Impact of Patient Device Experience on Acceptance and Adherence in Diabetes Mellitus

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Aim: To conduct a systematic literature review to examine how the patient experience with self-injectable insulin pen devices for diabetes mellitus impacts treatment acceptance and adherence, and to assess how well current methods capture all relevant patient attitudes and behavior that can impact adherence.

Background:
- Diabetes Mellitus (DM) affects nearly 415 million people worldwide, and is estimated to rise to over 622 million by 2040.
- Medication non-adherence is a common treatment issue and is associated with poor glucose control and consequently higher complication rates and societal costs.
- Non-adherence is variably defined across literature and often based on medication possession ratio, proportion of days covered, prescription refill rates, or any variation therein.
- Worldwide non-adherence rates for patients with diabetes ranges from 36-93%.
- Inconsistent characterization of adherence exacerbates difficulties with collective reporting and contributes to the variability of currently reported adherence rates.
- Measuring persistence in non-fixed dosing schedules of insulin from pen or injections further complicates accuracy of measure, and requires accounting for total quantity dispensed and variable treatment periods.
- ABC (Ascertaining Barriers to Compliance) Taxonomy and adherence outcome methodology varied with study follow-up.
- Longer-term variability in definition of terms may have resulted in incorrect comparisons across studies.
- Providers who understand adherence can help their patients achieve meaningful clinical results, such as HbA1c attainment, through dose optimization and adherence monitoring.
- HCP-relevant patient educational tools with clear definitions and appropriately inclusive components of adherence and standard reporting measures are needed.
- Lack of standardized descriptions and methods for measuring adherence may also produce a gap in provider and healthcare professional communication with patients and healthcare professionals.

Methods:
- A standardized review protocol was used to define the eligibility criteria for the search and screening of references using the PICO(TSS) framework, which outlines the population, interventions, comparators, outcomes, timing, setting, and study designs of interest (Table 1).
- Primary outcomes of interest were patient acceptance, patient satisfaction, medication adherence, and medication persistence.
- Medline (PubMed), Embase, OVID, and CENTRAL (Wiley) were searched during May 2017. Language was patient published (2012 onwards) and subject (human) limits were applied in each database.
- Bibliographies of relevant systematic reviews and meta-analyses were also searched for additional studies.
- Data extraction was conducted using the Digital Outcome Conversion (DOC) Data version 2.0 software platform (Doctor Evidence, LLC, Santa Monica, CA, USA) and its universal electronic extraction form, based on a standardized data configuration protocol. Each collected data point was extracted by two highly trained and proctored evidence analysts. All terms (characteristics and outcomes) were collected as reported in each paper and synonyms were “bound” before analysis using the DOC Ontology System.

Results:
- Adherence outcome methodology varied with medication possession ratio (MPR) being the most common measure. The adherence assessment did not account for the implementation component, but focuses almost entirely on persistence.
- Persistence was measured in studies both in continuous length of time spent receiving the medication, as well as the number of patients who were still receiving treatment at end of study follow-up.
- Long-term patient satisfaction is under-reported in the literature and heterogeneous in reporting methods. Only 6 studies measured satisfaction for at least 12 weeks, and the measurement used for satisfaction varied among studies, with only 2 studies using Diabetes Satisfaction Questionnaire (Table 2).
- Pen users had significantly higher adherence to insulin with vials (MPR mean difference 0.69%, 95% CI 0.84-7.54) at 1 year (Figure 3).
- Pen users had significantly longer persistence than those using vials (odds ratio 1.51; 95% CI 1.44-1.56) at 1 year.
- The search in MEDLINE, Embase and the Cochrane Library resulted in 562 potentially relevant references after duplicates were removed.
- 439 records were rejected during the title/abstract screening and 102 after reviewing the full-text (see Figure 1 for the flow of studies through the review).
- A total of 30 observational studies met eligibility criteria. Adherence and persistence were the most commonly measured outcomes (14 and 16 studies respectively), but there are differences in reporting methodologies as well as lack of methods disclosure (Figure 2).

Limitations:
- This study was conducted on observational studies rather than clinical trials, which is often considered a source of bias. For this topic, observational studies provide a more accurate assessment of patient behavior in the real world.
- While we attempted to find all relevant studies on this topic, it is possible that we missed some which would have informed our results in a different manner.
- Long-standing variability in definition of terms may have resulted in incorrect comparisons across studies.

Conclusions:
- This first ever systematic review of adherence with self-injection devices highlights the lack of scientific study in this area to date and identifies areas to improve collection and analyses of factors that impact the patient experience and outcomes.
- Pen users had significantly higher adherence and persistence than those using vials.
- Long-term patient satisfaction is both under-reported and inconsistently reported in this literature.
- This review identified a lack of standard definitions of adherence and absence of reporting of patient-reported outcomes associated with the use of self-administered devices to deliver medication.
- The ABC taxonomy provides a focus on acceptance and initiation, which are early components of adherence that are not considered in this body of literature.
- Acceptance and persistence should be measured more systematically and consistently, and capture aspects of treatment that are important to the patient, beyond technical specifications, as these components greatly contribute to adherence and overall patient experience.

Applications for Healthcare Practitioners:
- Lack of standardized descriptions and methods for measuring adherence may also produce a gap in provider and healthcare professional communication with the patient on the importance of adherence to treatment success.
- Healthcare providers should use clear definitions and appropriately inclusive components of adherence and standard reporting measures are needed.
- These tools can inform healthcare providers about patient satisfaction related to self-administration and guide conversations that optimize use of these devices.
- Providers who understand adherence can help their patients achieve meaningful clinical results, such as HbA1c attainment, through dose optimization and adherence monitoring.

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