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SCHNEIDER, Marie P.; KRUMMENACHER, Isabelle; FIGUEIREDO, Hugo; MARQUIS, Julien;
BUGNON, Oliver

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International Series: Adherence

Adherence: a review of education, research, practice and policy in Switzerland

Marie P. SCHNEIDER, Isabelle KRUMMENACHER, Hugo FIGUEIREDO, Julien MARQUIS, Oliver BUGNON.

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ABSTRACT*

Nonadherence to medication treatment regimens is a major preventable risk behavior in both acute and chronic diseases. Community pharmacists are facilitators in community care for promoting medication adherence and they should implement interdisciplinary medication adherence programs. To do so, pharmacists should be educated in medication adherence, and new pharmaceutical care policies should be implemented. The healthcare system should evolve to better meet the specific needs of patients.

Aims: this article describes what has been undertaken in the last decade in medication adherence in terms of education, research, practice and policy in Switzerland.

Methods: Medline was searched, with the search limited to Switzerland. The three Swiss pharmacy schools were also contacted to collect information about the medication adherence content of both their courses and research programs. National policies related to medication adherence were also reviewed for relevant content.

Results: Education: two pharmacy schools offer courses devoted specifically to medication adherence. The number of hours dedicated to the topic varies between 4 to 13. Research: a total of 16 studies met the inclusion criteria. Chronic patients were the focus of 9 studies. Medication adherence was the primary outcome of all studies; 10 studies also measured clinical outcomes. Nine studies evaluated the prevalence of medication

nonadherence; three studies evaluated the feasibility of new technologies for monitoring adherence; three studies evaluated medication adherence enhancing programs. Policies: three cognitive pharmaceutical services are reimbursed by healthcare insurers, which are directly related to medication adherence.

Conclusions: Pharmacists in Switzerland have been actively involved in medication adherence research since the mid '90s. Specific medication adherence courses have entered the curriculum of pharmacy schools, and policies in Switzerland are slowly beginning to meet needs of chronic patients by the introduction of pharmaceutical cognitive services and reimbursement fees.

Keywords: Medication Adherence. Pharmacists. Switzerland.

CUMPLIMIENTO: REVISIÓN DE LA EDUCACIÓN, INVESTIGACIÓN, PRÁCTICA Y POLÍTICA EN SUIZA

RESUMEN

El incumplimiento de los tratamientos farmacológicos es un comportamiento de riesgo serio prevenible tanto en enfermedades agudas como crónicas. Los farmacéuticos comunitarios son facilitadores en atención primaria para promover la adhesión a la medicación y deberían implantar programas interdisciplinarios de cumplimiento medicamentoso. Para ello, los farmacéuticos deben ser educados en adhesión a la medicación y deben implantarse nuevas políticas de atención farmacéutica. El sistema sanitario debería evolucionar para cumplir mejor las necesidades específicas de los pacientes.

Objetivos: este artículo describe lo que se ha realizado en la última década sobre adhesión a medicación en términos de educación, investigación, práctica y política en Suiza.

Métodos: Se buscó en Medline, limitando la búsqueda a Suiza. Se contactó a las tres facultades de Farmacia de Suiza para recoger información tanto sobre sus cursos como sobre sus programas de investigación. También se revisaron las políticas nacionales a la búsqueda de contenidos relevantes. **Resultados:** Educación: Dos facultades de farmacia ofrecieron cursos específicamente dedicados a adhesión a la medicación. El número de horas dedicado a estos temas varió de 4 a 13.

Investigación: 16 estudios cumplieron los criterios de inclusión. Los pacientes crónicos fueron el foco de 9 estudios. El cumplimiento de la medicación

* Marie P. SCHNEIDER. RPh, PhD. Researcher and lecturer in Pharmacy Practice. Community Pharmacy, Dpt of ambulatory care and community medicine, University Hospital, Lausanne (Switzerland).

Isabelle KRUMMENACHER. RPh, PhD student. Pharmacy Practice Unit. Pharmacy School, Universities of Geneva and Lausanne (Switzerland).

Hugo FIGUEIREDO. RPh, PhD student. Pharmacy Practice Unit. Pharmacy School, Universities of Geneva and Lausanne (Switzerland).

Julien MARQUIS. RPh, PhD student. Pharmacy Practice Unit. Pharmacy School, Universities of Geneva and Lausanne (Switzerland).

Oliver BUGNON. RPh, PhD. Head of Pharmacy Practice Unit. Pharmacy School, Universities of Geneva and Lausanne (Switzerland).

Series editors:

Marie P. SCHNEIDER. PhD. Researcher and lecturer in Pharmacy Practice. Community Pharmacy, Dpt of ambulatory care and community medicine, University Hospital, Lausanne (Switzerland).

Parisa ASLANI. PhD. Senior Lecturer in Pharmacy Practice. Faculty of Pharmacy, University of Sydney (Australia).

fue el resultado principal de todos los estudios; 10 estudios también midieron resultados clínicos. 9 estudios evaluaron la prevalencia del incumplimiento; 3 estudios evaluaron la viabilidad de las nuevas tecnologías para el seguimiento de la adhesión; 3 estudios evaluaron programas de aumento de cumplimiento. Políticas: - servicios cognitivos farmacéuticos están siendo remunerados por las aseguradoras y están directamente relacionados con el cumplimiento de la medicación. Conclusiones: La farmacia en Suiza se ha involucrado activamente en investigación sobre cumplimiento de la medicación desde mediados de los 90. Cursos específicos de cumplimiento de la medicación han entrado a formar parte del currículo de las facultades de farmacia, y las políticas en Suiza están comenzando lentamente a satisfacer las necesidades de los pacientes crónicos con la introducción de servicios cognitivos farmacéuticos y remuneración.

Palabras clave: Adherencia a la medicación. Farmacéuticos. Suiza.

INTRODUCTION

Nonadherence to medication treatment regimens ('medication nonadherence') is a major preventable risk behavior in chronic diseases. Missing doses is a natural behavior – every patient misses doses once in a while usually without important clinical consequences - but it may become pernicious if it is frequent enough to impact negatively on therapeutic outcomes. This is exemplified in the treatment of the Human Immunodeficiency Virus (HIV). Since the mid '90, HIV patients have become chronic patients largely due to the new potent combined antiretroviral therapies. However, ongoing medication adherence to the treatments needs to remain high (>90%) to prevent (1) the emergence of drug resistance strains and (2) treatment failure.¹

Medication adherence has become the new MeSH term in Medline since January 2009 and replaces the old term, patient compliance. Adherence is an active, intentional and responsible process of care in which the patient works to maintain health in close collaboration with healthcare providers. Medication adherence implies two different behaviors. On the one hand, persistence, which means the duration of dosing before patient's premature interruption of treatment, and, on the other hand, good quality of execution, which describes the daily patterns of patient adherence behavior (e.g. percentage of days with correct dosing, percentage of correct dosing intervals, drug holidays).

It has long been recognized that healthcare systems need to evolve to better meet the specific needs of chronic patients.² Healthcare providers should support their chronic patients by prescribing and delivering pharmacologically-sound treatments adjusted to specific patient needs. To ensure

optimal use of treatment, healthcare providers must also explore patient knowledge and understanding of disease and its treatment, beliefs and expectations, motivation, self-efficacy and readiness to treatment, and behavioral skills to ensure optimal integration of treatment into patient life style. Medication adherence is a dynamic behavior, which changes with time according to life circumstances. Therefore, it should be tracked over the long-term.

Chronic patients encounter several healthcare providers along their way, among them, their general practitioner, specialist physicians and their pharmacist. Unfortunately, healthcare providers usually do not collaborate. In fact, care is often sequential and inefficient as potentially useful information is not consistently exchanged or reinforced by all care providers.

A key professional responsibility of community pharmacists is to promote medication adherence. In fact, pharmacists are well positioned to identify and address medication adherence issues with their patients and provide an adherence report for physician review. This would allow physicians to consider adherence results as part of their decision making. Pharmacists are ideal partners and facilitators in community care for promoting medication adherence as it is often less difficult for patients to address nonadherence issues with someone other than the prescribing physician, to whom they may feel bonded.

However, to fulfill this role, pharmacists as well as other healthcare providers must be educated in medication adherence. Specific courses should cover medication adherence theories, relevant communication skills and relevant practice guidelines. An example is the recently published British National Institute for Health and Clinical Excellence (NICE) medication adherence guidelines for professionals and patients.³

Meanwhile, patient expectations of pharmacist's role should also evolve. Patients need to be informed of the potential and progressive shift from pharmacists dispensing chronic medications to pharmaceutical care programs, which emphasize the resolution of drug related problems such as medication nonadherence. Medication nonadherence should be addressed specifically with patients very early on in the course of their chronic treatment before nonadherence has become such an issue that patients become reluctant to express concerns and perceived difficulties with prescribed treatments.

This article describes what has been undertaken in Switzerland in terms of the education, research, practice and policy of medication adherence.

METHODS

Medication adherence education, research and practice

The three Swiss pharmacy schools – Basel, Geneva, and Zurich - were contacted and were asked to fill in a structured self-completion questionnaire about medication adherence in their

curricula, their medication adherence related research and the practice of medication adherence specific services in community pharmacy. Two items of the questionnaire focused on pre-graduate and post-graduate education in medication adherence. Respondents were asked to provide detailed information about the way education in medication adherence is structured and when the courses are taught. One item requested information on past and on-going research into medication adherence and for any related references. Three items were devoted to practice in community pharmacy: (1) the way community pharmacists address medication adherence with their chronic patients, (2) whether community pharmacists run specific adherence intervention programs, and (3) whether any interdisciplinary collaboration exists between community pharmacists and other healthcare providers or the pharmaceutical industry for promoting medication adherence.

Research in medication adherence

The database MEDLINE was searched, with the search limited to Switzerland from 1975 to present. The following key-words were used: patient compliance OR patient adherence OR medication adherence OR pharmaceutical services OR pharmaceutical care. Searches were also conducted based on the names of key Swiss researchers in the areas of medication adherence and pharmaceutical services. The study was included if pharmacists were involved in measuring and/or supporting patients' adherence to chronic medication. All study designs were included. Each retrieved article was then reviewed based on the study design, methods for measuring medication adherence, study outcomes and results.

Policy

National policies related to medication adherence were also reviewed. The policies are published in an agreement (Convention tarifaire RBP III) between the Swiss Pharmacist Society and Swiss health insurers ('santé suisse').

RESULTS AND DISCUSSION

Medication adherence education

All three Swiss pharmacy schools responded to the questionnaire. They all offer the Bachelor, a 3-year undergraduate degree, and a 2-year Master of Pharmacy degree. During the Bachelor degree, students receive an education in basic medical and pharmaceutical sciences. Depending on the Pharmacy Schools, 2 types of Masters degree are available: 1) a Masters degree in Pharmacy and a Masters degree in industrial pharmaceutical sciences. During the first year Masters degree in Pharmacy, students complete a 6-months advanced pharmaceutical sciences course and a 16-weeks research project. During the second year of the Masters degree in Pharmacy, students complete 20 to 30 weeks internship in community pharmacies and 10 optional weeks in hospital pharmacies, and attend a 12-week on campus course. The Masters degree in Pharmacy is completed by the Federal

examination for registered pharmacists. Registered pharmacists can then work in community pharmacies. Advanced Masters or diploma are also available, for example a Master of Advanced Studies in hospital pharmacy, a Master in Pharmaceutical Economics and Policy, a Master in Public Health or a diploma in community health.⁴

The curriculum regarding medication adherence varies widely from one University to the other. Students of all pharmacy schools are taught the topic during the masters training program. Two pharmacy schools offer specific courses devoted to medication adherence and related topics such as patient empowerment, and communication skills and techniques. The number of dedicated hours during the Masters varies between 4 to 13 hours. The third school did not approach the issue specifically but teaches medication adherence when appropriate during other therapeutic courses. Table 1 summarizes the medication adherence courses in the three Swiss pharmacy schools.

In Swiss pharmacy schools, medication adherence is slowly becoming recognized as an important issue that needs to be taught specifically. Nevertheless, the topic probably deserves more attention as patient behavior towards prescribed medications is an important modifier of the effectiveness of community-based chronic treatment. Moreover, the topic is taught at the end of the curriculum, which then coincides with student training in community pharmacies. However, it is important to increase students' awareness earlier on and to give them the opportunity to develop relevant skills more gradually.

Ongoing education in medication adherence for registered pharmacists is regularly provided by Universities, and national or local organizations involved in pharmacists' continuous education, for example, the Swiss Pharmacists Association, pharmaSuisse, and its program pharmActuel⁵ or the Association of community pharmacists CAP⁶ (Centre d'animation des pharmaciens).

Medication adherence education is also provided by other healthcare professionals, for example the University of Geneva offers a diploma in therapeutic education for chronic patients.⁷ All healthcare professionals can attend this 3-year course.

Research in medication adherence

A total of 16 studies met the inclusion criterion (Tables 2 and 3). The first publication was in 1998. Fourteen studies took place at one site; one was two-centered⁸ and the last one was multi-centered.⁹ All studies have been published in peer-reviewed journals: pharmacology journals, specific medical journals, or technology in health-care journals.

Medication adherence was the primary outcome of all studies; 10 studies also measured clinical outcomes. Nine studies evaluated the prevalence of medication nonadherence as the primary outcome.¹⁰⁻¹⁸ Three studies evaluated the feasibility of new technologies for measuring adherence (electronic pill containers, for example the Medication Event Monitoring System, MEMSTM the

Intelligent Drug Administration System, IDAS II™ the MEMS™ monitor connected to a personal modem HomeLink™.¹⁹⁻²¹ Eight studies correlated nonadherence rate to clinical outcomes^{9,11,12,15,16,18,22,23} and, among them, five

applied linear regression or multivariate analysis methods.^{9,15,16,18,22} One study evaluated predictors of nonadherence.¹⁰ Three studies evaluated medication adherence enhancing programs.^{8,9,23}

Table 1 Medication adherence courses in Swiss pharmacy schools.				
University	Degree (years)	Course	Content	Assessment
Basel	Master (4)	2-hour course on medication adherence	Theoretical basis, i.e. definition, measurement, intervention in the field of adherence in ambulatory care.	Oral exam
	Master (5)	4-hour workshop on medication adherence	Workshop on adherence with asthma treatment, patient education and monitoring.	Oral exam
		4-hour workshop on life style adherence	Workshop on smoking cessation, stages of change, motivational interview.	
Geneva	Master (5)	4-hour course on medication adherence	Definition of medication adherence and persistence, prevalence, risks linked to nonadherence, psychological theoretical frameworks, methods for evaluating/measuring adherence, program and techniques for promoting and supporting adherence, case studies.	Oral exam
		1-hour on empathy	Definition and theory, translation into practice, case studies	Oral exam
		2-hour course on patient empowerment	Definition, associated concepts (coping, disease management), translation into practice, case studies.	
		2-hour therapeutic education	Definition and theory, translation into practice, case studies	
		2-hour motivational interviewing	Introduction to motivational interviewing, i.e. its specific concepts (resistance, self-efficacy, ambivalence) and clinical skills (empathy, reflective listening, summaries, etc.); case studies.	
		2-hour workshop on interviewing techniques	Discussion of case studies, which students encountered during training; role-play.	
Zurich	Master (5)	No specific course	Medication adherence is taught during other courses, especially courses devoted to chronic patient treatment, all year through.	-

Chronic patients were the subjects in 9 studies: hypertension^{9,11,12,20,22} (5), lipid-lowering therapy¹⁶ (1), tuberculosis¹³ (1), HIV⁸ (1), and epilepsy²³ (1). In thirteen studies, patients were included in the outpatient medical clinics of three University hospitals in Switzerland (Lausanne, Basel and Geneva). Only one study took place in the community (community pharmacists and GPs)⁹ and two included hospitalized patients.^{10,19}

Four studies were randomized.^{9,17,20,23} All studies except one¹⁰ used electronic monitoring to measure medication adherence. Other methods included: pill counts, urine testing, self-reported questionnaire, and structured interviews with patients. A composite score between electronic monitoring, pill count and validated pocket-doses was also defined.^{8,22}

Authors of all sixteen studies were pharmacists and physicians. Nurses also participated in one study.⁸ For the most part, physicians recruited study subjects according to clinical inclusion criteria and referred them to pharmacists for the study. This suggests that medication adherence is an issue of interest to various health-care professionals as they share the responsibility with their patients for successful adherence. Most of all, it illustrates that health-care professionals can collaborate with each other as an interdisciplinary team for promoting medication adherence and seamless care. However, we have to explore whether this kind of model can be transferred to community pharmacies

and primary care practices. An on-going study in Switzerland is currently addressing this question.

Among the eight studies, which correlated medication adherence to clinical outcomes, five showed a significant association between medication adherence and clinical outcomes: better medication adherence correlated with improved outcomes.^{12,15,16,18,22} In most studies, medication adherence was high, probably because subjects knew they were being monitored (Hawthorne effect). However, subjects had difficulties adhering to complex recommendations (e.g. food restriction, refrigerator storage).¹⁷ In most studies, attrition rate was low and most patients were satisfied with the protocol. Three studies evaluated adherence-enhancing programs in hypertension, HIV and epilepsy; these early results are promising. Adherence seems to drop faster in control vs. intervention groups⁸ and clinical outcomes appear to be superior in intervention vs. control group.⁹ Larger, randomized trials are needed to confirm these preliminary results.

The latest intervention⁸ combined medication adherence electronic feedback – measured with MEMS™ caps - with motivational interviewing (MI), an approach developed by Miller and Rollnick²⁴ to promote behavioral change.²⁵ Motivational interviewing is tailored to patient's needs and readiness to change behavior.²⁶ The pharmacist created an individualized, nonjudgmental and

supportive environment allowing each patient to become an active partner. The intervention relied on Fisher's information-motivation-behavioral skills theoretical framework (IMB), which states that adherence-related information, motivation, and behavioral skills are fundamental determinants of adherence to medication.^{27,28} The intervention was also inspired by social cognitive theory.^{29,30} During the interview, the pharmacist addressed barriers and facilitators (cognitive, emotional, behavioral and social issues) encountered by the patient, which impacted adherence. At the end of each session, the patient brought an adherence report and summary of the intervention to the subsequent physician visit.

In Switzerland, other healthcare professionals such as physicians³¹, nurses³², psychologists³³, statisticians¹ and health economists³⁴ are interested in medication adherence research. Part of this research is interdisciplinary: physicians-pharmacists^{12,16}, physicians-nurses³², physicians-psychologists.³³

Practice of adherence services and policy

Community pharmacists are well placed to play a key role in supporting patient medication adherence as they are easily accessible, can meet with patients regularly and share the responsibility with the prescriber and the patient for dispensing medications efficiently and safely. The pharmacist has to answer the patients' individual needs in terms of information, medication handling, and practical integration and social acceptance of treatment into daily routines. Ideally, the pharmacist should address adherence issues empathically with their patients from the first time a medication is dispensed and offer patients the opportunity to talk on an ongoing basis about issues they face with their chronic treatment. This requires establishing and maintaining an appropriate, nonjudgmental environment.

Patient medication history: a tool for detecting nonadherence

Most community pharmacies in Switzerland are equipped with software, which keeps patient medication histories: prescribed and dispensed medicines, pharmacist comments on clinical data, automatic drug interaction checks, and patient dosage cards. This history is a useful indicator of patient medication renewal rate (Table 4). However, the accuracy of such histories can be low especially if the patient does not renew his treatment systematically at the same pharmacy. If nonadherence is detected through the history, an assumption for nonadherence should be validated with the patient and the issue should be addressed empathically.

In Switzerland, many pharmacies are equipped with a little desk on the side, where pharmacists can confidentially interview their patients about adherence issues.

Remunerated cognitive pharmaceutical services

Six types of cognitive pharmaceutical services are reimbursed by healthcare insurers in Switzerland,

the relative costs of which have been defined using a system of rated points. In 2009, the cost of one rated point equals 0.72 Euros (including taxes).³⁵ The overall aim of these cognitive services is to specify pharmacist tasks when delivering prescribed medication to patients and increase trust of patients, other healthcare givers and insurers. Among these cognitive pharmaceutical services, two are directly related to medication adherence and both need to be requested by a physician:

1. Weekly medication adherence fixed fee for preparing pill organizers, including electronic monitors for patients with a chronic condition, who take at least three different medicines concomitantly (20 rated points/week).
2. Direct observed therapy (DOT) fixed fee when a patient takes medication in the pharmacy under the pharmacist's supervision (usually 10 rated points/delivery; score differs for delivery of methadone).

A new cognitive pharmaceutical service, called polymedication check, will be implemented during 2009. The pharmacist will be reimbursed for a 20 to 30-minute interview with chronic patients taking at least 4 different and concomitant medications with the possibility of dispensing a pill organizer during the 3 following months. The aim is to tackle complex patients who are at risk of drug-related problems and/or nonadherence, hence the 4 prescribed medications. The interview and the pill-organizer do not need to be requested by the physician for reimbursement. This service can be repeated every 6 months.³⁶ This service represents a major improvement as, for the first time, interview time with the patient is reimbursed and the service does not need to be requested by the physician.

CONCLUSIONS

Specific medication adherence courses have entered the curriculum of two out of the three pharmacy schools in Switzerland. Pharmacists in Switzerland have also been actively involved in medication adherence research since the mid nineteen nineties. Research has primarily focused on nonadherence prevalence. More recently researchers have developed and evaluated programs for supporting medication adherence to long-term treatment. Most of the programs have been developed in specific clinic settings, for example the community pharmacy of an outpatient medical clinic. Present research focuses on the transfer of these programs to other community pharmacies in Switzerland. In fact, the main limitation of the research is that the effectiveness of these programs have not been assessed in large, multi-centered randomized clinical trials. Moreover whether these programs can be implemented successfully in non clinic settings i.e. community pharmacy, is still unknown.

Policies in Switzerland are slowly meeting the needs of chronic patients via implementation of pharmaceutical cognitive services and reimbursement fees. However, much still needs to be done to improve interdisciplinary collaboration in

order to provide seamless care. The role of the community pharmacists must evolve to meet the adherence challenges of patients with chronic diseases. Patient awareness of this shift in the role of the pharmacist will also have to be promoted and monitored.

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CONFLICT OF INTEREST

None declared.

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Table 2: Swiss research studies evaluating adherence.				
Study characteristics		Measuring methods for adherence	Study outcomes	Results
Schneider et al. ²¹ Design: pilot, run-in period, longitudinal, one-site. Aim: to assess if on-line home monitoring of medication adherence is feasible and acceptable to chronic patients. Duration: 2 months Number of subjects at inclusion: 7		Medication adherence monitor (MEMS™) connected to a personal modem (Homelink™) installed on the subject's telephone line.	Taking adherence ^a	On-line monitoring was well accepted by subjects. Adherence improved in 3 patients (from 76% to 90%, 69% to 87%, and 83% to 89%).
Fallab-Stubi et al. ¹³ Design: longitudinal, one-site. Aim: to evaluate the usefulness of an electronic monitor for measuring adherence to preventive chemoprophylaxis of tuberculosis with isoniazid. Duration: 6 months. Subjects at inclusion: 30		Continuous electronic monitoring of medication adherence (MEMS™), pill count, urine test for isoniazid.	Taking adherence	Mean adherence measured by electronic monitors was 91% (+/-18.6%). Pill count and urine test tended to overestimate adherence when compared to electronic data. Combined intervention of pharmacist and physician improved medication adherence significantly but transiently in all 4 non-adherent patients.
Schwed et al. ¹⁶ Design: open, longitudinal, one-site. Aim: to monitor adherence to fluvastatin 40mg using an electronic device vs. pill count. Duration: 6 months Subjects at inclusion: 30		Continuous electronic monitoring of medication adherence (MEMS™), pill count.	Taking dosing adherence ^a , timing adherence ^a , total and LDL-cholesterol.	Total cholesterol and LDL-cholesterol decreased significantly (18% and 25%, p<.001) during the study. Taking adherence was 89% +/-13.5%, dosing adherence was 82% +/- 19.5% and timing adherence was 82% +/- 19.5%. Adherence by pill count was 93% +/- 9.5%. A significant correlation between adherence and decrease in LDL-cholesterol was observed when adherence was assessed electronically.
Arnet et al. ¹⁰ Design: transversal. Aim: to correlate patients' statements on their adherence before hospitalization with their personal knowledge and convictions about their treatment. Duration:- Subjects at inclusion: 100		One structured interview per patient during hospitalization on an internal medicine ward.	Self-reported adherence, specific knowledge as for example name of medications, personal perception of prescribed medication.	78% subjects reported good adherence, while 13% admitted nonadherence. Knowledge was significantly better in adherent patients (p=.048). Personal perception did not differ by adherers and nonadherers. Subjects used 3 main strategies to ensure adherence: visual aids (69%), coupling to a ritual (26%), supervision by a third person (6%).
Stubi et al. ¹⁷ Design: randomized, open, one-site. Aim: to assess adherence to oral combined to written recommendations vs. oral recommendations to live oral Ty21a typhoid vaccine in travelers regarding dosing, timing with respect to food intake. Duration: 5 days Intervention: 55 Control: 60		Continuous electronic monitoring of medication adherence (MEMS™), pill count, self-administered questionnaire.	Percentage of adherers: taking all 3 pills, on alternate days, at least one hour before a meal.	No difference in adherence was shown by group. All subjects took the 2 capsules but only 53% subjects adhere to all recommendations according to the electronic monitors and 68% to the questionnaire (p=.05).

Table 2: Swiss research studies evaluating adherence.

Study characteristics	Measuring methods for adherence	Study outcomes	Results
<p>Burnier et al.¹² Design: one-arm, observational, longitudinal, one-site. Aim: to evaluate benefits of electronic monitoring of medication adherence in the management of patients with resistant hypertension. Duration: 4 months Number of subjects at inclusion: 41</p>	<p>Continuous electronic monitoring of medication adherence (each single antihypertensive drug was delivered in a MEMS™ monitor). For the first 2 months, patient's usual treatment was provided in MEMS™ without any other intervention; for the next 2 months, treatment could be adapted if necessary.</p>	<p>Dosing adherence, blood pressure.</p>	<p>Monitoring of adherence alone was associated with an improvement in BP ($p<.01$). BP was normalized in one-third of patients. Patients with lowest adherence had higher diastolic BP ($p=.04$).</p>
<p>Bertholet et al.¹¹ Design: retrospective, one-site. Aim: to evaluate whether the use of electronic monitoring for medication adherence is a useful approach to identify compliance problems in hypertensive patients. Duration: 2 months Number of subjects at inclusion: 69</p>	<p>Continuous electronic monitoring of medication adherence (one MEMS™ monitor per medication)</p>	<p>Taking adherence, blood pressure.</p>	<p>Significant decrease in BP (from 159/104 \pm 23/12 mmHg to 143/92 \pm 20/15, $p<.001$) after inclusion. BP was normalized in one third of patients. Mean adherence of patients with normalized BP was 90.7% (range, 64-100%), and was similar in the non-normalized patients.</p>
<p>Arnet et al.¹⁹ Design: open, longitudinal, one-site. Aim: to evaluate accuracy of electronic adherence monitoring of an oral vitamin combination. Duration: 3 weeks Subjects at inclusion: 37</p>	<p>Continuous electronic monitoring of medication adherence (MEMS™), pill count, patient interviews.</p>	<p>Taking adherence</p>	<p>Taking adherence was 102%. Pill boxes were opened >once a day by 10 patients on a least one monitored day. In 7 patients, the number of openings exceeded the number of capsules provided but only 2 patients admitted overconsumption.</p>
<p>Wermelle et al.¹⁸ Design: longitudinal, one-site. Aim: to evaluate if poor adherence is a predictor of low Helicobacter pylori eradication. Duration: one week Subjects at inclusion: 78</p>	<p>Continuous electronic monitoring of medication adherence (MEMS™).</p>	<p>H. pylori eradication rate, percentage of subjects taking more than 85% of their doses.</p>	<p>H. pylori eradication rate was 65% (95% CI: 54.8-76.0%). 89% of subjects were adherers. On multivariate analysis, H. pylori eradication was inversely associated with poor adherence ($p=.029$). Poor adherence and bacterial resistance explained 40% of failures.</p>
<p>Schneider et al.¹⁵ Design: one-arm, longitudinal, one-site. Aim: to characterize use of a nicotine nasal spray (NNS) in smoking cessation. Duration: 18 months Number of subjects at inclusion: 92</p>	<p>Nasal spray use was monitored by a microchip fixed on the spray unit (microswitch-actuated metered-dose inhaler chronolog, MDILog™).</p>	<p>Number of abstainers at 12 and 4 months; pattern of use of NNS.</p>	<p>Success rate was 17.4% at 12 and 9.8% at 24 months. Abstainers use NNS more than failures (12 vs. 6 puffs/day, $p=.05$), use it less in the morning compared with failures (26.6 vs. 32.8% of total median daily dose, $p=.03$) but used it more in the evening/night (35.3 vs. 26.7% of total median daily dose, $p=.007$).</p>

Table 2: Swiss research studies evaluating adherence.				
Study characteristics		Measuring methods for adherence	Study outcomes	Results
Landry et al. ¹⁴	Design: open, longitudinal, observational. Aim: to assess adherence to mefloquine malaria chemoprophylaxis in adult travelers to sub-Saharan Africa. Duration: variable Number of subjects at inclusion: 81	Continuous electronic monitoring of medication adherence (MEMS™), self-administered questionnaire on drug intake	Taking of all the tablets at the right day.	Only 26 travelers (32%) took all the doses at the expected date. 19/81 (24%) took them with intervals of +/- 1 day.
Santschi et al. ²⁰	Design: randomized, cross-over. Aim: to evaluate acceptability of IDAS II, a new electronic device for monitoring adherence in hypertension Duration: 2x2 months Number of subjects at inclusion: 24	Intelligent Administration System (IDAS II™ electronic monitor) vs. MEMS™ monitor as control.	Patients' opinion on both devices, rates of adherence, blood pressure.	Patients found MEMS™ easier to use than IDAS™ (p<.001) but appreciated IDAS™ blister packs better than MEMS™ bulk packaging (p<.01). Median taking adherence was 99% and comparable with both devices. No difference in blood pressure between groups.
Figueiredo et al. ²²	Design: retrospective, one site. Aim: to describe systolic blood pressure (SBP) and model it during an adherence-enhancing intervention program in patients resistant to their treatment. Duration: variable Subjects: 89	Continuous electronic monitoring of medication adherence (MEMS™), combined to repeated interviews with subjects. Composite adherence score between electronic monitoring, pill count and validated pocket-doses.	Quality of execution ^a , blood pressure.	Quality of execution was high and stable over time. The average decrease in SBP from baseline was 15mmHg. SBP decreased as quality of execution increases with a maximum around 85% adherence.
^a Taking adherence is the percentage of openings of the device divided by the number of prescribed doses. Dosing adherence is the percentage of days with correct dosing. Timing adherence is the percentage of openings of the device with a correct timing (+/-25% of prescribed interval). Quality of execution: data are summarized in a sequence of binary data, Z _{ij} , indicating whether yes (1) or no (0), at least one of the medicines was taken as prescribed on day i by patient j.				

Table 3: Swiss research studies evaluating medication adherence enhancing programs.

Study characteristics	Intervention	Study outcomes	Study results
Schneider et al. ²³ Design: randomized, controlled, open, one-site Aim: to evaluate the benefit of online telemonitoring of medication adherence in epilepsy. Duration: 8 months Intervention: 12 Control: 14	Electronic monitors of medication adherence (MEMS TM) connected to a personal modem (Homelink TM) installed on the subject's telephone line vs. electronic monitors only in controlled subjects. Pharmacist called patient at home in case of drug omission.	Taking, dosing and timing adherence, seizure frequency.	Dosing adherence was high and similar in both groups. There was a trend towards less epileptic events in the intervention vs. the control group (p=.07).
Santschi et al. ⁹ Design: cluster randomized, controlled, and multi-sites. Aim: to examine whether monitoring medication adherence with an electronic system improves BP control in uncontrolled patients followed by GPs. Duration : 12 months Intervention : 34 Control : 34	Electronic monitoring of medication adherence (MEMS TM), plus non-structured repeated interviews at the pharmacy in the intervention group vs. electronic monitors only in control group.	Normalized BP (<140/90 mmHg)	Likelihood of reaching target BP was higher in intervention group compared to control group (p<.05). At 4 months, 38% patients in intervention group reached target BP vs. 12% patients in control. (p<.05), and 21% vs. 9% at 12 months (p=ns). Multivariate analysis showed that being allocated to intervention group was associated with a greater odds of reaching target BP at 4 (p<.01) and 12 months (p=.051).
Krummenacher et al. ⁸ Design: pilot, quasi-experimental, two-sites. Aim: to evaluate the feasibility of an interdisciplinary and multifactorial adherence program in HIV patients starting a first or a second antiretroviral therapy line. Duration: 6 months Intervention: 21 Control: 11	Continuous electronic monitoring of medication adherence (MEMS TM), combined to repeated motivational interviewing in intervention vs. blinded medication adherence electronic monitoring in control group. Composite adherence score between electronic monitoring, pill count and validated pocket-doses.	Quality of execution and persistence.	The study was feasible in one site but not in the other one. Quality of execution was high in both groups (97% vs. 95%) but decreased statistically more over time in the control versus the intervention group (p<.0001).

Table 4: Example of a patient's medication history showing the timing of dispensation and the number of tablets dispensed per month.

2008															
Mr O.V. 81 years old															
	Dosage	Regimen		JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	DEC
Acetylsalicylic acid	300mg	1-0-0-0				90		90			90			90	
Enalapril	20mg	1-0-0-0				100	100				100			100	
Indapamide SR	1.5mg	1-0-0-0		90			90			90			90		
Amlodipine	5mg	1-0-0			30	100			100			100			100
Nateglinide	60mg	1-1-1				168	84	84		168	84		168	84	
Atorvastatin	10mg	1-0-0						30	30	100			100		
Calcium/cholecalciferol	500mg/400UI	2-0-0		120			120	120		120			120	120	
Acetaminophen	1000mg	1 to 2 tab/24h		80		20	40	60			80		20	40	
Acetaminophen	500mg									32					