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# SUCCESS OF A SUSTAINED PHARMACEUTICAL CARE SERVICE WITH ELECTRONIC ADHERENCE MONITORING IN A DIABETIC PATIENT OVER 12 MONTHS



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# Submission template

**TITLE OF CASE**

SUCCESS OF A SUSTAINED PHARMACEUTICAL CARE SERVICE WITH ELECTRONIC ADHERENCE MONITORING IN A DIABETIC PATIENT OVER 12 MONTHS

**SUMMARY**

We report of the first polypharmacy adherence monitoring over 371 days, integrated in a pharmaceutical care service (counselling, electronic multidrug punch cards, feedback on recent electronic records) for a 65-year old male diabetic patient after hospital discharge. The initial 4-times daily regimen with 15 daily pills changed after 79 days into a 2-times daily regimen with 9 daily pills for the next 292 days. The patient removed all medication from the multidrug punch cards (taking adherence 100%) and had 96.9% correct dosing intervals (timing adherence). The 57 evening doses showed the least variation in intake times at 17h 45min ± 8min. Over the observation year, the patient was clinically stable. The patient was very satisfied with the multidrug punch card use and the feedbacks on electronic records. In conclusion, long-term monitoring of polypharmacy was associated with the benefit of successful disease management.

**BACKGROUND**

According to its latest definition, *"Pharmaceutical Care is the pharmacist's contribution to the care of individuals in order to optimize medicines use and improve health outcomes"*.[1] Thus, medication adherence, i.e., the extent of a patient following the recommendations by a health-care professional, represents a central concern in pharmacy practice. With typical adherence rates for oral prescription medication of approximately 50-76% ,[2, 3] non-adherence has been designated as one of the largest health care problems in society ,[3-5] since it impairs clinical outcomes and quality of life, and generates costs.[6-10]
Polypharmacy, i.e. the use of multiple drugs administered to the same patient ,[11] has been described as a factor strongly related to non-adherence.[12, 13] However, polypharmacy has become common because of e.g. clinical practice relying on multidrug combinations, increased rates of comorbidities and the aging population. In this context, dose-dispensing aids such as multidrug punch cards are suggested to improve adherence to polypharmacy and clinical outcomes.[14-16]
Electronic monitoring is considered nearest to gold standard in adherence measurement.[17] Several studies used a pill bottle with a computer chip equipped cap that records each opening of the bottle. Because of the design of this pill bottle, one lead drug can be monitored at one time.[18-22] The recent development of printed electric circuitries and RFID technology made it possible to monitor polypharmacy by using a paper foil and a chip collecting real time data (Confrérie Clinique S.A., Lausanne, Switzerland) affixed on the back of a multidrug punch card.[23] The POlypharmacy Electronic Monitoring System (POEMS) records date, time, and location of medication removal of the whole therapy regimen.

We report of the first polypharmacy adherence monitoring over 12 months, integrated in a pharmaceutical care service for a diabetic patient after hospital discharge. The patient was recruited within a pilot study to prove feasibility of a pharmaceutical care service with electronic adherence monitoring (ClinTrials.gov Identifier: NCT01759095).

**CASE PRESENTATION**

We report of a 65-year old male patient who was hospitalized for a sepsis by *Staphylococcus aureus* at a large Swiss university hospital from January 28th to February 18th 2013. His actual diagnoses included late onset autoimmune diabetes in the adult ($HbA_{1C}$: 8%, 30.01.2013) with manifest complications (diabetic foot with chronic osteomyelitis, non-proliferative retinopathy, polyneuropathy), coronary heart disease with double stenting during the actual hospitalisation (LDL: 2.83 mmol/l, 01.02.2013; TG: 1.82 mmol/l,

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01.02.2013), and a beginning heart failure (LVEF 40%, blood pressure: 183/93 mmHg, 18.02.2013). Signs of a beginning dementia were reported but not further investigated. He was retired, lived independently and alone in a middle-sized city, and self-managed his medication by the use of a weekly pillbox. In January 2013, he was newly prescribed basal insulin by the general physician (GP) in addition to rapid-acting insulin that had been initiated years before. Amputation of digits I and II on the left foot had occurred after emergency hospitalisation in October 2010. He had no allergies and was a current smoker (30 pack years). At discharge, the patient was prescribed ten different medications representing 15 pills in a 4-times daily regimen (Table 1). Medication reconciliation, i.e. the comparison of pharmacotherapy before and after hospitalisation, showed that three medications were newly introduced, one dosing frequency was reduced, one strength was augmented, and intake times changed from 2-times daily to 4-times daily.

## INVESTIGATIONS

Adherence to polypharmacy was measured by POlypharmacy Electronic Monitoring System (POEMS) affixed on a disposable weekly multidrug frame card with 28 unit-of-use doses spread over 7x4 plastic cavities, filled by the community pharmacist with all oral solid medication.

## TREATMENT

During hospitalisation, a clinical pharmacist recommended to refer the patient to a pharmaceutical care service consisting of individualized counselling (knowledge of medication), packaging of solid oral medication into multidrug punch cards (facilitation of polypharmacy management), and electronic adherence monitoring (measurement-guided medication management). Insulin management did not require further instruction. The responsible physician approved the recommendation and the patient provided written informed consent.

Two days prior to discharge, the pharmacist counselled the patient on indication, long-term benefit, adverse effects, and correct use of all discharge medication using standardized information sheets. The sheets were handed out instead of official package inserts upon the patient's request. The pharmacist instructed the use of the multidrug punch card and tested the patient's dexterity to remove tablets.

At discharge, the patient was provided with one multidrug punch card equipped with POEMS, containing all prescribed oral solid medication for one week and his medication plan (Table 1, Figure 1).

**Table 1: Medication plan handed out to the patient at hospital discharge.**
HTC, hydrochlorothiazide; n.p., no picture available.

Medication plan for [patient name] *[year of birth] — Universitätsspital Basel

**Physician** _____ **Date** dd.mm.yyyy
**Ward** _____ **Visum** _____

**Hotline: xxx xxx xx xx**

| Medication | | Dosage | | | | Picture | Indication | Note |
|---|---|---|---|---|---|---|---|---|
| Name | Dose | morning | noon | evening | night | | | |
| Irbesartan / htc | 300/12.5 mg | 1 | | | | | Blood pressure | |
| Aspirine® | 100mg | 1 | | | | | Blood thinning | Before meal |
| Atorvastatin | 40mg | | | 1 | | | Blood fat | |
| Pantoprazol | 40mg | 1 | | | | | Gastric acid | |
| Bisoprolol | 2.5mg | 1 | | 1 | | n.p. | Blood pressure | |
| Clopidogrel | 75mg | 1 | | | | | Blood thinning | |
| Metformin | 1000mg | 1 | | 1 | | | Sugar | |
| Clindamycin | 300mg | 2 | 2 | | 2 | | Infection | Stop on 07.05.13 |
| | | | | | | | | |
| Insulin Lisprum | | | | | | n.p. | Sugar | According to scheme |
| Insulin Glargine | | | | | | n.p. | Sugar | According to scheme |
| | | | | | | | | |

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Five days after discharge, the patient was called to consolidate the safe and correct management of the electronic multidrug punch card. Exchange of empty multidrug punch cards for new filled ones occurred every 2-4 weeks at a predefined community pharmacy. The electronic records of the previous week were discussed following a protocol for measurement-guided medication management (MGMM) [17] and using elements of motivational interviewing [24] like open-ended questions, reflective listening, affirmative style, enhancement of personal motivation, setting goals and obtainment of a change of plan.

## OUTCOME AND FOLLOW-UP

The monitoring period lasted from February 18th 2013 (discharge day) until February 23rd 2014 and covered 371 days. In total, 54 multidrug punch cards with 899 unit-of-use doses were handed out. All returned multidrug punch cards were empty (taking adherence by pill count of 100%). Eleven multidrug punch cards (20.4%) and 9 random days were not readable (technical failure), and 17 event times were not recorded, leading to lost data for 218 doses (24.2%). The patient removed 8 pocket doses in anticipation of intakes away from home, which were excluded from the calculation. The summary of adherence statistics was derived from 673 electronic records.

The first 79 days of treatment comprised 4-times daily intakes (QID) due to antibiotic treatment until 7th May 2013, and covered 21.3% of the observation period. On May 8th 2013, the GP augmented bisoprolol from 2.5mg to 5mg twice daily without influence on the number of pills or the intake times. The next 292 days comprised twice-daily intakes (BID). A total of 278 doses were retrieved in the morning (QID: 63, BID: 215) in average at 7h 34min ± 55min (QID: 7h 24min ± 27min, BID: 7h 36min ± 1h 1min). The antibiotics assigned to be taken at noon (63 doses) and at night (65 doses) were taken in average at 12h 22min ± 2h 6min and at 21h 44min ± 44min, respectively. A total of 267 doses were retrieved in the evening (QID: 57, BID: 210) in average at 17h 39min ± 1h 1min (QID: 17h 45min ± 8min, BID: 17h 37min ± 1h 14min). The electronic records over the whole year are displayed in Figure 2.

A dosing interval was defined as correct if the time between doses was within 25% of the prescribed dosing interval, i.e., ± 3h for a 12-hour period (BID) and ± 1.5h for a 6-hour period (QID). Overall 96.9% of the dosing intervals were correct. All morning and evening doses of the QID regimen were taken in the grace period of 1.5 hrs, while 10/63 doses at noon and 4/65 doses at night were taken earlier or later, representing 5.4% of all QID doses. Of the BID regimen, 2/215 doses in the morning and 5/210 doses in the evening were taken outside the grace period of 3 hrs, representing 1.6% of all BID doses.

The patient kept all 17 planed appointments for multidrug punch card exchange and feedback sessions. He went on vacations thrice for several weeks. During the 9 feedback sessions conducted regularly every 1-2 months, the patient confirmed the safe and correct use of the punch card. He was very satisfied with his electronic records and emphasized his efforts for a highly regular taking and timing adherence. He reported a strong integration of the process of medication taking into his daily routine, i.e. coupled to mealtimes and insulin injection.

The patient was satisfied with the intervention and declared a feeling of increased medication safety owing to the multidrug punch card use. The electronic records used during the feedback sessions helped the patient to gain confidence in medication management and to maintain perfect regularity of the intakes. The electronic monitoring did not bother him. At the beginning, the removal of the medication out of the multidrug punch card caused him trouble because the back layer was hard to push through. However, he got used to it quickly, reported no more problems and wished to keep the punch cards after end of monitoring.

During the 12 months of monitoring, the patient had no readmission to hospital and no emergency visit. Laboratory values remained stable (LDL: 2.9 mmol/l, 29.01.2014; TG: 2.2 mmol/l, 29.01.2014; blood pressure: 193/88, 31.01.2014). $HbA_{1C}$ decreased to 7% (31.01.2014).

## DISCUSSION

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We found 3 close case reports in literature. First, a 79-year old Japanese female with type 2 diabetes and mild cognitive impairment took all medication 3-times daily from a sounding and light flashing electronic device.[25] After 6 months, adherence by pill count was one missed dose per week (95%) and $HbA_{1C}$ decreased from 8.0 to 7.1%, demonstrating the efficacy of the electronic reminder device. Second, a 17-year old female treated for Fanconi Anaemia with 8 drugs daily had an estimated adherence of 25%.[26] She received 35 motivational interviewing sessions over 17 months. Adherence to the lead medication levothyroxine measured by electronic pill bottle showed a significant improvement up to 82%, demonstrating the efficacy of motivational interviewing. Third, a 65-year old Swiss male with epilepsy and suspected abuse of sleeping pills was monitored with electronic multidrug punch cards over 3 weeks.[27] Inadequate medication intake behaviour could be corrected with feedback sessions.

Our case with pharmaceutical care service including electronic monitoring of adherence to polypharmacy and regular feedback on electronic records was successful to maintain perfect adherence and clinical stability during one year. A glycosylated haemoglobin ($HbA_{1C}$) level of 7% was reached during the one-year monitoring period and represents the target level recommended by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) for elderly comorbid patients.[28] The lowering of the $HbA_{1C}$ by 1% is known to improve micro- and macrovascular clinical endpoints significantly and to reduce all-cause mortality by 14%.[29] In our case, the $HbA_{1C}$ reduction probably followed from the adjustment of insulin therapy one month before hospitalisation. However, the impact of multidrug punch cards was demonstrated by a mean $HbA_{1C}$ reduction of 0.95% in 36 diabetic patients with oral antidiabetics after 8 months in a randomized controlled trial.[30] We thus can suppose that for our patient, the multidrug punch card acted as a railing and interrelated the oral therapy with the insulin therapy.

The challenging therapy plan of 4-times daily intake for over a fifth of the observation time and changes in daily routine like vacation had no influence on the patient's adherence. Because frequent dose dispensing and interruption in daily life were reported to negatively affect adherence [31-33] we assume that the multidrug punch card (as practical tool) coupled to the continuous feedback sessions (as external motivator) were able to consolidate and maintain perfect adherence. This assumption is supported by a meta-analysis attributing a large effect to the intervention of feedback on electronic dosing history.[34]

We acknowledge some limitations. The substantial loss of data due to technical flaws of our first generation POEMS is inherent in newly developed technologies. The subsequent generation of electronic foils will be improved. Electronic monitoring is often criticized to assume rather than prove the patient's actual medication intake. However, we observed that patients usually accept monitoring and thus swallow the removed medication.[35] Finally, the patient's being aware of observation is supposed to have an impact on the outcomes. However, a recent study showed that the use of an electronic device leads to a small, non-significant increase in adherence compared to standard packaging.[36] In conclusion, this case is to our knowledge the first report of long-term monitoring of polypharmacy associated with the benefit of successful disease management.

**LEARNING POINTS/TAKE HOME MESSAGES *3 to 5 bullet points***

- The pharmaceutical care intervention - comprising electronic monitoring of adherence to polypharmacy and recurrent feedback sessions – maintained optimal adherence and stabilized disease management.
- The patient accepted the electronic monitoring of adherence to polypharmacy over one year and was satisfied with the service. He was even willing to continue with this service after study end.
- Electronic monitoring of polypharmacy was feasible over one year and yielded valuable results.

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**FIGURE/VIDEO CAPTIONS**

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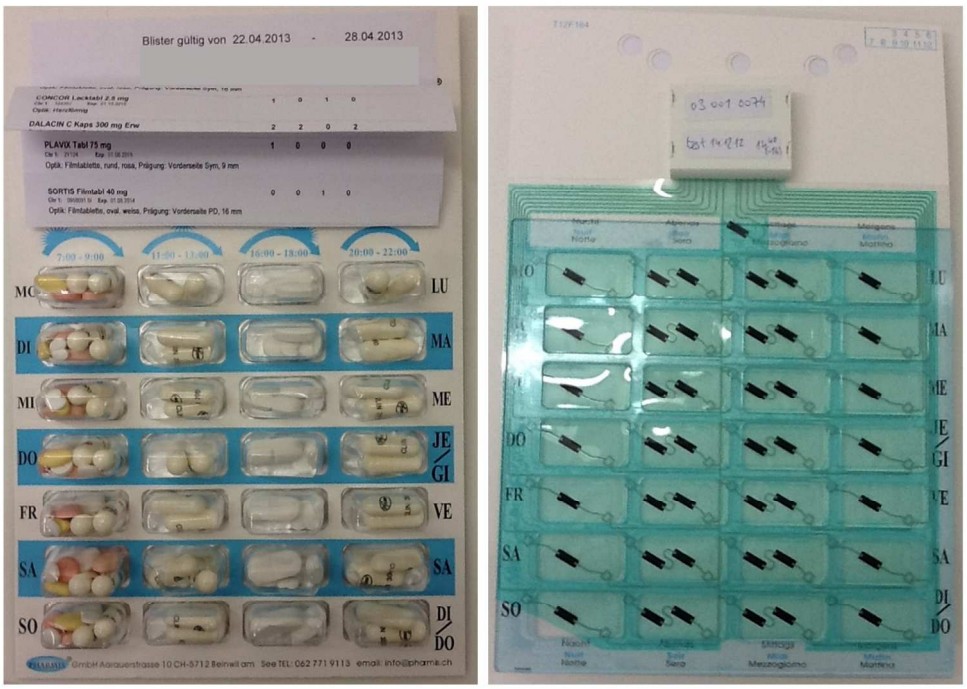
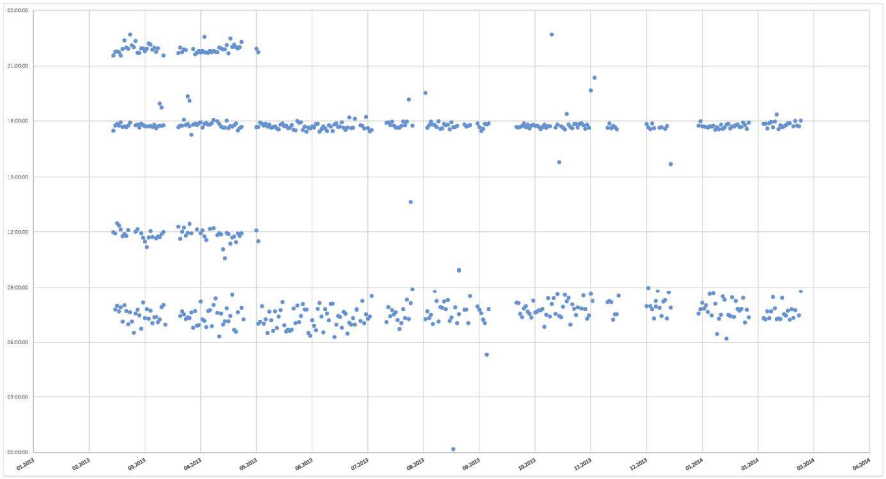
Figure 1. Electronic multidrug punch card front (left) and back with affixed POlymedication Electronic Monitoring System (POEMS; right).

Figure 2. Electronic records over the one-year monitoring period.




Electronic multidrug punch card front (left) and back with affixed POlymedication Electronic Monitoring System (POEMS; right).



Electronic records over the one-year monitoring period.
297x210mm (300 x 300 DPI)