Appendix 1: published research about the medication adherence program

Article	Aim of the study	Studied population and study duration	Design	Outcomes	Results
Fallab-Stubi et al., 1998 [28]	Evaluate the usefulness of EMs, comparing with pill count method and urine test.	Tuberculin positive patients treated with isoniazid N = 30 Period: 6 months	Prospective study: Visits planned every 4 weeks + Combined intervention (physician and pharmacist) with non-adherent patients at 3 and 6 months.	- Medication adherence	Adherence with EMs: 91.5 +- 18.6 %, With pill count: 96.2 +- 15.2 %, With urine test: 91.3 +- 22.2 %. EMs appeared to be more reliable than the pill count and urine test, which tended to overestimate the overall adherence. Combined intervention enhanced adherence in non-adherent patients.
Schneider et al., 1998 [29]	Assess if on-line monitoring of medication adherence is feasible and acceptable to patients.	Patients with chronic uncomplicated diseases (diabetes, hypertension, hypercholesterolaemia) N = 7 Period: 2 months	Open pilot study: - 4-weeks running phases with EMs - After 1 month: a modem connected to the pharmacy was installed on the patient's telephone line and EMs were installed on the modem every evening by the patient - In the end of the study: patients completed a satisfaction questionnaire.	- Medication adherence	Adherence > 95 % : 4 patients Adherence < 95 %: 3 patients but adherence increased during the on-line monitoring period. On-line monitoring seems to be feasible and acceptable to patients.
Schwed et al., 1999 [30]	Determine adherence to lipid-lowering therapy, using an EMs vs. pill count. Illustrate pattern of non adherence. Evaluate the relationship between adherence and response to fluvastatin.	Hypercholesterolemia N = 39 Period: 9 months	Open label study: - Dietetic phase: 3 months with 3 clinical visits - Active treatment phase (fluvastatin): 6 months with 3 clinical visits (at 1, 3 and 6 months).	- Medication adherence - Pattern of non adherence - Total cholesterol and LDL cholesterol	Lipid profile was improved during the active treatment phase but not during dietetic phase. Adherence was > 80 % at each visit but decreased over time. Pill count overestimated adherence data. Patterns of non adherence observed: drug holiday, missed doses, multiple daily doses, or toothbrush effect. Correlation between rate of adherence and decrease in LDL cholesterol: significant with EMs but not with pill count.

Bertholet et al., 2000 [31]	Evaluate the effect of the use of EMs on identifying and correcting adherence problems and its ultimate effect on enhancing the clinical outcome	Hypertensive patients (BP > 140/90 mm Hg) N = 69 Period: no information	Prospective study: Antihypertensive therapy dispensed in EMs.	- Medication adherence - Blood pressure	Decrease of blood pressure (from 159/104 +/- 23/12 to 143/92 +/- 20/15 mm Hg) for the group but: The use of electronic monitors had a positive effect on enhancing the therapy of antihypertensive patients.
Burnier et al., 2001 [19]	Evaluate the potential benefits EMs in the management of patients with resistant hypertension.	Hypertensive patients resistant to a 3-drug regimen N = 41 Period: 4 months	Prospective study: 2 months follow-up with EMs. After this period, patients could continue with EMs during 2 more months and treatment was adapted if necessary	- Medication adherence - Blood pressure	At 2 months: significant improvement of blood pressure. Patients with lowest adherence had higher diastolic blood pressure. At 4 months (n=30/41): further significant decrease in blood pressure.
Schneider et al., 2003 [32]	Evaluate the efficacy of a nicotine nasal spray in smoking cessation and characterize the pattern of use of the nasal spray with a special electronic monitor to assess factors associated with cessation success or failure.	Patient referred to the smoking cessation unit from October 1996 to April 1997 N = 92 Period: 24 months	Open prospective exploratory study: patients received a nicotine nasal spray with a microchip (MDILog) for 18 months. Follow-up visits were scheduled at week 2 and at 1,2, 3, 4, 6, 9, 12, 15, 18, 21 and 24 months.	- Number of abstainers at 12 and 24 months - Use of the spray	First 2 weeks: abstinence was significantly associated with cessation success at 6 and 24 months. First month: median use of 12 puffs/day in abstainers and 6 puffs/day in failures. Abstainers used the spray less in the morning but more in the evening/night compared with failures. Mean daily consumption of the nicotine nasal spray remained lower than expected in most participants, particularly in failures.
Schneider et al., 2003 [33]	Evaluate the benefit of an online telemonitoring of medication adherence.	Epileptic patients N = 26 (12 in the intervention group) Period: 8 months	Pilot randomized controlled study: - Control: antiepileptic drugs in EMs - Intervention: EMs combined with online telemonitoring. The pharmacist called patients if adherence problems occurred.	- Medication adherence	Percentage of days with correct dosing: > 90 % in control and intervention groups. Number of interventions performed by pharmacists: 78 (4 patients had more than 10 interventions). Intervention group: trend to fewer epileptic events vs. control.

Landry et al., 2006 [34]	Evaluate adherence to malaria chemoprophylaxis with weekly mefloquine. Compare EMs adherence with usual care questionnaire.	Adult travellers to sub-Saharan Africa N = 81 Period: March to April 1997	Before Travelling: oral and written information received about malaria and mefloquine + questionnaire on demographic and travel data, medical history and current medical treatment + patients received mefloquine in EMs. After travelling: second questionnaire on protective measures, drug intake and adverse events.	- Medication adherence - Demographics and Travel Characteristics - Adverse events	Electronic adherence data: - 75.3% took all tablets: 32.1% at the expected date, 9.9% starting late, 23.5% with intervals of ± 1 day from the right date and 9.9% took pills in a random way - 24.7% missed some doses mainly after return. Questionnaire: higher strict adherence data, some answers not reliable (21 cases with discordant results).
Santschi et al., 2007 [35]	Evaluate the acceptability of a new electronic drug adherence monitor (IDAS II).	Hypertensive patients treated with irbesartan N = 24 Period: 4 months	randomised two-way cross-over study: Device 1, 2 months: IDAS II Device 2, 2 months: MEMS	- Patient's opinion on both devices - Medication adherence - Blood pressure	Both devices: reliable reminders Preferences: MEMS (10/24), IDAS II (11/24), no preference (3/24) MEMS: easier to use than IDAS II IDAS II: better packaging than MEMS Adherence: 99.2 % with both devices, higher regularity of drug intake timing with IDAS II.
Santschi et al., 2008 [36]	Investigate if having the possibility to use EMs with interdisciplinary networks improved blood pressure control.	Uncontrolled hypertensive patients N = 68 (34 in the intervention group) Period: 12 months	Pragmatic cluster randomised controlled study: Intervention: medication adherence monitored with EMs Control: usual care.	- Target office BP<140/90 mmHg	Significantly more patients reached target BP in the intervention group at 4 and 12 months vs. control group.

Krummenacher et al., 2010 [20]	Evaluate the feasibility of a comprehensive, interdisciplinary adherence program	HIV patients followed by the Swiss HIV Cohort Study in 2 centres: Lausanne and Basel (Switzerland) N = 32 (21 in the intervention group) Period: 6 months, November 2006 to July 2007	Pilot study, quasi-experimental with 2 arms: - intervention: usual care + EMs + motivational interviews with a pharmacist. - control: usual care + blinded EMs	- Rate of patients' acceptance to take part in the program - Rate of patients' retention in intervention and control groups - Adherence, implementation and persistence	Study was not feasible in Basel: the recruitment stopped because unsuccessful inclusion. But feasible in Lausanne: - Inclusion rate intervention vs. control: 84% vs 52 % - Retention rate: 91% vs 82% - Adherence: 93% vs 87% but adherence decreased more quickly in the control group - Implementation: 97% vs 95% and decrease with time in both groups - Persistence: 97% vs 81%.
Krummenacher et al., 2011 [21]	Analyze the interdisciplinary HIV-adherence program	HIV patients referred to the program N = 104 Period: August 2004 to April 2008	Retrospective cohort study	- Socio-demographic data - Reasons for inclusion - Adherence rate - Clinical data (VL and CD4 cells) - Description of the pharmacy visits - Reasons for antiretroviral treatment adjustments - Reasons for interruption of the program.	59% women, 42% black ethnicity and median age = 39. 77% patients were ART-experienced and 59% had a protease inhibitor. Retention rate in the program: 92% Reasons for inclusion: naive patients, non adherence or suboptimal clinical outcomes Adherence: 87% persistence and 88% implementation. Number of undetectable patients increased during the study. Median time of interview: 35 minutes ART Adjustments: 45% (41% treatment simplification, 20% adverse events, 20% clinical issues)

Krummenacher et al., 2012 [22]	Describe demographic and clinical characteristics of HIV patients referred to the adherence program in comparison to the entire HIV population.	HIV patients referred to the adherence program N = 73 HIV patients followed in the same infection disease department N = 494 Period: August 2007 to November 2007	Retrospective descriptive cross-sectional study	- Socio-demographic data - Clinical data: VL and CD4 cells	Subjects referred to the adherence program differed from the entire HIV population: - Women more often included (66%) - Protease inhibitor more often prescribed than NNRTI - Lower CD4 cell count - Patients more often under salvage therapy.
Gertsch et al., 2013 [24]	Describe adherence of pregnancy and postpartum HIV women referred to the adherence program.	Pregnant HIV women referred to the adherence program N = 25 Period: 2004 to 2012	Exploratory, retrospective study	- Socio-demographic data - Adherence data	68% black ethnicity, 44% naive patients, median age= 29 96% has a protease inhibitor and NRTIs Women who stopped the program: - 24% during pregnancy, 12% at childbirth and 16% during postpartum period - 62% kept on ART, 3 stopped ART after childbirth and 2 stopped without physician's agreement Unattended visits: increased from 17% during pregnancy to 38% during postpartum Probability of correct ART intake: 97% during pregnancy, 93% at childbirth and increased again during postpartum.
Krummenacher et al., 2014 [23]	Identify barriers and facilitators encountered by HIV patients with suboptimal medication adherence.	HIV patients referred to the adherence program N = 17 Period: August 2004 to May 2008	Retrospective, qualitative, thematic content analysis of pharmacists' notes during interviews conducted within the adherence program.	- Barriers and facilitators	Three main categories of barriers/facilitators: - Cognitive, emotional and motivational - Environmental, organisational and social - Treatment and disease.

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