

Supplementary Figures:

Supplementary Figure 1: Inclusion and Exclusion criteria for study participants.

Subject Criteria

Inclusion Criteria:

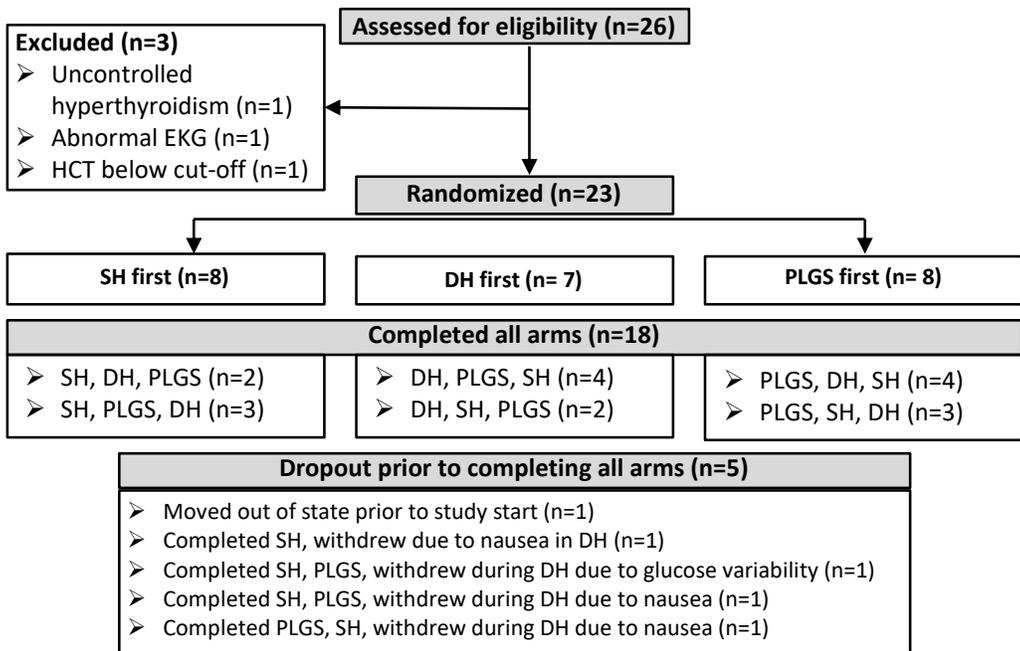
1. Diagnosis of type 1 diabetes mellitus for at least 1 year.
2. Male or female subjects 21 to 50 years of age.
3. Physically willing and able to perform 45 min of exercise (as determined by the investigator after reviewing the subjects activity level)
4. Current use of an insulin pump for at least 3 months with stable insulin pump settings for >2 weeks.
5. Lives with another person age 18 or older who will be present while subject exercises at home and that can attend the training on using the system.
6. Lives within 40 miles of OHSU main campus.
7. HbA1c \leq 10% at screening.
8. Total daily insulin requirement is less than 139 units/day.
9. Current use of a phone or other device so can be contacted by study staff off-campus
10. Willingness to follow all study procedures, including attending all clinic visits.
11. Willingness to sign informed consent and HIPAA documents.

Exclusion Criteria:

1. Female of childbearing potential who is pregnant or intending to become pregnant or breast-feeding, or is not using adequate contraceptive methods. Acceptable contraception includes birth control pill / patch / vaginal ring, Depo-Provera, Norplant, an IUD, the double barrier method (the woman uses a diaphragm and spermicide and the man uses a condom), or abstinence.
2. Any cardiovascular disease, defined as a clinically significant EKG abnormality at the time of screening or any history of: stroke, heart failure, myocardial infarction, angina pectoris, or coronary arterial bypass graft or angioplasty. Diagnosis of 2nd or 3rd degree heart block or any non-physiological arrhythmia judged by the investigator to be exclusionary.
3. Renal insufficiency (GFR < 60 ml/min, using the MDRD equation as reported by the OHSU laboratory).
4. Liver failure, cirrhosis, or any other liver disease that compromises liver function as determined by the investigator.
5. Hematocrit of less than 36% for men, less than 32% for women.
6. Hypertensive subjects with systolic blood pressure \geq 160 mmHg or diastolic blood pressure \geq 100 mmHg despite treatment or who have treatment-refractory hypertension (e.g. requiring four or more medications).
7. History of severe hypoglycemia during the past 12 months prior to screening visit or hypoglycemia unawareness as judged by the investigator. Subjects will complete a hypoglycemia awareness questionnaire. Subjects will be excluded for four or more R responses.
8. History of Diabetes Ketoacidosis during the prior 6 months prior to screening visit, as diagnosed on hospital admission or as judged by the investigator.
9. Adrenal insufficiency.
10. Any active infection.
11. Known or suspected abuse of alcohol, narcotics, or illicit drugs.
12. Seizure disorder.
13. Active foot ulceration.
14. Severe peripheral arterial disease characterized by ischemic rest pain or severe claudication.

15. Major surgical operation within 30 days prior to screening.
16. Use of an investigational drug within 30 days prior to screening.
17. Chronic usage of any immunosuppressive medication (such as cyclosporine, azathioprine, sirolimus, or tacrolimus).
18. Bleeding disorder, treatment with warfarin, or platelet count below 50,000.
19. Allergy to aspart insulin.
20. Allergy to glucagon.
21. Need for uninterrupted treatment of acetaminophen.
22. Current administration of oral or parenteral corticosteroids.
23. Any life threatening disease, including malignant neoplasms and medical history of malignant neoplasms within the past 5 years prior to screening (except basal and squamous cell skin cancer).
24. Beta blockers or non-dihydropyridine calcium channel blockers.
25. Current use of any medication intended to lower glucose other than insulin (ex. use of liraglutide).
26. Diagnosis of pheochromocytoma, insulinoma, or glucagonoma, personal or family history of multiple endocrine neoplasia (MEN) 2A, MEN 2B, neurofibromatosis or von Hippel-Lindau disease.
27. History of severe hypersensitivity to milk protein.
28. Current use of any medication with strong anticholinergic properties, such as antihistamines, sleep aids, and antidiarrheal medications.
29. Current use of indomethacin.
30. Conditions that may result in low levels of releasable glucose in the liver and an inadequate reversal of hypoglycemia by glucagon such as prolonged fasting, starvation or chronic hypoglycemia as determined by the investigator.
31. A positive response to any of the questions from the Physical Activity Readiness Questionnaire with one exception: subject will not be excluded if he/she takes a single blood pressure medication that doesn't impact heart rate and blood pressure is controlled on the medication (blood pressure is less than 140/90 mmHg).
32. Any chest discomfort with physical activity, including pain or pressure, or other types of discomfort.
33. Any clinically significant disease or disorder which in the opinion of the Investigator may jeopardize the subject's safety or compliance with the protocol.

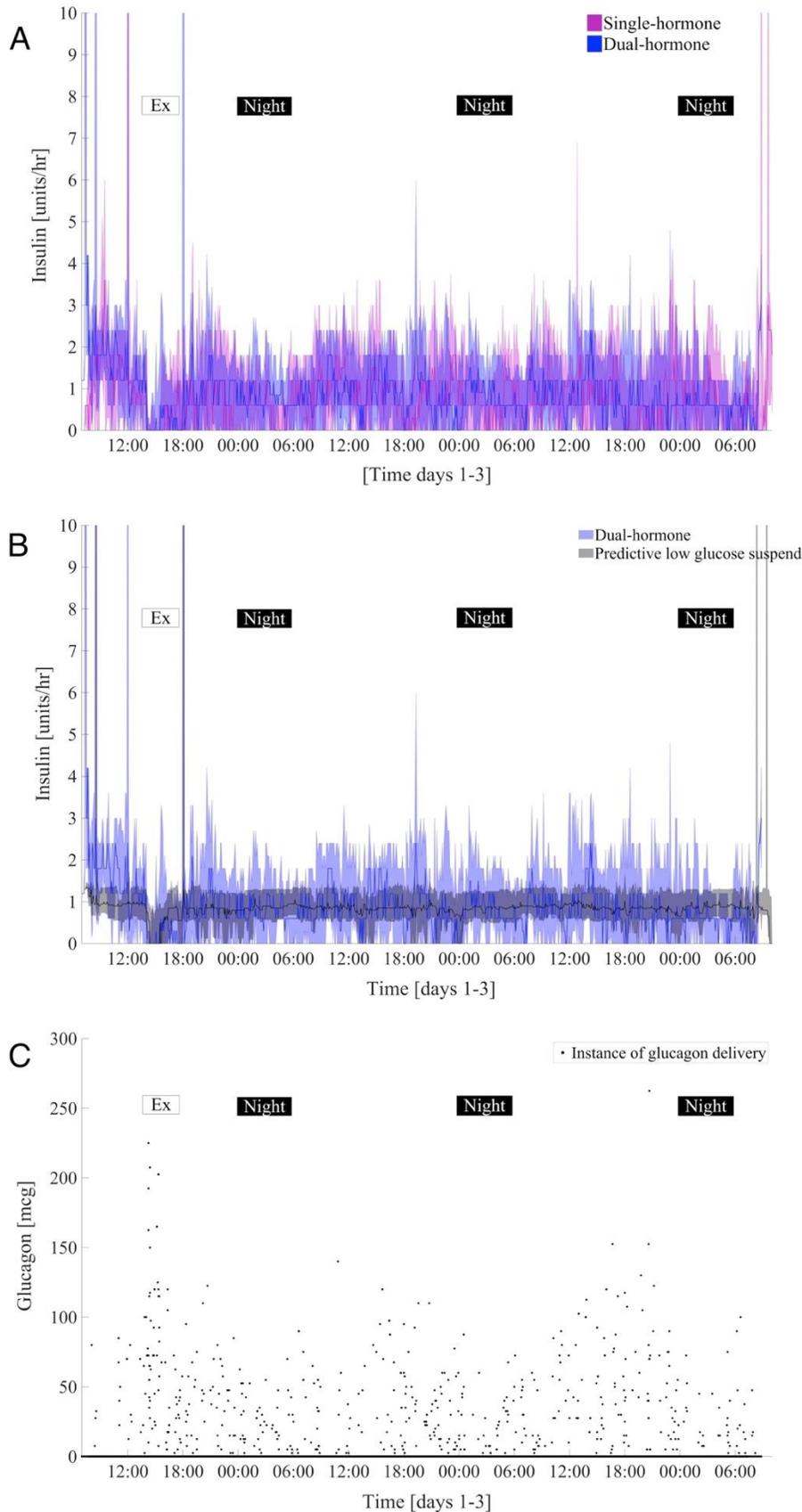
Supplementary Figure 2: Participant Flow Diagram.



Supplementary Figure 3: Study Design. In-clinic exercise-treadmill for 45 mins at 60% VO_{2max} two hours after lunch. Home exercise- ad lib exercise for 45 mins.

	Day 1	Day 2	Day 3
Dual hormone	In-clinic exercise	At home	At home exercise
Single hormone	In-clinic exercise	At home	At home exercise
PLGS	In-clinic exercise	At home	At home exercise

Supplementary Figure 4: Full study insulin and glucagon delivery. The 25% and 75% interquartile ranges are shown with colored graph and the median with the solid line. A) Insulin infusion (units/hr) for single-hormone (SH) in magenta versus dual-hormone (DH) in blue. B) Insulin infusion (units/hr) for dual-hormone (DH) in blue versus predictive low glucose suspend (PLGS) in grey. C) Glucagon delivery (mcg) for DH, each instance of glucagon delivery shown with black dot. “Ex” box indicates exercise start until 4 hours after. “Night” box indicates overnight period (12am-6am).



Supplementary Figure 5: In-clinic exercise period insulin and glucagon delivery. Treadmill exercise for 45 mins at 60% VO_{2max} occurred from minutes 0-45. The 25% and 75% interquartile ranges are shown with colored graph and the median with the solid line. A) Insulin infusion (units/hr) for single-hormone (SH) in magenta versus dual-hormone (DH) in blue. B) Insulin infusion (units/hr) for dual-hormone (DH) in blue versus Predictive low glucose suspend (PLGS) in grey. C) Glucagon delivery (mcg) for DH, each instance of glucagon delivery shown with black dot. “Exercise” box indicates the 45 minute exercise session.

