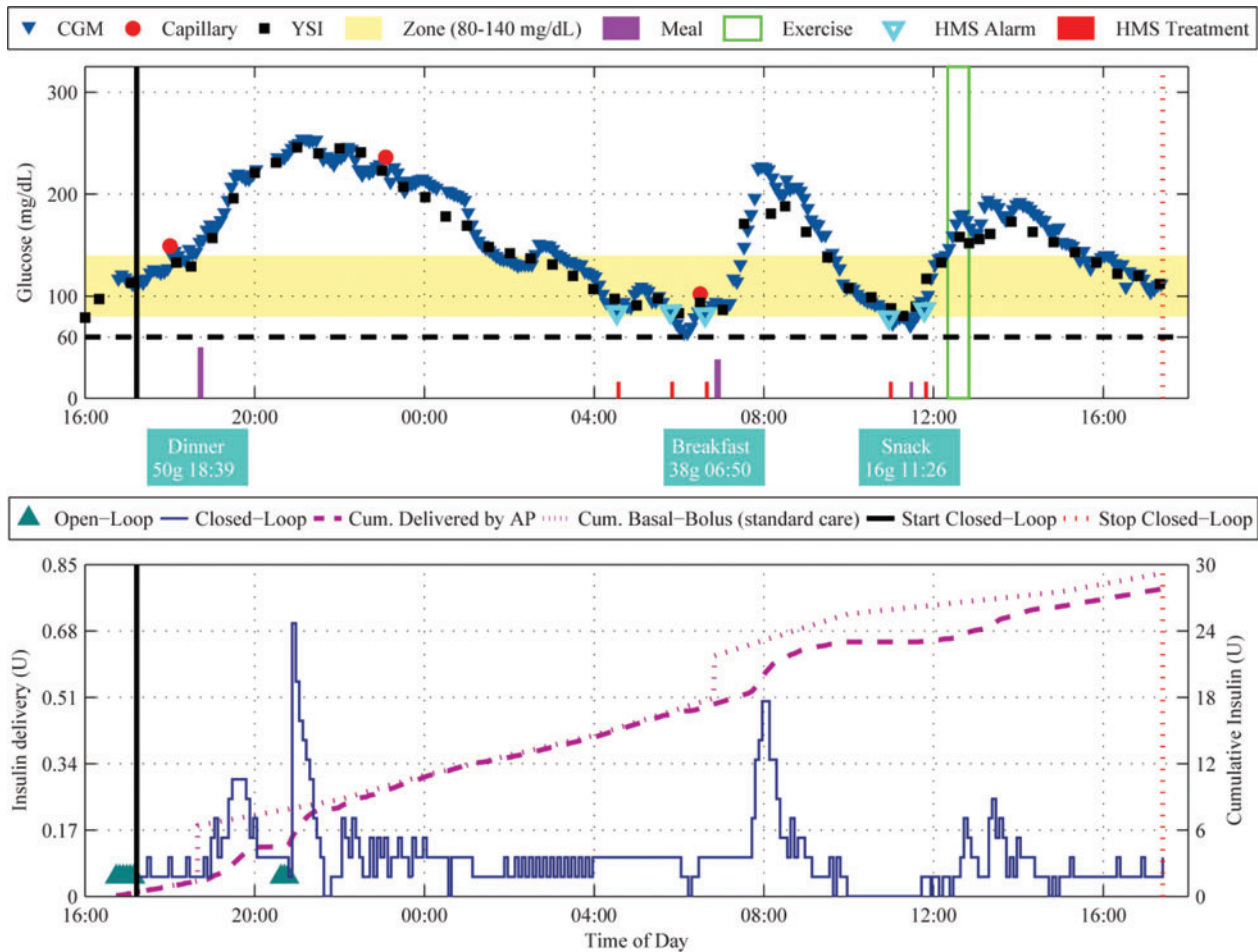
Supplementary Data



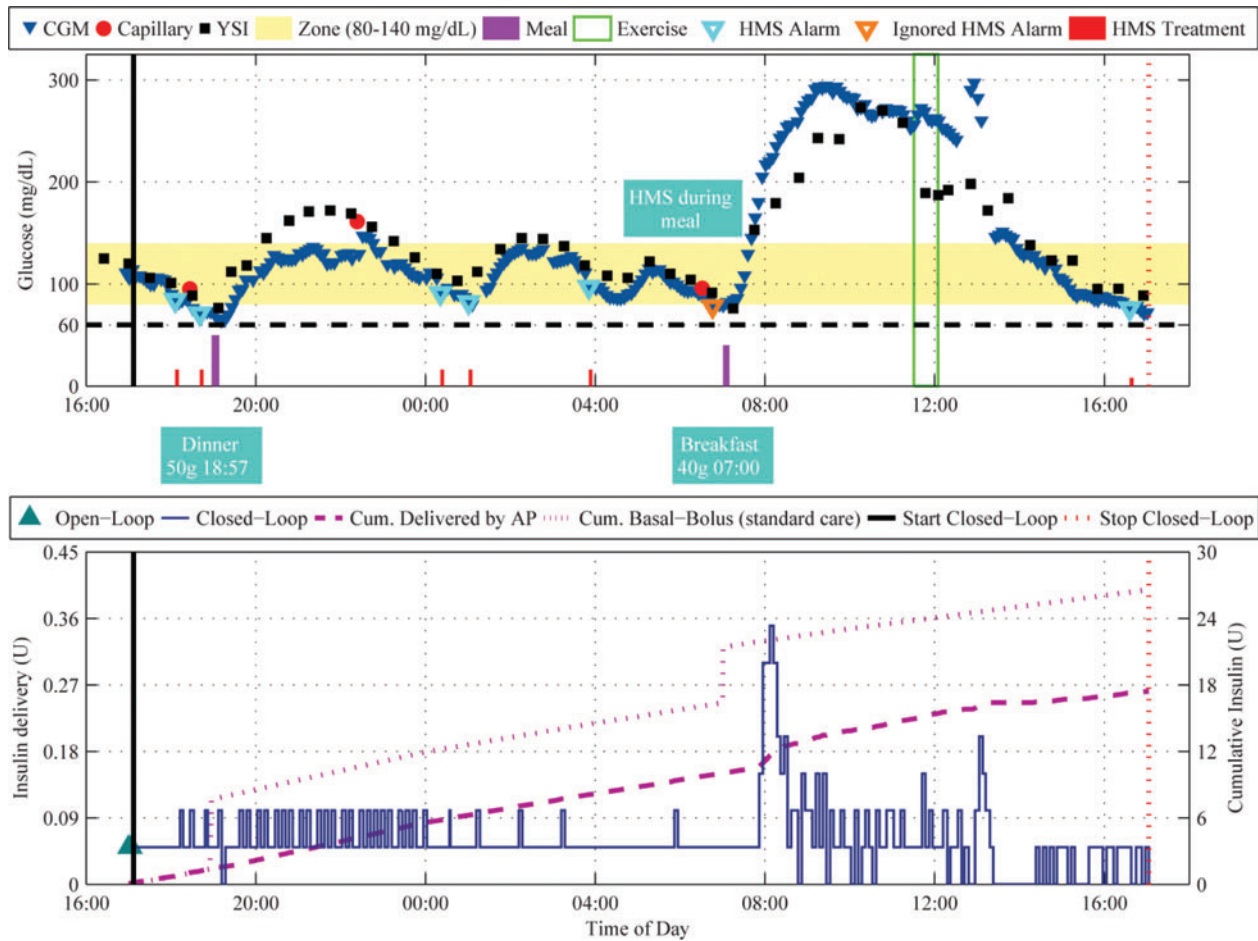
SUPPLEMENTARY FIG. S1. Clinical results output from closed-loop study number 1 demonstrating the ability of the design to effectively and safely overcome unannounced meal and unannounced exercise challenges. (**Upper panel**) Glucose tracing is shown with continuous glucose monitoring (CGM) in blue triangles, YSI (YSI glucose and lactate analyzer) in black squares, capillary calibrations in red circles, and the control zone in the yellow filled-in area. Meals and snacks are shown in purple bars, and rescue carbohydrates from health monitoring system (HMS) alarms are shown in red bars, with the alarms shown as blue triangles over the CGM measurement with which they coincided. The exercise session is shown in the green area. (**Lower panel**) Insulin delivery is shown with closed-loop delivery in blue. The cumulative (Cum.) insulin delivered during closed-loop is shown in purple dashed lines, compared with the standard care estimation (basal plus bolus for the dinner and breakfast meals) in purple dotted lines, both corresponding with the right axis. AP, artificial pancreas.



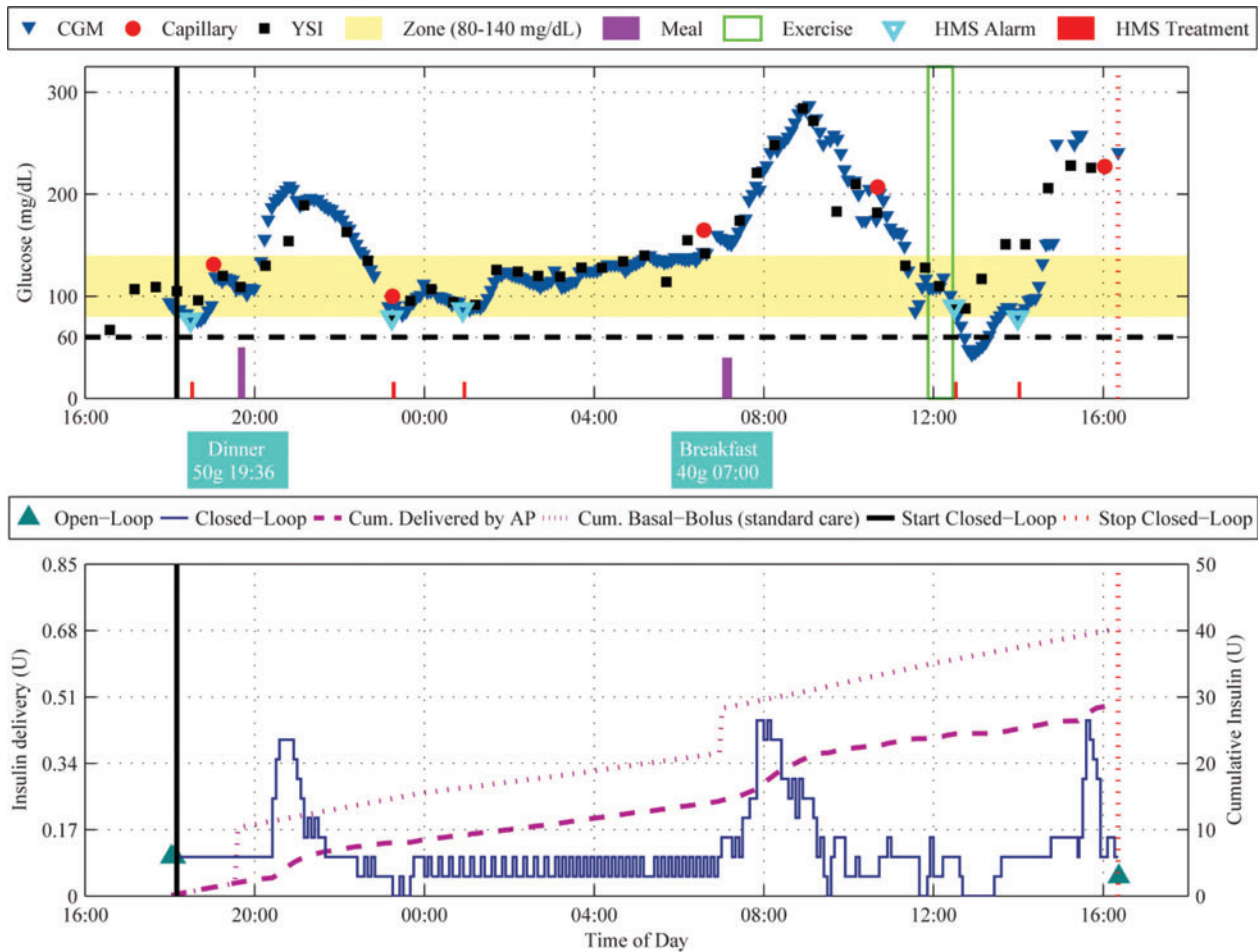
SUPPLEMENTARY FIG. S2. Clinical results output from closed-loop study number 2 demonstrating the ability of the design to effectively and safely overcome unannounced meal and unannounced exercise challenges. (**Upper panel**) Glucose tracing is shown with continuous glucose monitoring (CGM) in blue triangles, YSI (YSI glucose and lactate analyzer) in black squares, capillary calibrations in red circles, capillary measurements in red open circles, and the control zone in the yellow filled-in area. Meals and snacks are shown in purple bars, and rescue carbohydrates from health monitoring system (HMS) alarms are shown in red bars, with the alarms shown as blue triangles over the CGM measurement with which they coincided. The exercise session is shown in the green area. (**Lower panel**) Insulin delivery is shown with closed-loop delivery in blue. The cumulative (Cum.) insulin delivered during closed-loop is shown in purple dashed lines, compared with the standard care estimation (basal plus bolus for the dinner and breakfast meals) in purple dotted lines, both corresponding with the right axis. AP, artificial pancreas.



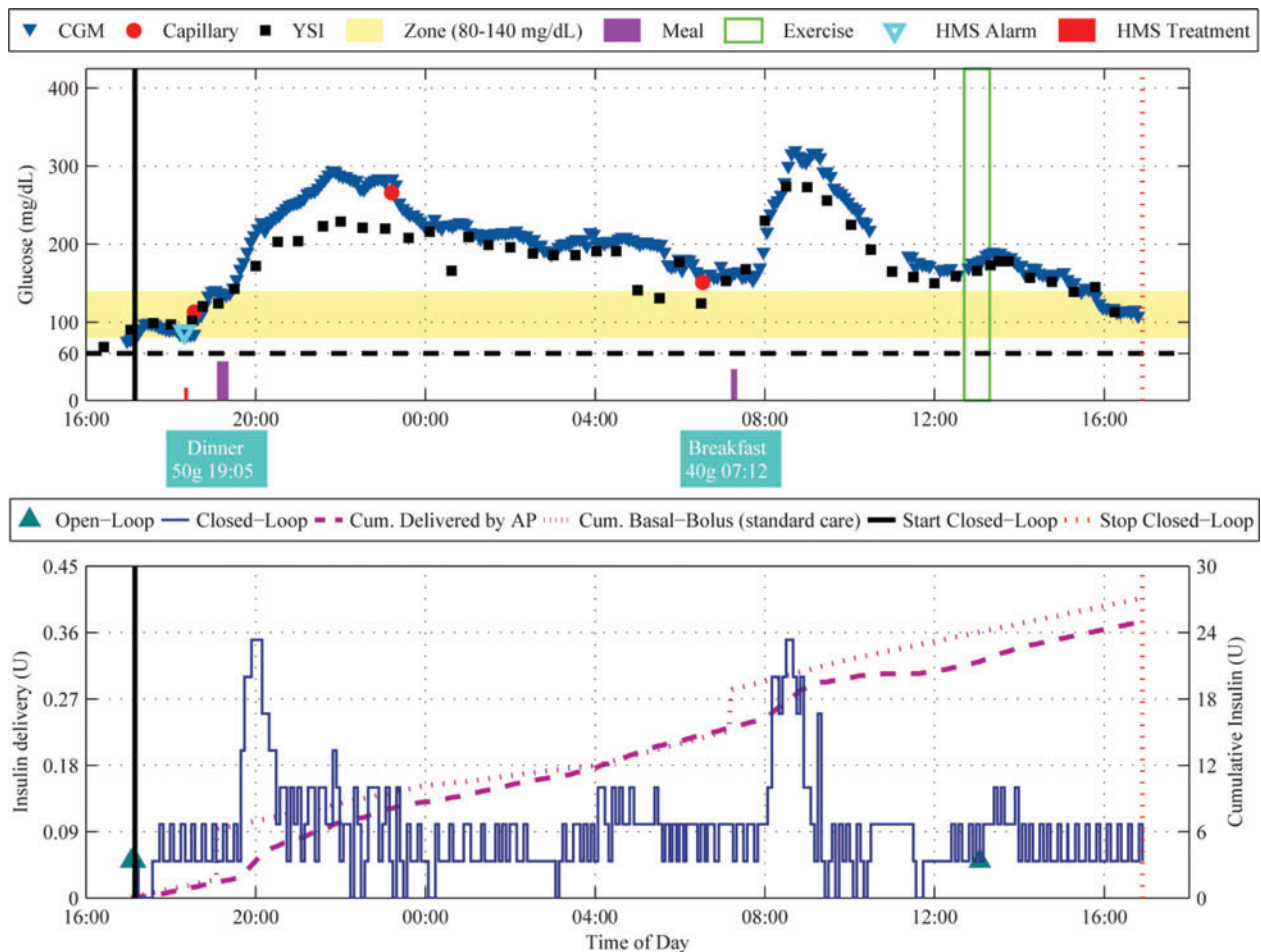
SUPPLEMENTARY FIG. S3. Clinical results output from closed-loop study number 3 demonstrating the ability of the design to effectively and safely overcome unannounced meal and unannounced exercise challenges. (**Upper panel**) Glucose tracing is shown with continuous glucose monitoring (CGM) in blue triangles, YSI (YSI glucose and lactate analyzer) in black squares, capillary calibrations in red circles, and the control zone in the yellow filled-in area. Meals and snacks are shown in purple bars, and rescue carbohydrates from health monitoring system (HMS) alarms are shown in red bars, with the alarms shown as blue triangles over the CGM measurement with which they coincided. The exercise session is shown in the green area. (**Lower panel**) Insulin delivery is shown with closed-loop delivery in blue. The cumulative (Cum.) insulin delivered during closed-loop is shown in purple dashed lines, compared with the standard care estimation (basal plus bolus for the dinner and breakfast meals) in purple dotted lines, both corresponding with the right axis. AP, artificial pancreas.



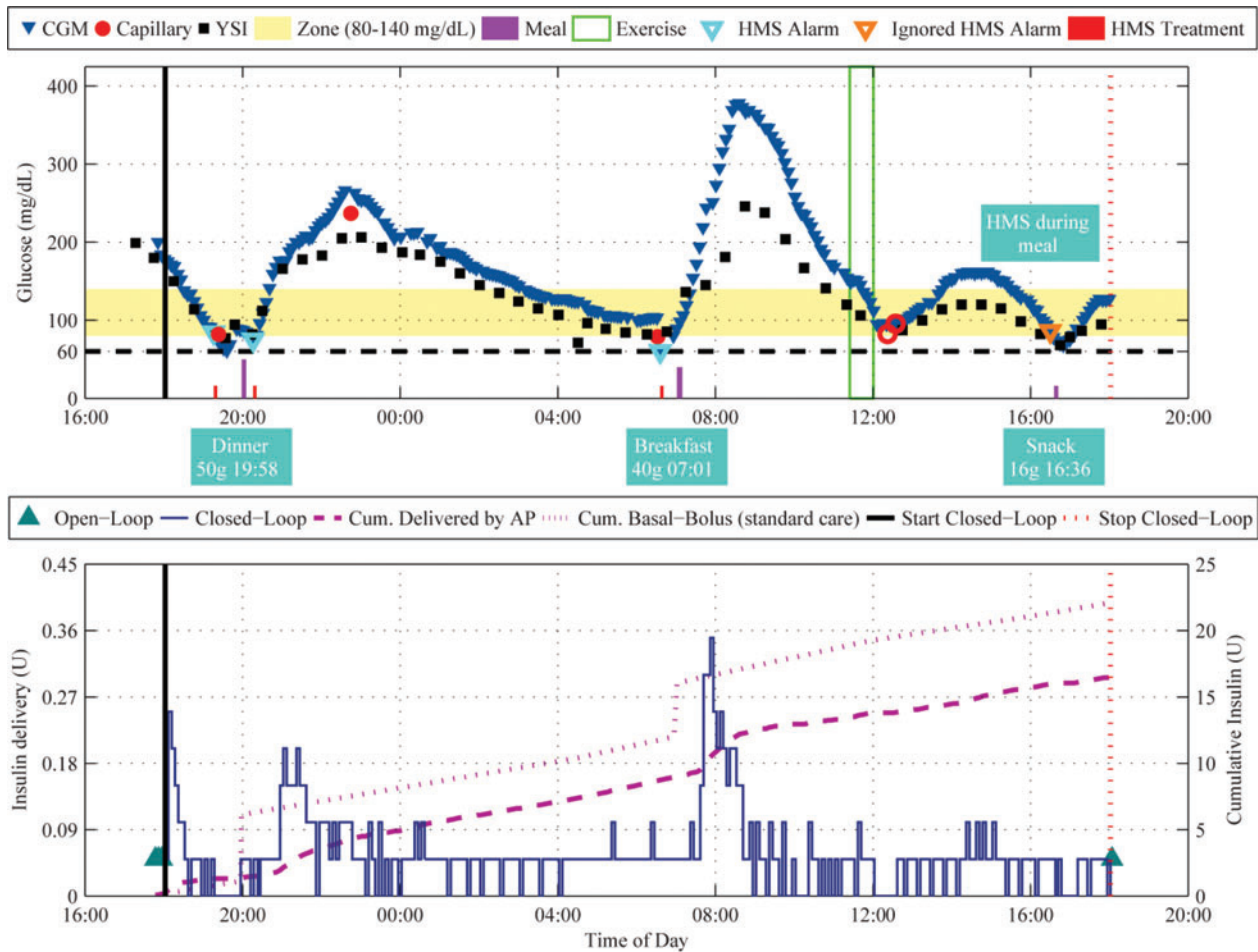
SUPPLEMENTARY FIG. S4. Clinical results output from closed-loop study number 4 demonstrating the ability of the design to effectively and safely overcome unannounced meal and unannounced exercise challenges. (**Upper panel**) Glucose tracing is shown with continuous glucose monitoring (CGM) in blue triangles, YSI (YSI glucose and lactate analyzer) in black squares, capillary calibrations in red circles, and the control zone in the yellow filled-in area. Meals and snacks are shown in purple bars, and rescue carbohydrates from health monitoring system (HMS) alarms are shown in red bars, with the alarms shown as blue triangles over the CGM measurement with which they coincided. Orange triangles indicate alarms that were ignored because of coincidence with meals, per protocol. The exercise session is shown in the green area. (**Lower panel**) Insulin delivery is shown with closed-loop delivery in blue. The cumulative (Cum.) insulin delivered during closed-loop is shown in purple dashed lines, compared with the standard care estimation (basal plus bolus for the dinner and breakfast meals) in purple dotted lines, both corresponding with the right axis. AP, artificial pancreas.



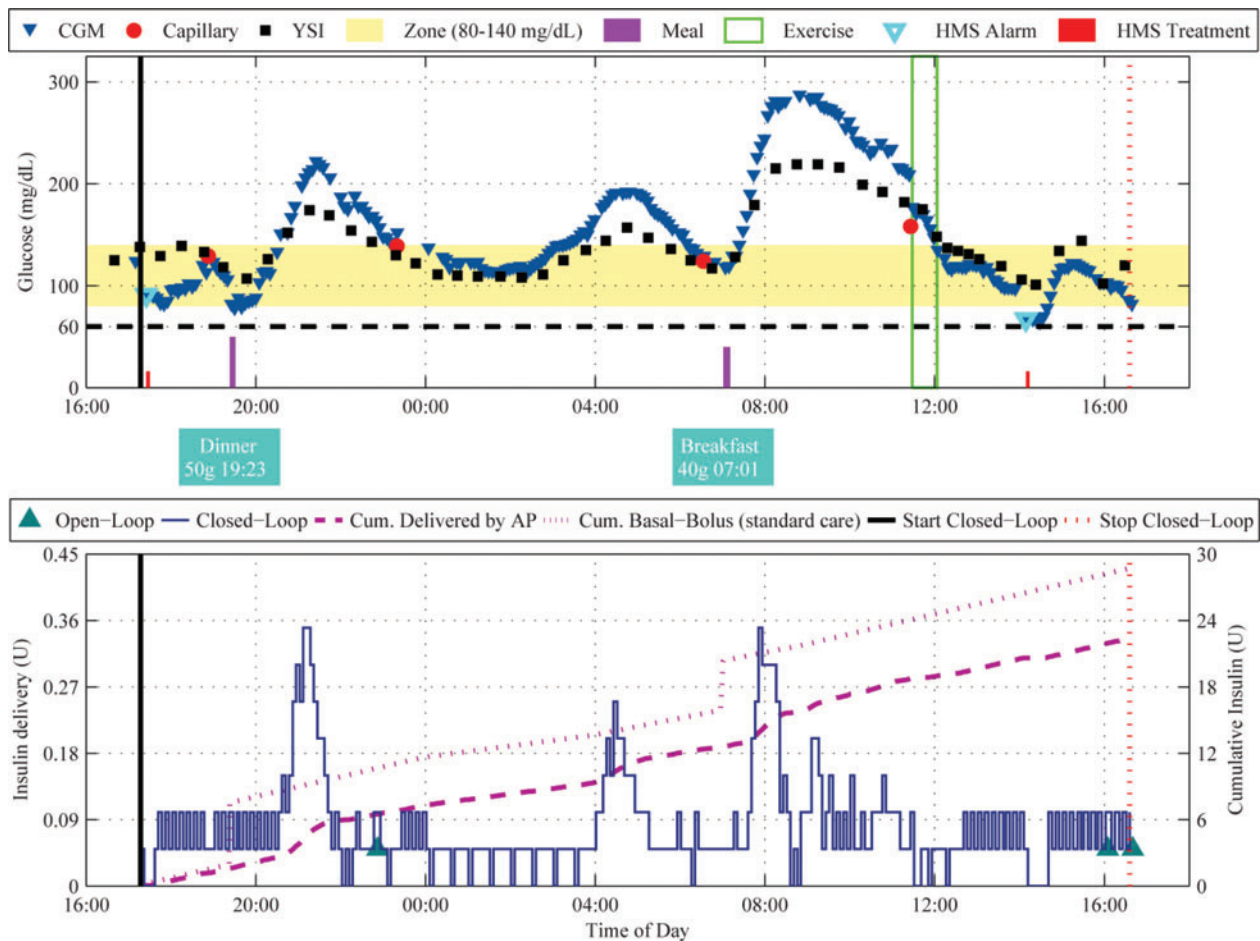
SUPPLEMENTARY FIG. S5. Clinical results output from closed-loop study number 5 demonstrating the ability of the design to effectively and safely overcome unannounced meal and unannounced exercise challenges. (**Upper panel**) Glucose tracing is shown with continuous glucose monitoring (CGM) in blue triangles, YSI (YSI glucose and lactate analyzer) in black squares, capillary calibrations in red circles, and the control zone in the yellow filled-in area. Meals and snacks are shown in purple bars, and rescue carbohydrates from health monitoring system (HMS) alarms are shown in red bars, with the alarms shown as blue triangles over the CGM measurement with which they coincided. The exercise session is shown in the green area. (**Lower panel**) Insulin delivery is shown with closed-loop delivery in blue. The cumulative (Cum.) insulin delivered during closed-loop is shown in purple dashed lines, compared with the standard care estimation (basal plus bolus for the dinner and breakfast meals) in purple dotted lines, both corresponding with the right axis. AP, artificial pancreas.



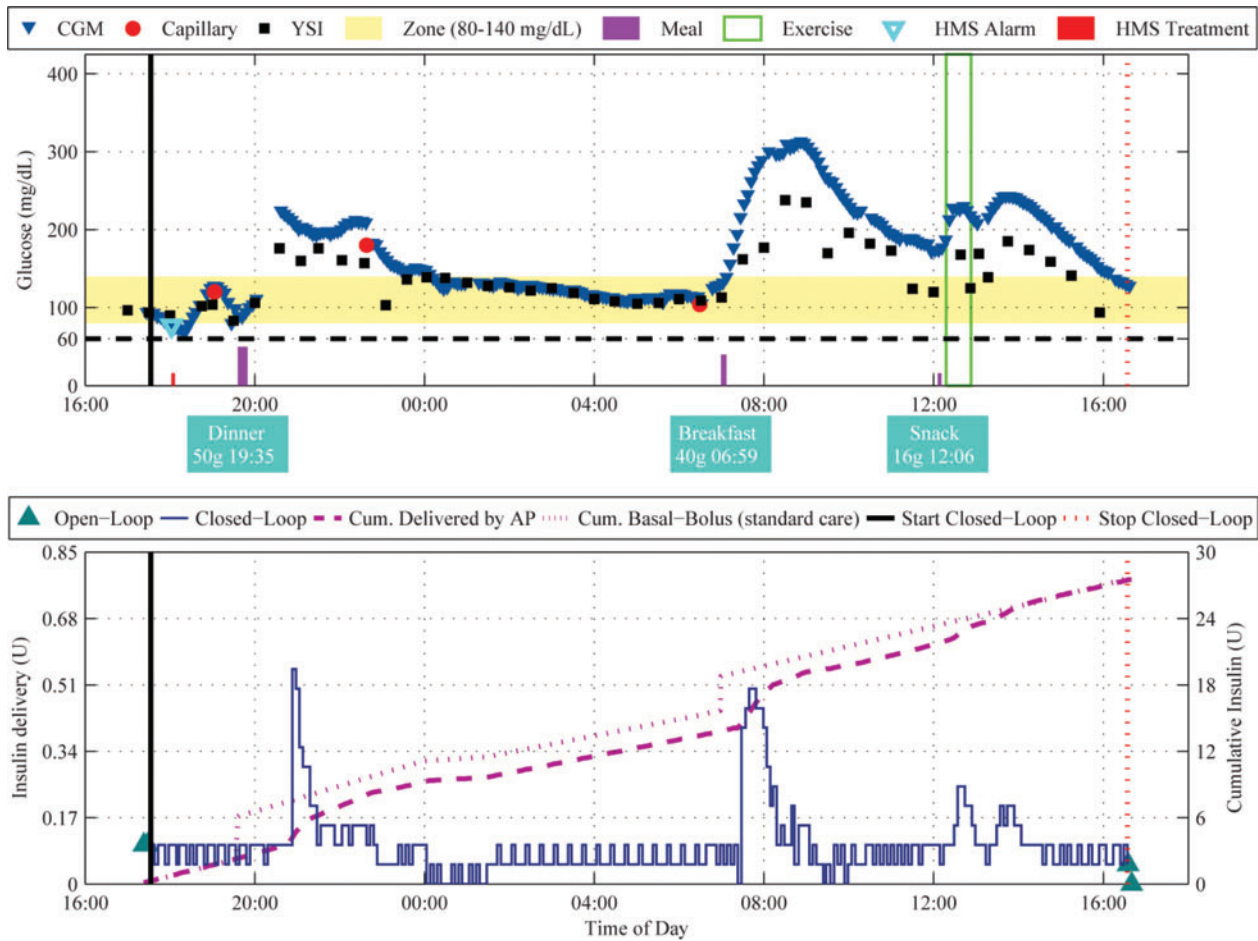
SUPPLEMENTARY FIG. S6. Clinical results output from closed-loop study number 6 demonstrating the ability of the design to effectively and safely overcome unannounced meal and unannounced exercise challenges. (**Upper panel**) Glucose tracing is shown with continuous glucose monitoring (CGM) in blue triangles, YSI (YSI glucose and lactate analyzer) in black squares, capillary calibrations in red circles, and the control zone in the yellow filled-in area. Meals and snacks are shown in purple bars, and rescue carbohydrates from health monitoring system (HMS) alarms are shown in red bars, with the alarms shown as blue triangles over the CGM measurement with which they coincided. The exercise session is shown in the green area. (**Lower panel**) Insulin delivery is shown with closed-loop delivery in blue. The cumulative (Cum.) insulin delivered during closed-loop is shown in purple dashed lines, compared with the standard care estimation (basal plus bolus for the dinner and breakfast meals) in purple dotted lines, both corresponding with the right axis. AP, artificial pancreas.



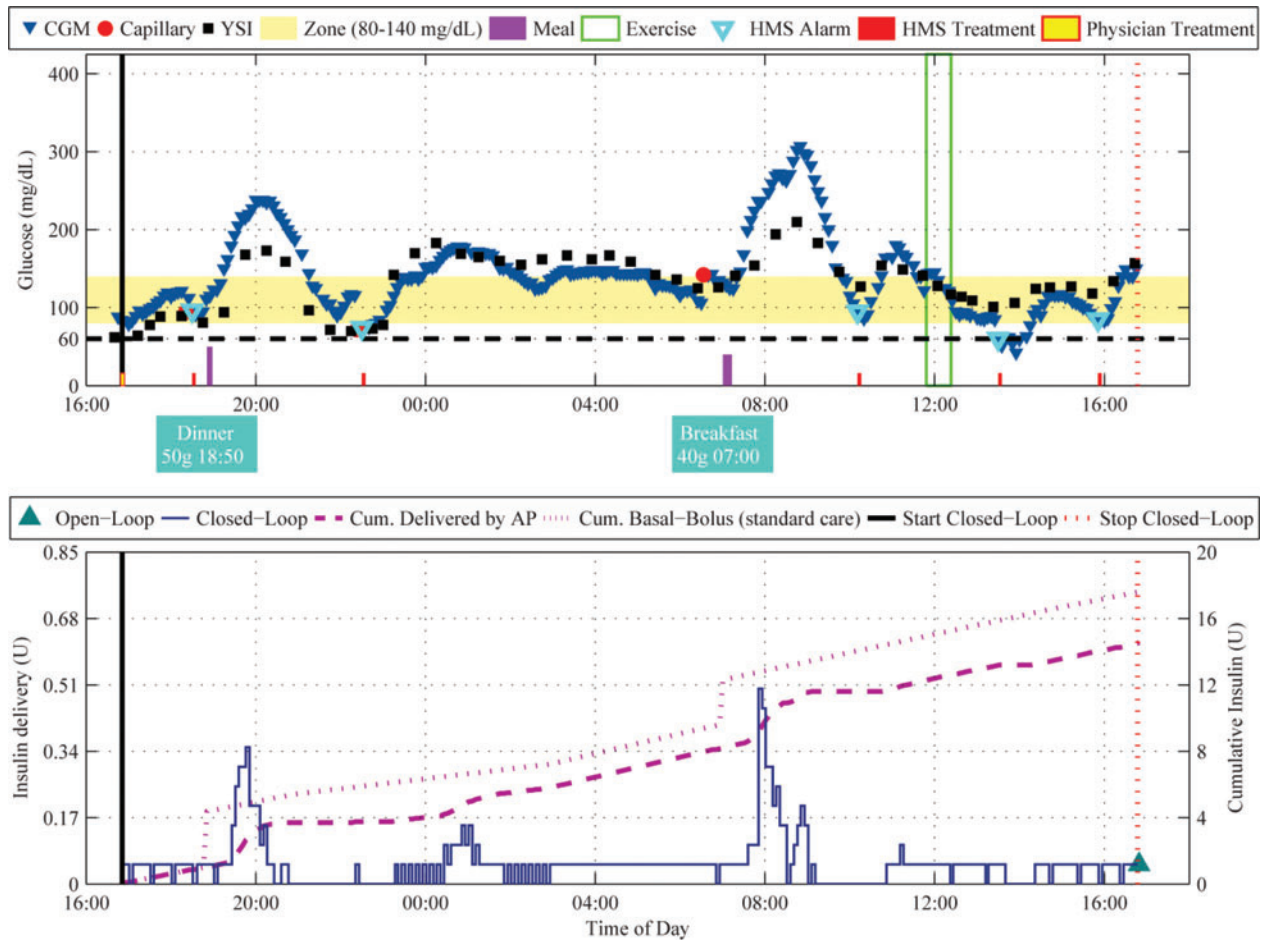
SUPPLEMENTARY FIG. S7. Clinical results output from closed-loop study number 7 demonstrating the ability of the design to effectively and safely overcome unannounced meal and unannounced exercise challenges. (**Upper panel**) Glucose tracing is shown with continuous glucose monitoring (CGM) in blue triangles, YSI (YSI glucose and lactate analyzer) in black squares, capillary calibrations in red circles, and the control zone in the yellow filled-in area. Meals and snacks are shown in purple bars, and rescue carbohydrates from health monitoring system (HMS) alarms are shown in red bars, with the alarms shown as blue triangles over the CGM measurement with which they coincided. Orange triangles indicate alarms that were ignored because of coincidence with meals, per protocol. The exercise session is shown in the green area. (**Lower panel**) Insulin delivery is shown with closed-loop delivery in blue. The cumulative (Cum.) insulin delivered during closed-loop is shown in purple dashed lines, compared with the standard care estimation (basal plus bolus for the dinner and breakfast meals) in purple dotted lines, both corresponding with the right axis. AP, artificial pancreas.



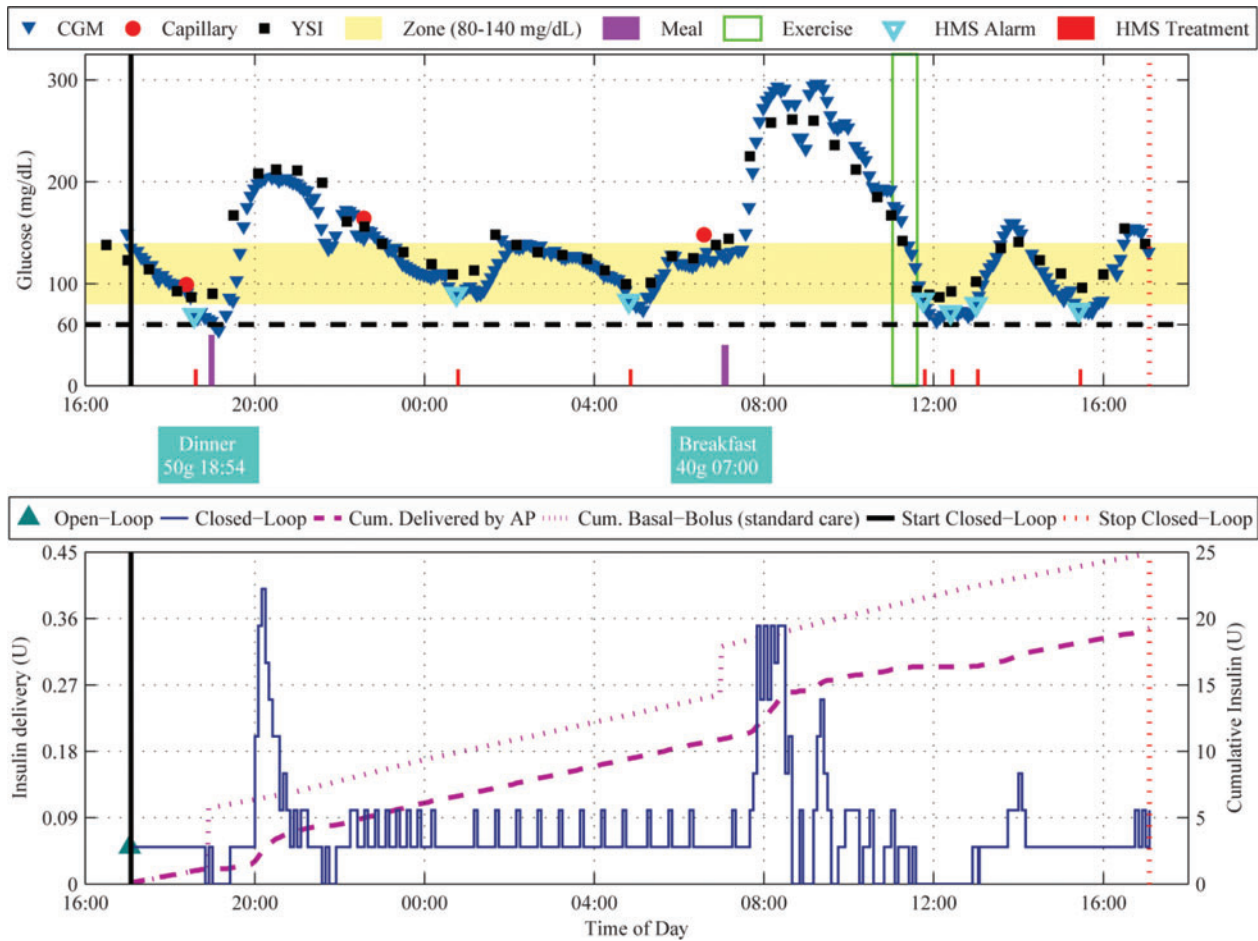
SUPPLEMENTARY FIG. S8. Clinical results output from closed-loop study number 8 demonstrating the ability of the design to effectively and safely overcome unannounced meal and unannounced exercise challenges. (**Upper panel**) Glucose tracing is shown with continuous glucose monitoring (CGM) in blue triangles, YSI (YSI glucose and lactate analyzer) in black squares, capillary calibrations in red circles, and the control zone in the yellow filled-in area. Meals and snacks are shown in purple bars, and rescue carbohydrates from health monitoring system (HMS) alarms are shown in red bars, with the alarms shown as blue triangles over the CGM measurement with which they coincided. The exercise session is shown in the green area. (**Lower panel**) Insulin delivery is shown with closed-loop delivery in blue. The cumulative (Cum.) insulin delivered during closed-loop is shown in purple dashed lines, compared with the standard care estimation (basal plus bolus for the dinner and breakfast meals) in purple dotted lines, both corresponding with the right axis. AP, artificial pancreas.



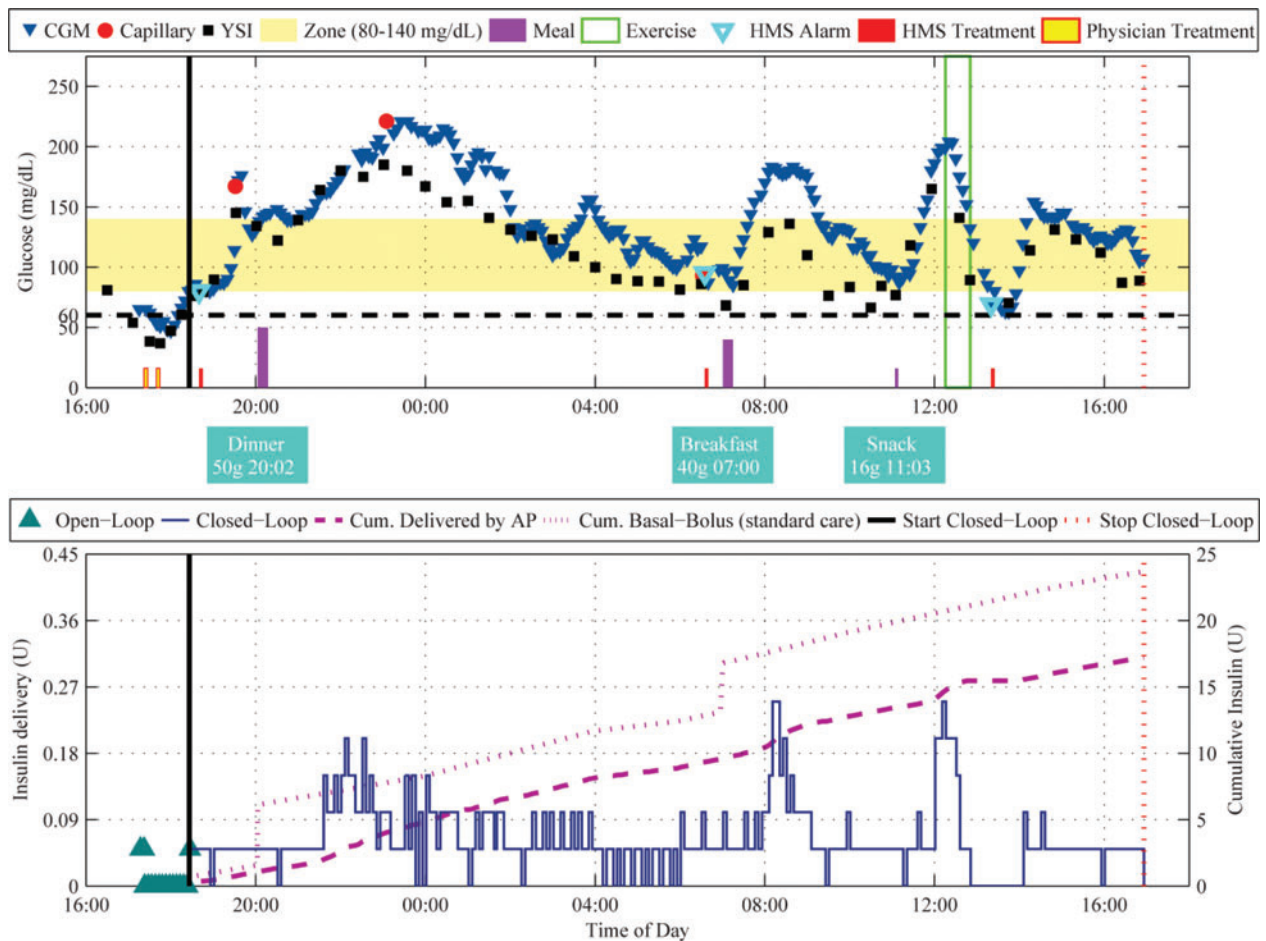
SUPPLEMENTARY FIG. S9. Clinical results output from closed-loop study number 9 demonstrating the ability of the design to effectively and safely overcome unannounced meal and unannounced exercise challenges. (**Upper panel**) Glucose tracing is shown with continuous glucose monitoring (CGM) in blue triangles, YSI (YSI glucose and lactate analyzer) in black squares, capillary calibrations in red circles, and the control zone in the yellow filled-in area. Meals and snacks are shown in purple bars, and rescue carbohydrates from health monitoring system (HMS) alarms are shown in red bars, with the alarms shown as blue triangles over the CGM measurement with which they coincided. The exercise session is shown in the green area. (**Lower panel**) Insulin delivery is shown with closed-loop delivery in blue. The cumulative (Cum.) insulin delivered during closed-loop is shown in purple dashed lines, compared with the standard care estimation (basal plus bolus for the dinner and breakfast meals) in purple dotted lines, both corresponding with the right axis. AP, artificial pancreas.



SUPPLEMENTARY FIG. S10. Clinical results output from closed-loop study number 10 demonstrating the ability of the design to effectively and safely overcome unannounced meal and unannounced exercise challenges. (**Upper panel**) Glucose tracing is shown with continuous glucose monitoring (CGM) in blue triangles, YSI (YSI glucose and lactate analyzer) in black squares, capillary calibrations in red circles, and the control zone in the yellow filled-in area. Meals and snacks are shown in purple bars, and rescue carbohydrates from health monitoring system (HMS) alarms are shown in red bars, with the alarms shown as blue triangles over the CGM measurement with which they coincided. Physician-ordered treatments are shown with yellow bars with red edges; these were given prior to the trial because of low blood glucose level, per protocol. The exercise session is shown in the green area. (**Lower panel**) Insulin delivery is shown with closed-loop delivery in blue. The cumulative (Cum.) insulin delivered during closed-loop is shown in purple dashed lines, compared with the standard care estimation (basal plus bolus for the dinner and breakfast meals) in purple dotted lines, both corresponding with the right axis. AP, artificial pancreas.



SUPPLEMENTARY FIG. S11. Clinical results output from closed-loop study number 11 demonstrating the ability of the design to effectively and safely overcome unannounced meal and unannounced exercise challenges. (**Upper panel**) Glucose tracing is shown with continuous glucose monitoring (CGM) in blue triangles, YSI (YSI glucose and lactate analyzer) in black squares, capillary calibrations in red circles, and the control zone in the yellow filled-in area. Meals and snacks are shown in purple bars, and rescue carbohydrates from health monitoring system (HMS) alarms are shown in red bars, with the alarms shown as blue triangles over the CGM measurement with which they coincided. The exercise session is shown in the green area. (**Lower panel**) Insulin delivery is shown with closed-loop delivery in blue. The cumulative (Cum.) insulin delivered during closed-loop is shown in purple dashed lines, compared with the standard care estimation (basal plus bolus for the dinner and breakfast meals) in purple dotted lines, both corresponding with the right axis. AP, artificial pancreas.



SUPPLEMENTARY FIG. S12. Clinical results output from closed-loop study number 12 demonstrating the ability of the design to effectively and safely overcome unannounced meal and unannounced exercise challenges. (**Upper panel**) Glucose tracing is shown with continuous glucose monitoring (CGM) in blue triangles, YSI (YSI glucose and lactate analyzer) in black squares, capillary calibrations in red circles, and the control zone in the yellow filled-in area. Meals and snacks are shown in purple bars, and rescue carbohydrates from health monitoring system (HMS) alarms are shown in red bars, with the alarms shown as blue triangles over the CGM measurement with which they coincided. Physician-ordered treatments are shown with yellow bars with red edges; these were given prior to the trial because of low blood glucose level, per protocol. The exercise session is shown in the green area. (**Lower panel**) Insulin delivery is shown with closed-loop delivery in blue. The cumulative (Cum.) insulin delivered during closed-loop is shown in purple dashed lines, compared with the standard care estimation (basal plus bolus for the dinner and breakfast meals) in purple dotted lines, both corresponding with the right axis. AP, artificial pancreas.