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# Multiple daily injection insulin regimen is an effective, and more economical, alternative to continuous insulin infusion for type 1 diabetics

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**ABSTRACT** A clinical decision report using:

Heller S, White D, Lee E, et al. A cluster randomised trial, cost-effectiveness analysis and psychosocial evaluation of insulin pump therapy compared with multiple injections during flexible intensive insulin therapy for type 1 diabetes: the REPOSE Trial. *Health Technol Assess.* 2017 Apr;21(20):1-278. <https://doi.org/10.3310/hta21200>

for a patient with type 1 diabetes.

**Keywords:** *type 1 diabetes, multiple daily injection, continuous insulin, cost*

## Clinical-Social Context

Susie Miller (pseudonym) is a 22 year old African American woman with type 1 diabetes mellitus (T1DM), diagnosed at age 6, who presented to the emergency department with diabetic ketoacidosis (DKA) after removing her insulin pump 2 days prior. Her past medical history includes four prior hospitalizations for DKA in the past 2 years and obesity (BMI 33 kg/m<sup>2</sup>). Of note, Ms. Miller was previously on a subcutaneous basal-bolus insulin regimen until the age of 20, when she switched to an insulin pump. Upon speaking with Ms. Miller, she stated that she removed her insulin pump because it “is inconvenient and uncomfortable” and prevents her from “working out how” she wants. Ms. Miller is highly motivated to improve her blood glucose levels and stated that she would like to lose weight, but her pump gets in the way during exercise and the insertion site becomes sore. Additionally, she states her family makes up a strong support system but because her mother is a single working parent with two younger children at home, Ms. Miller is responsible for paying for her school tuition and other expenses such as gasoline, food, and medications. Ms. Miller states that she works part time as a line chef in a local restaurant to cover her monthly expenses, but she does not have any significant savings, something she would like to work on increasing. During her hospital stay, she inquired if an injection regimen would be cheaper than the insulin pump, as she preferred the injection regimen for her lifestyle. Significantly, the cost of this life maintaining therapy was in direct contrast to her goal of acquiring financial savings. This is an excellent example of how kinship structures in resource limited environments are related to acquiring capital reserves.<sup>1</sup> Ms. Miller then requested to be switched back to a multiple daily injection (MDI) regimen to work better with her goals and current circumstances.

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## Clinical Question

How does the cost-benefit ratio compare between continuous insulin infusion (CII) therapy and MDI therapy for type 1 diabetics?

## Research Article

Heller S, White D, Lee E, et al. A cluster randomised trial, cost-effectiveness analysis and psychosocial evaluation of insulin pump therapy compared with multiple injections during flexible intensive insulin therapy for type 1 diabetes: the REPOSE Trial. *Health Technol Assess*. 2017 Apr;21(20):1-278. <https://doi.org/10.3310/hta21200><sup>2</sup>

## Description of Related Literature

Related literature was found via PubMed using the phrases “insulin pump”, “multiple injections”, “type 1 diabetes”, and “cost”. Initial search yielded 61 results, which after screening for randomized control trials (RCTs), left 8 results. Four of the RCTs were immediately eliminated because they did not answer the clinical question. The first analyzed time costs, instead of financial costs, of pump therapy vs. a MDI regimen and found that those on pump therapy experienced higher time costs.<sup>3</sup> The second analyzed the psychosocial benefits of a MDI regimen vs. CII therapy in children and their families, finding that both the children and their families experienced psychosocial benefits with CII therapy compared to a MDI regimen.<sup>4</sup> The third was a study protocol and did not include any results.<sup>5</sup> The fourth compared pregnant women with type 1 or type 2 diabetes using faster aspart insulin with those using insulin aspart and found that both were safe to use with no differences in fetal growth or hemoglobin A1c (HbA1c).<sup>6</sup>

Similarly, 2 more of the RCTs were eliminated. Although one examined cost-effectiveness and found that a MDI regimen is less expensive than pump therapy, it did not compare glycemic control, a necessary factor to consider when choosing Ms. Miller's regimen.<sup>7</sup> The second compared MDI with an implantable pump, which is different from the exterior pump Ms. Miller had, therefore excluding her from the study.<sup>8</sup>

Due to the low yield on PubMed, the same search terms were searched on Google Scholar. It is important to note that Google Scholar search results are influenced by the user's past search history, meaning the number of results may differ between users. After screening for RCTs, and ones that answer the clinical question, one additional paper was found. The SCUPI RCT compared CII and MDI for newly diagnosed type 1 diabetics in their first year of insulin treatment.<sup>9</sup> However, because Ms. Miller has had diabetes for over 15 years, she did not fit the study population. Additionally, the study participants were all under the age of 15.

The DIAMOND RCT randomized 75 adults with T1DM who use continuous glucose monitoring to either initiate CII or continue MDI and compared cost-effectiveness and quality of life (QOL) as well as glycemic control.<sup>10</sup> The study found that initiating CII was less cost-effective and did not improve QOL. This study was ultimately not used because Ms. Miller does not have a continuous glucose monitoring device and this was a qualifying aspect of the trial.

The RCT chosen for appraisal was a study conducted by Heller et. al. called the REPOSE trial.<sup>2</sup> The trial assigned 267 adults with T1DM to partake in a baseline nutrition course with approximately half of the participants initiating CII and half of the participants continuing MDI as the control. Of note, only 248 of the participants had a complete data collection at 24-months follow-up. The study concluded that initiating CII in adults with T1DM did not significantly improve glycemic control and is not a cost-effective option. The trial shares similar findings of previous papers. The study was ultimately selected because it answers the clinical question in terms of cost-effectiveness and glycemic control, the two concerns of Ms. Miller when she requested to be switched to MDI from her CII regimen.

According to the strength of recommendation taxonomy (SORT), the REPOSE trial has a level A Strength of Recommendation.<sup>11</sup> It achieves this level because there are at least two other quality RCTs with consistent findings: the DIAMOND and SCUPI trials. Both RCTs similarly found no significant advantage of CII over MDI in type 1 diabetics.

## Critical Appraisal

The REPOSE trial is a multicenter, cluster randomized clinical trial that recruited patients from eight diabetes centers in the United Kingdom.<sup>2</sup> A total of 317 participants (mean age = 41 years) with T1DM were recruited for participation, with a total of 267 participants included in analysis and 248 of those generating complete primary outcome data at 24 months. Both study groups were similar in sex, age, years since diagnosis, and baseline HbA1c. Inclusion criteria included being at least 18 years old and having T1DM for at least 1 year. Exclusion criteria included having renal impairment, uncontrolled hypertension, heart disease, or other serious medical conditions, or having used an insulin pump in the last 3 years. Ms. Miller conforms to the inclusion and exclusion criteria except for having used an insulin pump in the last 3 years.

Once participants were selected, they were assigned to a baseline nutrition course. They then began CII or continued MDI. Participants received their treatment for 2 years and outcomes were measured at 6, 12, and 24 months. The minimum clinically significant difference in HbA1c after treatment was set as a difference of 0.5%. According to SORT criteria, the trial is considered level 1 evidence.<sup>11</sup>

The primary outcome assessed was the change in HbA1c at the 2-year follow-up for participants with a baseline HbA1c greater than or equal to 7.5%. HbA1c was also evaluated at 6 and 12 months to assess shorter term effects. The mean decrease in HbA1c of the MDI group and CII group was 0.42% and was 0.85%, respectively. After adjusting for treatment center, nutrition course, and baseline HbA1c, t-test found no statistically significant difference between the two groups ( $p=0.098$ ).

A secondary outcome assessed the cost-effectiveness of CII compared with MDI. The study determined that at its annual cost, the pump would need to reduce the HbA1c by at least 1.0% to be considered cost-effective compared with MDI. The results of the study show the mean decrease of the pump HbA1c to be 0.85% which is less than 1.0%, and therefore, not cost-effective.

Participants were recruited in several ways that included direct contact to those on waiting lists for nutrition courses or people who had an appointment with a PI, referral by non-trial clinicians, and paper advertisements in clinics. Three hundred and seventeen participants were recruited, however 50 were excluded because they withdrew before baseline data was collected or before the nutrition course. Although 50 participants were lost, the number of participants who completed primary outcome data collection was almost identical for each group (120 MDI and 128 pump) meaning there was little to no attrition bias. Additionally, there is no indication bias as both groups were similar at baseline. There is also no apparent funding bias. The trial was funded by the National Institute for Health Research Health Technology Assessment program. The pumps were provided for free by Medtronic and multiple authors report personal fees from various companies, however none played any role in the design or conduction of the study.

The study may be prone to selection bias because of its exclusion criteria. If participants had other diseases such as renal and heart disease, they were not eligible. Although Ms. Miller did not have any excluded comorbidity, it is unlikely the general T1DM population is the same.

The study was not double blinded so it may be prone to performance bias. It was not double blinded due to the need to schedule participants in a nutrition course that would work with their schedule; however, the allocation of pump vs. MDI was blinded. Outcome measurement was not blinded due to the necessity of clinicians to collect the data, however HbA1c is an objective measurement and was calculated in an external laboratory.

The trial may be prone to participation bias because participants presented to a diabetes clinic for care or they were seeking out nutrition courses. This means that all participants, to some degree, took initiative to play an active role in their disease management. These participants may not be representative of the general patient with T1DM.

Another weakness of the trial is the study location. The trial was conducted in the United Kingdom and the majority of participants were white. Cultural, economic, and environmental differences might contribute to Ms. Miller, and others, experiencing different results.



## Clinical Application

Ms. Miller requested to be switched from her CII regimen to a MDI regimen, so long as it would not negatively impact her glycemic control. Ms. Miller requested this switch due to the pump's inconvenience during her daily activities and her financial concerns as she is currently paying her way through college. Based on the findings of the REPOSE trial, the clinical team informed Ms. Miller that a MDI regimen can indeed offer comparable blood glucose control to a CII regimen, when followed correctly, and is more cost-effective. Along with the REPOSE trial findings, the clinical team also felt confident switching Ms. Miller to a MDI regimen because of her personal preference and motivation. When medications/regimens are equivalent, as in this case, it is imperative to consider patient preference as it will impact adherence, therefore effecting disease management and longterm health. Before discharge, Ms. Miller was informed that it is essential that she follow her new MDI regimen as to avoid episodes of hypo- and hyperglycemia and to avoid further hospitalizations due to DKA. Because Ms. Miller has a high educational status, the clinical team felt that she would be able to successfully adhere to the new regimen. Ms. Miller was happily discharged from the hospital with her new MDI regimen and a follow-up appointment in 4 weeks to assess how she is managing her new plan.

## New Knowledge Related to Clinical Decision Science

Ms. Miller presented with DKA and poorly controlled T1DM not simply due to non-adherence, but due to much more intricate reasons. It was clear that Ms. Miller was working hard on bettering her health, however her current treatment regimen was not compatible with her daily activities, leading to worsening of her diabetes. Ms. Miller's case represents the importance of patient-based decision making in the clinical setting. It is imperative that clinicians understand a patient's wishes, goals, and motivations, as well as the patient's social determinants of health, and incorporate these into the decision-making process when selecting treatment regimens with the patient. If the patient is placed on a treatment plan they are not in agreement with or cannot adhere to, there is the potential for negative health outcomes, such as with Ms. Miller.

Although MDI regimens are viewed as second line to CII for type 1 diabetics, clinicians must weigh the risks and rewards of choosing a second line therapy when first line therapy is not compatible with a patient. In this manner, physicians can avoid practicing paternalistic medicine, where there is little discussion about or consideration of patient factors and instead decision making solely depends on the physician. In the case of Ms. Miller, the MDI regimen was found to be just as effective as the CII regimen, and it has the added benefit of being more cost-effective, a detail about which Ms. Miller was concerned. This emphasizes the importance of clinicians exploring all treatment options for patients, even if there is a distinct first line treatment.

Clinical Decision Science involves the astute use of information to optimize the treatment given to the patient. Treatments that patients can complete that are suboptimal otherwise are nonetheless better than theoretically optimal treatment regimens that the patient is unable to complete for a particular social reason. While clinical trials focus only on strict efficacy of one treatment over another, one wonders how frequently social issues preventing the proper employment of newer and purportedly better regimens result in the old ways being better in practice.

## Conflict Of Interest Statement

The author declares no conflicts of interest.

## References

1. Turco B, Agrusa V, Abdallah L, Meza JP. Translational Social Science: Kinship, gift exchange, and the management of diabetes. *Clin Res Prac*, Feb 22 2024;9(2):eP3582. <https://doi.org/10.22237/crp/1705536000>
2. Heller S, White D, Lee E, et al. A cluster randomised trial, cost-effectiveness analysis and psychosocial evaluation of insulin pump therapy compared with multiple injections during flexible intensive insulin therapy for type 1 diabetes: the REPOSE Trial. *Health Technol Assess*. 2017 Apr;21(20):1-278. <https://doi.org/10.3310/hta21200>

3. Kamble S, Weinfurt KP, Schulman KA, Reed SD. Patient time costs associated with sensor-augmented insulin pump therapy for type 1 diabetes: results from the STAR 3 randomized trial. *Med Decis Making*. 2013 Feb;33(2):215-24.  
<https://doi.org/10.1177/0272989X12464824>
4. Mueller-Godeffroy E, Vonthein R, Ludwig-Seibold C, et al.; German Working Group for Pediatric Pump Therapy (AGIP). Psychosocial benefits of insulin pump therapy in children with diabetes type 1 and their families: The pumpkin multicenter randomized controlled trial. *Pediatr Diabetes*. 2018 Dec;19(8):1471-1480. <https://doi.org/10.1111/pedi.12777>. Erratum in: *Pediatr Diabetes*. 2020 Feb;21(1):144-145
5. White D, Waugh N, Elliott J, et al.; REPOSE group. The Relative Effectiveness of Pumps Over MDI and Structured Education (REPOSE): study protocol for a cluster randomised controlled trial. *BMJ Open*. 2014 Sep 3;4(9):e006204.  
<https://doi.org/10.1136/bmjopen-2014-006204>
6. Nørgaard SK, Søholm JC, Mathiesen ER, et al. Faster-acting insulin aspart versus insulin aspart in the treatment of type 1 or type 2 diabetes during pregnancy and post-delivery (CopenFast): an open-label, single-centre, randomised controlled trial. *Lancet Diabetes Endocrinol*. 2023;11(11):811-821. [https://doi.org/10.1016/S2213-8587\(23\)00236-X](https://doi.org/10.1016/S2213-8587(23)00236-X)
7. Kamble S, Schulman KA, Reed SD. Cost-effectiveness of sensor-augmented pump therapy in adults with type 1 diabetes in the United States. *Value Health*. 2012 Jul-Aug;15(5):632-8. <https://doi.org/10.1016/j.jval.2012.02.011>
8. Haardt MJ, Selam JL, Slama G, et al. A cost-benefit comparison of intensive diabetes management with implantable pumps versus multiple subcutaneous injections in patients with type I diabetes. *Diabetes Care*. 1994 Aug;17(8):847-51.  
<https://doi.org/10.2337/diacare.17.8.847>
9. Blair J, McKay A, Ridyard C, et al. Continuous subcutaneous insulin infusion versus multiple daily injections in children and young people at diagnosis of type 1 diabetes: the SCIPI RCT. *Health Technology Assessment* (Winchester, England). 2018 Aug;22(42):1-112. <https://doi.org/10.3310/hta22420>
10. Wan W, Skandari MR, Minc A, et al. Cost-effectiveness of Initiating an Insulin Pump in T1D Adults Using Continuous Glucose Monitoring Compared with Multiple Daily Insulin Injections: The DIAMOND Randomized Trial. *Med Decis Making*. 2018 Nov;38(8):942-953. <https://doi.org/10.1177/0272989X18803109>
11. Ebell MH, Siwek J, Weiss BD, et al. Strength of Recommendation Taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. *J Am Board Fam Med*. 2004;17(1):59-67. <https://doi.org/10.3122/jabfm.17.1.59>

