Medication and Symptom Management in Persons Living with HIV: Perceptions and Collaboration of Persons Living with HIV, their Close Support Persons and Healthcare Providers

Inauguraldissertation

zur Erlangung der Würde eines Doktors der Pflegewissenschaft

vorgelegt der Medizinischen Fakultät der Universität Basel

von

Dunja Nicca,

von Sufers und Donath / Graubünden

Basel, 2009

Genehmigt von der Medizinischen Fakultät

auf Antrag von:

Fakultätsverantwortliche	Prof. Rebecca Spirig
Dissertationsleitung	Prof. Rebecca Spirig
Co-Referat	Prof. Wolf Langewitz
Externe Experin	Prof. Sally H. Rankin

Basel, den 28.10.2009

Dekan

Prof. Albert Urwyler

Table of Content

Acknowledgements **3**

Summary **5**

Introduction **13**

Chapter 1 Collaborative medication and symptom management in the context of chronic HIV management **16**

Treatment success and future challenges for the management of HIV/AIDS 16

The management of chronic conditions 18

Self-management: a collaborative endeavor 19

Self-management of PLWH 21

Collaboration in medication and symptom management 24

Medication and symptom management *24*

PLWH's collaboration with close support persons and healthcare providers *27*

Role of Self-management programs for PLWH 28

HIV self-management in the Swiss context 29

Chapter 2 Aims of the research program **38**

Chapter 3 Comprehensive Clinical Adherence Interventions to Enable Antiretroviral Therapy: A Case Report **41**

Abstract 42

Introduction 43

Presentation of the case study 44

Background of the intervention strategies 46

Implementation of interventions and clinical progress 49

Discussion and implications for practice 52

Chapter 4 Literaturzusammenfassung zur Frage: „Welche Interventionen bewirken eine Verbesserung der Adhärenz von HIV-Patienten unter ART?“ Interventions to Enhance Adherence of Patients with HIV on ART: A Literature Review **56**

Zusammenfassung 57

Abstract 57

Einleitung 58

Literatursuche 59

Beschreibung der Studien 60

Zusammenfassung der Resultate 67

Schlussfolgerung und Empfehlung 68

Chapter 5 Keeping a grip on HIV: A Qualitative Investigation on Collaborative Medication and Symptom Management Experiences of Persons with HIV living in Switzerland **74**

Abstract 75

Introduction 76

Methodology and Methods 77

Results 78
Discussion 86
Chapter 6 Symptom management in HIV/AIDS: A mixed methods approach to describe collaboration and concordance between persons living with HIV and their close support persons 94
Abstract 95
Introduction 96
Methodology and Methods 97
Results 100
Discussion 112
Chapter 7 Discussion 118
Discussion of key findings 118
The complexity of HIV self-management 118
PLWH as active self-managers 120
Self-management collaboration 122
Discussion of methods 124
Implications for future research and clinical practice 127
Future research 127
Implications for clinical practice 128
Conclusion 133
Curriculum Vitae 145

Acknowledgements

My deepest gratitude goes to my advisor, **Prof. Rebecca Spirig,** who introduced me to the world of research, then accompanied and supported my development for many years. I appreciate most her critical perspective on research and social phenomena, which broadened my own perspective through her provocative and inspiring discourses.

I also wish to express special thanks to the other members of my PhD committee, who have all given close support and guidance throughout the dissertation process on numerous levels, enabling my learning and progress. I want to thank **Prof. Kim Moody**, of the University of Southern Maine, for her extremely cheerful and motivating mentorship throughout the process. She also gave me the opportunity to gain an in-depth knowledge of the academic and clinical work of nurses in the US, which provided me with a vision to guide my learning process. I greatly appreciated **Prof. Manuel Battegay's,** quick and substantial feedback and his continuous structural guidance throughout the process of my PhD studies. Many thanks also to **Prof. Marcel Tanner**, whose broad experience in mentoring PhD students, which was apparent in the calm and structured guidance he provided, I appreciated very much.

I gratefully thank **Prof. Langewitz,** for his spontanous effort as faculty co-evaluator of this thesis. I enjoyed working with him in different projects and in particular learned from his expertise in patient-provider communication. His feedbacks were always substantial and motivating.

And I also gratefully thank **Prof**. **Sally Rankin**, of the University of California, San Francisco, for her willingness to evaluate this thesis as an external expert. I greatly respect her broad scientific expertise in HIV and other chronic illness management, and her openness and willingness to share her expertise.

I especially wish to thank **Prof. Sabina De Geest**, head of the Institute of Nursing Science, University of Basel, for providing personal support and a rich scientific environment, allowing constant learning opportunities and inspiration from her network of renowned international researchers. I also want to thank her for chairing the defense colloquium as representative and chair of the Medical Faculty's PhD Commission (University of Basel).

I wish to express my deepest gratitude to **Katharina Fierz** and **Dr. Jan Fehr** who have both been most supportive colleagues for many years. They were always reliable and inspiring discussion partners for a range of questions that arose throughout my study process and contributed substantially, as co-authors, to the improvement of my dissertation project.

Many thanks also go to the following persons, all of whom contributed substantially to this dissertation project:

Prof. Mary Beth Happ who introduced me into mixed method research and has been an appreciated mentor throughout the process of data analysis and description.

Christine Spitz for her contributions regarding qualitative data analysis, which included many inspiring discussions.

Sabine Bigler who has been an appreciated colleague in many HIV related projects, contributed to data collection and conducted a broad literature review on adherence interventions.

Christine Vincenzi who contributed in data collection and added appreciated input in research meetings.

Dr. Luigia Elzi who contributed by collaboratively caring for patients and discussing and writting up the case report

The study nurses and physicians at the SHCS centers in Basel, Bern, St. Gallen and Zürich, who were involved in recruitment of participants and therefore supported the research process substantially.

Chris Shultis and **Leslie Nicholls,** for their careful editing of my manuscripts and dissertation. Working with them improved my writing and English language skills considerably.

All participants who shared their stories

During my PhD education, I also had the excellent opportunity to work part time at the HIV outpatient clinic in St. Gallen. I want to give a special thanks to the **“Infekt-Team”**, who supported my work by providing an atmosphere where new ideas could be discussed and clinical care and research processes were reflected thoughtfully. I therefore wish to thank every member of the team for their contributions.

I am deeply thankful to **Prof. Pietro Vernazza**, head of the Division of Infectious Diseases and Hospital Hygiene, Cantonal Hospital, Basel, for giving me the opportunity to work in a setting with regular scientific and clinical exchange, and for introducing me to many experts in the field of HIV care and research. Diverse discussions and his visionary attitude inspired and broadened my own perspectives.

Many thanks go to **Marianne Graf,** from department of organizationl developement at the University of Basel for her thoughtful coaching and encouragement.

I am also extremely grateful to the **Ebnet Foundation** for their grant support, their careful supervision of the research process, and their encouraging feedback.

Finally, my profound personal thanks go to my partner, **Marcel Zürcher**, for his ongoing commitment and support throughout this project, and to my closest friends, who encouraged my work but provided me with many pleasant diversions to replenish my energy.

Summary

Over the past two decades, developments in the treatment and monitoring of HIV Infection have radically reduced morbidity and mortality rates among those affected by it [1]. Between 1996 and 2005, the estimated life expectancy for persons living with HIV (PLWH) placed on combined antiretroviral therapy (cART) at age 20 rose from 36.1 to 49.4 years [2].

Focusing on the improvement of health outcomes for the estimated 33 million PLWH worldwide, the situation differs considerably between low- and high-resource settings. Broader access to cART should substantially improve health outcomes for PLWH in low-resource settings, where supplies currently meet only 31% of the estimated global need [3]. However, such steep improvements are no longer a realistic option for high-resource settings. In western and central Europe, for example, long-term treatment is already provided to 90 -100% of PLWH and initial drops in mortality and morbidity have been sustained [4].

In high resource settings, though, long-term treatment experiences have shown that non-adherence to medication regimens is a serious issue. Since ART demands a constant level of medication to suppress viral replication, once started it has to continue without interruption. Compelling evidence has linked treatment interruptions, including medically guided ones, with poorer clinical outcomes compared to continuous treatment, i.e., near-perfect adherence [5].

However, long term adherence is complicated by a range of barriers, including the medications' adverse effects: estimates of prescribed cART doses actually taken in Europe and Northern America range from 60%-70% [5-8]. As a result, medications' adverse effects, opportunistic infections and co-morbidities keep the prevalence of symptoms consistently high, averaging 8-14 symptoms per person [9-12]; and a high number of distressing symptoms has been shown to further complicate adherence to cART [9].

Regarding the stabilization of health outcomes for this treatment-experienced population of PLWH, major advances are no longer possible based solely on treatment access. It is clearly necessary to formulate new management strategies that consider multiple aspects of this chronic condition, focusing in particular on the skills needed by PLWH and their close support persons (CSPs) to manage their condition at home on a daily basis.

In order to improve health outcomes for patients with chronic conditions, various studies have shown a need for profound changes across diverse levels of the health care system [9, 13, 14]. The WHO publication 'Innovative Care for Chronic Conditions' structures chronic care management areas requiring change into micro, meso, and macro levels, with each level interacting with and dynamically influencing the others. The macro level consists of policy makers who influence standards and incentives for quality care; the meso level includes healthcare organizations and communities; and the micro level is the level of patient interaction, where patients' self management and collaboration

between health care providers and patients are key issues [15]. By providing a fuller understanding of PLWH's self-management and collaboration with CSPs and health care providers (HCPs) within the care process, the research represented here should help answer questions of how and where to improve care for PLWH on the micro (patient) level.

In the context of chronic disease management, "self-management" has become a widely used term, encompassing the day-to-day activities a chronic illness patient performs to minimize the consequences of his or her condition. Such actions vary based on the person's perceptions, experiences and expertise, but share the focus of optimizing health outcomes, whether by retarding deterioration, maintaining a given level of health, or improving overall wellness [16-18]. Additionally self-management is increasingly recognized as a dynamic process that includes active collaboration with others, especially close support persons (e.g., partners, friends, family) and healthcare providers [18, 19]. Yet the skills that enable healthcare providers and close support persons to work with PLWH's self-management have only been vaguely described.

Although patient self-management shows similarities across a range of chronic conditions, every condition has unique challenges that require specialized self-management tasks. HIV specific self-management tasks have been summarized into eight categories: medication management, symptom management, substance use management, lifestyle management, emotional management, role management, transmission management, and social management. From a medical perspective with a focus on improving health outcomes, medication and symptom management may be regarded as the core tasks of HIV self-management. After all, a person's experience of symptoms is closely related to adherence to cART (i.e., adherence decisions are often based upon symptoms), and adherence is closely related to treatment success [9, 20, 21].

In the current literature, medication management and symptom management – the two self-management tasks upon which this thesis focuses – have mainly been described in a fragmented way, with close attention paid only to one or the other, despite considerable evidence linking the two closely [9, 21-23].

Medication management encompasses decisions related to initiating or changing cART regimens [24-26]. Once started, the new or changed regimens have to be integrated into daily life and adherence maintained over time. Eventually, this also entails the management of adherence related obstacles [6, 27]. Opportunistic diseases and/or co-morbidities often require further medication management.

Symptom management encompasses the assessment, evaluation and monitoring of symptoms [21]. Decisions are necessary on how to deal with symptoms, such as when to contact healthcare providers, whether or not to alter exercise or diet, and when to take — or not take — certain medications [28].

For PLWH, the formulation and adoption of many medication and symptom management strategies involves collaboration with their HCPs and CSPs; yet, despite the seemingly obvious benefits of such collaboration, the related processes are only vaguely understood. Since self-management activities regarding both medications and symptoms are closely associated with health outcomes, a fuller understanding of such activities is necessary to improve related services.

The overall aim of this exploratory mixed method research program was to describe PLWH's symptom and medication management activities, focusing on collaboration between PLWH, CSPs and HCPs, from the perspectives of all three groups. Four articles presented the results.

The first, a clinical case report, describes the complexity of self-management support in clinical care and illustrates how interventions that were individualized, culturally sensitive, and provided by a team of health care providers enabled the patient to optimize his adherence, which led to significant improvement in his clinical surrogate markers and subjective quality of life.

Second, a literature review summarized the evidence resulting from randomised controlled trials of interventions designed to enhance medication adherence to antiretroviral therapy. The review showed that effective programs combine several methods, and highlighted a continuing need for long term programs tailored to patient needs.

The third article dealt with PLWH's experiences with the management of medications and symptoms, along with their collaborations with close support persons and health care providers within this process. The narratives of 13 PLWH revealed that even small changes in health and treatment could change participants' impressions of maintaining or "losing their grip" on HIV. To keep their grip, participants constantly monitored their condition, developed expertise in care and symptom management, and included input from healthcare providers and close support persons in their management processes. Despite the clear need for partnerships with HCP, PLWH described this area of collaboration as sometimes supportive, sometimes a hindrance.

The final article reported on the use of an exploratory mixed methods approach to examine the collaboration of PLWH and their CSP within the process of symptom management, including a comparison of the two players symptom reports. Qualitative results revealed that collaboration typically depended on distinct but integrative positions of PLWH and CSP, with the PLWH in a clear leadership role.

These roles were reflected in diverse themes of daily symptom management, and later confirmed in the quantitatively assessed symptom experience reports, where PLWH reported significantly more symptoms over the previous week – an average of 16 (Q_1=9; Q_3=24), compared to CSPs' 12 (Q_1=5; Q_3=17). This disproved two of our initial hypotheses – first, that certain symptoms would be reported more often by CSPs (this was never the case), and second, that where the PLWH reported symptoms as very distressing, symptom reports by PLWH and CSP would not differ.

The results of this research program contributed to the existing knowledge by using the conceptualization of Loring and Holman to describe HIV specific self-management tasks and skills

[17]. This comprehensive description can be used as a guiding framework to plan both clinical self-management support interventions and HIV self-management oriented research projects.

Another important contribution was the replication of the observation by Thorne et al. that chronically ill patients at some point made an active decision to control the effects of their condition [18]. The constitutive pattern “I have a grip on HIV - HIV has a grip on me” revealed a similar phenomenon. However, in contrast to earlier investigations, examining this phenomenon provided insights into a dynamic process. Throughout the course of the condition, health and/or treatment changes could influence the perception of “having a grip on HIV” or losing it. These alternating conditions could constitute a phenomenon more pregnant in HIV than in chronic conditions with more predictable illness trajectories. Additionally, since the “HIV has a grip on me” perception was associated with feelings of uncertainty, fear and loss of morale, and since depressive symptoms clearly hinder effective self-management, this phenomenon certainly warrants clinical examination [28-30].

A particularly important outcome of this research program is the deepening of our understanding of collaboration between PLWH and CSP. Concordant with earlier reports, the narratives of PLWH and CSP presented in Chapter Six revealed that PLWH collaborated closely with their CSPs to manage their condition [31-33]. Yet, in contrast to earlier investigations, this collaboration was characterized by distinct roles: as ‘managers’, the PLWH took a clear lead on the overall management of the condition, whereas, as ‘companions’, their CSPs tried to find and support aspects of self-management. The PLWH’s leadership role was, in fact, much clearer here than in previous studies, which emphasized the partnership aspects of the PLWH/CSP relationship. This insight into the collaboration of PLWH and CSP may provide a foundation upon which to integrate CSP into research based clinical interventions.

To our knowledge, concordance between the symptom reports of patients and their CSPs has never before been described for the PLWH population. We therefore provide the first recorded insights into the issue. Compared to earlier investigations in cancer populations, where CSPs reported more symptoms than patients [34, 35], PLWH in this study consistently reported significantly more.

Additionally, we described an inter-method inconsistency that indicates a need to better understand management of neurocognitive symptoms from PLWH’s and CSP’s perspectives. Our qualitative analysis revealed a cluster of neurocognitive symptoms that CSPs recognized but did not wish to discuss with their partners; and the quantitative assessment of concordance between symptom reports revealed that all symptoms were reported more often by the PLWH.

Regarding collaborations with HCPs, in accord with previous research, our results illustrated that this group can both hinder and enable PLWH’s self-management [36-38]. PLWH’s narratives provided insights into the respective negative and positive aspects of their relationships with HCPs. On one hand, the need for providers to use a patient centered approach, including recognizing each person as a unique human being, is highlighted and has already proved important in a broad range of studies [36, 38-40]. On the other hand, our findings also highlight the importance of HIV-specific competence on the part of healthcare providers. Second in importance to overall medical competence, this includes the ability to assess a patient’s symptom experience in a non-judgmental manner, to collaboratively develop medication and symptom management strategies, to provide ongoing education on those topics, and finally to assist patients in decision making and in the coordination of their various health problems.

Also significantly, this research program determined that CSP were only very slightly integrated into clinical care, meaning their collaboration with health care providers was marginal. Since PLWH need their CSPs to act as active partners to manage the disease, not integrating them into self-management support is a missed opportunity to strengthen PLWH’s self-management.

In summary, this study program provided new insights and raised further questions. Subsequent research should focus on a qualitative meta-synthesis and development of the phenomenon of “having a grip” or “being in control” of a chronic condition, descriptions of HCPs’ perspectives of collaboration, a better understanding of the concordance between PLWH’s symptom reports and those of CSP – particularly in relation to neurocognitive symptoms and regarding strategies for integrating CSP’s into intervention programs and clinical processes.

References

1. Sterne, J.A., et al., *Long-term effectiveness of potent antiretroviral therapy in preventing AIDS and death: a prospective cohort study.* Lancet, 2005. **366**(9483): p. 378-84.
2. Hogg, R.S.S., J. A.; Graber, S.; Battegay, M.; Bonarek, M.; D'Arminio Monforte, A.; Esteve, A.; Harris, R.; Justice, A.; Hayden, A.; Lampe, F.; Mocroft, A.; Mugavero, M. J.; Staszewski, S.; Wasmuth, J.C.; van Sighem, A.; Kitahata, M.; Guest, J.; Egger, M.; May, M., *Life expectancy of individuals on combination antiretroviral therapy in high-income countries: a collaborative analysis of 14 cohort studies.* Lancet, 2008. **372**(9635): p. 293-9.
3. Unaids, *2008 Report on the global Epidemic*. 2008, WHO Library Cataloguing-in-Publication Data.
4. Mocroft, A., et al., *Decline in the AIDS and death rates in the EuroSIDA study: an observational study.* Lancet, 2003. **362**(9377): p. 22-9.
5. Burman, W., et al., *Episodic antiretroviral therapy increases HIV transmission risk compared with continuous therapy: results of a randomized controlled trial.* J Acquir Immune Defic Syndr, 2008. **49**(2): p. 142-50.
6. Deschamps, A.E., et al., *Prevalence and correlates of nonadherence to antiretroviral therapy in a population of HIV patients using Medication Event Monitoring System.* AIDS Patient Care STDS, 2004. **18**(11): p. 644-57.
7. Simoni, J.M., et al., *Self-report measures of antiretroviral therapy adherence: A review with recommendations for HIV research and clinical management.* AIDS Behav, 2006. **10**(3): p. 227-45.
8. Sitta, R., et al., *No Variability Across Centers in Adherence and Response to HAART in French Hospitals: Results From the ANRS-EN12-VESPA Study.* J Acquir Immune Defic Syndr, 2009.
9. Ammassari, A., et al., *Self-reported symptoms and medication side effects influence adherence to highly active antiretroviral therapy in persons with HIV infection.* J Acquir Immune Defic Syndr, 2001. **28**(5): p. 445-9.
10. Harding, R., et al., *Is antiretroviral therapy associated with symptom prevalence and burden?* Int J STD AIDS, 2006. **17**(6): p. 400-5.
11. Karus, D., et al., *Patient reports of symptoms and their treatment at three palliative care projects servicing individuals with HIV/AIDS.* J Pain Symptom Manage, 2005. **30**(5): p. 408-17.
12. Silverberg, M.J., et al., *Prevalence of clinical symptoms associated with highly active antiretroviral therapy in the Women's Interagency HIV Study.* Clin Infect Dis, 2004. **39**(5): p. 717-24.
13. Handford, C.D., et al., *Setting and organization of care for persons living with HIV/AIDS.* Cochrane Database Syst Rev, 2006. **3**: p. CD004348.
14. Schoen, C., et al., *In chronic condition: experiences of patients with complex health care needs, in eight countries, 2008.* Health Aff (Millwood), 2009. **28**(1): p. w1-16.
15. WHO, *Innovative Care for Chronic Conditions*. 2002, Geneva: WHO library Cataloging-in-Publication.
16. Gifford, A.L. and S. Sengupta, *Self-management health education for chronic HIV infection.* AIDS Care, 1999. **11**(1): p. 115-30.
17. Lorig, K.R. and H. Holman, *Self-management education: history, definition, outcomes, and mechanisms.* Ann Behav Med, 2003. **26**(1): p. 1-7.
18. Thorne, S., B. Paterson, and C. Russell, *The structure of everyday self-care decision making in chronic illness.* Qual Health Res, 2003. **13**(10): p. 1337-52.

19. Epping-Jordan, J.E., et al., *Improving the quality of health care for chronic conditions.* Qual Saf Health Care, 2004. **13**(4): p. 299-305.

20. Harrigan, P.R., et al., *Predictors of HIV drug-resistance mutations in a large antiretroviral-naive cohort initiating triple antiretroviral therapy.* J Infect Dis, 2005. **191**(3): p. 339-47.

21. Portillo, C.J., W.L. Holzemer, and F.Y. Chou, *HIV symptoms.* Annu Rev Nurs Res, 2007. **25**: p. 259-91.

22. Wilson, H.S., S.A. Hutchinson, and W.L. Holzemer, *Reconciling incompatibilities: a grounded theory of HIV medication adherence and symptom management.* Qual Health Res, 2002. **12**(10): p. 1309-22.

23. Simoni, J.M., et al., *Efficacy of interventions in improving highly active antiretroviral therapy adherence and HIV-1 RNA viral load. A meta-analytic review of randomized controlled trials.* J Acquir Immune Defic Syndr, 2006. **43 Suppl 1**: p. S23-35.

24. Enriquez, M., et al., *Assessment of readiness for adherence by HIV-positive males who had previously failed treatment.* J Assoc Nurses AIDS Care, 2004. **15**(1): p. 42-9.

25. Nicca, D., et al., *[Ready for antiretroviral therapy? Therapy decision making experiences of persons living with HIV].* Pflege, 2005. **18**(5): p. 289-98.

26. Nordqvist, O., et al., *Assessing and achieving readiness to initiate HIV medication.* Patient Educ Couns, 2006. **62**(1): p. 21-30.

27. Vervoort, S.C., et al., *Adherence in antiretroviral therapy: a review of qualitative studies.* Aids, 2007. **21**(3): p. 271-81.

28. Spirig, R., et al., *Symptom management in HIV/AIDS: advancing the conceptualization.* ANS Adv Nurs Sci, 2005. **28**(4): p. 333-44.

29. Eller, L.S., *Depressive symptoms in HIV disease.* Nurs Clin North Am, 2006. **41**(3): p. 437-53, vii.

30. Fehr, J.S., et al., *Starting or changing therapy - a prospective study exploring antiretroviral decision-making.* Infection, 2005. **33**(4): p. 249-56.

31. Bischofberger, I. and R. Spirig, *[The work profile of family caregivers of persons affected by HIV/AIDS].* Pflege, 2004. **17**(3): p. 176-86.

32. Powell-Cope, G.M., *HIV disease symptom management in the context of committed relationships.* J Assoc Nurses AIDS Care, 1996. **7**(3): p. 19-28.

33. Spirig, R., *In invisibility and isolation: the experience of HIV-affected families in German-speaking Switzerland.* Qual Health Res, 2002. **12**(10): p. 1323-37.

34. Kurtz, M.E., et al., *Concordance of cancer patient and caregiver symptom reports.* Cancer Pract, 1996. **4**(4): p. 185-90.

35. McPherson, C.J., et al., *Family caregivers' assessment of symptoms in patients with advanced cancer: concordance with patients and factors affecting accuracy.* J Pain Symptom Manage, 2008. **35**(1): p. 70-82.

36. Beach, M.C., J. Keruly, and R.D. Moore, *Is the quality of the patient-provider relationship associated with better adherence and health outcomes for patients with HIV?* J Gen Intern Med, 2006. **21**(6): p. 661-5.

37. Furler, J., et al., *The emotional context of self-management in chronic illness: A qualitative study of the role of health professional support in the self-management of type 2 diabetes.* BMC Health Serv Res, 2008. **8**: p. 214.

38. McCoy, L., *HIV-positive patients and the doctor-patient relationship: perspectives from the margins.* Qual Health Res, 2005. **15**(6): p. 791-806.

39. Beach, M.C. and T. Inui, *Relationship-centered care. A constructive reframing.* J Gen Intern Med, 2006. **21 Suppl 1**: p. S3-8.

40. Schneider, J., et al., *Better physician-patient relationships are associated with higher reported adherence to antiretroviral therapy in patients with HIV infection.* J Gen Intern Med, 2004. **19**(11): p. 1096-103.

Introduction

Over the past decades, developments in the treatment and monitoring of HIV-Infection have radically reduced morbidity and mortality of those affected by it [2]. In countries with broad access to combined antiretroviral therapy (cART), HIV infection has turned into a manageable chronic condition: persons living with HIV (PLWH) can carry on productive lives, often for decades after infection [1]. As with all chronic conditions, optimal health outcomes result from a combination of state of the art medical care and effective patient self-management [14, 41, 42]. For PLWH, self-management has two main aspects: first, the management of medications, since near-perfect adherence to long-term antiretroviral treatment is required [20, 43, 44]. Second, the management of symptoms linked to the disease itself, medications'adverse effects, opportunistic infections and co-morbidities have been shown to influence adherence to cART and health related quality of life [9, 21, 45, 46]. For PLWH, managing medications and managing symptoms have become two central and interwoven processes in their lifelong engagement with their chronic condition, their close support persons (CSPs), and their healthcare providers (HCPs) [22, 31]. For example, after discussing the management of side effects with a CSP, a PLWH might decide to see a healthcare provider, who might then assess symptoms and discuss self-management strategies or possible treatment changes.

So far, medication and symptom management strategies of PLWH have been described in rather fragmented ways, focusing either on adherence or on symptom management. Additionally, despite anecdotal reports praising the often complex collaboration between the different players (PLWH, CSPs, and HCPs), it has been largely neglected as a topic of research. A fuller understanding of collaborative support networks linking medication and symptom management is needed to improve long term clinical care and to inform the further development of comprehensive self-management support programs.

This thesis will address this need by exploring interactions between participants in HIV medication and symptom management, from the perspectives of PLWH and CSPs, using a mixed methods (qualitative/quantitative) approach. More specifically, since so little was understood of the collaboration between the various players, a exploratory design, with a greater emphasis on qualitative methodology, was chosen [47].

The project's first phase was qualitative: data were gathered through interviews with PLWH and CSPs. In the second, based on these data, which provided insight into the collaborative processes, hypotheses relating to the collaboration of PLWH and CSPs in symptom management were drawn and tested quantitatively with a larger sample of PLWH and CSPs. Results so far are presented in two articles, the first using qualitative data alone (chapter 5), and the second combining qualitative and quantitative data (chapter 6).

The research presented in this thesis was conducted within the framework of the larger multi-center **S**ymptoms and **o**ther **L**ife **Ex**periences and **A**dherence (SOLEXA) investigation (Spirig, 2003). From the perspective of patients and their close support persons, the SOLEXA study focuses on the relationships between symptom experience, symptom manageability, adherence, health related quality of life, and HIV progression. It is organized in collaboration within the Swiss HIV Cohort Study (SHCS), an ongoing multi-center research project established in 1988 and focusing on patient oriented HIV research. While seven HIV outpatient clinics across Switzerland are enrolled in the SHCS, to avoid the complications inherent in using translated questionnaires, the SOLEXA component, including the research presented here, is implemented only in Basel, Bern, St. Gallen, and Zürich, the four centers where German is the official and most spoken language.

This thesis is divided into seven chapters. **Chapter 1** provides a literature base introduction into the need for chronic illness management strategies for PLWH, with a focus on self-management. Further, this chapter elaborates the roles of symptom and medication management within overall HIV self-management and collaboration with others in these processes. **Chapter 2** describes the aims of the research program. The next four chapters incorporate publications. **Chapter 3** presents the publication *"Comprehensive Clinical Adherence Interventions to Enable Antiretroviral Therapy: A Case Report" (*the *Journal of the Association of Nurses in AIDS Care, Volume 18, Issue 6, pp 44-53).* Focusing on the complexity of self-management support in clinical care, this article provides evidence based support strategies with a focus on collaboration between PLWH and teams of healthcare providers. **Chapter 4** focuses on a structured literature review summarizing evidence on adherence interventions for PLWH, titled *"Interventions to Enhance Adherence of Patients with HIV on Antiretroviral Therapy"*. Originally published in German (*Pflege,* Volume 20, Issue 5 (Oct, 2007), pp 268-77) for maximum accessibility to German speaking nurses, this article was submitted to the publisher before the publication of a similar meta-analytic review on adherence interventions by Simoni et al. [23]. **Chapter 5** features *"Keeping a Grip on HIV: collaborative Medication and Symptom Management Experiences of Persons with HIV living in Switzerland"*. From the perspective of PLWH, this article summarizes the results of the qualitative exploration of the first phase of the current study. This article has been submitted for publication in *International Journal of Nursing Studies*. Similarly, **Chapter 6** incorporates mixed methods results of the same study phase, focusing on the collaboration of PLWH and CSPs in symptom management. This article, *"Symptom management in HIV/AIDS: A mixed methods approach to describe the collaboration and concordance of persons living with HIV and their close support persons",* has also been submitted for publication in *Journal of Mixed Methods Research*. In **Chapter 7** the findings are discussed as a whole and suggestions provided for further research and clinical implementations are made.

References

1. Hogg, R.S.S., J. A.; Graber, S.; Battegay, M.; Bonarek, M.; D'Arminio Monforte, A.; Esteve, A.; Harris, R.; Justice, A.; Hayden, A.; Lampe, F.; Mocroft, A.; Mugavero, M. J.; Staszewski, S.; Wasmuth, J.C.; van Sighem, A.; Kitahata, M.; Guest, J.; Egger, M.; May, M., *Life expectancy of individuals on combination antiretroviral therapy in high-income countries: a collaborative analysis of 14 cohort studies.* Lancet, 2008. **372**(9635): p. 293-9.
2. Sterne, J.A., et al., *Long-term effectiveness of potent antiretroviral therapy in preventing AIDS and death: a prospective cohort study.* Lancet, 2005. **366**(9483): p. 378-84.
3. Bodenheimer, T., E.H. Wagner, and K. Grumbach, *Improving primary care for patients with chronic illness.* Jama, 2002. **288**(14): p. 1775-9.
4. Schoen, C., et al., *In chronic condition: experiences of patients with complex health care needs, in eight countries, 2008.* Health Aff (Millwood), 2009. **28**(1): p. w1-16.
5. Sochalski, J., et al., *What works in chronic care management: the case of heart failure.* Health Aff (Millwood), 2009. **28**(1): p. 179-89.
6. Bangsberg, D.R., D.L. Kroetz, and S.G. Deeks, *Adherence-resistance relationships to combination HIV antiretroviral therapy.* Curr HIV/AIDS Rep, 2007. **4**(2): p. 65-72.
7. King, M.S., S.C. Brun, and D.J. Kempf, *Relationship between adherence and the development of resistance in antiretroviral-naive, HIV-1-infected patients receiving lopinavir/ritonavir or nelfinavir.* J Infect Dis, 2005. **191**(12): p. 2046-52.
8. Harrigan, P.R., et al., *Predictors of HIV drug-resistance mutations in a large antiretroviral-naive cohort initiating triple antiretroviral therapy.* J Infect Dis, 2005. **191**(3): p. 339-47.
9. Ammassari, A., et al., *Self-reported symptoms and medication side effects influence adherence to highly active antiretroviral therapy in persons with HIV infection.* J Acquir Immune Defic Syndr, 2001. **28**(5): p. 445-9.
10. Badia, X., et al., *Evaluating changes in health status in HIV-infected patients: Medical Outcomes Study-HIV and Multidimensional Quality of Life-HIV quality of life questionnaires. Spanish MOS-HIV and MQOL-HIV Validation Group.* Aids, 2000. **14**(10): p. 1439-47.
11. Hudson, A., K. Kirksey, and W. Holzemer, *The influence of symptoms on quality of life among HIV-infected women.* West J Nurs Res, 2004. **26**(1): p. 9-23; discussion 24-30.
12. Portillo, C.J., W.L. Holzemer, and F.Y. Chou, *HIV symptoms.* Annu Rev Nurs Res, 2007. **25**: p. 259-91.
13. Bischofberger, I. and R. Spirig, *[The work profile of family caregivers of persons affected by HIV/AIDS].* Pflege, 2004. **17**(3): p. 176-86.
14. Wilson, H.S., S.A. Hutchinson, and W.L. Holzemer, *Reconciling incompatibilities: a grounded theory of HIV medication adherence and symptom management.* Qual Health Res, 2002. **12**(10): p. 1309-22.
15. Creswell, J.W.P.C., V.L, *Designing and Conducting Mixed Methods Research.* 2007, Thousand Oaks: Sage Publications.
16. Simoni, J.M., et al., *Efficacy of interventions in improving highly active antiretroviral therapy adherence and HIV-1 RNA viral load. A meta-analytic review of randomized controlled trials.* J Acquir Immune Defic Syndr, 2006. **43 Suppl 1**: p. S23-35.

Chapter 1

Collaborative medication and symptom management in the context of chronic HIV management

This Chapter provides an introduction to the challenges of HIV care in the context of chronic disease management. The current state of evidence related to two important aspects of a chronic disease management approach - self-management of patients and collaboration between patients, families and healthcare providers - are described with a focus on HIV care.

Treatment success and future challenges for the management of HIV/AIDS

Since the introduction of **c**ombined and highly active **a**nti**r**etroviral **t**herapies (in the following abbreviated: cART) in the mid-nineties, improvements have been documented in diverse health outcomes such as quality of life, morbidity and mortality for PLWH in countries where treatment was available. For example, 14 linked cohort studies in high income countries illustrated an increase in estimated life expectancy for PLWH placed on cART at age 20 from 36.1 years to 49.4 years, for the period between 1996 and 2005 [2].

Nevertheless, more than a decade after the adoption of effective combination regimens, HIV/AIDS remains a global health problem. In 2007 an estimated 33 million people (30.3-36.1 million) were living with HIV, of whom Sub-Saharan Africa accounted for two thirds (67%). In North America and Western and Central Europe, the number of PLWA was estimated at approximately 2 million (1.4-2.8 million) [3]. Worldwide, ca. 2.7 million (2.2 - 3.2 million) new HIV infections and 2 Million (1.8-2.3 million) AIDS related deaths occurred last year [3].

So far, the number of new HIV infections globally continues to outstrip advances in treatment and accessibility to it [3]. Globally, this situation demands further advances in prevention and testing strategies. In particular, though it highlights the need for further improvements to treatment access in low and middle income countries, where, at the end of 2007, nearly 3 million people were receiving antiretroviral treatment. Even while this figure represents a striking one-year improvement of 45%, it covers only 31% of the estimated global need [3]. Another important global change in the epidemic has recently become evident: after decades of increasing mortality, the annual global number of AIDS deaths has declined, partly as a result of greater access to treatment in resource-limited settings [1, 3]. In resource-rich settings, AIDS death rates began to decline dramatically early in the cART era: since September, 1998, the incidence of AIDS or related deaths has fallen by 8% per 6-month period (rate ratio 0.92, 95% CI 0.88-0.95, $p<0.0001$) [4]. On the negative side, this trend toward higher life expectancy has also increased the need for long term treatment and care [2].

Treatment strategies differ strongly between resource-rich and resource-limited settings. In the latter, the provision of ART usually follows a public health approach [48], generally characterized by a limited number of standardized treatment regimens and standardized clinical and laboratory monitoring [49]. This strategy reflects the level of training of healthcare workers, the high patient burden and the limited number of drugs available in such settings. In contrast, HIV care in high income countries is usually provided in specialized facilities and includes highly individualized treatment strategies. Based on constantly updated treatment guidelines, frequent monitoring of important surrogate markers such as CD4 cell counts and viral loads, and medication resistance testing, individualized treatment regimens draw on a range of more than 20 approved antiretroviral drugs [50]. Developments in antiretroviral treatment over recent years have provided more convenient regimens with less problematic adverse effects, lower pill counts and treatment options including new drug classes. Still, while such regimens suppress viral replication, they do not eradicate the virus. Actual HIV eradication (via drugs, gene therapy or vaccines) will probably take many more years to develop, test and deploy [51-53].

Focusing on the improvement of health outcomes for PLWH, the situation is again somewhat different for low- and high-resource settings. Whereas broader access to ART and other treatment options should substantially improve health outcomes for PLWH in low-resource settings, this no longer seems possible for high-resource settings. In western and central Europe, for example, long-term treatment is already provided to 90-100% of PLWH and the initial drops in mortality and morbidity have been sustained [3, 4]. In those settings, though, long-term treatment experiences have shown that treatment comes at a price for PLWH. Since ART therapy demands a constant level of medication to suppress viral replication, once started it has to continue without interruption. Compelling evidence has linked treatment interruptions, including medical guided ones, with poorer clinical outcomes compared to continuous treatment (i.e., near-perfect adherence) [5]. Further, it has been shown that even newer and more potent regimens have to be taken very regularly in order to prevent or delay drug resistance, which is closely associated with treatment failure [20, 43, 44]. Despite the risks of non-adherence, though, many PLWH find it difficult to keep to their medication regimens for long periods. Estimates of prescribed doses taken range from 60%-70% for PLWH in Western Europe and Northern America, while various barriers have been shown to complicate PLWH’s cART adherence patterns [6-8].

Further, more than half of PLWH receiving ART experience some medication side effects [12, 54]. While some of these are minor and diminish over time, others can be very distressing or even life threatening. A high number and distressing symptoms have been shown to complicate adherence to ART [9, 21]. To complicate matters still further, HIV-related immune suppression is associated with a range of life threatening, debilitating, or otherwise distressing opportunistic infections [55]. In addition, PLWH frequently suffer from other chronic health conditions (e.g., tuberculosis, liver disease, heart disease and cancer), any of which can complicate HIV treatment and care [56, 57]. In sum, due to the adverse effects of cART, opportunistic infection and comorbidities symptoms prevalence is consistently high for many PLWH, averaging 8-14 symptoms per person [9-12].

Regarding the stabilization of health outcomes for the aging and treatment-experienced population of PLWH in affluent settings, major advances are no longer possible based solely on treatment access. It is clearly necessary to formulate new management strategies that consider multiple aspects of this chronic condition, including the medical complexity of the condition, the skills of healthcare providers, patients and the close support persons who manage the condition in their homes, and the need for long-term collaboration between and follow-up of patients and healthcare providers. Where accessibility to cART is high, then further improvement of health outcomes for PLWH will demand comprehensive healthcare services meeting these needs. In the long run, as accessibility issues are resolved in developing areas, such strategies, adapted to specific contexts, will become a global priority.

The management of chronic conditions

Through advances in treatment, HIV/AIDS is now widely accepted as a chronic condition. Healthcare needs of PLWH have become comparable to those of patients with other chronic conditions such as cardiovascular disease, cancer or diabetes, which also require comprehensive health support [58]. However, most healthcare systems in affluent countries were originally designed to respond to acute episodic illness. As a result, they often have difficulty focusing on the goals of containing a disease, slowing its progression, and supporting patients to deal with its challenges [14, 41]. A survey of chronically ill adults in eight high-income countries (Australia, Canada, France, Germany, the Netherlands, New Zealand, the United Kingdom, and the United states) found major differences between countries regarding access, safety, and care efficiency, indicating that the characteristics of national healthcare systems significantly influence the actions of persons with chronic conditions. Still, certain deficits were noted across all countries, particularly inadequate coordination regarding patients seen by multiple clinicians and weak efforts to engage or support patients to manage their conditions [14]. Focusing on institutional/organizational factors, Handford et al. examined the association between the organization of care at individual healthcare institutions and outcomes for PLWH across a range of studies (28 studies, 39,776 subjects). The results linked institutions treating higher volumes of HIV patients, especially those incorporating case management approaches, i.e., patient-centered care, with increased provision of cART and with lower mortality rates [13].

In order to improve healthcare and outcomes for patients with chronic conditions, Handford et al. indicate a need for fundamental changes to all of the studied healthcare systems. Historically this need was highlighted by researchers' observations that patients had changing needs depending on the phases of their illness [59]. In the late nineties Wagner et al. evaluated the efficacy of interventions across a range of programs, leading to their widely-adopted Chronic Care Model (CCM), which was later developed further by the WHO [15, 60, 61]. The WHO publication 'Innovative Care for Chronic Conditions', structures chronic care management areas requiring changes into micro, meso, and macro levels, with each level interacting with and dynamically influencing the others. At the micro level, i.e., the level of patient interaction, improvements require a primary focus on patient and close support persons' behaviors, and on the information they receive from their healthcare providers. The meso level refers to healthcare organizations and communities. At this level, care coordination requires evidence-based practice. This means integrating community resources, including information tracking systems, to plan, establish, implement and coordinate preventive interventions and long-term care processes. At the macro level, policy makers, i.e., government officials, rely on input from the micro and meso levels to inform their decisions and help them set standards and incentives for quality care in chronically ill populations [15].

While none of the various comprehensive approaches proposed to improve chronic care have yet been directly acknowledged as superior, the CCM is among the most widely applied. Several studies have investigated the impact of single or multiple elements of the CCM. For example, a meta-analysis by Tsai et al. found that no single element of it was essential for improving outcomes, but that changing the design of healthcare delivery systems based on the CCM framework significantly improved process outcomes, as did self-management [62]. A more recent structured qualitative review on the effectiveness of the CCM came to a similar conclusion: studies applying most elements of the model in ambulatory settings showed improved patient care and health outcomes [63]. However, much of the evidence supporting the CCM is still observational and causal inferences are difficult. Trials and reviews have mostly focused on specific areas of the model, such as patient self-management programs [64]. This is particularly true in the context of HIV/AIDS, where most trials have been conducted in fragmented areas of PLWH's self-management, such as adherence to ART or transmission prevention [23, 65].

However incomplete, the available evidence strongly suggests that a chronic care approach would improve current HIV/AIDS management strategies. Importantly, the CCM and related approaches provide only a framework for changes at diverse levels of the healthcare system: meeting the specific challenges of any chronic condition requires strategies tailored to fit the context and needs of each patient. The research presented in this thesis provides evidence to better answer the question of how and where to improve care for PLWH on the micro level (patient), by providing a fuller understanding of PLWH's self-management and collaboration with CSPs and HCPs within the process.

The two aspects of the chronic care mode – self-management and collaboration – will be discussed below.

Self-management: a collaborative endeavor

In the context of chronic disease management, “self-management” has become a widely used term, encompassing the day-to-day activities a chronic illness patient performs to minimize the consequences of his or her condition. Such actions vary based on the person's perceptions, experiences and expertise, but share the focus of optimizing health outcomes, whether by retarding deterioration, maintaining a given level of health, or improving overall wellness [16-18]. Lorig and Holman conceptualize the essence of these processes more succinctly: they incorporate diverse tasks and required skills [17]. In their 2003 study, based on an earlier investigation by Corbin and Strauss, three self-management tasks were observed across a range of chronic conditions: medical management, role management and emotional management [66]. Medical management included, for example, medication taking, or adhering to a special diet; role management included maintaining, changing and creating new life roles according to the challenges of the condition; and emotional management involved dealing with such emotions as anger, fear, and frustration, all of which are commonly experienced during chronic illness trajectories. Regarding these tasks, five self-management skills were described: 1) problem solving: isolating problems, gathering information, implementing solutions, and evaluating results; 2) decision making: applying information and training to distinguish medically serious symptoms from less serious problems and reacting appropriately; 3) resource utilization: navigating through health information sources and identifying the most relevant material; 4) formation of provider partnerships: appropriately discussing developments regarding the course of illness with healthcare providers to allow informed decisions; and, 5) action planning and self-tailoring: developing and implementing short-term action plans [17].

As suggested in the CCM, self-management should be viewed not as an isolated theory but rather in the contexts of broader systems (e.g., policy, healthcare organizations, communities and families). In these contexts, self-management is increasingly recognized as a dynamic process that includes active collaboration with others, especially close support persons (e.g., partners, friends, family) and healthcare providers [19].

The term “collaboration” is widely used but often misunderstood to signify any form of teamwork. A more useful definition is ‘a recursive process where two or more people or organizations work together in an intersection of common goals by sharing knowledge, learning and building consensus. Collaboration does not require leadership and can sometimes bring better results through decentralization and egalitarianism’ [67]. In the context of chronic care models it is proposed that collaboration of the different players is most effective when every member of the team is informed, motivated, prepared and able to communicate and manage the chronic condition [15, 61, 68]. It can therefore be proposed that effective self-management collaboration requires special skills not only of patients but also of the other key players. Yet the skills that enable healthcare providers and close support persons to work with PLWH’s self-management have only been vaguely described. Existing evidence is summarized in ‘Collaboration in medication and symptom management’. Given the importance of the types of collaboration described in the CCM, developing them will require a deeper understanding of the specific collaborative processes, tasks and skills demanded of each player [15, 61, 68].

Self-management of PLWH

Patient self-management shows similarities across a range of chronic conditions, particularly the tasks of medical, role, and emotional management. Nevertheless, every chronic condition has special challenges, and self-management tasks can be described most usefully with reference to their specific characteristics.

In order to provide an overview of HIV specific self-management tasks and to position the two aspects of self-management at the focus of this thesis, i.e., medication and symptom management, within the broader context of HIV self-management, a literature review was conducted on themes described under the umbrella of HIV self-management. Based on this review and combined with the broader self-management conceptualization described by Lorig and Holman [17].

HIV self-management tasks have been divided into eight categories: medication management, symptom management, substance use management, lifestyle management, emotional management, role management, transmission management, and disclosure management. A short description of each task is provided in Box 2 (below).

Box 2: HIV Self-management Tasks

Medication management

Decisions related to initiating or changing cART regimens often require collaboration with healthcare providers. Once started, the new or changed regimens have to be integrated into daily life and adherence maintained over time. Eventually, this also entails the management of adherence related obstacles, which often requires the support of others. Additionally opportunistic diseases and/or comorbidities often require medication management.[7, 25, 27, 30, 69]

Symptom management

The diverse symptoms that can occur throughout the illness trajectory have to be recognized, evaluated and monitored. Decisions are necessary on how to deal with symptoms, such as when to contact healthcare providers, whether or not to alter exercise or diet, and when to take — or not take — certain medications.[16, 28, 70-72]

Substance use management

The use of substances including tobacco, alcohol and diverse illicit drugs can interfere with health either directly or by hindering the management and treatment of HIV. Treatment strategies have to take substance use into account, and harmful behaviors have to be changed or reduced. Such behavioral change sometimes requires collaboration with healthcare providers.[73-77]

Lifestyle management

HIV infection generally requires lifestyle changes. Initiation of health promoting activities may be perceived as needed and helpful. Often-cited changes include eating healthier food, using food supplements (e.g., vitamins) and special precautions against food-related infections. Many PLWH also take steps to reduce stress and increase their physical fitness. [18, 70, 78, 79]

Emotional management

Awareness of HIV infection alters ones view of the future, often leading to emotions such as anger, fear, frustration and depression. Learning to manage those emotions is part of the process of managing the condition. [17, 80-84]

Role management

The trajectory of HIV may involve diverse changes in health. Despite such changes, important life roles have to be maintained or adapted and meaningful new roles and behaviors developed. For example, a woman suffering severe fatigue might need to reduce household tasks in order to be able to take care of her child. [17, 85-87]

Transmission management

Prevention of virus transmission is complex and particularly influences sexuality and reproduction. Knowledge about prevention of transmission has to be gained and strategies have to be implemented into daily life. This often requires discussion with others (partners, families, friends, healthcare providers) and evaluation of risks taken. Own worries and fears and feelings of shame have to be managed. [65, 88-91]

Disclosure (social) management

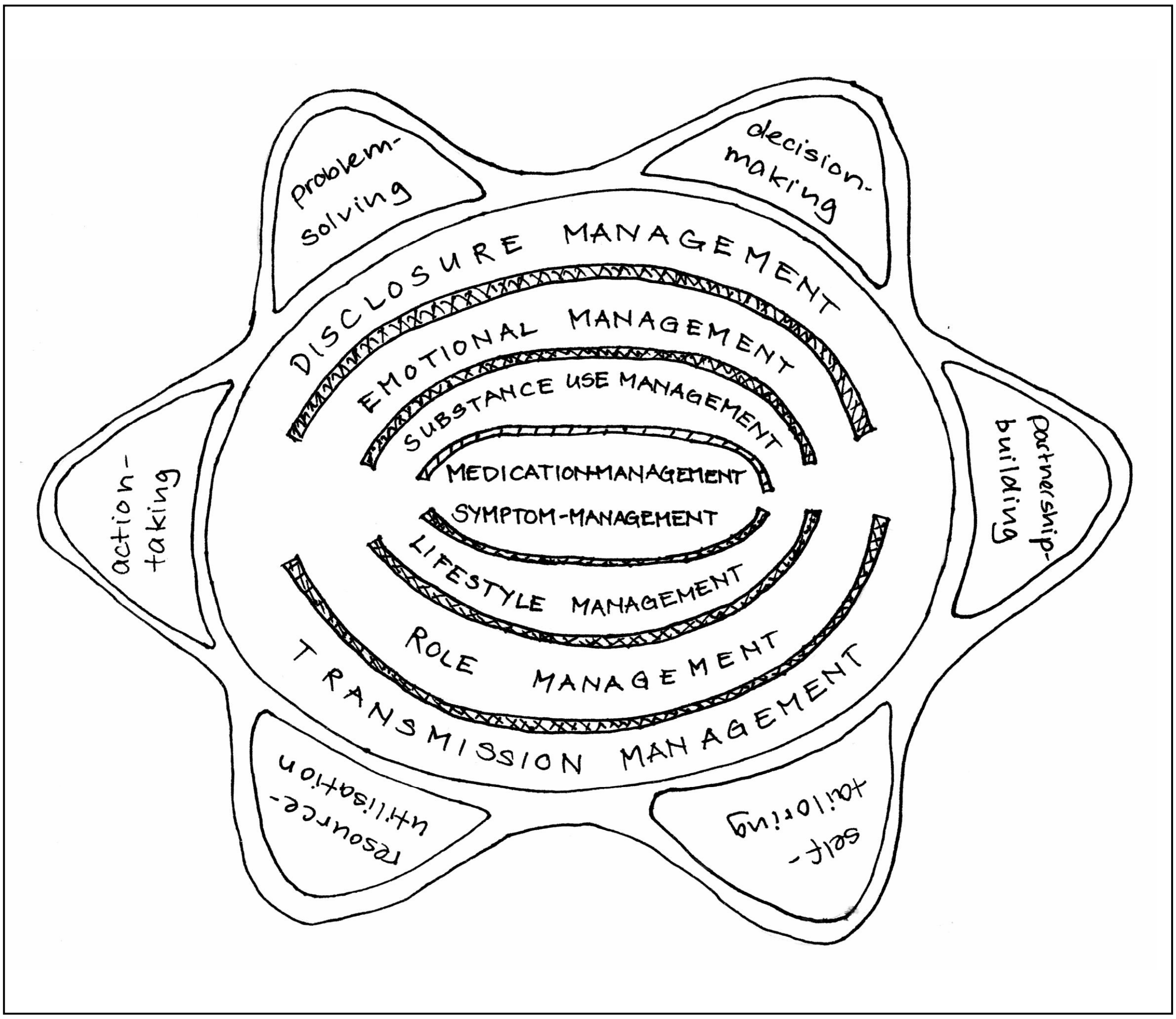
To prevent stigmatization and other negative consequences, pros and cons of disclosure have to be constantly evaluated. This includes consideration of consequences for close persons such as children or partners. Once the decision is made, disclosure often involves educating others about HIV. Further decisions are also required regarding active participation in political and advocacy work. [17, 92-96]

The self-management tasks outlined here are distinct but mutually influential: the management of one task, such as medication management, can be influenced by the way other tasks such as disclosure or symptoms are managed. Still, the four tasks of medication, symptom, substance use, and lifestyle management are closely related to improvement of health and could therefore be categorized more broadly, as Lorig and Holman suggest, as “medical management”. Likewise, based on Lorig and Holman’s conceptualization, the two tasks of emotional and role management have not been further refined. These terms summarize much descriptive HIV research very well, requiring no further differentiation. However, both transmission risk management and disclosure management represent newly defined task categories. The tasks they describe fit poorly alongside any of the previously existing general self-management tasks (medical, emotional, and role management). For use across diverse chronic conditions, a more general term such as ‘social management’ might be useful, under which disclosure management and other aspects specific to the respective conditions could be summarized.

From a medical perspective, with a focus on improvement of health outcomes, medication and symptom management may be regarded as the core tasks of HIV self-management. After all, a person’s experience of symptoms is closely related to adherence to cART, and adherence is closely related to treatment success [9, 20, 21, 91]. From the patient’s perspective, however, medication and symptom management might not always be the main focus. For example, if problems arise from illicit drug use or the stress involved in disclosing one’s HIV infection to a new partner, medication or symptom management might fade at least temporarily into the background. Nevertheless, it can be assumed that, over the trajectory of the disease, every PLWH will have to deal with symptoms, medication intake or both and both tasks will inevitably require self-management strategies.

Additionally, the self-management tasks described thus far demand specific skills. Figure 1 (below) provides an overview on HIV self-managment tasks and skills. The set of core skills described by Lorig and Holman (for description see last chapter) was added to the HIV specific self-management tasks [17]. In figure 1, these skills surround the self-management tasks, reflecting their importance regarding the described tasks. The skills are drawn as cogs of a gear, which, if complete, can mesh smoothly with other gears to achieve a desired outcome, thus illustrating that active, successful self-management always includes and is influenced by collaboration with others, such as close support persons or healthcare providers.

Figure 1: HIV self-managment tasks and skills



Collaboration in medication and symptom management

In the current literature, medication management and symptom management – the two self-management tasks upon which this thesis focuses – have mainly been described in a fragmented way, with close attention paid only to one or the other, despite the fact that several studies have linked them closely [9, 17, 21, 22]. The two tasks will therefore be introduced separately before their associations and the collaborations within the management process are further elaborated.

Medication and symptom management

Medication management for PLWH includes decision making related to starting or changing medical treatments such as cART or medication to treat opportunistic diseases or co-morbidities [24-26, 97]. Once a decision is made, medication intake has to be integrated into daily life, where adherence choices will be made on a dose-by dose basis [22, 69]. Most studies of HIV medication management have focused on cART adherence, often broadly defined as the extent to which a patient's medication taking behavior corresponds with the agreed recommendations of the healthcare provider [98].

Even though this definition implies collaboration, the current concept of adherence has been criticized for maintaining a paternalistic and provider oriented perspective on medication management [99]. If cART initiation, for example, is determined not by consensus but by guidelines. The start of cART is recommended with the decline of immune functions, as reflected by the prevalence of T-cells, especially the CD4 cell count. Current guidelines recommend a treatment initiation threshold of 350 CD4 cells/µ L; later starts have been associated with worse health outcomes [50]. Additionally, it is recommended that symptomatic patients start cART regardless of their CD4 cell counts. On the other hand, even for those feeling absolutely healthy, cART is recommended if CD4 cell counts are near the threshold, although treatment can be associated with diverse adverse effects. This may mean that some patients are pressured to initiate cART before they are convinced of the need for it.

For timely treatment starts, however, PLWH's readiness, i.e., the affected individual's awareness that a particular change will be beneficial, is an important issue. Since the patient is ultimately responsible for taking the medication, potential barriers to adherence have to be identified, and the patient has to accept responsibility for initiation of the behaviour. Finally, the individual must retain a sense of control and impending action [26]. There is evidence that readiness and adherence to cART are distinct concepts. More specifically, readiness is viewed as a distinct factor that influences adherence, and therefore treatment outcomes, and should be examined as a subcategory of self-management support related to medication management [97]. Additionally, readiness to ART has been shown to be influenced by the PLWH - HCP collaboration [25].

Once the decision is made to initiate cART, the treatment's success is profoundly influenced by each person's ability to ingest the complete regimen, every day at exact times, over a long period of time [100]. Early studies showed that 95% of the prescribed doses had to be taken as prescribed; more recent results illustrate that some combinations of drugs allow less stringent adherence to achieve viral suppression [43, 44]. Nevertheless, irregularities can lead to insufficient plasma drug levels, increasing the risk of drug resistant mutations, cross-resistance to other medications, which can ultimately lead to ineffectiveness of the medication.

Further, multi resistant virus strains can be transmitted through the community [20]. As a result, a combined sense of public and individual responsibility motivates or even forces PLWH to develop medication management strategies to integrate their regimens into their lives [99].

Still, problems with adherence to cART are widespread. Across Europe and North America cross sectional studies have determined that, on average, only 60%-70% of doses prescribed are actually taken [23, 101]. In a study incorporating long term follow-ups (median 8.3 years IQR 3.13-9.30), only 32.78% of patients (n=540) achieved and maintained continuous adherence [102].

Not surprisingly, qualitative and quantitative research shows that adherence can be complicated by multiple factors. These cover five dimensions: 1) Socioeconomic factors, e.g., age, gender, and income; 2) therapy related factors, e.g., the number of daily doses, pill counts and side effects; 3) condition related factors, e.g., viral load, time since diagnosis and HIV related symptoms; 4) patient related factors, e.g., low self-efficacy, treatment beliefs and depression; 5) healthcare team and system related factors, e.g., medication distribution, reimbursement, and support of healthcare providers [6, 27]. However, few factors have demonstrated a consistent negative influence on adherence. The issue of why people fail to manage their medication sufficiently, even when lapses may shorten their lives, belies simple explanations of influencing factors [103].

The task of symptom management is important for PLWH throughout the course of HIV infection. In the early stages, acute HIV infection can be associated with mild influenza- like symptoms lasting several days. After this comes a so-called asymptomatic phase, where a strong immune response controls viral replication, often for years, and opportunistic infections are rare [104]. Nevertheless, PLWH can still experience symptoms during this phase. For example, depression, fatigue and anxiety have been reported throughout the course of HIV [21, 104].

When the function of the immune system declines and cART is started, whether in symptomatic or asymptomatic patients, it can be associated with a range of adverse effects. For example, among PLWH who changed therapy regimens, clear therapy associated reasons included diarrhea, nausea, vomiting, myalgias, paresthesias, and body fat redistribution [12]. Additional symptoms might occur in the context of opportunistic infections or comorbidities [105].

Given such a range of reasons for symptoms, it is unsurprisingly that, across a range of studies, the symptom prevalence has remained high through the pre- and post-cART eras [11, 12, 21, 105, 106]. Two studies conducted after the advent of cART documented an overall symptom prevalence of around 70%. More specifically, Newshan et al. reported that 68% of an outpatient cohort sample (n=484) reported at least one symptom, whereas, of those, 96% reported multiple symptoms [107]. The second study investigated symptom prevalence in a sample of HIV-positive women (n=1256). In that case, 67% of the women not receiving therapy and 69% of women receiving therapy showed at least one symptom [12]. These results indicate that symptom prevalence has not been reduced in the context of cART.

Congruent with the findings of the study of women, a study of men (n=374) reported a higher number of symptoms in the men receiving cART (n=210, 56%). The cART group displayed an average of 14 symptoms, compared to an average of 10 among the non-cART group (p=0.001) [10].

Across a range of more recent studies, averages of 8 to 14 symptoms per PLWH have been described, depending on the scales used [9-12, 105]. Yet not only the prevalence of symptoms but also their intensity and the distress they cause have shown severe influences on PLWH's adherence to cART and their health related quality of life [10, 106, 108, 109].

Effective symptom management is therefore crucial, encompassing day-to-day decisions about dealing with symptoms, such as when to contact healthcare providers, whether or not to alter exercise or diet, and when to take—or not take—certain medications [16, 28].

One line of research provides further descriptions of the different types of activities PLWH perform to self-manage symptoms. These include distraction techniques, dietary measures, complementary therapies, medications, exercise, and substances such as alcohol and marijuana [70, 82, 110, 111].

Additionally, symptom management can be disrupted by various factors, most of which are summarized or described in different models of HIV symptom management [28, 71, 112, 113]. As described for barriers to adherence, these factors can be grouped into 4 dimensions: 1) socioeconomic factors, e.g., age, gender, literacy and social support; 2) condition related factors, e.g., co-morbidities, immune status and treatment success; 3) patient related factors, e.g., illness representations, loss of control or self-efficacy; 4) healthcare team and system related factors, e.g., sources of information, self-management programs and collaboration with healthcare providers [28, 71, 112, 113].

For PLWH the two self-management tasks of medication and symptom management appear closely related and similarly important to health outcomes [22]. In particular, insufficient symptom management can negatively affect a person's health seeking behaviors, quality of life and adherence to cART [21]. Across a range of studies, patients with more symptoms scored lower in health related quality of life [45, 46, 114-118]. More specifically, in a study investigating changes in virological markers, quality of life, and symptom profiles over time, quality of life was less sensitive to immunological or virological changes than it was to responsiveness to symptoms [119].

Further, prevalence of symptoms has also been linked, across diverse studies, to PLWH's adherence to ART. For example in a cross sectional multi-center study (n=358), non-adherent patients had higher mean scores both for overall symptoms (12.3 +/- 9.2 versus 8.1 +/- 6.6; p<.001) and for medication's adverse effects (2.9 +/- 2.7 versus 1.9 +/- 1.9; p<.001) when compared with adherent patients [9]. Another study, showing similar results, also highlighted a negative association related to collaboration with healthcare providers: PLWH (n=420) with higher symptom scores were also less likely to adhere to medications, follow providers' advice, or attend scheduled medical visits [120].

PLWH's collaboration with close support persons and healthcare providers

Collaboration appears integral to HIV self-management processes, since PLWH must continually make decisions such as whether to seek support or with whom they will interact in order to achieve positive health outcomes [18]. Primarily, they collaborate with two other groups regarding medication and symptom management: healthcare providers and close support persons.

Close support persons are individuals who share deep personal connections with PLWH and provide various forms of support in times of need [33, 121], whether as family members, life partners or friends [33]. However, such support can by no means be expected: even the closest relationships show the influence of persistent social stigmatization of HIV/AIDS and those affected by it [33, 93, 96]. In a qualitative investigation in Switzerland, for example, only a small subgroup of family members of PLWH actually provided support for them. They did this very privately to avoid rejection and moral judgement of others [33].

Nevertheless, the presence of at least one close and informed support person is clearly beneficial to PLWH's health. A prospective cohort study demonstrated that stable partnerships have been associated with slower rates of disease progression in PLWH receiving cART [122]. More specifically, high levels of social support have been associated with fewer depressive symptoms and enhanced treatment adherence [123-125].

Narratives of close support persons show that they consistently provide both instrumental support, such as preparing medications, and emotional support, such as listening or conversing [31]. However, for persons with chronic conditions, collaboration with CSPs is generally described as unidirectional, with the CSP assuming the role of caregiver [126]. Still, in the post-cART era, with declining HIV related morbidity allowing many PLWH to maintain active work and social lives, such collaboration has been researched only marginally, leaving significant knowledge gaps, such as that regarding how PLWH and their CSPs collaborate on the health-inflluencing tasks of medication and symptom management.

Healthcare providers monitor symptoms, prescribe medications, and support PLWH's self-management efforts. Nevertheless, nurses and physicians typically demonstrate little skill at predicting patients' symptom experiences, readiness for cART or adherence to cART [30, 127-129]. Therefore, mutual patient-provider communication is crucial element of effective support, beginning with the accurate assessment of symptoms and adherence. Beach and colleagues, for example found a single item — the patient's perception of "being known as a person"— significantly and independently associated with receiving appropriate cART, adhering to cART, and having undetectable serum HIV RNA [36]. Qualitative data also confirm that for patients, healthcare providers are an important source of information and decision making assistance, as long as they are able to acknowledge the patient's expertise and judgement [25].

Results of adherence and symptom management intervention studies show that while healthcare professionals are able to provide effective support, most intervention programs have been conducted outside routine clinical care [23, 65, 72, 130]. Additionally, focusing on the triad of PLWH, CSP and healthcare provider, details of collaborative activities between CSPs and healthcare providers regarding self-management processes remain unclear.

Role of Self-management programs for PLWH

Self-management is increasingly recognized as an active process linking the social systems of PLWH with healthcare providers [19, 64]. The dynamics of this process have been applied to self-management of diverse other chronically ill populations, in group or individual based programs, by educated peers, lay workers, nurses, psychologists, pharmacists and physicians [16, 23, 130].

Yet, while multiple studies have confirmed the positive association between social support and health-related outcomes such as adherence [123, 124, 131], few HIV self-management interventions have focused on the roles of close support persons. One exception was a study by Remien et al., who demonstrated the effectiveness of a couple based adherence-promoting intervention. Although, in most cases, effects diminished with time, the intervention group showed very significantly higher mean cART adherence (proportion of doses taken) than controls (76 % vs. 60%) [132].

HIV specific self-management programs' have generally been directed toward specific self-management tasks, such as transmission risk management, symptom management or medication management (focusing on adherence). A meta-analytic review on the efficacy of adherence interventions, for example, indicated that across studies, participants in intervention groups were more likely than those in control groups to achieve 95% adherence (OR 1.50, 95% CI:1.16-1.94) [23]. And while Gifford et al. developed a comprehensive HIV self-management program, their main outcome measure was symptom status. Their randomized controlled trial illustrated a decrease in the experimental group's symptom severity index (i.e., the number of symptoms with moderate or greater severity), alongside an increase in that of the control group (-0.9 versus +0.5; $p<.03$) [16].

Many symptom management intervention programs focus on individual symptoms such as diarrhea or depressive symptoms [133, 134]. Some smaller studies of interventions focusing on overall symptom management measured adherence, quality of life, emotional distress and perception of health as outcomes. All showed a tendency for improvements in their intervention groups' measured outcomes [130, 135]. A recent randomized controlled trial testing the effectiveness of a symptom management manual (compared to a Nutrition Manual) illustrated in a mixed model growth analysis significantly greater declines in symptom frequency and intensity scores for the intervention group compared to controls ($t=2.36$, $P=0.018$) [72].

Such programs illustrate the possibility to improve individual self-management behaviors in chronically ill populations in general and among PLWH in particular. Likewise, in the field of HIV-self-management, the majority of self-management interventions limit their focus to very specific tasks. Unfortunately, such specificity fails to reflect the life situations of PLWH, who, as illustrated by the close connection of symptom and medication management, often find themselves managing multiple tasks simultaneously. Additionally, self-management behavior is complex and changing. And while interventions often show short-term improvements, long term programmatic efforts are necessary to maintain those effects. This is supported by recent evidence that not every person profits from stand alone programs, while long term benefits may require ongoing collaborative processes between PLWH, CSPs and HCPs [23, 136].

HIV self-management in the Swiss context

The chronic condition management, especially self-management, is strongly context-dependent. Since the research summarized in this thesis was conducted in Switzerland, a broad overview of Swiss national conditions is provided below.

The Swiss healthcare system is well developed, with a mandatory health insurance system covering ambulatory care, laboratory testing, and prescription medications offered at specialized clinics – in this case, HIV outpatient clinics. For patients unable to pay standard premiums or deductible amounts, the Swiss social insurance system provides subsidized coverage. In theory, this means that the approximately 25’000 PLWH in Switzerland, including migrants and asylum seekers, have full access to specialized HIV care and treatment [3].

The seven ambulatory centers of the Swiss HIV Cohort Study (SHCS) provide the majority of specialized HIV outpatient treatment, caring for about 70% of PLWH in Switzerland [137]. In 2008, 86% of Swiss PLWH were male and 82% were caucasian. Transmission paths broke down as follows: men having sex with men (MSM), 37%; heterosexual contact, 39%; and intravenous drug use (IDU), 20.9% (SHCS, 2008). The centers provide highly individualized treatment and care. Over 20 approved antiretroviral agents from four drug classes are prescribed according to the international guidelines [50, 138]. Five of these clinics are part of University hospitals; the remaining two belong to Cantonal hospitals.

In high level practice and educational settings such as these, physicians tend to change frequently, while nurses usually work many years in the same setting. Since the Swiss system of academic nursing education is a fairly recent development, most nurses working in such settings are educated at the diploma level.

All of the SHCS outpatient clinics use the SHCS Adherence Questionnaire (SHCS-AQ) to assess patient self-reported adherence at least every 6 months [139]. In a recent survey of 3607 SHCS participants, 31.1% reported missing doses over the preceding 4 weeks, with individual clinics’ non-adherence scores averaging from 26.1% to 41.5% [101]. One explanation of the broad variability of adherence rates between centers is that some provide structured adherence interventions whereas others do not. Symptoms and medication side effects are regularly assessed and treated in regular medical consultations by healthcare providers. To date, though, no structured or standardized patient education has been implemented regarding symptom management. Such education is generally provided during one-to-one consultations, and therefore depends largely on individual providers' perceptions and skills. Additionally, CSPs have not been systematically integrated into clinical care or self-management support, depending instead on the priorities of individual centers and providers.

To summarize, limited and highly fragmented information is available about PLWH's collaboration experiences regarding medication and symptom management. In fact, the available evidence suggests that healthcare providers do not sufficiently recognize or address this population's symptom and medication management processes [10, 128]. The Swiss healthcare system provides near-universal access to very individualized HIV-specific treatment at specialized outpatient clinics. However, regarding symptom and medication management support for both PLWH's and their CSPs, interventions are less structured, depending instead on center- and provider-specific variables. Nevertheless, medication and symptom management activities are key predictors of non-adherence to cART, a known risk factor for poor outcomes in HIV populations. PLWH's and their CSPs' descriptions of such activities, including their collaborative efforts to develop effective self-management skills and strategies, are important resources for healthcare providers concerned with offering the best possible care.

References

1. Hogg, R.S.S., J. A.; Graber, S.; Battegay, M.; Bonarek, M.; D'Arminio Monforte, A.; Esteve, A.; Harris, R.; Justice, A.; Hayden, A.; Lampe, F.; Mocroft, A.; Mugavero, M. J.; Staszewski, S.; Wasmuth, J.C.; van Sighem, A.; Kitahata, M.; Guest, J.; Egger, M.; May, M., *Life expectancy of individuals on combination antiretroviral therapy in high-income countries: a collaborative analysis of 14 cohort studies.* Lancet, 2008. **372**(9635): p. 293-9.
2. Unaids, *2008 Report on the global Epidemic*. 2008, WHO Library Cataloguing-in-Publication Data.
3. Sterne, J.A., et al., *Long-term effectiveness of potent antiretroviral therapy in preventing AIDS and death: a prospective cohort study.* Lancet, 2005. **366**(9483): p. 378-84.
4. Mocroft, A., et al., *Decline in the AIDS and death rates in the EuroSIDA study: an observational study.* Lancet, 2003. **362**(9377): p. 22-9.
5. Keiser, O., et al., *Public-health and individual approaches to antiretroviral therapy: township South Africa and Switzerland compared.* PLoS Med, 2008. **5**(7): p. e148.
6. WHO, *Antiretroviral Therapy for HIV Infection in Adults and Adolescents: Recommendations for public health approach*. 2006, WHO Library Cataloguing-in-Publication Data: Geneva.
7. Hammer, S.M., et al., *Antiretroviral treatment of adult HIV infection: 2008 recommendations of the International AIDS Society-USA panel.* Jama, 2008. **300**(5): p. 555-70.
8. Marsden, M.D. and J.A. Zack, *Eradication of HIV: current challenges and new directions.* J Antimicrob Chemother, 2009. **63**(1): p. 7-10.
9. Shen, L., et al., *Dose-response curve slope sets class-specific limits on inhibitory potential of anti-HIV drugs.* Nat Med, 2008. **14**(7): p. 762-6.
10. Whitney, J.B., et al., *T cell vaccination reduces SIV in semen.* J Virol, 2009.
11. Burman, W., et al., *Episodic antiretroviral therapy increases HIV transmission risk compared with continuous therapy: results of a randomized controlled trial.* J Acquir Immune Defic Syndr, 2008. **49**(2): p. 142-50.
12. Bangsberg, D.R., D.L. Kroetz, and S.G. Deeks, *Adherence-resistance relationships to combination HIV antiretroviral therapy.* Curr HIV/AIDS Rep, 2007. **4**(2): p. 65-72.
13. Harrigan, P.R., et al., *Predictors of HIV drug-resistance mutations in a large antiretroviral-naive cohort initiating triple antiretroviral therapy.* J Infect Dis, 2005. **191**(3): p. 339-47.
14. King, M.S., S.C. Brun, and D.J. Kempf, *Relationship between adherence and the development of resistance in antiretroviral-naive, HIV-1-infected patients receiving lopinavir/ritonavir or nelfinavir.* J Infect Dis, 2005. **191**(12): p. 2046-52.
15. Deschamps, A.E., et al., *Prevalence and correlates of nonadherence to antiretroviral therapy in a population of HIV patients using Medication Event Monitoring System.* AIDS Patient Care STDS, 2004. **18**(11): p. 644-57.
16. Simoni, J.M., et al., *Self-report measures of antiretroviral therapy adherence: A review with recommendations for HIV research and clinical management.* AIDS Behav, 2006. **10**(3): p. 227-45.
17. Sitta, R., et al., *No Variability Across Centers in Adherence and Response to HAART in French Hospitals: Results From the ANRS-EN12-VESPA Study.* J Acquir Immune Defic Syndr, 2009.
18. Fellay, J., et al., *Prevalence of adverse events associated with potent antiretroviral treatment: Swiss HIV Cohort Study.* Lancet, 2001. **358**(9290): p. 1322-7.
19. Silverberg, M.J., et al., *Prevalence of clinical symptoms associated with highly active antiretroviral therapy in the Women's Interagency HIV Study.* Clin Infect Dis, 2004. **39**(5): p. 717-24.

20. Ammassari, A., et al., *Self-reported symptoms and medication side effects influence adherence to highly active antiretroviral therapy in persons with HIV infection.* J Acquir Immune Defic Syndr, 2001. **28**(5): p. 445-9.
21. Portillo, C.J., W.L. Holzemer, and F.Y. Chou, *HIV symptoms.* Annu Rev Nurs Res, 2007. **25**: p. 259-91.
22. Brooks, J.T., J.E. Kaplan, and H. Masur, *What's New in the 2009 US Guidelines for Prevention and Treatment of Opportunistic Infections Among Adults and Adolescents with HIV?* Top HIV Med, 2009. **17**(3): p. 109-14.
23. French, A.L., et al., *Trends in mortality and causes of death among women with HIV in the United States: a 10-year study.* J Acquir Immune Defic Syndr, 2009. **51**(4): p. 399-406.
24. Marin, B., et al., *Non-AIDS-defining deaths and immunodeficiency in the era of combination antiretroviral therapy.* Aids, 2009.
25. Harding, R., et al., *Is antiretroviral therapy associated with symptom prevalence and burden?* Int J STD AIDS, 2006. **17**(6): p. 400-5.
26. Karus, D., et al., *Patient reports of symptoms and their treatment at three palliative care projects servicing individuals with HIV/AIDS.* J Pain Symptom Manage, 2005. **30**(5): p. 408-17.
27. Beaglehole, R., et al., *Improving the prevention and management of chronic disease in low-income and middle-income countries: a priority for primary health care.* Lancet, 2008. **372**(9642): p. 940-9.
28. Bodenheimer, T., E.H. Wagner, and K. Grumbach, *Improving primary care for patients with chronic illness.* Jama, 2002. **288**(14): p. 1775-9.
29. Schoen, C., et al., *In chronic condition: experiences of patients with complex health care needs, in eight countries, 2008.* Health Aff (Millwood), 2009. **28**(1): p. w1-16.
30. Handford, C.D., et al., *Setting and organization of care for persons living with HIV/AIDS.* Cochrane Database Syst Rev, 2006. **3**: p. CD004348.
31. Thorne, S. and B. Paterson, *Shifting images of chronic illness.* Image J Nurs Sch, 1998. **30**(2): p. 173-8.
32. Wagner, E.H., et al., *Improving chronic illness care: translating evidence into action.* Health Aff (Millwood), 2001. **20**(6): p. 64-78.
33. Wagner, E.H., et al., *Quality improvement in chronic illness care: a collaborative approach.* Jt Comm J Qual Improv, 2001. **27**(2): p. 63-80.
34. WHO, *Innovative Care for Chronic Conditions*. 2002, Geneva: WHO library Cataloging-in-Publication.
35. Tsai, A.C., et al., *A meta-analysis of interventions to improve care for chronic illnesses.* Am J Manag Care, 2005. **11**(8): p. 478-88.
36. Coleman, K., et al., *Evidence on the Chronic Care Model in the new millennium.* Health Aff (Millwood), 2009. **28**(1): p. 75-85.
37. Singh, D., *How can chronic disease management programmes operate across care settings and providers?* 2008, Copenhagen: WHO, European Observatory of Health Systems.
38. Crepaz, N., et al., *Do prevention interventions reduce HIV risk behaviours among people living with HIV? A meta-analytic review of controlled trials.* Aids, 2006. **20**(2): p. 143-57.
39. Simoni, J.M., et al., *Efficacy of interventions in improving highly active antiretroviral therapy adherence and HIV-1 RNA viral load. A meta-analytic review of randomized controlled trials.* J Acquir Immune Defic Syndr, 2006. **43 Suppl 1**: p. S23-35.

40. Gifford, A.L. and S. Sengupta, *Self-management health education for chronic HIV infection.* AIDS Care, 1999. **11**(1): p. 115-30.

41. Lorig, K.R. and H. Holman, *Self-management education: history, definition, outcomes, and mechanisms.* Ann Behav Med, 2003. **26**(1): p. 1-7.

42. Thorne, S., B. Paterson, and C. Russell, *The structure of everyday self-care decision making in chronic illness.* Qual Health Res, 2003. **13**(10): p. 1337-52.

43. Corbin, J. and A. Strauss, *Unending Work and Care: Managing Chronic Illness at Home.* 1988, San Francisco: Jossey-Bass.

44. Epping-Jordan, J.E., et al., *Improving the quality of health care for chronic conditions.* Qual Saf Health Care, 2004. **13**(4): p. 299-305.

45. Wikipedia, *Collaboration*. 2009. http://en.wikipedia.org/wiki/Collaboration

46. Bodenheimer, T., E.H. Wagner, and K. Grumbach, *Improving primary care for patients with chronic illness: the chronic care model, Part 2.* Jama, 2002. **288**(15): p. 1909-14.

47. Fehr, J.S., et al., *Starting or changing therapy - a prospective study exploring antiretroviral decision-making.* Infection, 2005. **33**(4): p. 249-56.

48. Gray, J., *Becoming adherent: experiences of persons living with HIV/AIDS.* J Assoc Nurses AIDS Care, 2006. **17**(3): p. 47-54.

49. Nicca, D., et al., *[Ready for antiretroviral therapy? Therapy decision making experiences of persons living with HIV].* Pflege, 2005. **18**(5): p. 289-98.

50. Vervoort, S.C., et al., *Adherence in antiretroviral therapy: a review of qualitative studies.* Aids, 2007. **21**(3): p. 271-81.

51. Chou, F.Y., *Testing a predictive model of the use of HIV/AIDS symptom self-care strategies.* AIDS Patient Care STDS, 2004. **18**(2): p. 109-17.

52. Reynolds, N.R., et al., *HIV illness representation as a predictor of self-care management and health outcomes: a multi-site, cross-cultural study.* AIDS Behav, 2009. **13**(2): p. 258-67.

53. Spirig, R., et al., *Symptom management in HIV/AIDS: advancing the conceptualization.* ANS Adv Nurs Sci, 2005. **28**(4): p. 333-44.

54. Wantland, D.J., et al., *A randomized controlled trial testing the efficacy of an HIV/AIDS symptom management manual.* J Pain Symptom Manage, 2008. **36**(3): p. 235-46.

55. Elzi, L., et al., *A smoking cessation programme in HIV-infected individuals: a pilot study.* Antivir Ther, 2006. **11**(6): p. 787-95.

56. Nijhawan, A., S. Kim, and J.D. Rich, *Management of HIV Infection in Patients With Substance Use Problems.* Curr Infect Dis Rep, 2008. **10**(5): p. 432-8.

57. Reynolds, N.R., *Cigarette smoking and HIV: more evidence for action.* AIDS Educ Prev, 2009. **21**(3 Suppl): p. 106-21.

58. Voggensperger, J., et al., *[Smoking cessation for HIV infected patients].* Pflege, 2003. **16**(5): p. 283-8.

59. Conen, A., et al., *Self-reported alcohol consumption and its association with adherence and outcome of antiretroviral therapy in the Swiss HIV Cohort Study.* Antivir Ther, 2009. **14**(3): p. 349-57.

60. Hand, G.A., et al., *Moderate intensity exercise training reverses functional aerobic impairment in HIV-infected individuals.* AIDS Care, 2008. **20**(9): p. 1066-74.

61. Hendricks, K.M., et al., *Dietary patterns and health and nutrition outcomes in men living with HIV infection.* Am J Clin Nutr, 2008. **88**(6): p. 1584-92.

62. Coleman, C.L., et al., *Gender differences in use of prayer as a self-care strategy for managing symptoms in African Americans living with HIV/AIDS.* J Assoc Nurses AIDS Care, 2006. **17**(4): p. 16-23.

63. Fitzpatrick, A.L., et al., *Survival in HIV-1-positve adults practicing psychological or spiritual activities for one year.* Altern Ther Health Med, 2007. **13**(5): p. 18-20, 22-4.

64. Kemppainen, J.K., et al., *Strategies for self-management of HIV-related anxiety.* AIDS Care, 2006. **18**(6): p. 597-607.

65. Plattner, I.E. and N. Meiring, *Living with HIV: the psychological relevance of meaning making.* AIDS Care, 2006. **18**(3): p. 241-5.

66. Riley, T.A., et al., *Low-income HIV-infected women and the process of engaging in healthy behavior.* J Assoc Nurses AIDS Care, 2008. **19**(1): p. 3-15.

67. Braveman, B., et al., *Occupational identity, occupational competence and occupational settings (environment): influences on return to work in men living with HIV/AIDS.* Work, 2006. **27**(3): p. 267-76.

68. Davies, S.L., et al., *MOMS: formative evaluation and subsequent intervention for mothers living with HIV.* AIDS Care, 2009. **21**(5): p. 552-60.

69. Merenstein, D., et al., *Association of child care burden and household composition with adherence to highly active antiretroviral therapy in the Women's Interagency HIV Study.* AIDS Patient Care STDS, 2009. **23**(4): p. 289-96.

70. Kalichman, S.C., *Co-occurrence of treatment nonadherence and continued HIV transmission risk behaviors: implications for positive prevention interventions.* Psychosom Med, 2008. **70**(5): p. 593-7.

71. Fisher, J.D. and L. Smith, *Secondary prevention of HIV infection: the current state of prevention for positives.* Curr Opin HIV AIDS, 2009. **4**(4): p. 279-87.

72. van der Straten, A., et al., *Managing HIV among serodiscordant heterosexual couples: serostatus, stigma and sex.* AIDS Care, 1998. **10**(5): p. 533-48.

73. Fox, J., et al., *Reductions in HIV transmission risk behaviour following diagnosis of primary HIV infection: a cohort of high-risk men who have sex with men.* HIV Med, 2009. **10**(7): p. 432-8.

74. Bairan, A., et al., *A model of HIV disclosure: disclosure and types of social relationships.* J Am Acad Nurse Pract, 2007. **19**(5): p. 242-50.

75. Chenard, C., *The impact of stigma on the self-care behaviors of HIV-positive gay men striving for normalcy.* J Assoc Nurses AIDS Care, 2007. **18**(3): p. 23-32.

76. Plach, S.K., P.E. Stevens, and S. Keigher, *Self-care of women growing older with HIV and/or AIDS.* West J Nurs Res, 2005. **27**(5): p. 534-53; comment 554-8.

77. Schuster, M.A., et al., *Perceived discrimination in clinical care in a nationally representative sample of HIV-infected adults receiving health care.* J Gen Intern Med, 2005. **20**(9): p. 807-13.

78. Mahajan, A.P., et al., *Stigma in the HIV/AIDS epidemic: a review of the literature and recommendations for the way forward.* Aids, 2008. **22 Suppl 2**: p. S67-79.

79. Wilson, H.S., S.A. Hutchinson, and W.L. Holzemer, *Reconciling incompatibilities: a grounded theory of HIV medication adherence and symptom management.* Qual Health Res, 2002. **12**(10): p. 1309-22.

80. Enriquez, M., et al., *Assessment of readiness for adherence by HIV-positive males who had previously failed treatment.* J Assoc Nurses AIDS Care, 2004. **15**(1): p. 42-9.

81. Nordqvist, O., et al., *Assessing and achieving readiness to initiate HIV medication.* Patient Educ Couns, 2006. **62**(1): p. 21-30.

82. Sodergard, B., et al., *A structural equation modeling approach to the concepts of adherence and readiness in antiretroviral treatment.* Patient Educ Couns, 2007. **67**(1-2): p. 108-16.

83. World Health Organisation, *Adherence to long term therapies: Evidence for Action.* 2003, Geneva: World Health Organisation.

84. Broyles, L.M., A.M. Colbert, and J.A. Erlen, *Medication practice and feminist thought: a theoretical and ethical response to adherence in HIV/AIDS.* Bioethics, 2005. **19**(4): p. 362-78.

85. Gross, R., et al., *A simple, dynamic measure of antiretroviral therapy adherence predicts failure to maintain HIV-1 suppression.* J Infect Dis, 2006. **194**(8): p. 1108-14.

86. Glass, T.R., et al., *Correlates of self-reported nonadherence to antiretroviral therapy in HIV-infected patients: the Swiss HIV Cohort Study.* J Acquir Immune Defic Syndr, 2006. **41**(3): p. 385-92.

87. Knobel, H., et al., *Impact of different patterns of nonadherence on the outcome of highly active antiretroviral therapy in patients with long-term follow-up.* HIV Med, 2009. **10**(6): p. 364-9.

88. Wong, W.K. and J. Ussher, *How do subjectively-constructed meanings ascribed to anti-HIV treatments affect treatment-adherent practice?* Qual Health Res, 2008. **18**(4): p. 458-68.

89. Levy, J.A., *HIV and the pathogenesis of AIDS.* 3rd ed. 2007, Washington: ASM Press.

90. Bova, C., et al., *The Symptom Experience of HIV/HCV-Coinfected Adults.* J Assoc Nurses AIDS Care, 2008. **19**(3): p. 170-80.

91. Mathews, W.C., et al., *National estimates of HIV-related symptom prevalence from the HIV Cost and Services Utilization Study.* Med Care, 2000. **38**(7): p. 750-62.

92. Newshan, G., J. Bennett, and S. Holman, *Pain and other symptoms in ambulatory HIV patients in the age of highly active antiretroviral therapy.* J Assoc Nurses AIDS Care, 2002. **13**(4): p. 78-83.

93. Benjamini, Y.H., Y., *Controlling the false discovery rate: A practical and powerful approach to multiple testing. Journal of the Royal Statistical Society.* 1995. **Series B, 57**: p. 289-300.

94. Holzemer, W.L., et al., *Validation of the Sign and Symptom Check-List for Persons with HIV Disease (SSC-HIV).* J Adv Nurs, 1999. **30**(5): p. 1041-9.

95. Nicholas, P.K., et al., *Symptom management and self-care for peripheral neuropathy in HIV/AIDS.* AIDS Care, 2007. **19**(2): p. 179-89.

96. Nicholas, P.K., et al., *Unhealthy behaviours for self-management of HIV-related peripheral neuropathy.* AIDS Care, 2007. **19**(10): p. 1266-73.

97. Dodd, M., et al., *Advancing the science of symptom management.* J Adv Nurs, 2001. **33**(5): p. 668-76.

98. Sousa, K.H., S.S. Tann, and O.M. Kwok, *Reconsidering the assessment of symptom status in HIV/AIDS care.* J Assoc Nurses AIDS Care, 2006. **17**(2): p. 36-46.

99. Badia, X., et al., *Evaluating changes in health status in HIV-infected patients: Medical Outcomes Study-HIV and Multidimensional Quality of Life-HIV quality of life questionnaires. Spanish MOS-HIV and MQOL-HIV Validation Group.* Aids, 2000. **14**(10): p. 1439-47.

100. Bastardo, Y.M. and C.L. Kimberlin, *Relationship between quality of life, social support and disease-related factors in HIV-infected persons in Venezuela.* AIDS Care, 2000. **12**(5): p. 673-84.

101. Benedict, R.H., et al., *Impact of human immunodeficiency virus type-1-associated cognitive dysfunction on activities of daily living and quality of life.* Arch Clin Neuropsychol, 2000. **15**(6): p. 535-44.

102. Hudson, A., K. Kirksey, and W. Holzemer, *The influence of symptoms on quality of life among HIV-infected women.* West J Nurs Res, 2004. **26**(1): p. 9-23; discussion 24-30.

103. Lorenz, K.A., et al., *Changes in symptoms and health-related quality of life in a nationally representative sample of adults in treatment for HIV.* Qual Life Res, 2006. **15**(6): p. 951-8.

104. Sousa, K.H., et al., *Dimensions of health-related quality of life in persons living with HIV disease.* J Adv Nurs, 1999. **29**(1): p. 178-87.

105. Burgoyne, R.W. and D.H. Tan, *Prolongation and quality of life for HIV-infected adults treated with highly active antiretroviral therapy (HAART): a balancing act.* J Antimicrob Chemother, 2008. **61**(3): p. 469-73.

106. Burgoyne, R.W., et al., *Long-term quality-of-life outcomes among adults living with HIV in the HAART era: the interplay of changes in clinical factors and symptom profile.* AIDS Behav, 2004. **8**(2): p. 151-63.

107. Holzemer, W.L., et al., *Predictors of self-reported adherence in persons living with HIV disease.* AIDS Patient Care STDS, 1999. **13**(3): p. 185-97.

108. Levine, C., *AIDS and changing concepts of family.* Milbank Quarterly, 1990. **68**(1): p. 33-58.

109. Spirig, R., *In invisibility and isolation: the experience of HIV-affected families in German-speaking Switzerland.* Qual Health Res, 2002. **12**(10): p. 1323-37.

110. Young, J., et al., *Stable partnership and progression to AIDS or death in HIV infected patients receiving highly active antiretroviral therapy: Swiss HIV cohort study.* Bmj, 2004. **328**(7430): p. 15.

111. Burgoyne, R.W., *Exploring direction of causation between social support and clinical outcome for HIV-positive adults in the context of highly active antiretroviral therapy.* AIDS Care, 2005. **17**(1): p. 111-24.

112. DiMatteo, M.R., *Social support and patient adherence to medical treatment: a meta-analysis.* Health Psychol, 2004. **23**(2): p. 207-18.

113. Ingram, K.M., et al., *Social support and unsupportive social interactions: their association with depression among people living with HIV.* AIDS Care, 1999. **11**(3): p. 313-29.

114. Bischofberger, I. and R. Spirig, *[The work profile of family caregivers of persons affected by HIV/AIDS].* Pflege, 2004. **17**(3): p. 176-86.

115. Lingler, J.H., et al., *Conceptual challenges in the study of caregiver-care recipient relationships.* Nurs Res, 2008. **57**(5): p. 367-72.

116. Miller, L.G., et al., *How well do clinicians estimate patients' adherence to combination antiretroviral therapy?* J Gen Intern Med, 2002. **17**(1): p. 1-11.

117. Reilly, C.A., et al., *A comparison of patient and nurse ratings of human immunodeficiency virus-related signs and symptoms.* Nurs Res, 1997. **46**(6): p. 318-23.

118. Berg, K.M. and J.H. Arnsten, *Practical and Conceptual Challenges in Measuring Antiretroviral Adherence.* J Acquir Immune Defic Syndr, 2006. **43**: p. 79-87.

119. Beach, M.C., J. Keruly, and R.D. Moore, *Is the quality of the patient-provider relationship associated with better adherence and health outcomes for patients with HIV?* J Gen Intern Med, 2006. **21**(6): p. 661-5.

120. Chiou, P.Y., et al., *A programme of symptom management for improving quality of life and drug adherence in AIDS/HIV patients.* J Adv Nurs, 2006. **55**(2): p. 169-79.

121. Simoni, J.M., P.A. Frick, and B. Huang, *A longitudinal evaluation of a social support model of medication adherence among HIV-positive men and women on antiretroviral therapy.* Health Psychol, 2006. **25**(1): p. 74-81.

122. Remien, R.H., et al., *Couple-focused support to improve HIV medication adherence: a randomized controlled trial.* Aids, 2005. **19**(8): p. 807-14.

123. Anastasi, J.K., et al., *Symptom management of HIV-related diarrhea by using normal foods: A randomized controlled clinical trial.* J Assoc Nurses AIDS Care, 2006. **17**(2): p. 47-57.

124. Neidig, J.L., B.A. Smith, and D.E. Brashers, *Aerobic exercise training for depressive symptom management in adults living with HIV infection.* J Assoc Nurses AIDS Care, 2003. **14**(2): p. 30-40.

125. Inouye, J., L. Flannelly, and K.J. Flannelly, *The effectiveness of self-management training for individuals with HIV/AIDS.* J Assoc Nurses AIDS Care, 2001. **12**(5): p. 71-82.

126. Kennedy, A., A. Rogers, and M. Crossley, *Participation, roles, and the dynamics of change in a group-delivered self-management course for people living with HIV.* Qual Health Res, 2007. **17**(6): p. 744-58.

127. Gebhardt, M., M. Rickenbach, and M. Egger, *Impact of antiretroviral combination therapies on AIDS surveillance reports in Switzerland. Swiss HIV Cohort Study.* Aids, 1998. **12**(10): p. 1195-201.

128. Clumeck, N., A. Pozniak, and F. Raffi, *European AIDS Clinical Society (EACS) guidelines for the clinical management and treatment of HIV-infected adults.* HIV Med, 2008. **9**(2): p. 65-71.

129. Deschamps, A.E., et al., *Diagnostic value of different adherence measures using electronic monitoring and virologic failure as reference standards.* AIDS Patient Care STDS, 2008. **22**(9): p. 735-43.

Chapter 2

Aims of the research program

In countries with broad access to antiretroviral therapy, mortality and morbidity rates among PLWH have fallen significantly, with HIV/AIDS now generally accepted as a treatable chronic condition[2]. Recent evidence further suggests that improvements in health outcomes require an approach based not on traditional acute care models but on modern comprehensive chronic illness management [14]. Across diverse chronic conditions, such services have proved successful with changes at the levels of policy, healthcare organization and the individual patient [15].

At the patient level, self-management and collaboration between patients, close support persons and healthcare organizations are now seen as the most important aspects related to health outcomes [19]. In HIV/AIDS, medication and symptom management tasks are key to successful self-management, but have been described mainly in fragmented ways, with most research focusing either on symptoms or on cART adherence, despite the fact that PLWH's symptom experiences are closely associated with adherence to cART [19, 22, 23, 28].

For PLWH, the formulation and adoption of many medication and symptom management strategies involves collaboration with their HCPs and CSPs; yet, despite the seemingly obvious benefits of such collaboration, the related processes are only vaguely understood. Since self-management activities regarding both medications and symptoms are closely associated with health outcomes, a fuller understanding of such activities is necessary to improve related services.

The overall aim of this exploratory research program was to describe PLWH's symptom and medication management activities, focusing on collaboration between PLWH, CSPs and HCPs, from the perspectives of all three groups. This involved focusing on the specific aims outlined below:

- to present a clinical case report from the HCP's perspective, with individualized evidence based medication and symptom management interventions (based on literature review);
- to review the evidence on adherence support interventions for PLWH (based on literature review);
- to describe the experiences of PLWH regarding medication and symptom management, with reference to collaboration with HCPs and CSPs (based on qualitative results); and
- to explore the collaborative activities between PLWH and their CSPs within the process of symptom management, including the concordance between both players' symptom reports (based on qualitative and quantitative results).

This study was conducted according to an exploratory mixed methods design [47]. In a first step, the goal was to gain a clearer understanding of PLWH's and CSPs' medication and symptom management experiences, including their collaboration with each other and HCPs. Therefore, in-depth interviews were conducted with PLWH and CSPs and qualitatively analyzed. In the second phase, based on the findings of the first, questions related to the concordance of PLWH's and HCPs' symptom reports were formulated and tested quantitatively in a larger sample.

References

1. Hogg, R.S.S., J. A.; Graber, S.; Battegay, M.; Bonarek, M.; D'Arminio Monforte, A.; Esteve, A.; Harris, R.; Justice, A.; Hayden, A.; Lampe, F.; Mocroft, A.; Mugavero, M. J.; Staszewski, S.; Wasmuth, J.C.; van Sighem, A.; Kitahata, M.; Guest, J.; Egger, M.; May, M., *Life expectancy of individuals on combination antiretroviral therapy in high-income countries: a collaborative analysis of 14 cohort studies.* Lancet, 2008. **372**(9635): p. 293-9.
2. Schoen, C., et al., *In chronic condition: experiences of patients with complex health care needs, in eight countries, 2008.* Health Aff (Millwood), 2009. **28**(1): p. w1-16.
3. WHO, *Innovative Care for Chronic Conditions*. 2002, Geneva: WHO library Cataloging-in-Publication.
4. Epping-Jordan, J.E., et al., *Improving the quality of health care for chronic conditions.* Qual Saf Health Care, 2004. **13**(4): p. 299-305.
5. Simoni, J.M., et al., *Efficacy of interventions in improving highly active antiretroviral therapy adherence and HIV-1 RNA viral load. A meta-analytic review of randomized controlled trials.* J Acquir Immune Defic Syndr, 2006. **43 Suppl 1**: p. S23-35.
6. Spirig, R., et al., *Symptom management in HIV/AIDS: advancing the conceptualization.* ANS Adv Nurs Sci, 2005. **28**(4): p. 333-44.
7. Wilson, H.S., S.A. Hutchinson, and W.L. Holzemer, *Reconciling incompatibilities: a grounded theory of HIV medication adherence and symptom management.* Qual Health Res, 2002. **12**(10): p. 1309-22.
8. Creswell, J.W.P.C., V.L, *Designing and Conducting Mixed Methods Research*. 2007, Thousand Oaks: Sage Publications.

Chapter 3

Comprehensive Clinical Adherence Interventions to Enable Antiretroviral Therapy: A Case Report

Dunja Nicca[1,2], Kimberly Moody[3], Luigia Elzi[2], Rebecca Spirig[1]

[1] Division of Clinical Nursing Science, University Hospital Basel

[2] Division of Infectious Diseases and Hospital Epidemiology, University Hospital Basel

[3] College of Nursing and Health Professions, University of Southern Maine & Maine Medical Center, Portland, Maine, USA

Corresponding author, e-mail: spirigr@uhbs.ch

Published in:

Journal of the Association of Nurses in AIDS Care (JANAC), 2007, 18 (6): p. 44-53

Abstract

Adherence to antiretroviral therapy is key for successful treatment in HIV-infected persons. In order to enhance adherence, multilevel interventions are necessary. This is often a challenge as this case of an HIV-infected man with a history of poor adherence and multiple virological failures demonstrates.

With a multidisciplinary approach, comprehensive intervention strategies were used to facilitate the patient’s adherence to an enfurvirtide-based regimen. The interventions are described in detail and include adherence support with modified daily observed therapy, support regarding symptom management, and social relationships. The patient’s clinical progress was monitored using indicators such as clinical surrogate markers, adherence to ART and HIV-related symptom and depression scores.

The case illustrates how interventions that were individualized, culturally sensitive, and provided by a team of health care providers enabled a patient to optimize his adherence which led to significant improvement in his clinical surrogate markers and subjective quality of life.

Introduction

Potent antiretroviral therapy (ART) for HIV-infection requires nearly perfect adherence[1] on a long-term basis, since non-adherence by HIV-infected patients has been associated with incomplete viral suppression, the development of drug resistance, disease progression, and mortality (Bangsberg et al. 2003). Unfortunately, recommended levels of adherence to medication are not often achieved. In clinical practice, non-adherence rates in the HIV-infected population fall somewhere between 20% and 50% depending on operational definitions and methods of measurement (WHO, 2003). Adherence is complex and influenced by multiple factors including: (1) the complexity of the regimen; (2) frequency and severity of side effects and symptoms; (3) social and psychological factors such as depression; (4) treatment and health beliefs; (5) social and provider support; and (6) personal attributes such as clinical status, sex, age and substance use (Fogarty et al. 2002). Thus, multileveled adherence support is crucial.

In order to integrate medical, psychosocial, and behavioral interventions in patients with HIV, a chronic illness management approach is recommended. Patients need to become invested and knowledgeable partners in managing their chronic condition in daily life (Bodenheimer, Lorig, Holman & Grumbach, 2002). Within that context, patient's health outcomes are optimized by state-of-the-art medical therapy and interventions related to adherence and symptom management. The interventions should be performed over time and include combinations of educational, behavioral and social support approaches (Yeni et al. 2004; Reynolds 2004).

Incorporating multilevel approaches that meet an individual patient's needs in clinical practice is often a challenge. Strategies need to flex and adapt to the ever changing physical and psychosocial states of a patient who struggles with the management of ART. Providers need time and expertise to provide a safe and therapeutic environment for change to occur. Yet they are often less skilled at enabling behavioral change than they are at educating and advising. The practice setting also creates barriers to comprehensive intervention strategies in terms of time allotted for short visits with an emphasis on physiological rather than psychological outcomes.

The following case report offers an opportunity to analyze comprehensive evidence-based clinical interventions to facilitate adherence to a complex antiretroviral treatment regimen for an HIV-infected man who had a history of long term non-adherence and multiple virological failures, intravenous drug use, and clinical depression. After the case presentation, the evidence-based theoretical background of the selected intervention strategies will be described, before the implementation of interventions and the patient's clinical progress are illustrated.

---

[1] Adherence to ART is understood as the extent to which a patient's behavior, regarding taking medication corresponds with the agreed recommendations that were collaboratively developed with the health care provider (WHO, 2003).

Presentation of the case study

Mr. Angeli[2] was a 44 year old man attending an HIV Outpatient Clinic in a Swiss city for monitoring and treatment of his HIV Infection. The Clinic is one of the seven centres participating in the Swiss HIV Cohort Study (SHCS). Within the SHCS, standardized collection of socio-demographic, clinical, and laboratory data are integrated into the care of patients living with HIV (www.shcs.ch). Due to mandatory health insurance, all persons living with HIV in Switzerland (including migrants) have equal access to care and ART whether participating in the SCHS or not.

Mr. Angeli's primary care provider was a physician with a specialty in infectious disease. The patient's clinic visits had been infrequent and erratic. With interruptions, he had been taking various combinations of antiretroviral medications for the last 3 years. At the time of this case study, he presented to the clinic with therapy failure and multiple drug resistant mutations. Since his problems with adherence to ART had been documented numerous times, he was referred to a nurse-led adherence counseling program, funded in part by a nursing practice development grant.

Medical History

Mr. Angeli's HIV Infection (CDC C3) was first diagnosed in 1992. He had experienced opportunistic infections that included candida esoghagitis and herpes zoster, both in 1999. Additional comorbidities included hepatitis C infection, chronic obstructive lung disease, and peripheral polyneuropathy. Mr. Angeli had been an intravenous drug user from 1978-1987. Substance use had been routinely assessed within the SHCS every six months. Over the past 3 years Mr. Angeli had reported three instances of sporadic cocaine use. In the same time period, many episodes of high alcohol consumption, mostly during weekends, had been reported in his chart. However the patient did not meet the criteria for alcohol use disorder (ICD10).

Mr. Angeli presented to our clinic in April 2005 because of bloody diarrhea without abdominal pain or fever. In addition, he complained about dyspnea, generalized muscle pain, severe fatigue and depressed mood. CD4-T-count was 5 cells/µL and a viral load of 462991 copies/mL on ART with Didanosine, Tenofovir, and Nevirapine. Genotypic and phenotypic resistance testing showed broad resistance to protease inhibitors (M46IL, L90M), NNRTI (Y181I) and NRTI (M184V, K70KR). Due to his condition, the patient was hospitalized.

Social History

Born and raised in a little village in southern Italy, Mr. Angeli came to live and work in Switzerland 3 years prior. He moved to Switzerland because of a relationship with his girlfriend, but he stated that they had broken up a few months prior to this assessment. His ex-girlfriend was the only person who

---

[2] Name and information about the patient's changed to maintain his privacy.

knew about his HIV status. Mr. Angeli had a few friends with whom he socialized occasionally, but he could not name a close support person. He had been working in a large bakery and had recently lost his job due to long unexplained absences from work. Mr. Angeli complained about severe fatigue and weakness and was not always able to cope with the heavy work and the night shifts at the bakery. Still, he did not want his physician to provide documentation to his boss, because he feared disclosure of his HIV status at work.

Even though he had been working in a German speaking Swiss town for 3 years, he was not able to understand, read, write or speak German. At work he spoke Italian; he stated he did not have the energy to go to German classes because he was exhausted from work. His ex-girlfriend had handled all his paperwork and financial affairs for him until they separated. Mr. Angeli explained that he was now overwhelmed by the papers and bills due to his health problems and did not feel that he could cope anymore.

Treatment and Adherence History

Mr. Angeli was treated with Zidovudine, Lamivudine, and Nelfinavir from 1999 to 2003. Several treatment interruptions were reported in his chart, most of them because of fear of drug interactions and concomitant use of alcohol and cocaine. Due to cumulative drug resistance, he was treated in 2003 with a new experimental regimen with Indinavir and Lopinavir/Ritonavir administered once a day. Mr. Angeli complained of the high pill burden and interrupted the treatment. A few months later, in 2004, a simpler regimen with Didanosine, Tenofovir, and Nevirapine was started. Reduction of the daily pill count from 10 to 4 was achieved. Other possible adherence influencing factors were frequently documented such as high alcohol consumption, depression, unstable work situation, and relationship problems.

A present assessment of adherence, based on the motivation to change medication taking behavior (Highstein, Willey & Mundy 2006) and on barriers and facilitators to adherence (WHO, 2003) revealed that Mr. Angeli was motivated to try another antiretroviral regimen in order to feel better. The conversation about his former medication taking behavior revealed additional barriers such as: having a hard time maintaining a daily schedule; fear of HIV disclosure; not wanting to be reminded of his HIV status; and loneliness.

Since the high alcohol consumption reported in the chart represented a risk factor for adherence problems, Mr. Angeli's alcohol consumption was assessed with the Alcohol Use Disorders Identification Test (AUDIT). The AUDIT is a questionnaire that helps practitioners identify a potentially harmful drinking pattern or dependence (WHO 2001). Mr. Angeli's AUDIT Score represented a medium-level alcohol problem and indicated that brief counseling and continued monitoring were appropriate interventions. The first counselling session was held immediately after the assessment. Monitoring was integrated in the assessment of the SHCS every six months.

Background of the intervention strategies

Mr. Angeli is a complex patient with diverse interrelated problems. In order to optimize health outcomes, individualized evidence-based intervention strategies had to be implemented. Therefore a trusting relationship between Mr. Angeli and his health care providers (nurse/physician) had to be established. This was especially important because of language barriers and his former negative experiences with the health care system. Further, Mr. Angeli had to be included in the decision-making process related to treatment and support interventions, since his active participation was needed. On the basis of a trusting relationship and the process of shared decisions, Mr. Angeli needed support in the areas of adherence, symptom management and social support. A modified daily observed therapy program (mDOT) seemed an appropriate adherence intervention for Mr. Angeli: it would help him to structure his days and provide support in the administration of medication. Further, the regular visits would permit nurse-led counseling for a longer time in the areas of adherence, symptom management, and social support.

Shared Decision Making

Participation by chronically ill patients in the process of treatment decision making has demonstrated a positive influence on patient satisfaction and motivation for treatment (Bodenheimer et al. 2002). In HIV care, good patient-provider communication and a shared process of treatment decision making has been shown to influence a patient’s readiness for ART (Fehr et al. 2005). Further, a positive patient provider relationship has been shown to have a significant influence on an HIV-infected patient’s adherence to ART (Fogarty et al. 2002). Schneider et al. (2004) found that multiple dimensions such as communication, HIV specific information, participatory decision making, trust, and the quality of dialogue regarding adherence were significantly associated with adherence to ART. Decision making regarding symptom management involves a collaborative process aimed at making changes in medication and health behavior (Spirig, Moody, Battegay & De Geest, 2005). Thus, patient-provider interaction plays an important role related to interventions and health care outcomes.

Modified Daily Observed Therapy and Adherence Counselling

A growing body of evidence has demonstrated that directly observed therapy (DOT) can be a successful approach to enhance adherence to ART in patients who are hard to reach or have been unsuccessful in previous attempts of ART (Altice et al. 2004). To date, the existing programs have been conducted in structured institutional settings such as methadone maintenance clinics, HIV clinics, skilled nursing facilities or prisons, or communities and resource-poor countries (Mitty & Flanigan 2004). The strategies used differ depending on the population they planned to reach. Few programs use DOT strategies and observe every dose of medication taken. The majority use modified daily observed therapy strategies (mDOT), which includes, for example, the observation of one dose of a twice daily regimen for five days of the week. Additionally many DOT/mDOT programs include enhanced services such as adherence counselling and linkages to community and health care resources (Mitty et al. 2004).

To date experience with DOT/mDOT (for ART) is limited to pilot studies, preliminary results of randomized clinical trials or observational (comparative) studies (Altice et al. 2004). Even with these limited data, results for DOT and mDOT are promising, as Macalino et al. (2004) found in their pilot study: 25 individuals with active substance use disorders and documented history of non-adherence received a 6 month DOT intervention. Full viral suppression (less than 50 copies/mL) was achieved by 47% of patients after 2 to 3 months and 70% after 3 to 6 months. However, DOT alone will not eliminate non-adherence and successful programs include the following additional characteristics: (1) be highly individualized and flexible; (2) build a trusting relationship with patient; (3) address facilitators and barriers of adherence; (4) include enhanced services; (5) have good communication of different providers (Mitty et al. 2004; Frederick et al. 2004). Programs that include those components have shown to be well accepted by patients and have been an important link for comprehensive health care services for hard to reach patients when addressing the above mentioned clinical outcomes.

Further DOT/mDOT programs might be one of many different useful strategies to support patients with a history of long term non-adherence who have developed multiple resistant mutations and could profit from complex regimens including Enfurvirtide (ENF). ENF has to be administered twice daily by subcutaneous injection; it typically takes approximately 20 minutes for ENF to dissolve fully. Trials have found that injection site reactions were the most common adverse event and nearly all patients reported at least one reaction. In clinical trials, acceptance of ENF by patients is reported to be high. However some barriers such as subjective acceptance by patients, readiness for treatment, and adoption in daily clinical practice have been observed (Clotet et al. 2004). In the Swiss HIV Cohort Study, about 40% of patients starting ENF discontinued the treatment after a median time of 6 months (Elzi et al. 2005). Many factors may be involved in the high rate of stopping ENF. Former IV drug users objected to the use of ENF as the subcutaneous administration revived negative experiences associated with their substance dependence. Reactions at the injection site were rarely found to be treatment limiting – however they may have also contributed to the psychological barriers of adoption and administration of ENF therapy. Complexity of ENF adoption and administration can be further increased by the high psychosocial and behavioral risk profiles of these patients. Patient education materials alone have proved not to be sufficient to support some of the patients on ENF in their self-management (Kempner, 2005). For the “typical” ENF patient, injection site reactions, HIV-related symptoms, changing therapy because of optimal background, and pill- and injection-fatigue may converge to create a complex clinical scenario. This impacts patients’ self-management and adherence behaviors necessitating a much more individualized approach than would have been expected based on the findings of the trials establishing efficacy of treatment.

Support in the Management of Symptoms and Side Effects

Symptom management encompasses how a person living with HIV makes day-to-day decisions about dealing with symptoms, such as when to contact the health care provider, whether to take certain medications, and whether or not to alter exercise or diet (Gifford, Laurent, Gonzales, Chesney & Lorig 1998; Spirig et al. 2005). When symptoms are poorly managed, adherence becomes a problem resulting in rapid disease progression and negative effects on quality of life (Bastardo & Kimberlin 2000). Effective symptom management therefore is imperative. Providers have to be sensitive to the broad range of physiological and psychological symptoms and side effects that might occur and assess them systematically and regularly. Patients typically experience multiple signs and symptoms. Mathews and colleagues (2000) recently found that only 9.1% of the HIV-infected patients in their study (N = 4042) reported no signs and symptoms during a 6 month period. Frequently reported symptoms include: (1) fatigue (between 20%—85%); (2) sadness (82%); (3) diarrhea (40%—75%); and (4) pain (76%) (Vogl et al. 1999; Matthews et al. 2000). A patient's active self-management of symptoms is important and involves teaching for monitoring and managing symptoms by providers. Gifford and colleagues discovered, for example, that after receiving a self management program HIV patients improved their attitudes and abilities to deal with their symptoms and reduced unscheduled hospital visits (1998). Chou and colleagues (2004) tested a symptom management program that emphasized self care education related to medication side effects. They also reported significant differences in unscheduled hospital visits between groups but no differences in self esteem.

Social Support and Stabilization of Living Conditions

Reports from studies of patients living with chronic illnesses show that the availability of social support from a social network, especially a primary support person, is an important determinant of well-being (DiMatteo, 2004). A longitudinal descriptive study using the data from the Swiss HIV Cohort Study (N = 5350) demonstrated that the presence of a stable partnership was a significant predictor of slower progression of disease (Young et al. 2003). More specifically, effective self-management of HIV-infected persons, including adherence to ART, is enhanced when there is a social network and the presence of one primary support person (DiMatteo, 2004). Providers should assess a HIV-infected person's social network and also provide primary support persons with information and guidance or use a systemic approach that focuses interventions on families. This might be important since qualitative data show, that patient and support persons are often very close, live withdrawn lives, and provide important support to each other but do not exchange much with others outside of their close circle (Spirig, 2002). Additionally, health care providers can provide links to other sources of social support. DOT/mDOT programs provided social support by enhancing conncetions to existing community-based resources (Mitty et al.2004).

Implementation of interventions and clinical progress

Mr. Angeli's primary physician had known him for 6 months. She was a cultural match for him as she was a native Italian speaker and thus able to converse with Mr. Angeli, which allowed them to establish a trusting relationship. During the week of Mr. Angeli's hospitalization, the physician introduced him to the Advanced Practice Nurse (APN) who had expertise in adherence counselling. The physician and nurse met with Mr. Angeli for short visits on the hospital unit, listening to his worries and problems and conveying to him prospects for future support. The visits gave the nurse the opportunity to establish and strengthen their relationship. This facilitated conducting the adherence-related assessment at the first outpatient clinic visit after discharge from the hospital.

Due to Mr. Angeli's multiple drug resistances, possible future treatment options were discussed in an interdisciplinary team of HIV-experienced physicians and nurses. A salvage regimen with Enfurvitide (ENF) and Tenofovir, Efavirenz, Lamivudine, Zidovudine, and Didanosine was proposed. Additionally, antidepressant treatment with Paroxetine was suggested since the patient screened positive for depression and anxiety scores as assessed by the Hospital Anxiety and Depression Scale (HADS) (Bjelland, Dahl, Haug & Neckelmann 2002).

In a joint session the patient, physician, and nurse discussed the proposed therapy options. Thorough discussion ensured that Mr. Angeli was able to express his worries, hopes, and former experiences with medications and adherence. For example, he said that he was afraid of needles and even though he had injected intravenous drugs, he never had injected his drugs himself. The physician brought issues of drug effectiveness and side effects of the proposed regimen into the discussion whereas the nurse brought in possible individualized adherence support strategies. In a process of shared decision making, they agreed that Mr. Angeli would start the proposed antiretroviral regimen with the support of a mDOT program as well as financial and housekeeping assistance. They decided not to start the antidepressant treatment, as Mr. Angeli believed that his mood would improve once he started feeling better with the ART. Ongoing nurse and physician consultations were planned with a comprehensive evaluation after 6 months. At that time, they had the option to stop or change the ART regimen if needed. This timeline was very important for the patient since he felt able to adhere to the plan for a period of 6 months if no adverse events occurred.

His twice daily regimen with Enfuvirtide and Tenofovir, Efavirenz, Lamivudine, Zidovudine included subcutaneous injections and oral medication intake every 12 hours. The individualized mDOT program included visits to the HIV outpatient clinic every morning during the week (20 minutes). Once a week Mr. Angeli had an individualized 25 minute counseling session with the APN. Community care nurses went to his home in the evening and on the weekends to administer the injections and oral medication. All services were covered by his health insurance. The community nurses were given background information by the APN at the HIV outpatient clinic. Consultations with the physician were scheduled at the outpatient clinic 2 weeks after start of treatment, at 1 month and then every 3 months.

Mr. Angeli kept his appointment at the outpatient clinic every day, even though he spent the rest of the day in bed during the early weeks of treatment. Within a few weeks his symptoms of fatigue and muscle pain were better controlled due to ART and effective pain management. By self-report on a Likert scale from 1 to 10 (1 = none, 10 = worst) his fatigue score decreased from 8 at baseline assessment to 5 after 4 weeks and his pain score decreased from 6 to 2. He began asking questions about HIV-infection and treatment. Counseling sessions included making drawings about his health beliefs and educational materials about biomedical issues as verbal communication was limited due to the language barrier.

After 3 months of treatment, Mr. Angeli showed a slight interest in the process of administering ENF by injection. He began to observe the nurse doing the injection when previously he had turned his head away. The nurse explained what she was doing and further counseling sessions included education regarding preparation of the vials and later, injection of medications. Educational material in Italian was used for this purpose. A few weeks later the patient was ready to do the ENF-injections by himself. He rated his self efficacy (perceived capabilities to perform the task) with administration of ENF as 7 on a 1-10 scale with 1 indicating not at all confident and 10 totally confident (Schwarzer, Bässler, Kwiatek, Schröder & Zhang, 1997). Community nursing service was stopped and Mr. Angeli did the evening and weekend injections himself. Even so, he still wanted to come to the outpatient clinic for his morning injections but he administered the medication himself. One of the nurses always checked how he was doing and gave assistance if needed. They called him when he did not arrive at the clinic, but this only happened a few times.

Mr. Angeli’s viral load decreased from 462991 copies/mL below 400 copies within a year after treatment change. Accordingly his CD4 count slowly increased from 5 cells/μL to 106 cells/μL after 3 months, 101 after 6 months, and 127 after 24 months.

Counseling sessions after the patient began the injections himself focused on issues around injection site reactions, side effects, and symptom management. With the help of the nurse, Mr. Angeli developed an injection schema which made injection site reactions, such as painful indurations, manageable. He learned to palpate the indurations and change injection site carefully, since he had limited sites for injection.

During the first 6 months of treatment Mr. Angeli suffered several episodes of a fever or cough. This frightened him so his counseling included education to differentiate between symptoms where he needed the assistance of professionals and those that he could manage himself. Discussion also included a differentiation of symptoms connected to HIV-infection and those probably as a result of depression. After education about depression related symptoms and treatment possibilities, Mr. Angeli decided to start antidepressant treatment, 5 months after the initiation of ART. Mr. Angeli’s subjective quality of life increased while the depression score (measured by HADS) decreased to a negative score (see Table 1) (Bjelland et al. 2002).

Table 1: Anxiety and Depression Scores according to the HADS

	Depression Score		**Anxiety Score**	
Baseline	14	positive	12	positive
3 months after mDOT start	14	positive	9	questionable
6 months after mDOT start *	9	questionable	5	negative
12 months after mDOT start	5	negative	7	negative

Score: negative 0-7 / questionable 8-10 / positive >10

*3 month after start with antidepressant

Mr. Angeli's alcohol and drug consumption was been assessed at 3, 6 and 12 months with the assessing consumption/amount of consumption questionnaire routinely used at the SCHS. At every assessment, he indicated that he had stopped alcohol and drug use completely. His aspartate and alanine aminotransferases were within the normal range thus no additional laboratory tests were done. Asked about his reasons of stopping, Mr. Angeli described a trigger event: A few days after starting with the new regimen he had 2 glasses of wine there after he fainted in the bathroom. That was the moment when he realized this was his last treatment option and he did not want to ruin this chance.

At the beginning of the ENF treatment, Mr. Angeli had been referred to the local HIV Agency for help with his paperwork and financial issues. He also received community services for cleaning because he was too weak to do it himself. The HIV Agency paid for both services. After his HIV-infection and depression were better controlled he took over both tasks independently.

Issues during counseling shifted to disclosure of his HIV-positive status. During this time Mr. Angeli disclosed his HIV-positive status to two close friends and brought them to the outpatient clinic. In an interactive session they received information about HIV infection from Mr. Angeli and the nurse. During the conversation, Mr. Angeli demonstrated how much he had learned and that he had become quite knowledgeable about his HIV infection. His friends were very touched and willing to give support where needed.

The nurse and physician met regularly to discuss the Mr. Angeli's progress and upcoming problems. The joint brief sessions with him after 3 and 6 months demonstrated that the initial plan with interventions related to adherence symptom management and social support had been successful. While Mr. Angeli enhanced his self management skills, his clinical markers (CD4/VL) improved, his symptoms were controlled and his subjective quality of life increased significantly. The interdisciplinary approach and shared process with him allowed adaptation of the interventions to the ever-changing clinical situation.

Discussion and implications for practice

This case illustrates how a patient with many adherence-related barriers and multiple genotypic drug resistances was able to adhere to a complex ART regimen, which led to a significant improvement in his health status. Former adherence related interventions during the patient's outpatient clinic visits had failed. Those interventions had predominantly focused on acute problems: for example a high pill burden from the patient's perspective or a failing regimen from the provider's perspective. Clinical strategies used had been based on advice and education by different providers without structured follow-ups. Mr. Angeli's outcomes demonstrated that this approach was not sufficient. We suggest that in our case, the highly structured multilevel approach over time, with culturally relevant information and skill building strategies, was pivotal for the improvements his in health outcomes. This is in accordance with the existing literature, which concludes that knowledge of ART is a necessary component of adherence, yet educational strategies alone are not sufficient in promoting adherence. In addition, motivational, cognitive, behavioural, and affective strategies have to be included in repetitive interventions (Reynolds, 2004). We propose that such interventions should be included early in the treatment process in order to prevent treatment failure due to adherence problems.

Planning and implementation of the above described multilevel approaches in clinical practice is demanding, as many issues have to be assessed and different providers have to coordinate their interventions. We used the Self Regulatory HIV Symptom Management Model (SSMM-HIV) to understand the relationships between key factors influencing adherence to ART and HIV-related management. The SSMM-HIV, developed by our team and described elsewhere (Spirig et al. 2005), provided a framework for assessment of key factors influencing Mr. Angeli's symptom management and adherence. Whereas the SSMM-HIV helped to identify problem areas, for example medication management, interventions had to be further individualized. In the case of Mr. Angeli's problems with medication management, the mDOT approach was selected. Other patients might need different approaches. A patient's needs and feasibility of interventions related to different health care settings have to be carefully considered. To date there is limited evidence showing which intervention strategy is most effective related to diverse problem behaviors or different groups of HIV-infected patients. More specific research in this area is needed. Meanwhile clinical expertise and good patient-provider communication seem to be essential for successful interventions. A DOT strategy may be viewed as intrusive and controlling by patients and thought of as paternalistic by professionals (Mitty et al. 2004). However, we chose the treatment regimen and adherence supportive intervention in collaboration with the patient. This enabled him to benefit from the structure of regular visits and counselling without feeling controlled. Less structural help was needed as he developed his self management skills and actively took over his medication management.

According to Bodenheimer et al. (2002), optimal chronic care is achieved when an informed, activated patient interacts with a prepared, proactive practice team. Further, the support of a larger network of health professionals has been identified as an adherence supporting factor (Reynolds, 2004). In our case an adherence specialization nurse and a physician at the HIV outpatient clinic, different community care nurses, and a social worker in town interacted with the patient. We suggest that not only the support of the different health care providers was important but also their collaboration and the coordination of interventions. In our case, it was the nurse’s role to coordinate interventions and to educate non-HIV specialized providers about key issues related to interaction with the patient. In complex clinical cases, orchestrated teamwork with broad HIV- and adherence-related knowledge and expertise are important issues for successful interventions. Further, teams need to be able to constantly evaluate and adapt their interventions to the clinical situation, since ART regimens have to be monitored closely. Adherence is being recognized as a dynamic behavior influenced by interrelated factors that change over time (Reynolds, 2004). For that, cases like Mr. Angeli’s are important because knowledge generated from reflection and critical review enhances the understanding of providers about adherence, adherence intervention, symptom management, and multidisciplinary collaboration. It is especially important that teams analyze such cases carefully in order to better understand patient behavior and provider support.

References

Altice, F. L., Mezger, J. A., Hodges, J., Bruce, R. D., Marinovich, A., Walton, M. et al. (2004). Development of a directly administrated antiretroviral therapy intervention for HIV-infected drug users: Implications for program replication. *Clinical Infectious Diseases, 38*(Suppl 5), 376-387.

Bangsberg, D.R., Charlebois, E.D., Grant, R.M., Holodniy, M., Deeks, S.G., Perry, S., et al. (2003). High levels of adherence do not prevent accumulation of HIV drug resistance mutations. *AIDS*, *17,* 1925-1932.

Bastardo, Y.M. & Kimberlin, C.L. (2000). Relationship between quality of life, social support and disease-related factors in HIV-infected persons in Venezuela. *AIDS Care*, *12* (5), 673-684.

Bjelland, I., Dahl, A. A., Haug, T. T., Neckelmann, D. (2002). The validity of the Hospital Anxiety and Depression Scale. An updated review. *Journal of Psychosomatic Research, 52* (2), 69-77.

Bodenheimer, T., Lorig, K., Holman, H. & Grumbach, K. (2002). Patient self-management of chronic disease in primary care. *JAMA*, *288*(19), 2469-2475.

Chou, F.Y., Kou, B. I., Lee, M., Chen, Y., Wu, S. & Lin, L. (2004). A program of symptom management for improving self-care for patients with HIV/AIDS.

Clotet, B., Raffi, F., Cooper, D., Delfaissy, J.F., Lazzarin, A., Moyle, G. et al. (2004). Clinical management of treatment-experienced, HIV-infected patients with fusion inhibitor enfuvirtide: consensus recommendations. *AIDS, 18,* 1137-1146.

Di Matteo, R.M. (2004). Social support and patient adherence to medical treatment: A meta-analysis. *Health Psychology, 23*(2), 207-218.

Elzi, L., Kaufmann, G., Weber, R., Hirschel, B., Cavassini, M., Furrer, H. et al. (2005). Long term (144 weeks) efficacy and safety of Enfurvirtide (T-20) in the Swiss HIV Cohort Study. 3rd IAS, Rio de Janeiro, Brazil, 24-27July.

Fehr, J., Nicca, D., Sendi, P., Wolf, E., Wagels, T., Kiss, A., et al. (2005). Starting or changing therapy—a prospective study exploring antiretroviral decision-making. Infection, 33, 249-256.

Fogarty L., Roter D., Larson S., Burke, J., Gillepsie, J. & Levy, R. (2002). Patient adherence to HIV medication regimens: A review of published and abstract reports. *Patient Education and Counselling, 46*, 93-108.

Gifford A.L., Laurent, D.D., Gonzales, V.M., Chesney, M.A. & Lorig, K.R. (1998). Pilot randomized trial of education to improve self-management skills of men with symptomatic HIV/AIDS. *Journal of Acquired Immune Deficiency Syndromes*, *18*, 136-144.

Highstein, G. R., Willey, C. & Mundy, L. M. (2006). Development of stage of readiness and decisional banlance instruments: Tools to enhance clinical decision-making for adherence to antiretroviral therapy. *AIDS and Behavior*, *10*(5), 563-573.

Kempner, T. (2005). Development of nursing guidelines for the administration of Enfurvirtide. *Journal of the Association of Nurses in AIDS Care*, *16*(2), 49-51.

Macalino, G. E., Mitty, J. A., Bazerman, L. B., Singh, K., McKenzie, M. & Flanigan, T. (2004). Modified directly observed therapy for the treatment of HIV-seropositive substance users: lessons learned from a pilot study. *Clinical Infectious Diseases, 38*(Suppl 5), 393-397.

Mathews, W. C., McCutchan, J. A., Asch, S., Turner, B. J., Gifford, A. L., Kuromiya, K., et al. (2000). National estimates of HIV-related symptom prevalence from the HIV cost and services utilization study. *Medical Care, 38* (7), 750-762.

Mitty, J.A. & Flanigan, T.P. (2004). Community based interventions for marginalized populations. *Clinical Infectious Diseases*, *38*(Suppl 5), 373-375.

Reynolds, N. R. (2004). Adherence to antiretroviral therapies: State of the science. *Current HIV Research*, *2*, 207-214.

Schneider, J., Kaplan, S.H., Greenfield, S., Li, W. & Wilson, I.B. (2004). Better physician-patient relationships are associated with higher reported adherence to antiretroviral therapy in patients with HIV infection. *Journal of General Internal Medicine, 19*, 1096-1103.

Schwarzer, R., Bäßler, J., Kwiatek, P., Schröder, K., & Zhang, J. X. (1997). The assessment of optimistic self-beliefs: Comparison of the German, Spanish, and Chinese versions of the General Self-Efficacy Scale. *Applied Psychology: An International Review, 46*(1), 69-88.

Spirig, R., Moody, K., Battegay, M. & De Geest, S. (2005). Symptom management in HIV/AIDS: advancing the conceptualization. *Advances in Nursing Science, 28*(4), 333-344.

Spirig, R. (2002). In invisibility and isolation:The experience of HIV-affected families in German-speaking Switzerland. *Qualitative Health Research, 12*(10), 1323-1337.

Vogl, D., Rosenfeld, B., Breitbart, W., Thaler, H., Passik, S., McDonald et al. (1999). Symptom prevalence, characteristics, and distress in AIDS outpatients. *Journal of Pain and Symptom Management*, 18(4), 253-262.

World Health Organisation (2003). *Adherence to long-term therapies: Evidence for action*. Geneva: WHO.

World Health Organisation (2001). *AUDIT The Alcohol Use Disorders Identification Test: Guidelines for Use in Primary Care*: Geneva: WHO.

Yeni, P.G., Hammer, S.M., Hirsch, S.M., Saag, M.S., Schechter, M., Carpenter, C.C., et al. (2004). Treatment for adult HIV infection 2004 Recommendations of the International AIDS Society-USA Panel. *JAMA, 292* (2), 251-265.

Young, J., De Geest, S., Spirig, R., Flepp, M., Rickenbach, M. & Furrer, H., et al. (2004). Stable partnership and progression to AIDS or death in HIV-infected patients receiving highly active antiretroviral therapy: Swiss HIV Cohort Study. *BMJ, 328*, 1-6.

Chapter 4

Literaturzusammenfassung zur Frage: „Welche Interventionen bewirken eine Verbesserung der Adhärenz von HIV-Patienten unter ART?“

Interventions to Enhance Adherence of Patients with HIV on ART: A Literature Review

Sabine Bigler[1,2], Dunja Nicca[1,2,3], Rebecca Spirig[1,2]

[1]Abteilung Klinische Pflegewissenschaft, Universitätsspital Basel, Schweiz

[2] Institut für Pflegewissenschaft, Universität Basel, Schweiz

[3] Infektiologie, Kantonsspital St. Gallen, Schweiz

Corresponding author, email: rspirig@uhbs.ch

Published in: Pflege, 2007, 20 (5), p. 268-277

Zusammenfassung

Durch die Entwicklung einer hochwirksamen antiretroviralen Kombinationstherapie der HIV Infektion konnte die Lebenserwartung und die Lebensqualität vieler HIV positiver Menschen im Vergleich zu vor 10 Jahren massgeblich verbessert werden. Diese positive Entwicklung wird dadurch beeinträchtigt, dass viele Betroffene nicht best möglich von der Therapie profitieren können, da eine Vielzahl von Faktoren dazu beitragen, dass ihre Adhärenzrate nicht im optimalen Bereich liegt. Dies kann unter anderem zu therapieresistenten Mutationen des Virus führen. Sowohl Ärzte und Ärztinnen, wie auch das Pflegefachpersonal sind deshalb gefordert, eine angepasste und wirkungsvolle Unterstützung mit dem Ziel einer Adhärenzverbesserung zu bieten. Evidenzbasierte Empfehlungen, wie solche Interventionsprogramme für die Praxis konkret aussehen sollen fehlen bislang. Diese Literaturzusammenfassung geht ausgehend von randomisierten kontrollierten Studien der Frage nach, wie Interventionsprogramme aufgebaut und welche Elemente darin enthalten sein sollen, damit die Adhärenz der Patienten best möglich unterstützt und gesteigert werden kann. Es zeigt sich, dass Interventionsprogramme wirkungsvoller sind, wenn sie verschiedene methodische Ansätze kombinieren und theoriebasiert sind. Für die Praxis kann empfohlen werden, den Patienten zusätzlich zu generalisierten Kurzinterventionen eine kontinuierliche und auf ihre jeweilige individuelle Situation angepasste Betreuung zukommen zu lassen.

Abstract

The introduction of potent antiretroviral therapy led to a reduction of HIV associated mortality and morbidity in industrial countries. HIV infection has changed from a lethal disease to a chronic illness that can be treated effectively. It can be assumed, that people who receive correct treatment now have a normal life expectancy. However one of the most crucial predictors to ensure the effectiveness of ART is a nearly perfect adherence to the medication regime. Evidence based guidelines on adherence intervention programs are missing so far. This literature review summarizes the evidence resulting of randomised controlled trials which were conducted to enhance medication adherence to antiretroviral therapy. It shows that effective programs need to combine several methods. Generalized short term interventions are easier to be tested by randomized controlled trials. However, for nursing guidelines we suggest long term programs which are tailored to the need of the patient.

Einleitung

Die Immunschwächekrankheit HIV / AIDS war lange Zeit eine Krankheit, welche nicht effektiv therapiert werden konnte. Seit der Entwicklung der hochaktiven antiretroviralen Kombinationstherapien (Highly Active Antiretroviral Therapy [ART]) Mitte der 1990er Jahren konnte in Industrieländern die Mortalität bis ins Jahr 2004 um 86% gesenkt werden [1]. Unter der Behandlung von ART können die Betroffenen ein Absinken der Viruslast und ein Anstieg der CD4 Zellzahl erfahren; verbunden mit weniger Hospitalisationen und einem langsameren Fortschreiten der Krankheit hin zu AIDS [140, 141]. HIV / AIDS hat sich damit zu einer behandelbaren chronisch verlaufenden Krankheit gewandelt, mit deren Symptomen und Anforderungen die Betroffenen und ihre Bezugspersonen umgehen und leben lernen müssen.

Der Erfolg der Therapie ist jedoch nicht ohne Vorbehalte garantiert und kann z.B. durch Medikamentenresistenzen limitiert werden. Diese entstehen durch ungenügende Wirkstoffspiegel, welche unter anderem durch Interaktionen und Malabsorptionen der Medikamente verursacht werden und deshalb von Patient zu Patient[3] variieren. Einer der wichtigsten Einflussfaktoren auf den Wirkstoffspiegel stellt die Therapietreue der Patienten (im Folgenden Adhärenz[4] genannt) dar, indem dieser schon durch die kleinste Abweichung vom verordneten Regime absinken kann [44, 141, 143, 144]. Eine ungenügende Adhärenzrate hat damit aber nicht nur negative Auswirkungen auf das Individuum, sondern ebenso auf die Epidemie als Ganzes, da vermehrt Übertragungen mit teilresistenten HIV Viren stattfinden.

Trotz der ernst zu nehmenden Auswirkungen einer mangelhaften Therapiebefolgung, ist der Anteil von Patienten, welche eine Adhärenzrate von 95% nicht erreichen in der HIV Population hoch. Je nach Definition und Messmethode liegt er zwischen 20% und 50% [142]. In der Schweiz konnte mittels einer Erhebung mit einem Fragebogen gezeigt werden, dass 31.1% der Patienten mindestens eine Medikamenteneinnahme im Monat vergessen [145].

Die Gründe für eine mangelhafte Adhärenz sind mannigfaltig. Eine grosse Anzahl Studien untersuchte im Verlauf der letzten Jahre Faktoren, die Einfluss auf das Adhärenzverhalten der HIV Patienten ausüben [6, 146, 147]. Analog dem WHO Schema [142] finden sich verschiedene patienten-, sowie therapie- und krankheitsbezogene Faktoren, welche stark negativ mit der Adhärenz korrelieren, wie z.B. ein fehlender Glaube in die Therapie, Depression, aktiver Drogen- und Alkoholkonsum, die Komplexität der Therapie oder unerwünschte kurz- und langfristige Arzneimittelwirkungen [120, 140, 148-154]. Positiv mit der Adhärenzrate korrelieren ein gutes Verhältnis zwischen dem Patienten und

---

[3] Im Text wird die männliche Form ‚Patient' stellvertretend für beide Geschlechter verwendet.

[4] Die World Health Organisation 142. WHO, *Adherence to long-term therapies. Evidence for action.* 2003. definiert Adhärenz als „das Ausmass, mit welchem das Verhalten eines Patienten mit den Empfehlungen übereinstimmt, die er von einer Person aus dem Gesundheitsbereich erhalten und mit denen er sich einverstanden erklärt hat." (WHO 2003).

dem Arzt / dem Betreuungsteam, sowie regelmässige Nachkontrollen. Klare Instruktionen zur Verwaltung der Medikamente und Wissen zur Krankheit und zum Zusammenspiel von Adhärenz und Krankheitsverlauf sind ebenfalls Faktoren, welche signifikant positiv mit der Adhärenz korrelieren [155, 156]. Sozioökonomische Faktoren, wie z.B. Alter, Geschlecht, Einkommen oder Bildungsstand zeigen dagegen in den verschiedenen Studien keine konstante Korrelation mit der Adhärenz [6, 155].

Heute, 10 Jahre nach der Entwicklung von ART, liegt der Fokus vieler Beteiligten weniger auf der Untersuchung der Einflussfaktoren als vielmehr auf der Entwicklung wirkungsvoller Interventionsprogramme, welche zum Ziel haben, die Patienten bei der regelmässigen und korrekten Einnahme der Medikamente zu unterstützen und so eine hohe Adhärenzrate zu gewährleisten. Viele dieser Programme sind dabei explizit auf die oben beschriebenen Einflussfaktoren der Adhärenz ausgerichtet. Im Verlauf der letzten Jahre wurden mittels experimenteller randomisierter Studien diverse Interventionsprogramme wissenschaftlich getestet. Diese Literaturzusammenfassung will eine Übersicht über die Ergebnisse solcher publizierter Interventionsprogramme und deren Implikationen für die Praxis geben. Die Frage, welcher dabei nachgegangen wird, lautet: „Welche Interventionen bewirken eine Verbesserung der Adhärenz von HIV Patienten unter ART?“

Literatursuche

Um diese Suchfrage beantworten zu können, wurde von April bis August 2005 die nachfolgend beschriebene Literatursuche durchgeführt. Die Artikel wurden anhand folgender Einschlusskriterien ausgewählt:

- Die Probanden sind erwachsene HIV Patienten, die mit ART therapiert werden
- Der Publikationstyp ist entweder eine kontrollierte experimentelle Interventionsstudie (randomized controlled trial [RCT]) mit dem Ziel einer Adhärenz- Steigerung (Primärliteratur) oder eine Literaturzusammenfassung (Review) solcher Interventionsstudien.

Der Grund für die Einschlusskriterien liegt darin, dass bei diesen das höchste Evidenzniveau erwartet werden kann. Metaanalysen sind bezüglich der formulierten Zielfrage keine vorhanden. Ausgeschlossen wurden Machbarkeitsstudien und Pilotstudien.

Die Literatur-Suche wurde auf den Suchmaschinen PubMed / MEDLINE, PsychINFO und der Cochrane Library durchgeführt, wobei sich auf PsychINFO keine Artikel fanden und die Cochrane Library nur eine Review als Ergebnis lieferte. Als Suchbegriffe verwendet wurde HIV, ADHERENCE, COMPLIANCE und INTERVENTION. Die Suche mit den Stichworten HIV + INTERVENTION + ADHERENCE OR COMPLIANCE auf PubMed ergab 65558 Resultate, weshalb die Suche in Kombination mit Compliance rsp. Adherence einzeln durchgeführt wurde: HIV + INTERVENTION + COMPLIANCE ergab 175 Resultate, wobei bei inhaltlicher Durchsicht festgestellt wurde, dass es sich fast nur um unerwünschte Titel handelte, da sie sich vor allem auf die Wirksamkeit von Wirkstoffen konzentrierten. Die Suche nach HIV + INTERVENTION +

ADHERENCE dagegen zeigte 151 Resultate, welche gemäss der oben genannten Einschlusskriterien gesichtet wurden. Insgesamt fanden sich in der Literatursuche 13 RCTs und vier Reviews.

Da die Autorinnen in einem Verb und von Interessenten betreffend der Problematik der Adhärenz von HIV Patienten sind, wurden sie auf eine weitere Literaturzusammenfassung von Simoni, Frick, Pantalone und Turner [157] aufmerksam gemacht, welche in Form eines Buchkapitels veröffentlicht worden ist. In dieser Review haben Simoni et al. ihre vorhergehende Literaturzusammenfassung vom Jahr 2003 bis zum Januar 2005 aufdatierten. Da diese Review ebenfalls den Suchkriterien entsprach, wurde sie zusätzlich in die Ergebnisse mit einbezogen. Es zeigte sich, dass die von uns gefundenen RCTs bis auf einer später erschienenen Studie alle in dieser Review aufgeführt wurden.

Beschreibung der Studien

Nachfolgend werden die Resultate aus der Literatur-Suche beschrieben, welche in ausführlicherer Form in der Tabelle 1 dargestellt sind.

Die fünf Reviews und die darin beschriebenen Interventionsprogramme werden in chronologischer Abfolge dargestellt und anschliessend durch die aktuellere Interventionsstudie ergänzt. Nebst dem gesuchten Effekt auf die Adhärenz wird jeweils auch angegeben, ob gleichzeitig eine signifikante Verbesserung der klinischen Werte, wie z.B. eine Reduktion der Viruslast oder ein Anstieg der CD4+ Zellzahl vermerkt werden konnte. Diese klinischen Parameter wurden in den meisten Studien nebst der Adhärenzrate als zweite Outcome-Variabel erhoben.

Haddad, Inch, Glazier, Wilkins, Urbshott, Bayoumi & Rourke [158] beschreiben nebst sechs Kurzbeschreibungen als einzige publizierte Studie diejenige von Knobel, Carmona, Lopez, Gimeno, Saballs, Gonzalez, Guelar & Diez [159]. Dabei wurde in einem durch Pharmazeuten geleiteten RCT versucht, mittels Schulungen und telefonischer Nachbetreuung die Adhärenz der Patienten zu steigern. Die Adhärenzrate unterschied sich signifikant zwischen den beiden Gruppen, während aber die Unterschiede in der Viruslast nicht signifikant waren. Die Literaturzusammenfassung von Fogarty et al. [146] stellt 16 Interventionsprogramme vor, von welchen die einzigen vier publizierten RCTs erst als Pilotstudien vorlagen. Lediglich eine dieser Pilotstudien wies einen signifikanten Effekt auf die Adhärenz auf, welcher allerdings nur temporär anhaltend war [160]. Eine weitere Literaturzusammenfassung beschreibt RCTs, welche bis 2002 publiziert oder an der internationalen AIDS Konferenz in Barcelona im Juli 2002 vorgestellt worden waren [161]. Darin werden die drei publizierten Artikel von Knobel et al. (1999), Tuldra, Fumaz, Ferrer, Bayes, Arno, Balague, Bonjoch, Jou, Negredo, Paredes, Ruiz, Romeu, Sirera, Tural, Burger & Clotet et al. [162] und Rigsby, Rosen, Beauvais, Cramer, Rainey, O'Malley, Dieckhaus & Rounsaville [163], sowie vier RCTs aus der Konferenz vorgestellt. Die Intervention in der Studie von Tuldra et al. (2000) war psychoedukativer Art und bestand aus vier Behandlungen. Nach 48 Wochen erreichten 94% der Teilnehmer der Interventionsgruppe eine Adhärenzrate von mindestens 95%, während dies in der Kontrollgruppe nur 69% waren. Die Teilnehmer der Interventionsgruppe zeigten auch eine tiefere Viruslast. Die

Unterschiede in der Adhärenz erreichten jedoch nicht statistische Signifikanz. Rigsby et al., (2000) führten eine Intervention durch, bei welcher die Patienten angeleitet wurden, ihre Medikamente an eine fixe Aktivität zu koppeln (cue dose training), mit dem Ziel weniger Einnahmen zu vergessen. Dabei erhielt eine Gruppe zusätzlich eine monetäre Entlöhnung, wenn die Adhärenzrate zufrieden stellend war. Resultat: Nur die Gruppe mit der zusätzlichen Entlöhnung zeigte eine signifikant erhöhte Adhärenz, welche in einer späteren Kontrollmessung ebenfalls nicht mehr nachgewiesen werden konnte.

Die aktuellsten Reviews sind diejenigen von Simoni, Frick, Pantalone & Turner [164] und (2005), welche die vorhergehenden Reviews bis zum Januar 2005 aufdatieren und auch nach laufenden Studien suchen, welche durch den amerikanischen Nationalfonds unterstützt werden. In der Literaturzusammenfassung von 2003 finden sie nebst den bereits erwähnten drei Reviews 21 publizierte Studien und 39 laufende Studien. Unter den publizierten Studien befinden sich eine Pilotstudie und vier weitere RCTs: Das Kurzinterventionsprogramm von Safren, Otto, Worth, Salomon, Johnson, Mayer & Boswell [165] enthielt lediglich eine Einzellektion, basierend auf kognitiver und verhaltensorientierter Therapie und auf Techniken der motivierenden Gesprächsführung. Die Interventionsgruppe erfuhr einen anhaltenden, signifikanten Adhärenzanstieg. In einer weiteren Studie wurden die Probanden der Interventionsgruppe häufiger über ihre HIV-1 RNA Werte informiert als diejenigen der Kontrollgruppe [166]. Diese Intervention zeigte keinen Effekt auf das Adhärenz Verhalten. Mann [167] wählte für seine Interventionsstudie einen gefühlsorientierten Ansatz: die Teilnehmer wurden aufgefordert, zwei Mal pro Tag positive Gedanken bezüglich der Zukunft und ihrer Therapie aufzuschreiben. Diese Studie zeigte ebenfalls keine signifikanten Ergebnisse.

In der aufdatierten Review von Simoni et al. [157] finden sich bereits 15 RCTs, darunter drei Pilotstudien, und 51 laufende Studien, was deutlich aufzeigt, wie stark das Interesse an dieser Frage innerhalb dieses Zeitraumes zugenommen hatte. Smith, Rublein, Marcus, Brock und Chesney [168] führten mit 43 Probanden eine kontrollierte randomisierte Intervention durch, welche eine Entwicklung von Fertigkeiten in den Bereichen Zielsetzung, Selbstkontrolle, Selbstbelohnung und soziale Unterstützung enthielt und während drei Monaten je eine Visite beinhaltete. Die Intervention zeigte zwar, dass die Probanden im Vergleich zur Kontrollgruppe eine höhere Selbstwirksamkeit[5] entwickeln konnten und eine signifikant höhere Adhärenzrate hatten; die beiden Gruppen unterschieden sich in der Viruslast jedoch nicht signifikant. Die Studie ist unter anderem auch deshalb interessant und wegweisend, weil die Entwicklung des Interventionsprogrammes theoriebasiert erfolgte indem sie sich auf die ‚social cognitive theory' stützt [170]. Goujard, Bernard, Sohier,

---

[5] Mit dem Begriff der Selbstwirksamkeit (self-efficacy) bezeichnet man die individuelle Überzeugung, dass man in einer bestimmten Situation die angemessene Leistung erbringen kann 169. Bandura, A., *Social foundations of thougt and action: A social cognitive theory.* 1986, NJ: Prentice Hall: Englewood Cliffs..

Peyramond, Lancon, Chwalow, Arnould & Delfraissy [171] führten ein Schulungsprogramm durch, welches auf das Wissen der Patienten und den organisatorischen Umgang mit der Therapie (Erinnerungshilfen, Medikamentendispenser,...) gerichtet war. Die Resultate zeigten eine Verbesserung der Adhärenz und der Gesundheitssituation, nicht jedoch einen signifikanten Unterschied in den klinischen Werten zwischen Interventions- und Kontrollgruppe. Rawlings, Thompson, Farthing, Brown, Racine, Scott, Crawford, Goodwin, Tolson, Williams & Shaefer [172] beschreiben eine aufwändige Schulung mit 11 Modulen, die sowohl die Patienten, wie auch deren Bezugspersonen besuchten (Bestärkung zur Zielerreichung mit Wissensvermittlung und Vermittlung von Fähigkeiten zur Verbesserung von Selbstpflege, Adhärenz, Lebensqualität und Zufriedenheit). Die Studie konnte keinen Unterschied zwischen Interventions- und Kontrollgruppe aufzeigen, weder in der Adhärenzrate noch in den klinischen Werten. Auch in der Studie von Pradier, Bentz, Spire, Tourette-Turgis, Morin, Souville, Rebillon, Fuzibet, Pesce, Dellamonica & Moatti [173] wurde der Interventionsgruppe empathische individuelle Beratung und Schulung zuteil, die das Gefühl der Selbstwirksamkeit stärken sollte. Die Interventionsgruppe zeigte in der Nachkontrolle einen anhaltend höheren Anteil an adhärenten Patienten und eine signifikante Abnahme der Viruslast. In einer anderen Studie wurde ein Pager als Erinnerungshilfe für die Medikamenteneinnahem eingesetzt. Auch hier zeigte sich eine signifikante Adhärenz Steigerung in der Interventionsgruppe [174]. In zehn Gruppenlektionen wurde in der Studie von Jones, Ishii, LaPerriere, Stanley, Antoni, Ironson, Schneiderman, Van Splunteren, Cassells, Alexander, Gousse, Vaughn, Brondolo, Tobin & Weiss [175] durch Therapeuten Stressmanagement und Ausdruckstherapie vermittelt. Die Kontrollgruppe erhielt eine ähnliche Schulung mittels Video-Lektionen. Es konnten keine signifikanten Gruppenunterschiede erkannt werden.

Ergänzend wird noch die Studie von Remien, Stirratt, Dolezal, Dognin, Wagner, Carballo-Dieguez, El-Bassel & Jung [132] beschrieben, die wir in unserer Literatursuche zusätzlich gefunden haben. Diese führten eine paarfokussierte Intervention durch und verwendete das von ihnen entwickelte SMART Programm (sharing medical Adherence Responsibility together), welches auf der social action theory von Ewart, (1991) basiert. Es beinhaltet Schulungen zum Wissen über die Krankheit und die Therapie und soll dazu dienen, Schwierigkeiten in der Befolgung der Therapie aufzudecken und Strategien zur Problemlösung und Kommunikation zwischen dem Patienten und seiner Bezugsperson zu entwickeln, mit dem Ziel einer optimierten Unterstützung durch den Partner und einem erhöhten Vertrauen in die Selbstwirksamkeit. Es konnte zwar eine Adhärenz-Steigerung ausgemacht werden, die Adhärenzrate lag aber weiterhin im suboptimalen Bereich und fiel in den Nachkontrollen nach drei und sechs Monaten wieder ab.

Autor, Jahr,	**Stichprobe**	**Intervention**	**Resultate**
Knobel et al., 1999	Patienten aus Barcelona mit einer Viruslast >5'000 und CD4 Zahl < 200 N=170	Gruppe 1: Eine Einzellektion mit einem Pharmazeuten welcher ein individuelles Assessment durchführte und Ratschläge abgab und telefonische Unterstützung anbot n=60 Gruppe 2: Kontrollgruppe mit Standardbetreuung n=110	Nachkontrolle nach 24 Wochen: - Adhärenzrate über 90% bei 77% der Teilnehmer von Gruppe 1 gegenüber 53% in Gruppe 2 p<.002 - Keine Gruppenunterschiede bezüglich einer nicht nachweisbaren Viruslast
Tuldra et al., 2000	Konsekutive Patienten, welche die erste oder zweite antiretrovirale Behandlung begonnen N=116	Gruppe 1: eine Einzellektion durch einen Psychologen über die Wichtigkeit von Adhärenz und darüber, wie ausgehend von der Selbstwirksamkeits- Theorie mit Problemen bezüglich der Adhärenz umgegangen werden kann. Bei den nachfolgenden Sitzungen nach 4, 24 und 48 Wochen wurde die Adhärenz erneut betont und es wurden spezifische Probleme angegangen n=55 Gruppe 2: Kontrollgruppe mit Standardbetreuung n=61	Nachkontrolle nach 48 Wochen (N=70): - 94% der Gruppe 1 erreichten eine selbst rapportierte Adhärenz Rate von mindestens 95%, gegenüber 69% in der Gruppe 2 - 89% der Gruppe 1 zeigten HIV-1 RNA Levels von höchstens 400 Stk/ml, gegenüber 66% in der Gruppe 2
Rigsby et al., 2000	Hauptsächlich männliche Afro Amerikaner mit vorgängigem Drogenkonsum aus West Haven und Hartford, CT N=55	Während einem Monat jede Woche eine Lektion über: Gruppe 1: Durch einen Berater geführte cue dose Trainings (Patienten stellten tägliche Hilfestellungen auf, die sie an die Medikamenteneinnahme erinnern) und Rückmeldungen der EEM[6] Messung n=22 Gruppe 2: Dasselbe plus eine wöchentliche monetäre Belohnung für zeitlich korrekte Medikamentenflaschenöffnungen Gruppe 3: Kontrollgruppe, mit Ermutigung bezüglich der Adhärenz.	- Während der Intervention (Woche 0 bis 4) zeigte nur die Gruppe 2 eine höhere Adhärenz im Vergleich zur Kontrollgruppe - In den Nachkontrollen (Woche 5 bis 12) zeigte die Gruppe 2 einen signifikanten Adhärenz Rückgang im Vergleich zur Kontrollgruppe (Gruppe 1 nicht)
Haubrich et al., 2001	Vorwiegend Patienten mit geringem Einkommen von fünf der Universität angegliederten HIV Kliniken in Kalifornien N=206	Gruppe 1: während einem Jahr alle zwei Monate Rückmeldung zu den HIV-1 RNA Werten Gruppe 2: halbjährliche Rückmeldungen dazu	- Es konnten keine signifikanten Unterschiede in der selbst rapportierten Adhärenz und der CD4 Zahl zwischen den Gruppen beobachtet werden - Gruppe 1 wies im Vergleich mit der Gruppe 2 eine signifikant grössere Reduktion der Viruslast auf (p=.003)

---

[6] electronic event monitoring (EEM) ist eine Messmethode der Adhärenz

Autor, Jahr,	Stichprobe	Intervention	Resultate
Mann, 2001	Multiethnische Frauen mit tiefem sozioökonomischem Status (40% Afro Amerikanerinnen, 35% Hispanic) N=44	Gruppe 1: Pro Tag mindestens zwei Mal je 10 Minuten über das Thema „eine positive Zukunft, in welcher ich zur Behandlung von HIV täglich nur eine Tablette einnehmen muss“ schreiben n=21 Gruppe 2: Keine Schreibübung n=23	Nachkontrolle nach 4 Wochen: - diejenigen Probanden mit tiefer Adhärenz zeigten einen (nicht signifikanten) Trend Richtung einer höheren Adhärenz, während die Probanden mit hoher Ausgangsadhärenz eine Verschlechterung der Adhärenzrate zeigten.
Safren et al., 2001	Patienten aus der Gemeindepflege in Boston, welche als gefährdet angesehen werden für eine Non-Adhärenz weil sie entweder einen Therapiestart oder eine –änderung erlebten oder in der Visite in den letzten zwei Wochen vor dem Einschluss eine Adhärenz von weniger als 100% rapportierten N=56	Gruppe 1: Eine Einzellektion durch einen Arzt oder via Videoband basierend auf kognitiver und verhaltensorientierter Therapie, Problemlösungsstrategien und Techniken aus der motivierenden Gesprächsführung und einer telefonischen Nachbetreuung nach einer Woche n=30 Gruppe 2: Minimaler Kontakt während zwei Wochen und Selbstkontrolle durch ein Medikamententagebuch n=26	Nachkontrolle nach zwei Wochen: - Gruppe 1 rapportierte einen signifikanten Anstieg der Adhärenz seit den Ausgangsdaten (von 74% auf 95%), während in der Gruppe 2 eine minimale Zunahme von 84% auf 90% stattfand. Nachkontrolle nach 12 Wochen: Die Adhärenzraten waren konstant gegenüber Woche 2
Goujard et al., 2003	Patienten aus verschiedene Kliniken in Frankreich, N=367	Gruppe 1: Ärzte und Pflegefachpersonal mit speziellem Vorbereitungstraining entwickeln eine individuellen Schulungsplan, basierend auf den persönlichen Schwierigkeiten bezüglich der Adhärenz, bestehend aus einer Zeitplanung mit Aufkleber, drei einstündigen Schulungslektionen und einem Medikamentendispenser. N=188 Gruppe 2: Kontrollgruppe n=179	Nachkontrolle nach 6 Monaten: Die Teilnehmer der Interventionsgruppe zeigten eine signifikante Zunahme der Adhärenz zwischen Ausgangsmessung und sechs Monaten, welche nach 12 und 18 Monaten beibehalten wurde. - Keine direkte Auswirkung auf die Viruslast oder CD4 Zahl.

Autor, Jahr,	**Stichprobe**	**Intervention**	**Resultate**
Jones et al., 2003	Multiethnische Teilnehmerinnen (54% Afro Amerikaner, 18% Hispanics) aus Florida, New York und New Yersey N= 174	Gruppe 1: Zehn Gruppen-Lektionen mit Therapeuten über kognitives und verhaltensorientiertes Stressmanagement und unterstützende Ausdruckstherapie n=92 Gruppe 2: Video-Lektionen mit ähnlichem Inhalt, aufgeteilt in 10 Lektionen à 45 Minuten Schulung und 75 Minuten Unterhaltung n=82	Nachkontrolle nach 15 Monaten: - keine signifikante Unterschiede in der Adhärenz zwischen den Gruppen - Diejenigen mit sehr tiefer Adhärenz zeigten in beiden Gruppen nach der Intervention eine Adhärenz-Zunahme von 0-40% (Gruppe 1 p<.001 und Gruppe 2 p<.01)
Pradier et al., 2003	Patienten unter HAART welche in eine medizinische Nachkontrolle am Universitätsspital von Nizza kamen. N=246	Gruppe 1: dreimalige Einzellektion mit einer Pflegefachperson mit individueller Beratung und Schulung basierend auf motivierender Psychologie und patientenzentrierte emphatische Therapie mit dem Ziel, das Gefühl der Selbstwirksamkeit und weitere Fähigkeiten zu steigern n=124 Gruppe 2: Kontrollgruppe mit Standardbetreuung n=122	Nachkontrolle nach 6 Monaten: - Gruppe 1 zeigte einen signifikant höheren Anteil an adhärenten Patienten und eine signifikante Abnahme der Viruslast - Zwischen den Gruppen zeigte sich kein Unterschied in der nicht nachweisbaren Viruslast
Rawlings et al., 2003	HIV positive Frauen mit einer nachweisbaren Viruslast, rekrutiert aus 25 Kliniken N=195	Gruppe 1: Vier vorgegebene Module zu Schulung und Beratung mit Patientinnen und deren persönlichen Bezugspersonen plus Standardberatung betreffend Adhärenz durch einen Gesundheitsfachperson (health care provider) n=96 Gruppe 2: einfache Standardberatung betreffend Adhärenz n=99	Nachkontrolle nach 20 Wochen: - Kein Unterschied zwischen den beiden Gruppen zu keinem Zeitpunkt, weder in der selbst rapportierten noch in der durch EEM erhobenen Messung - Keine Unterschiede in virologischen Indikatoren beobachtet
Smith et al., 2003	Patienten einer Klinik in North Carolina, welche einen Therapiestart oder –wechsel erlebten N=43	Gruppe 1: Individuell gestaltetes Schulungsprogramm und Training von Fähigkeiten, durch eine Pflegefachperson oder einen Pharmazeuten in vier Sitzungen. Das Programm enthielt Informationenaustausch , Entwicklung von Fähigkeiten, Selbstkontrolle, Setzen von Zielen und soziale Unterstützung und Selbstbelohnungen n=22 Gruppe 2: Kontrollgruppe mit Standardtherapie n=21	Nachkontrolle nach 12 Wochen: - Gruppe 1 zeigte erhöhte und höhere Adhärenzwerte an als die Kontrollgruppe (p<.0017) - Bezüglich der virologischen Indikatoren konnten keine Gruppenunterschiede festgestellt werden

Autor, Jahr,	Stichprobe	Intervention	Resultate
Safren et al., 2003	Patienten aus der Gemeindepflege in Boston, USA, welche in der zweiwöchigen Adhärenz-Messung mit EEM eine Adhärenzrate von weniger als 90% aufwiesen N=44	Gruppe 1: Nachrichtensystem via Pager als Erinnerungshilfe für die Medikamenteneinnahme, die Mahlzeiten und die Arzttermine und EEM Messung ohne Rückmeldung n=34 Gruppe 2: Nur EEM Messung n=36	Am Ende der 12 wöchigen Intervention zeigte die Gruppe 1 eine signifikant höhere Verbesserung in der durch EEM gemessenen Adhärenz als die Gruppe 2 (p<.004)
Remien et al., 2005	Patienten von zwei ambulanten Kliniken in NY mit weniger als 80% Adhärenz und ihre Partner N=215	Gruppe 1: Vier Lektionen à 45-60 min innerhalb von 5 Wochen durch eine Pflegende mit dem selbst entwickelten Programm „sharing medical Adherence Responsibilities together” (SMART), basierend auf Ewart's social action theory. Das Programm beinhaltete Schulung über Therapie und Adhärenz, das Finden von Hindernissen bezügl. dem Erreichen einer guten Adhärenz, das Entwickeln von Kommunikations- und Problemlösungsstrategien, die Optimierung der Unterstützung durch den Partner und der Aufbau einer Zuversicht in das Erreichen einer optimalen Adhärenz n=106 Gruppe 2: Kontrollgruppe mit Standardtherapie n=109	Nachkontrolle nach 8 Wochen (zwei Wochen nach Intervention): - signifikant höhere Adhärenz in Gruppe 1,sowohl bezüglich der eingenommenen Dosen wie auch der zeitlichen Adhärenz, jedoch immer noch im suboptimalen Bereich Nachkontrollen nach drei und sechs Monaten: - kein nachweisbarer Effekt mehr

Zusammenfassung der Resultate

Die oben aufgeführten Interventionsprogramme werden nachfolgend bezüglich Methodologie, Interventionslänge und –ansatz (Einzel-, Paar-, Gruppensitzung) und dem Inhalt des Interventionsprogramms vergleichend dargestellt.

Methodologie

Die Zahl der Probanden in den Interventionsgruppen ist durchschnittlich 67, mit 21 als kleinste und 188 als grösste Anzahl. Sie ist vor allem in den früheren Studien häufig kleiner als 60 Personen, was die Erreichung einer statistisch genügend grossen Teststärke erschwert.

Die angewendeten Messmethoden zur Erhebung der Adhärenz sind je nach Studien unterschiedlich. Die Adhärenz wird sowohl elektronisch gemessen, was zurzeit als zuverlässigste Messmethode angesehen wird, wie auch durch Zählung der verbliebenen Anzahl Tablette bei der Arztvisite oder durch Fragebogen, welche sich wiederum im Umfang und dem Inhalt der Fragen stark unterscheiden. Der unterschiedliche Validitätsgrad der verschiedenen Messmethoden, welcher sich in verschieden hoher Sensitivität und Spezifität äussert, hat eine erhebliche Auswirkung auf die erhobene Adhärenzrate. Eine Vergleichbarkeit der Studien wird dadurch erschwert. Positiv ist zu vermerken, dass mit Ausnahme von Safren et al., 2003 bei allen Interventionsstudien regelmässige Nachkontrollen bis zu einem Jahr nach der Intervention statt fanden. Von den Studien, welche signifikante Effekte nachweisen konnten, waren die Nachkontrollen frühestens nach drei Monaten erfolgt. Bei dieser Zeitspanne kann man davon ausgehen, dass der Effekt längerfristig anhaltend ist.

Anzahl Sitzungen

Die Interventionsdauer unterscheidet sich in den verschiedenen Studien mit einer Spannbreite von einer bis zu mehr als 10 Sitzungen erheblich. Signifikante Erfolge verzeichneten dabei sowohl Kurzinterventionsprogramme von nur einer Sitzung, wie auch Programme mit zwei bis fünf Sitzungen. Von den drei Studien, welche mehr als fünf Sitzungen beinhalteten, wies allerdings keine einen signifikanten Effekt auf. Dies steht möglicherweise mit den Interventionsprogrammen in Zusammenhang: Die eine Intervention ist rein kognitiver Art; die anderen basieren auf standardisierten Schulungsprogrammen, in welchen kaum individuell angepasste Inhalte vermittelt werden können (Jones et al., 2003; Haubrich et al., 2001).

Ansatz der Intervention

Bei 10 der 13 Studien wurde das Programm einzig mit dem Patienten selbst durchgeführt; davon konnte in sieben eine signifikante Adhärenz-Steigerung nachgewiesen werden. Die beiden Programme, in welchen die Partner mit einbezogen wurden, wie auch die Gruppenintervention zeigten keinen, rsp nur einen kurzfristigen Erfolg. Dies kann wiederum damit zusammen hängen, dass bei zwei Studien ein generalisiertes Programm angeboten wurde, wodurch möglicherweise nicht genügend auf die jeweiligen Bedürfnisse der Probanden oder der Paare eingegangen werden konnte

(Jones et al., 2003; Remien et al., 2005). Darüber hinaus kann der Erfolg des Programms auch davon abhängen, wie gut die Intervention auf die spezifischen Charakteristika der jeweiligen Population der Probanden abgestimmt ist (Rawlings et al., 2003).

Art der Intervention

Insgesamt sind nur zwei der 13 Studien umfassend theoriegeleitet ausgearbeitet worden. Bei den anderen ist die Entwicklung der Intervention mangelhaft bis gar nicht beschrieben, obwohl diese häufig Elemente aus verschiedenen Modellen verwenden, wie z.B. die Selbstwirksamkeit oder die motivierende Gesprächsführung.

Bezüglich der Inhalte der Interventionsprogramme lässt sich die Entwicklungstendenz der letzen Jahre folgendermassen beschreiben: Während von den ersten Interventionsprogrammen bis 2001 die Hälfte relativ einfach konzipiert waren und beispielsweise ausschliesslich auf kognitiven oder emotionalen Inhalten basierten, weisen die neueren Programme ab 2001 in fünf von sieben Programmen einen breiten Ansatz auf, indem sie kognitive und verhaltensorientierte Schulung kombinierten. Es fällt auf, dass Interventionen, die verschiedene Ansätze kombinierten und auf eine Verhaltensänderung hinzielten häufiger zu einer signifikanten Adhärenz-Steigerung führten. Im weiteren lassen sich die Studien hinsichtlich dem Kriterium vergleichen, ob das Interventionsprogramm standardisiert oder individuell konzipiert ist: Von den acht Studien, welche ein individuell angepasstes Programm allein oder kombiniert mit standardisierten Inhalten anboten, zeigten sechs signifikante Erfolge bezüglich eines Adhärenz-Anstieges, während bei den standardisierten Programmen nur eines von fünf einen signifikanten Effekt aufweisen konnte.

Schlussfolgerung und Empfehlung

Die Adhärenz ist einer der wesentlichsten Einflussfaktoren einer erfolgreichen antiretroviralen Therapie. Die Pflegefachpersonen und Ärzte sind deshalb gefordert, den Patienten eine angepasste und wirkungsvolle Unterstützung mit dem Ziel einer Adhärenz Verbesserung zu bieten. Eine evidenzbasierte Empfehlung, wie solche Interventionsprogramme konkret aussehen sollen, fehlt jedoch bislang. Die hier beschriebenen randomisierten kontrollierten Studien zeigen Tendenzen auf, welche wichtige Hinweise für die Planung zukünftiger Praxisprogramme liefern. Der Nutzen der RCTs in Bezug auf die klinische Umsetzung, wie auch deren Limiten werden nachfolgend diskutiert.

Wie eingangs dargestellt wurde, handelt es sich bei der Adhärenz um ein komplexes Phänomen, welches vielen Einflussfaktoren unterliegt. Die Entwicklung der letzten Jahre zeigt, dass die ersten Interventionsprogramme dieser Komplexität zu wenig Rechnung trugen, indem sie sich primär auf den Patienten und kaum auf sein Umfeld konzentrierten und vor allem Interventionen im psychologischen und kognitiv-verhaltensorientierten Bereich anwendeten, wobei die Ansätze selten kombiniert wurden. In den letzten Jahren wurden die Interventionsprogramme zunehmend komplexer: Es wurden vermehrt individuell angepasste Programme angeboten, die kognitive und verhaltensorientierte Schulung kombinieren. Sie sind jedoch nach wie vor stark auf den Patienten ausgerichtet und kaum auf die weiteren Einflussfaktoren der Adhärenz wie sie die WHO (2003) formuliert hat. Angesichts der wichtigen Rolle, welche die soziale Unterstützung in einer effektiven Adhärenz-Erhaltung spielt, sollte bei zukünftigen Studien insbesondere vermehrt Augenmerk auf die fachliche Betreuung durch das Gesundheitspersonal und die soziale Unterstützung durch private Bezugspersonen gelegt werden.

In den Resultaten zeigt sich die Tendenz, dass Studien, die auf einem Modell basieren der Multidimensionalität besser Rechnung tragen und auch erfolgsversprechende Resultate zeigen. Dies kommt daher, weil die Adhärenz hierbei als Verhaltensänderung verstanden wird, die in engem Zusammenspiel mit Aspekten wie z.B. der Selbstwirksamkeit und Motivation steht, welche entsprechend ins Interventionsprogramm integriert werden. Bei der Mehrzahl der oben beschriebenen Studien liegt dem Interventionsprogramm aber kein theoretisches Modell zu Grunde, was als deutliches Manko bezeichnet werden kann und bei der Planung zukünftigen Studien beachtet werden soll.

Bezüglich der Interventionsdauer ist auffallend, dass komplexe Programme nicht nur bei Interventionen über einen längeren Zeitraum hinweg, sondern bereits in Form von Einzellektionen signifikante Effekte auslösen können. Ausgehend von den Resultaten könnte vermutet werden, dass Kurzinterventionen durchaus wirkungsvoll sein können, wenn sie in Form von generalisierten Programmen durchgeführt werden (Schulungen im Plenum, etc), während längerfristige Interventionen gezielt auf den individuellen Patienten zugeschnitten sein müssen, um seinen Bedürfnissen gerecht zu werden und ihn in seiner Verhaltensänderung angepasst und best möglich begleiten zu können.

Die beschriebene Tendenz in Richtung breit angelegter und individualisierter Programme die sich nach Sichtung der Studien zeigt, stimmt mit Schlussfolgerungen aus allgemeiner Literatur zu Adhärenz überein: Haynes, Montague, Oliver, McKibbon, Brouwers & Kanani [176] beschreiben in einer umfassenden Review, dass Wissensvermittlung zwar ein notwendiger Bestandteil eines erfolgreichen Adhärenz-Programms ist, die Schulungen alleine jedoch nicht genügen, um eine anhaltende Verhaltensänderung herbei zu führen. Er kommt zum Schluss, dass umfassende multidimensionale Interventionen effektiver zu sein scheinen. Diese zeichneten sich durch eine komplexe Kombination von Information, Erinnerungshilfen, Beratung, Selbstüberwachung, Bestärkung, Familientherapie und weitere Formen von supervisorischer Hilfe durch Fachpersonen aus.

Programme, die eine solche Komplexität aufweisen sind jedoch schwieriger zu testen, da sie den Anforderungen einer randomisierten kontrollierten Interventionsstudie kaum entsprechen können. Es gelingt zudem selten, grossen Gruppen von Patienten ein einheitliches Interventionsprogramm zukommen zu lassen, das bei allen Probanden unabhängig ihrer individuellen Situation eine gleichermassen effektive Wirkung zeigt. Dies kann als Limitation dafür verstanden werden, Interventionsprogramme mit dem Ziel einer Adhärenz-Steigerung mittels RCTs zu testen und mag nebst den methodologischen Mängeln ein Grund dafür sein, dass in den beschriebenen Studien oft nur kleine Interventionseffekte gemessen werden konnten. Insofern ist die Aussagekraft von RCTs bezüglich der Testung idealer Interventionsprogramme beschränkt. Trotzdem ist die Durchführung solcher Studien unumgänglich, da sie im Vergleich zu den deskriptiven Studien ein höheres Evidenzniveau aufweisen und ihre Resultate wegweisend für die Entwicklung von zukünftigen Praxisprogrammen sind.

Für die klinische Pflegepraxis bedeuten die obigen Schlussfolgerungen, dass die Praxisprogramme theoriebasiert erstellt werden sollen und verschiedene Methodenansätze beinhalten sollen. Optimistisch stimmt dabei der Umstand, dass auch standardisierte Kurzinterventionen gute Wirkung zeigen können, was angesichts der beschränkten Ressourcen ein wichtiger Aspekt für das klinische Arbeitsfeld darstellt. Hingegen bietet sich in der klinischen Pflegepraxis zudem die Möglichkeit, die Patienten kontinuierlich und auf ihre individuelle Situation angepasst zu betreuen, wodurch die Adhärenz noch wirkungsvoller unterstützt werden kann.

Bei der Implementation aller Praxisprogramme muss allerdings beachtet werden, dass auch hier eine vorausgehende Einschätzung der Adhärenz zentral ist und die mit der Intervention beauftragten Personen bezüglich der verschiedenen Programmelemente speziell geschult werden, damit sie über die für die Intervention notwendigen Kompetenzen verfügen.

Literaturverzeichnis

Ammassari, A.; Murri, R.; Pezzotti, P.; Trotta, M.P.; Ravasio, L.; De Longis, P.; Lo Caputo, S.; Narciso, P.; Pauluzzi, S.; Carosi, G.; Nappa, S.; Piano, P.; Izzo, C.M.; Lichtner, M.; Rezza, G.; Monforte, A.; Ippolito, G.; d'Arminio Moroni, M.; Wu, A.W.; Antinori, A.; Gallicano, K.; De Luca, A.; Cingolani, A.; Jacobson, D.: Self-reported symptoms and medication side effects influence adherence to highly active antiretroviral therapy in persons with HIV infection

Patient-reported nonadherence to HAART is related to protease inhibitor levels. J Acquir Immune Defic Syndr, 2001, 28: 445-449.

Arnsten, J.H.; Demas, P.A.; Farzadegan, H.; Grant, R.W.; Gourevitch, M.N.; Chang, C.J.; Buono, D.; Eckholdt, H.; Howard, A.A.; Schoenbaum, E.E.: Antiretroviral therapy adherence and viral suppression in HIV-infected drug users: comparison of self-report and electronic monitoring. Clin Infect Dis, 2001, 33: 1417-1423.

Bandura, A.: Self-efficacy: toward a unifying theory of behavioral change. Psychol Rev, 1977, 84: 191-215.

Bandura, A.: Social foundations of thougt and action: A social cognitive theory. Englewood Cliffs, NJ: Prentice Hall, 1986.

Bangsberg, D.R.; Hecht, F.M.; Charlebois, E.D.; Zolopa, A.R.; Holodniy, M.; Sheiner, L.; Bamberger, J.D.; Chesney, M.A.; Moss, A.: Adherence to protease inhibitors, HIV-1 viral load, and development of drug resistance in an indigent population. Aids, 2000, 14: 357-366.

Catz, S.L.; Kelly, J.A.; Bogart, L.M.; Benotsch, E.G.; McAuliffe, T.L.: Patterns, correlates, and barriers to medication adherence among persons prescribed new treatments for HIV disease. Health Psychol, 2000, 19: 124-133.

Chesney, M.: Adherence to HAART regimens. AIDS Patient Care STDS, 2003, 17: 169-177.

Deschamps, A.E.; Graeve, V.D.; van Wijngaerden, E.; De Saar, V.; Vandamme, A.M.; van Vaerenbergh, K.; Ceunen, H.; Bobbaers, H.; Peetermans, W.E.; de Vleeschouwer, P.J.; de Geest, S.: Prevalence and correlates of nonadherence to antiretroviral therapy in a population of HIV patients using Medication Event Monitoring System. AIDS Patient Care STDS, 2004, 18: 644-657.

Duran, S.; Spire, B.; Raffi, F.; Walter, V.; Bouhour, D.; Journot, V.; Cailleton, V.; Leport, C.; Moatti, J.P.: Self-reported symptoms after initiation of a protease inhibitor in HIV-infected patients and their impact on adherence to HAART. HIV Clin Trials, 2001, 2: 38-45.

Fogarty, L.; Roter, D.; Larson, S.; Burke, J.; Gillespie, J.; Levy, R.: Patient adherence to HIV medication regimens: a review of published and abstract reports. Patient Educ Couns, 2002, 46: 93-108.

Garcia, R.; Schooley, R.T.; Badaro, R.: An adherence trilogy is essential for long-term HAART success. Braz J Infect Dis, 2003, 7: 307-314.

Gifford, A.L.; Groessl, E.J.: Chronic disease self-management and adherence to HIV medications. J Acquir Immune Defic Syndr, 2002, 31 Suppl 3: S163-166.

Glass, T.R.; De Geest, S.; Weber, R.; Vernazza, P.L.; Rickenbach, M.; Furrer, H.; Bernasconi, E.; Cavassini, M.; Hirschel, B.; Battegay, M.; Bucher, H.C.: Correlates of Self-Reported Nonadherence to Antiretroviral Therapy in HIV-Infected Patients: The Swiss HIV Cohort Study. J Acquir Immune Defic Syndr, 2006, 41: 385-392.

Goujard, C.; Bernard, N.; Sohier, N.; Peyramond, D.; Lancon, F.; Chwalow, J.; Arnould, B.; Delfraissy, J.F.: Impact of a patient education program on adherence to HIV medication: a randomized clinical trial. J Acquir Immune Defic Syndr, 2003, 34: 191-194.

Haddad, M.; Inch, C.; Glazier, R.H.; Wilkins, A.L.; Urbshott, G.; Bayoumi, A.; Rourke, S.: Patient support and education for promoting adherence to highly active antiretroviral therapy for HIV/AIDS. Cochrane Database Syst Rev, 2000: CD001442.

Haubrich, R.H.; Currier, J.S.; Forthal, D.N.; Beall, G.; Kemper, C.A.; Johnson, D.; Dube, M.P.; Hwang, J.; Leedom, J.M.; Tilles, J.; McCutchan, J.A.: A randomized study of the utility of human immunodeficiency virus RNA measurement for the management of antiretroviral therapy. Clin Infect Dis, 2001, 33: 1060-1068.

Haynes, R.B.; Montague, P.; Oliver, T.; McKibbon, K.A.; Brouwers, M.C.; Kanani, R.: Interventions for helping patients to follow prescriptions for medications. Cochrane Database Syst Rev, 2000: CD000011.

Holzemer, W.L.; Corless, I.B.; Nokes, K.M.; Turner, J.G.; Brown, M.A.; Powell-Cope, G.M.; Inouye, J.; Henry, S.B.; Nicholas, P.K.; Portillo, C.J.: Predictors of self-reported adherence in persons living with HIV disease. AIDS Patient Care STDS, 1999, 13: 185-197.

Hubbard, M.: Dealing with the obstacles in adhering to highly active antiretroviral therapy. J Assoc Nurses AIDS Care, 2006, 17: 18-25.

Ickovics, J.R.; Meade, C.S.: Adherence to HAART among patients with HIV: breakthroughs and barriers. AIDS Care, 2002, 14: 309-318.

Jones, D.L.; Ishii, M.; LaPerriere, A.; Stanley, H.; Antoni, M.; Ironson, G.; Schneiderman, N.; Van Splunteren, F.; Cassells, A.; Alexander, K.; Gousse, Y.P.; Vaughn, A.; Brondolo, E.; Tobin, J.N.; Weiss, S.M.: Influencing medication adherence among women with AIDS. AIDS Care, 2003, 15: 463-474.

King, M.S.; Brun, S.C.; Kempf, D.J.: Relationship between adherence and the development of resistance in antiretroviral-naive, HIV-1-infected patients receiving lopinavir/ritonavir or nelfinavir. J Infect Dis, 2005, 191: 2046-2052.

Knobel, H.; Alonso, J.; Casado, J.L.; Collazos, J.; Gonzalez, J.; Ruiz, I.; Kindelan, J.M.; Carmona, A.; Juega, J.; Ocampo, A.: Validation of a simplified medication adherence questionnaire in a large cohort of HIV-infected patients: the GEEMA Study. Aids, 2002, 16: 605-613.

Knobel, H.; Carmona, A.; Lopez, J.L.; Gimeno, J.L.; Saballs, P.; Gonzalez, A.; Guelar, A.; Diez, A.: [Adherence to very active antiretroviral treatment: impact of individualized assessment]. Enferm Infecc Microbiol Clin, 1999, 17: 78-81.

Mann, T.: Effects of future writing and optimism on health behaviors in HIV-infected women. Ann Behav Med, 2001, 23: 26-33.

Murphy, D.A.; Roberts, K.J.; Martin, D.J.; Marelich, W.; Hoffman, D.: Barriers to antiretroviral adherence among HIV-infected adults. AIDS Patient Care STDS, 2000, 14: 47-58.

Paterson, D.L.; Swindells, S.; Mohr, J.; Brester, M.; Vergis, E.N.; Squier, C.; Wagener, M.M.; Singh, N.: Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. Ann Intern Med, 2000, 133: 21-30.

Pradier, C.; Bentz, L.; Spire, B.; Tourette-Turgis, C.; Morin, M.; Souville, M.; Rebillon, M.; Fuzibet, J.G.; Pesce, A.; Dellamonica, P.; Moatti, J.P.: Efficacy of an educational and counseling intervention on adherence to highly active antiretroviral therapy: French prospective controlled study. HIV Clin Trials, 2003, 4: 121-131.

Rawlings, M.K.; Thompson, M.A.; Farthing, C.F.; Brown, L.S.; Racine, J.; Scott, R.C.; Crawford, K.H.; Goodwin, S.D.; Tolson, J.M.; Williams, V.C.; Shaefer, M.S.: Impact of an educational program on efficacy and adherence with a twice-daily lamivudine/zidovudine/abacavir regimen in underrepresented HIV-infected patients. J Acquir Immune Defic Syndr, 2003, 34: 174-183.

Remien, R.H.; Stirratt, M.J.; Dolezal, C.; Dognin, J.S.; Wagner, G.J.; Carballo-Dieguez, A.; El-Bassel, N.; Jung, T.M.: Couple-focused support to improve HIV medication adherence: a randomized controlled trial. Aids, 2005, 19: 807-814.

Rigsby, M.O.; Rosen, M.I.; Beauvais, J.E.; Cramer, J.A.; Rainey, P.M.; O'Malley, S.S.; Dieckhaus, K.D.; Rounsaville, B.J.: Cue-dose training with monetary reinforcement: pilot study of an antiretroviral adherence intervention. J Gen Intern Med, 2000, 15: 841-847.

Safren, S.A.; Hendriksen, E.S.; Desousa, N.; Boswell, S.L.; Mayer, K.H.: Use of an on-line pager system to increase adherence to antiretroviral medications. AIDS Care, 2003, 15: 787-793.

Safren, S.A.; Otto, M.W.; Worth, J.L.; Salomon, E.; Johnson, W.; Mayer, K.; Boswell, S.: Two strategies to increase adherence to HIV antiretroviral medication: life-steps and medication monitoring. Behav Res Ther, 2001, 39: 1151-1162.

Simoni, J.M.; Frick, P.A.; Pantalone, D.W.; Turner, B.J.: Antiretroviral adherence interventions: a review of current literature and ongoing studies. Top HIV Med, 2003, 11: 185-198.

Simoni, J.M.; Pantalone, D.W.; Frick, P.A.; Turner, B.J.: Best Practices in the Behavioral Management of Chronic Disease, enhancing antiretroviral adherence a review of published reports of RTCs and on going NIH funded research. Vol. Volume II, Chapter 3. Institute for Disease Management, Los Altos, CA, 2005.

Smith, S.R.; Rublein, J.C.; Marcus, C.; Brock, T.P.; Chesney, M.A.: A medication self-management program to improve adherence to HIV therapy regimens. Patient Educ Couns, 2003, 50: 187-199.

Sterne, J.A.; Hernan, M.A.; Ledergerber, B.; Tilling, K.; Weber, R.; Sendi, P.; Rickenbach, M.; Robins, J.M.; Egger, M.: Long-term effectiveness of potent antiretroviral therapy in preventing AIDS and death: a prospective cohort study. Lancet, 2005, 366: 378-384.

Tuldra, A.; Fumaz, C.R.; Ferrer, M.J.; Bayes, R.; Arno, A.; Balague, M.; Bonjoch, A.; Jou, A.; Negredo, E.; Paredes, R.; Ruiz, L.; Romeu, J.; Sirera, G.; Tural, C.; Burger, D.; Clotet, B.: Prospective randomized two-Arm controlled study to determine the efficacy of a specific intervention to improve long-term adherence to highly active antiretroviral therapy. J Acquir Immune Defic Syndr, 2000, 25: 221-228.

Wagner, G.J.: Predictors of antiretroviral adherence as measured by self-report, electronic monitoring, and medication diaries. AIDS Patient Care STDS, 2002, 16: 599-608.

Wall, T.L.; Sorensen, J.L.; Batki, S.L.; Delucchi, K.L.; London, J.A.; Chesney, M.A.: Adherence to zidovudine (AZT) among HIV-infected methadone patients: a pilot study of supervised therapy and dispensing compared to usual care. Drug Alcohol Depend, 1995, 37: 261-269.

Walsh, J.C.; Mandalia, S.; Gazzard, B.G.: Responses to a 1 month self-report on adherence to antiretroviral therapy are consistent with electronic data and virological treatment outcome. Aids, 2002, 16: 269-277.

WHO: Adherence to long-term therapies. Evidence for action. 2003.

Chapter 5

Keeping a grip on HIV: A Qualitative Investigation on Collaborative Medication and Symptom Management Experiences of Persons with HIV living in Switzerland

Dunja Nicca [1,2], Jan Fehr[3], Katharina Fierz [1], Kimberly Moody [4], Rebecca Spirig [1]

[1] Institute of Nursing Science, University of Basel and Department of Clinical Nursing Science, University Hospital Basel, Switzerland

[2] Division of Infectious Diseases and Hospital Epidemiology, Cantonal Hospital of St. Gallen, Switzerland

[3] Division of Infectious Diseases and Hospital Hygiene, University Hospital Zuerich, Switzerland

[4] University of Southern Maine, Portland, Maine, USA

Corresponding author, e-mail: dunja.nicca@kssg.ch

Submitted to: International Journal of Nursing Studies

Abstract

Objectives: the purpose of this study was to gain an understanding of the experiences of persons living with HIV and their medication and symptom management in light of collaboration with close support persons and healthcare providers.

Design/Methods: Open ended interviews were conducted with adult participants on antiretroviral therapy who were receiving care at four different HIV outpatient clinics in Switzerland. Data were analyzed using a critical hermeneutical approach.

Results: Narratives revealed that already small changes in health and treatment could change participant's impression of “having a grip” on HIV or “losing it.” To keep a grip, participants constantly monitored their condition, developed expertise in care and symptom management, and included healthcare providers and close support persons in their management.

Conclusions: Patients' impressions of their abilities to manage their condition appeared to be a phenomenon that could guide future support. Collaboration with healthcare providers and close support persons enabled or hindered a patient's management. Suggestions to improve support are made.

Introduction

Over the past several decades, developments in the treatment and monitoring of HIV have radically improved the prospects of those living with the disease. In countries with broad access to long-term combined antiretroviral therapy (cART), usually monitored through outpatient services, the morbidity and mortality of people living with HIV (PLWH) have been sharply reduced (Sterne et al., 2005). As a result HIV is now considered a manageable chronic condition.

In order to improve outcomes for patients with chronic conditions, fundamental changes across health care systems have been suggested (Schoen, Osborn, How, Doty, & Peugh, 2009). The WHO publication ‘Innovative Care for Chronic Conditions’, structures chronic care management areas requiring changes into macro, meso, and micro levels, with each level interacting with and dynamically influencing the others (WHO, 2002). The macro level refers to policy decisions and standards, the meso level to health care organization and the community and finally the micro level to patient interactions. On the micro level, patient’s self management and the patient-provider collaboration have been described as key issues influencing health outcomes (Epping-Jordan, Pruitt, Bengoa, & Wagner, 2004; Schoen et al., 2009).

Patient self-management includes diverse tasks, such as dealing with emotions related to the condition, maintaining meaningful behaviors despite fluctuation in health, and most notably, handling medical management on a daily basis (Corbin & Strauss, 1988). For PLWH this medical management includes two main components: the management of medications and the management of symptoms (Spirig, Moody, Battegay, & De Geest, 2005).

Both aspects are closely related and are important for optimal health outcomes. Symptom prevalence remains high for many PLWH and insufficient symptom management can negatively influence medication adherence and quality of life (Ammassari et al., 2001; Badia, Podzamczer, Casado, Lopez-Lavid, & Garcia, 2000). Lack of medication adherence has been linked with the development of drug resistant mutations along with the loss of viral suppression and immune functions (Bangsberg, Kroetz, & Deeks, 2007; King, Brun, & Kempf, 2005). Additionally, qualitative research has highlighted the interface between symptom management and medication adherence choices (Wilson, Hutchinson, & Holzemer, 2002). Research and clinical practice further show that, for day-to-day management of medications and symptoms, collaboration with supportive others and with healthcare providers is vital (Thorne, Paterson, & Russell, 2003). In the current literature, PLWH’s medication and symptom management has been described in a very fragmented way, focusing either symptom management or medication adherence. Necessary collaborations within those processes have been largely neglected. Traditionally medication and symptom management were considered the territory of healthcare providers, conducted in a rather paternalistic way without an emphasis on a patient’s illness, work, or educational needs (Bodenheimer, Wagner, & Grumbach, 2002a). Nevertheless the benefits of collaborative approaches have been discussed in the literature and it can be assumed that these approaches have made their way into clinical practice (Joosten et al., 2008). In order to reflect and improve current practice, it is important to focus on the patient's perspective. The aim of this investigation was therefore to gain understanding of PLWH's experiences with medication and symptom management in light of collaboration with healthcare providers and close support persons.

Methodology and Methods

This study is part of a larger mixed method research project investigating the perceptions of PLWH, their close support persons and healthcare providers, regarding symptom and medication management. This particular report describes PLWH experiences within medication and symptom management including their perspectives on collaborations with close support persons and healthcare providers.

The study is rooted in critical hermeneutics (Allen, 1995). By employing the principles of critical hermeneutics, this study focused on language and understanding in the interviews with participants and in the study of texts, in relation to wider socio-cultural aspects (Allen, 1995; Koch, 1996).

Socio-cultural Setting

The study has been conducted in HIV outpatient clinics in the Swiss healthcare system. Ambulatory care prescription medications are covered with a mandatory health insurance system. For patients unable to pay standard premiums or deductible amounts, the Swiss social insurance system provides subsidized coverage.

Seven ambulatory centers of the Swiss HIV Cohort Study (SHCS) provide the majority of specialized HIV outpatient treatment, caring for around 70% of PLWH in Switzerland (Gebhardt, Rickenbach, & Egger, 1998). This study has been conducted in four SHCS centers, three located within University hospitals and one within Cantonal hospitals. In high level practice and educational settings such as these, physicians tend to change frequently. In contrast, nurses usually work many years in the same setting.

Data Collection

Over a six month period, nurses at the SHCS centers offered adult HIV patients, coming for medical consultations, the opportunity to participate in this study. Ethics review boards of all study centers had approved the investigation. To be eligible for inclusion, participants had to be German speaking, on antiretroviral therapy and have a close support person. A close support person was defined as someone who, by birth, marriage, friendship or declared commitment, shared deep personal connections with the participant and provided various forms of support in times of need (Levine, 1990). Participants (PLWH) from the convenience sample in the larger study had been asked whether they would be willing to participate in qualitative interviews. From the group who had consented to this, a sample of 13 PLWH was purposefully selected based on center, gender and transmission group. Written informed consent was given prior to the interviews.

The critical hermeneutic experience is characterized by open dialogue (Koch, 1996). A broad interview guide with open questions to facilitate the dialogue on medication- and symptom management and the collaboration with others was used. Interviews, which lasted 50 to 90 minutes, were recorded and later transcribed verbatim. In critical hermeneutics it is argued that the conversations are influenced by social and political norms that shape the involved relationships and interviewers are not perceived as neutral observers (Allen, 1995). In this study three nurses with a Masters Degree and experience in HIV research and clinical care were involved in the process of data collection. None of them were involved in clinical care of participants. All had received extensive interview training and the process was reflected after every interview in the research team.

Data Analysis

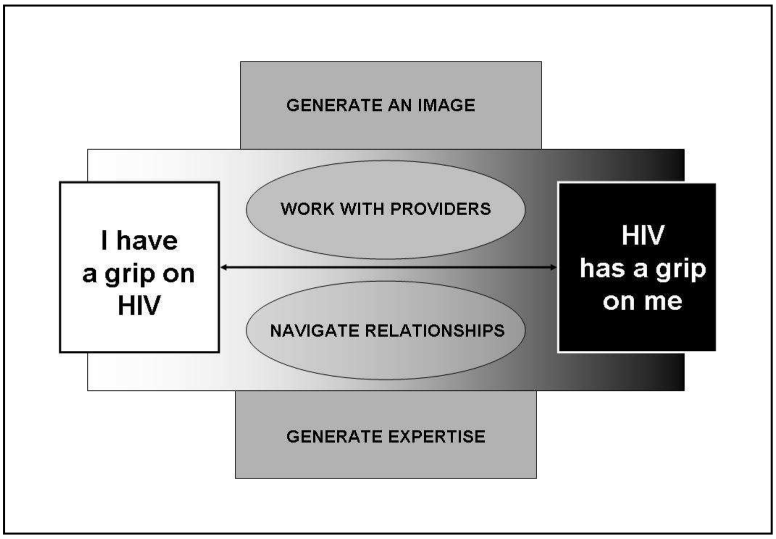
The interview analysis was started after the first three interviews and it influenced further data collection. After ten interviews themes seemed to be repeating and no new aspects were considered. Three more interviews were conducted to ensure this observation. To analyze and interpret data, the hermeneutic approach suggested by Diekelmann and Allen (1989) was used. It involves multiple steps such as a) developing an overall understanding of the texts; b) defining categories for each interview; c) developing relational themes (themes that cut across all texts); and d) building constitutive patterns (patterns present in all documents, expressing the relationships of the relational themes). Atlas software supported this process (Atlas.ti 5.2 Scientific Software Development, Berlin, Germany). Two researchers with expertise in HIV care and research were involved in each step of the data analysis, building of categories and relational themes involved consensus discussions. To ensure the quality of data analysis, the process itself and the relational themes were regularly discussed in the research group and with two PLWH that were not study participants. The data analysis was undertaken in German, the language in which the interviews were conducted. The final description of the findings was written in English, quotes were back worth translated.

Results

Five women and seven men between 27 and 50 years of age (mean: 41.2) participated in the interviews. Their living circumstances in rural and urban areas of Switzerland were diverse: some lived in homo- or heterosexual partnerships, others in families with children or by themselves with close contact with friends or family members. Five of them had a history of illicit drug use. Participants' stories revealed a broad experience of living with HIV and managing cART and symptoms within diverse relationships in the Swiss healthcare context.

The constitutive pattern generated from the interview data and illustrated in figure 1 *"I have a grip on HIV—HIV has a grip on me"* describes the participants' ongoing evaluation of their own condition with respect to their medication and symptom management. Four relational themes influenced this process. They illustrated the participants' continuous work in relation to medication and symptom management. Two themes *"generate images"* and *"generate expertise,"* revealed processes conducted by participants in order to keep up a meaningful daily life despite changes in their health. The other two themes, oriented toward the same goal, were *"work with healthcare providers"* and *"navigate relationships"*, which showed interactive processes with others.

Figure 1: "Keeping a grip on HIV"



I Have a Grip on HIV—HIV Has a Grip on Me

Participants reported that developments in antiretroviral treatment options increased their prospects of a long and relatively healthy life. Yet, living with HIV/AIDS left them prone to multifaceted health problems throughout the course of the condition. If not sufficiently managed, even small changes in health or treatment were reported to severely impact daily life. A woman commented on this situation,

> *I can talk like this, because I am alright at the moment. If something comes up and the whole situation could change quickly.*

Related to this management, participants described two interchanging conditions. At one pole they felt fully able to manage the difficulties of their chronic disease and keep up a meaningful life. At the other they felt overwhelmed by difficulties and unable to manage. The two conditions reflected in "I have a grip on HIV" and "HIV has a grip on me," and the dynamics between them, experienced by all participants irrespective of their years of experience with HIV, will be further explored.

"I have a grip on HIV" reflects the condition where participants felt able to master the challenges of living with HIV. In their stories, issues of everyday life were more present than those of illness management. Many negated having any disease or medication related symptoms. Still, some explained that, although they experienced symptoms such as diarrhea or fatigue, they were untroubled by them, because they had successfully integrated their management into daily life. Additionally, they had integrated the intake of antiretroviral regimens into their daily routines. Participants were able to take their medications on a regular basis without difficulty or even much awareness. Significant others were often part of this routine. Even in exceptional situations, such as vacations, medication intake could be handled without difficulty and was not a key issue. A woman with children typified this condition with this comment:

> *For us it's a normal life. I don't have any troubles and don't even think about it. The only thing is to take my meds. I just do it every day at lunch. Otherwise it's not a topic anymore.*

If changes in health and treatment were not sufficiently manageable, participants described an incremental process of radical changes that influenced the perception of their condition. Such changes could occur throughout the illness course.

"HIV has a grip on me" reflects this more daunting condition, where participants felt driven by their HIV infection itself. Issues of the illness management, such as uncontrolled symptoms or problems with the medical regimen, could become all-dominant and threaten their ability to keep up the normality of their daily lives. Reflecting on this change, a male participant said,

> *I had a huge combination of medications, but I felt fine for years. Even though I had this fatigue, I was able to do everything, like going out or exercising. But two years ago the body aches and the loss of energy really started. Now, I have to say this can not be it! Some days before getting up, I feel like I can't handle daily life and work.*

Various other participants recounted stories about their "most difficult symptoms," including for example almost unbearable skin itching, changes in body fat distribution, or warts. In particular, changes in body fat and warts negatively impacted a participant's body image. They also feared stigmatization due to forced disclosure of their HIV status because of visible symptoms.

> *Visible symptoms are more difficult. Every time others look at you, they will think, something is wrong with her. That forces you to explain yourself and is very stressful, besides the fact that you don't like yourself looking like this.*

Diverse difficulties involving their antiretroviral regimens seemed to further complicate their everyday lives. For some, the medications were a constant reminder of their HIV infection, which was still painful. Others talked about problems integrating medication intake into their routines, or experienced distressing side effects. One man shared such an experience:

> *Often it is very difficult to open the medication box. Especially if we have relatives visiting, it is difficult. They do know about it, but then my wife acts extraordinarily and puts the box on the table right in front of me. I am completely stressed in those situations.*

If those difficulties could not be resolved over time, people reported a sense of losing their "grip" on HIV. This could lead to uncertainty, fear, and loss of morale. In order to get back the "grip on HIV" again, participants described various strategies, revealed by following four themes: generate an image, generating expertise, working with providers, and navigating relationships.

Generate an image

Participants seemed to be aware that health changes could occur any time and influence their ability to have a “grip on HIV”. To minimize the impact of such changes on their everyday life, they talked about constantly monitoring their own state of health and related behavior. Along with the effect of medical treatment or their current adherence behavior, they kept a close watch for any new or changing symptoms. In order to create an overall image of their situation, participants talked about evaluating their observations, which helped them to make management decisions. Generating an image was an important, but often difficult task to keep a grip on HIV as this example illustrates:

> *If I can isolate something (symptom) concretely, the situation is simply different from when I don’t know where it’s coming from. That makes it possible to get a grip on it. It’s positioning something, not even what you can do about it that makes the difference.*

To generate an image, participants seemed to base their interpretations on frames of reference they had developed for themselves regarding their knowledge of symptoms, their bodies, their labs, and their personal adherence requirements. These frames which will be further described.

Participants’ knowledge of medication side effects or their experiences of diverse symptoms allowed them to distinguish between known and unknown symptoms.

> *By now I know my symptoms. They repeat themselves, I can differentiate between the ones I know and those I don’t, then I watch more carefully.*

They further stated that compared to the beginning of their chronic condition, over time they had built up a keen sense for their individual body changes, recognizing, for example, small sensations before trouble arose.

> *With time, you really get the feeling for your body, a lot more than any healthy person does that is for sure.*

All participants knew the courses and current states of their surrogate markers; some used this to combine and interpret their current parameters with occurring symptoms or the effect of medical regimens, whereas others combined it with their body feelings only.

Additionally over time participants had defined what level of adherence was sufficient for them. With this in mind, they could monitor their adherence behavior regarding timing, doses, and dietary restrictions. Such personal perception of adherence requirements seemed not always in concordance with provider recommendations, but with their lab parameters or body feeling.

> *I take them regularly. I only forget them two or three times a month. But I never eat with them, as I am supposed to. It just did not work out while working. Anyway my lab is always fine, I am doing alright.*

Participants seemed to link all of these reference points to form an overall picture of their condition and to arrive at management decisions. For some, the monitoring processes were so well integrated into their daily routines they almost did not notice them. For others, these processes demanded more attention and energy, especially if they had not yet developed expertise in managing symptoms and medications.

Generate expertise

Participants revealed that they developed expertise in handling the challenges of medication and symptom management. Many described a difficult learning process at the beginning, with many trials and errors before they were able to solve the problems. Such situations could lead to the impression of loosing ‘the grip on HIV’. Nevertheless diverse experiences and increases in knowledge made management easier. Yet, participants were aware that irrespective of their current knowledge new health challenges could always occur. In order to ‘keep a grip on HIV’ they continuously and actively developed their expertise. This included learning processes related to making decisions, finding out what works, organizing medications, and understanding HIV that will be further described.

Skills seemed to grow as participants built up their knowledge to make decisions related to symptoms and medications, observing, for example, the criteria healthcare providers used to make such decisions. Many also sought information on the Internet or other media sources. Even negative experiences yielded knowledge for future decisions:

> *I have problems with my eyes and it’s my fault: I waited too long (to seek treatment). Because it was at the beginning of the disease, at that time you don’t know how to handle it. I would recommend a newly infected person to see the doctor for every bloody thing. They should really see about what’s important and what’s not. It’s a real advantage when you know how to manage the disease.*

Participants shared, that they had to work out personal strategies to manage their symptoms, based on recommendations from different sources such as providers, diverse media and peer support. To manage diarrhea, for example, one woman describes how she used prescribed medications, changed her diet and tried over the counter medications until she found a working strategies for herself.

> *I have this diarrhea and the doc gave me Imodium (loperamid). But with time I learned to better manage it. I used Bioflorin which rebuilds the intestinal mucosa, it works out for me now. I have also tried with food, for a while I ate bananas.*

Participants also seemed to develop systems that allowed them to take their antiretroviral regimen according to the perception of their own adherence requirements. For example, they used diverse technical reminder systems, adjusted times, and experimented with food until they had found a system that worked for them. Such a working system often needed time to be developed. One woman talked about this:

> *I organized myself over time. Now I have these boxes for fourteen days. Every other Sunday I fill them up, and then I take the medication every morning and every evening. I am accurate; I take them pill by pill in the same order. First*

> *before breakfast I take the thyroid medication and then after breakfast with a sip of coffee, the HIV medication.*

All participants seemed to have developed broader perspectives on HIV and related issues, including opportunistic diseases and possible symptoms, functions of the immune system, interpretation of lab parameters, and the benefits and side effects of antiretroviral agents. Information from diverse media, supportive others, and, in particular, healthcare providers served as a basis for knowledge and understanding. A woman describes this process.

> *I ask her (physician) many questions and she explains a lot. And every time it is like little bridges you cross to connect things. Knowing and understanding really helps.*

Work with providers

To manage symptoms and medications effectively, participants emphasized the importance of a close, participatory relationship with HIV specialized healthcare providers. This was particularly important to strengthen unsatisfactory self-evaluation and management strategies. And therefore to change from the condition of ‘HIV has a grip on me’ to ‘I have a grip on HIV’. The process of working with healthcare providers involves selecting the place to go for support, ones own contribution to the collaboration and dealing with provider relations.

Independent of their relationships with individual providers, participants experienced their HIV outpatient clinics as important institutions. A clinic was the place “where people really know me.” They were welcomed familiarly by nurses, their health histories were known and they did not have to repeat their case details at every visit. Additionally, many appreciated that, they had long term relations with nurses and that in their clinics, they could talk freely about their HIV infections and associated topics.

> *HIV is a topic there at the clinic. Well I somehow always feel I can talk about it there. The staff takes it seriously and I can discuss with them.*

Finally, if problems in symptom and medication management arose, the clinic was a place to call and where they were confident of receiving competent, HIV focused care.

Active participation was perceived as important for participants in their collaboration with individual healthcare providers, especially with physicians. One woman stated:

> *I think you have to work with them (physicians); if you don’t, the outcome is no good for both parties. I always prepare myself, I look things up and I tell them about my symptoms and my opinion.*

Participants stated that they could not expect to be asked about every symptom. It was therefore important to know about possible symptoms and clearly and actively communicate observations or even emotions. Further, textbook recommendations were often not experienced as sufficient to solve problems regarding symptom or medication management. Individualized solutions had to be worked out collaboratively to ‘keep a grip on HIV’. Participants prepared suggestions for symptom management strategies or therapy options to be discussed with their providers. They also intended to have an active exchange of expertise with their providers. While they actively sought information from experienced providers, they also educated newer ones about important experiences they had had in the past, including, for example, unusual side effects not yet described in the available literature. Finally, they coordinated general healthcare providers with their HIV specialized providers. When necessary, they also called to check about medication interactions. Some insisted on being treated by their HIV providers for general health problems. They questioned competence of non HIV specialized providers and feared to loose 'grip on HIV' with a less competent partners.

Relationships with providers were sometimes experienced as positive and supportive, other times as difficult and non-supportive. If the latter was the case, participants missed the active partner they needed to optimally manage the situation. Two women, with severe skin itching, shared two very different experiences. One was positive:

> *At one point I had this awful itching; I was really stressed about it. But I got the impression they really took it seriously, even though from an objective perspective it's not such a bad thing. I definitely liked that.*

The other woman experienced a non-supportive interaction:

> *I had very dry skin and awful itching, but absolutely no one took it seriously there (at the clinic). Especially during winter time, I had bleeding legs. As soon as the physician changed, he told me medications could do that. But before that, I told them many times and no one reacted to it.*

Participants talked about being deeply affected by such differences in relationships since it was very relevant for 'keeping a grip on HIV'. When mentioning providers with whom they experienced positive interactions, for example, they used inclusive language with phrases such as "we need to solve this" or "we will do this." In those cases, providers knew to listen carefully before acting and to focus on the patient comprehensively, as a person. Such providers educated and enabled participants to deal with difficulties, for example, by preparing them for medication intake. Such relationships fostered a sense in the participants that they could bring in their own perspectives—that they and their providers were genuine partners. This gave them a feeling of security, even if problems could not be solved immediately.

In contrast, some participants had the impression that their providers were not actually listening to their input, but simply pursuing their own agendas. To the participants, such providers seemed either uninterested or simply did not believe them. In particular, symptoms involving fatigue, neurological or cognitive problems, where a quick solution was not possible, appeared extremely difficult to discuss. The statement of a man with fatigue reflects this situation:

> *All went well for years. I had the impression they (physicians) appreciated how well I managed besides a full time job. Now I have this fatigue and everything changed. I sometimes think my lab results are still to good to be taken seriously. My last physician for example, in every consultation told me, that he*

> *wants to take me of the antibiotics and go back to work. He really scared me, I almost panicked. I always wanted to work that's not it, but now I think they don't take my problems seriously.*

Participants also occasionally questioned the competence of less communicative providers— for example, when they had not prepared them for possible side effects, or seemed not to react appropriately to symptoms. In such cases, participants felt they had not been taken seriously, and expressed difficulties speaking about their experiences. Some withdrew from the relationship and withheld information about symptoms. Others used more active strategies and insisted that their perspectives be acknowledged. “I fight for my rights and well being,” as one patient put it. Others considered changing providers.

For participants who had the feeling of having a grip on HIV, close collaboration was appreciated, but not essential. However, in cases where they felt HIV had a grip on them (also indicating that their own strategies were insufficient), full collaboration was indispensable. If it was absent, such participants expressed feelings of insecurity, distress, and even desperation.

Navigate relationships

Relationships with family members, partners, friends, colleagues at work and others were an important part of participants' everyday lives. With a focus on their illness management and in order to ‘keep a grip on HIV’, participants therefore carefully navigated relationships with significant others. This process included following issues that will be further described: the management of disclosure, things PLWH and the persons close to them did for one another and how they kept the balance.

Management of HIV disclosure was an important issue. All participants seemed to handle the disclosure of their HIV status with great care. Whereas some restrictively informed only the most important persons in their lives, others informed a broader group. Participants decided against disclosure to certain close relatives, including children or parents, to protect them from stigmatization or negative feelings. Their disclosure decisions seemed to be closely linked to issues of symptom and medication management. Participants informed others in order to receive support or at least to minimize disturbances in their management. For example, they informed others if symptoms became noticeable, began to hinder daily activities or work performance, or if they simply wanted to talk. They also informed others in order to take their antiretroviral medication openly, as the example of one participant illustrates:

> *Being HIV positive is not so important for me. But before I spend my vacation with someone, I usually tell them about it. I don't want to hide the medication intake or even lie about it. Usually I feel close to people I spend my vacation with. So it's not to bad, but you need to prepare them.*

The moment to disclose HIV status appeared to be chosen carefully, since it always demanded energy and time to talk. Even though some participants informed others very easily and openly, they had to take the reaction of the others into account. For others, the disclosure process was very distressing, especially if they felt forced to do so, for example by visible or bothersome symptoms.

To share issues surrounding symptom and medication management, it was important for participants that the people who supported them were informed about their HIV diagnosis and that they be trustworthy and understanding. Participants often shared all aspects of their daily lives and activities with such close support persons. Merged into these daily activities were diverse forms of mutual caregiving that reflected not only their close relationships but also various issues involving symptoms and medications. Participants explained, for example, that their close others were there for them to talk to or offered to drive or accompany them to clinic visits if those tasks were difficult or distressing. One woman talked about how her sister assumed certain household chores:

> *We don't have to talk about it. My sister recognizes if I'm tired or feeling down and helps me with little everyday tasks. She vacuums the house or helps me to feed the animals.*

On the other hand participants also explained that they provided similar support for their significant others. They might have taken over household tasks, because the support person had a heavy workload and were there to talk if any problems occurred. Additionally, close support persons, especially children and partners, were perceived as persons for whom it was important to live, and, in fact, to actively manage their chronic condition.

Close support persons were described as co-affected by the disease and its related challenges. Changes also obviously influenced their daily lives: they had to deal with the diagnoses of their loved ones and to keep abreast of issues of symptom and medication management . Sometimes they were able to provide support, other times, as one participant described, they struggled with difficult situations:

> *This fatigue came slowly, but it is very disturbing for us. My partner just can't handle it, he is completely stressed about it. We often argue about it, discussed it back and forth but I don't see a way out so far.*

In order to "keep a grip" on their own illness management and to reduce the burden on their close support persons, participants seemed to carefully balance their relationships according to their specific circumstances. Sometimes, for example, this would involve discussing symptom management decisions with them, whereas other times they might not even mention the symptoms they experienced. One woman, not wishing to disturb her husband before an important business meeting, did not talk to him about her symptoms, but went to see her doctor. Even after learning that she had to be hospitalized, she called her husband only after everything was set and his important meeting was concluded. Additionally, to allay the fears of those closest to them, participants provided HIV related knowledge and informed them about their conditions on an ongoing basis.

Discussion

Findings reflect medication and symptom management experiences of a group of PLWH receiving care at Swiss HIV outpatient clinics. The constitutive pattern "I have a grip on HIV—HIV has a grip on me" sheds light on the importance for PLWH to gain or maintain the feeling of being able to manage medications and symptoms. This stands in accordance with former qualitative investigations, where the decision of persons with a chronic condition to control the disease rather than being controlled by it has been described (Lorig & Holman, 2003; Thorne et al., 2003). In contrast to former research our results not only describe a one time decision but highlight a dynamic process of changes in the perception of "having a grip" across the course of the condition. This leads to the assumption that time-limited self management interventions as usually planned and tested in study programs might not sufficiently meet PLWH's needs. Ongoing screening of needs and provision of support should be integrated into clinical care. Additionally the phenomena of "keeping a grip or controlling HIV" should be further investigated. This is in particular important, since a limitation of this study was the mainly white population with a western cultural background. However a qualitative investigation in Australia revealed differences for an English- and an Arabic speaking group of diabetes patients: whereas the English speaking group emphasized the need to control the condition, the Arabic speaking group emphasized the need to reduce stress caused by the condition (Furler et al., 2008).

The ongoing and active self-management of PLWH to "keep a grip on HIV" can also be influenced by social aspects. In Switzerland, health and related productivity are become important values. Health, understood as an expression of an individual's well being, has become desirable and achievable for everyone. With that awareness, social expectations grew, such that individuals, including chronically ill persons, actively maintain their health (Kickbush, 2006). Nevertheless, some highly challenging illness related work, such as described by PLWH and other chronically ill populations, does not seem to be well recognized in society nor in the healthcare community (Lorig & Holman, 2003; Wiener, 1989). For PLWH in particular, the underrecognition of their contribution to health by society could be increased because of fear from stigmatization only a close circle of persons is informed about the chronic condition (Spirig, 2002). The underrecognition of PLWH's daily work by healthcare providers could be explained by the traditional stronger focus on biomedical issues, compared to behavioral aspects such as self management (Bodenheimer et al., 2002b). Managing a still stigmatized chronic condition, in a social context where individuals are expected to maintain optimal health, combined with underrecognition of self management support needs by professionals could put PLWH's at risk for negative health outcomes.

The results of this study clearly showed that interactions with healthcare providers and close support persons assisted or hindered PLWH's continuous management of medications and symptoms. However, independent of the experiences with individual providers, PLWH's connected their HIV outpatient clinics in two important respects. First, they described it as a place where they could talk about HIV freely. Even today fear of stigmatization and experiences of stigmatization by PLWH are described in diverse settings (Peretti-Watel, Spire, Pierret, Lert, & Obadia, 2006; Schuster et al., 2005). An investigation in a large teaching hospital in the UK for example illustrated that professionals working on units that regularly provided HIV-care, appeared to be more positive and less pejorative against PLWH than others (Hodgson, 2006). In such contexts, HIV specialized institutions with a less pejorative caring culture and attitudes seem to be important recourses for PLWH's. Second study participants described the clinics as places where they were known as a person and health history was familiar to providers. Interestingly in particular nurses were associated with the feeling of familiarity and being known. This supports recent discussions on the importance of high care continuity for persons with a chronic condition highlights the role nurses can play within continuity of care (Guthrie, Saultz, Freeman, & Haggerty, 2008). Both aspects, the non pejorative environment and care continuity, seem to be important conditions for patient-provider partnerships in HIV care.

The need of PLWH's to establish working partnerships with their healthcare providers as reflected in this research project, is described in studies across diverse chronically ill populations (Thorne et al., 2003). These findings provide insight into the details that constitute such partnerships with a focus on managing medications and symptoms. On one hand, the need for providers to use a patient centered approach, including recognizing each person as a unique human being, is described and has already been found to be important in a broad range of studies (Beach et al., 2006; McCoy, 2005; Schneider, Kaplan, Greenfield, Li, & Wilson, 2004). On the other hand, these findings highlight the importance of the need for HIV-specific competence on the part of healthcare providers. Next to a medical competence, this includes the ability to assess a patient's symptom experience in a non judgmental manner, to develop medication and symptom management strategies collaboratively with patients, to provide ongoing education within those topics, and finally to assist patients in decision making and in the coordination of different health problems. In PLWH's narratives physicians played a key role related to such needs. However meeting all of those needs can be a challenge for an individual physician in specialized outpatient clinics situated in academic hospitals. A team approach with an optimal mix of individual provider's skills seems to be needed. Nurses, who have traditionally strong focus on self management education, could probably expand their role in self management education.

Consistent with the literature, close support persons provided diverse forms of support and a reciprocal process of giving and taking support was described (Bischofberger & Spirig, 2004). In contrast former studies, PLWH seemed to manage relationships with the clear goal to 'keep a grip on HIV'. This gave them a leadership role in their collaboration with close support persons. For example, participants seemed to educate their close support persons about HIV related knowledge and their actual condition to allay their fears. Since they themselves often did rely on information and education of healthcare providers, they had to transfer the gained understanding to their close support person. PLWH who were having difficulties in medication and symptom management and who had a fearful support person, seemed, at times, to be overburdened with this work. This highlights the need for not only for patient but also for support person focused interventions. So far the Swiss healthcare and insurance system is strongly focused on and reimburses services at the individual patient level. As a result, healthcare providers have focused the individual patient as the center of care. Family focused interventions have rarely been integrated in the education curricula of nurses and physicians. For example nurses (*n* = 580) in a Swiss university hospital, who were directly engaged in patient care, rated their professional competences over seven dimensions. The dimension of “education for patients and families” received the lowest ratings with a median of 80% (1=not competent; 100=absolutely competent) (Martin et al., in press, 2009).

Conclusion

The sometimes hardly visible illness work of PLWH around medication and symptom management has to be recognized as such and adequately supported by healthcare providers in particular nurses need to expand self management support. Patients’ own perceptions of their ability to control their disease management could be one important marker of the needed support and should be further investigated. Since PLWH need active partners in their medication and symptom management, their close support persons should be included in support interventions. The process of supporting PLWH and their close support persons in medication and symptom management requires good communication, caring, respect and high medical competence by their healthcare providers. These needs might be best met by a chronic illness approach with well orchestrated teamwork by different healthcare providers.

References

Allen, D. G. (1995). Hermeneutics: philosophical traditions and nursing practice research. *Nursing Science Quarterly, 8*(4), 174-182.

Ammassari, A., Murri, R., Pezzotti, P., Trotta, M. P., Ravasio, L., De Longis, P., et al. (2001). Self-reported symptoms and medication side effects influence adherence to highly active antiretroviral therapy in persons with HIV infection. *Journal of Acquired Immune Deficiency Syndromes, 28*(5), 445-449.

Badia, X., Podzamczer, D., Casado, A., Lopez-Lavid, C., & Garcia, M. (2000). Evaluating changes in health status in HIV-infected patients: Medical Outcomes Study-HIV and Multidimensional Quality of Life-HIV quality of life questionnaires. Spanish MOS-HIV and MQOL-HIV Validation Group. *AIDS, 14*(10), 1439-1447.

Bangsberg, D. R., Kroetz, D. L., & Deeks, S. G. (2007). Adherence-resistance relationships to combination HIV antiretroviral therapy. *Current HIV/AIDS Reports, 4*(2), 65-72.

Beach, M. C., Keruly, J., & Moore, R. D. (2006). Is the quality of the patient-provider relationship associated with better adherence and health outcomes for patients with HIV? *Journal of General Internal Medicine, 21*(6), 661-665.

Bischofberger, I., & Spirig, R. (2004). [The work profile of family caregivers of persons affected by HIV/AIDS]. *Pflege, 17*(3), 176-186.

Bodenheimer, T., Wagner, E. H., & Grumbach, K. (2002a). Improving primary care for patients with chronic illness. *JAMA, 288*(14), 1775-1779.

Bodenheimer, T., Wagner, E. H., & Grumbach, K. (2002b). Improving primary care for patients with chronic illness: the chronic care model, Part 2. *JAMA, 288*(15), 1909-1914.

Broyles, L. M., Colbert, A. M., & Erlen, J. A. (2005). Medication practice and feminist thought: a theoretical and ethical response to adherence in HIV/AIDS. *Bioethics, 19*(4), 362-378.

Chiou, P. Y., Kuo, B. I., Chen, Y. M., Wu, S. I., & Lin, L. C. (2004). A program of symptom management for improving self-care for patients with HIV/AIDS. *Aids Patient Care and STDS, 18*(9), 539-547.

Chou, F. Y. (2004). Testing a predictive model of the use of HIV/AIDS symptom self-care strategies. *Aids Patient Care and STDS, 18*(2), 109-117.

Corbin, J., & Strauss, A. (1988). *Unending Work and Care: Managing Chronic Illness at Home*. San Francisco, CA: Jossey-Bass.

Deschamps, A. E., De Geest, S., Vandamme, A. M., Bobbaers, H., Peetermans, W. E., & Van Wijngaerden, E. (2008). Diagnostic value of different adherence measures using electronic monitoring and virologic failure as reference standards. *Aids Patient Care and STDS, 22*(9), 735-743.

Deschamps, A. E., Graeve, V. D., van Wijngaerden, E., De Saar, V., Vandamme, A. M., van Vaerenbergh, K., et al. (2004). Prevalence and correlates of nonadherence to antiretroviral therapy in a population of HIV patients using Medication Event Monitoring System. *Aids Patient Care and STDS, 18*(11), 644-657.

Diekelmann, N., & Allen, D. G. (1989). A hermeneutic analysis of the NLN criteria for the appraisal of baccalaureate programs. In N. Diekelmann, D. G. Allen & C. Tanner (Eds.), *The NLN* *criteria for the appraisal of baccalaureate programs: A critical hermeneutic analysis* (pp. 11–31). New York, NY: National League for Nursing.

DiMatteo, M. R. (2004). Social support and patient adherence to medical treatment: a meta-analysis. *Health Psychology, 23*(2), 207-218.

Epping-Jordan, J. E., Pruitt, S. D., Bengoa, R., & Wagner, E. H. (2004). Improving the quality of health care for chronic conditions. *Quality and Safety in Health Care, 13*(4), 299-305.

Fehr, J. S., Nicca, D., Sendi, P., Wolf, E., Wagels, T., Kiss, A., et al. (2005). Starting or changing therapy - a prospective study exploring antiretroviral decision-making. *Infection, 33*(4), 249-256.

Furler, J., Walker, C., Blackberry, I., Dunning, T., Sulaiman, N., Dunbar, J., et al. (2008). The emotional context of self-management in chronic illness: A qualitative study of the role of health professional support in the self-management of type 2 diabetes. *BMC Health Serv Res, 8*, 214.

Gebhardt, M., Rickenbach, M., & Egger, M. (1998). Impact of antiretroviral combination therapies on AIDS surveillance reports in Switzerland. Swiss HIV Cohort Study. *AIDS, 12*(10), 1195-1201.

Gifford, A. L., & Sengupta, S. (1999). Self-management health education for chronic HIV infection. *AIDS Care, 11*(1), 115-130.

Glass, T. R., De Geest, S., Weber, R., Vernazza, P. L., Rickenbach, M., Furrer, H., et al. (2006). Correlates of self-reported nonadherence to antiretroviral therapy in HIV-infected patients: The Swiss HIV Cohort Study. *Journal of Acquired Immune Deficiency Syndromes, 41*(3), 385-392.

Gross, R., Yip, B., Lo Re, V., 3rd, Wood, E., Alexander, C. S., Harrigan, P. R., et al. (2006). A simple, dynamic measure of antiretroviral therapy adherence predicts failure to maintain HIV-1 suppression. *Journal of Infectious Diseases, 194*(8), 1108-1114.

Guthrie, B., Saultz, J. W., Freeman, G. K., & Haggerty, J. L. (2008). Continuity of care matters. *BMJ, 337*, a867.

Hammer, S. M., Eron, J. J., Jr., Reiss, P., Schooley, R. T., Thompson, M. A., Walmsley, S., et al. (2008). Antiretroviral treatment of adult HIV infection: 2008 recommendations of the International AIDS Society-USA panel. *JAMA, 300*(5), 555-570.

Harding, R., Molloy, T., Easterbrook, P., Frame, K., & Higginson, I. J. (2006). Is antiretroviral therapy associated with symptom prevalence and burden? *International Journal of STD and AIDS, 17*(6), 400-405.

Harrigan, P. R., Hogg, R. S., Dong, W. W., Yip, B., Wynhoven, B., Woodward, J., et al. (2005). Predictors of HIV drug-resistance mutations in a large antiretroviral-naive cohort initiating triple antiretroviral therapy. *Journal of Infectious Diseases, 191*(3), 339-347.

Hodgson, I. (2006). Empathy, inclusion and enclaves: the culture of care of people with HIV/AIDS and nursing implications. *Journal of Advanced Nursing, 55*(3), 283-290.

Ingram, K. M., Jones, D. A., Fass, R. J., Neidig, J. L., & Song, Y. S. (1999). Social support and unsupportive social interactions: their association with depression among people living with HIV. *AIDS Care, 11*(3), 313-329.

Joosten, E. A., DeFuentes-Merillas, L., de Weert, G. H., Sensky, T., van der Staak, C. P., & de Jong, C. A. (2008). Systematic review of the effects of shared decision-making on patient satisfaction, treatment adherence and health status. *Psychotherapy and Psychosomatics, 77*(4), 219-226.

Kickbush, I. (2006). *Die Gesundheitsgesellschaft Megatrends der Gesundheit und deren Konsequenzen für Politik und Gesellschaft*. Gamburg: Verlag für Gesundheitsförderung.

King, M. S., Brun, S. C., & Kempf, D. J. (2005). Relationship between adherence and the development of resistance in antiretroviral-naive, HIV-1-infected patients receiving lopinavir/ritonavir or nelfinavir. *Journal of Infectious Diseases, 191*(12), 2046-2052.

Koch, T. (1996). Implementation of a hermeneutic inquiry in nursing: philosophy, rigour and representation. *Journal of Advanced Nursing, 24*(1), 174-184.

Levine, C. (1990). AIDS and changing concepts of family. *Milbank Quarterly, 68*(1), 33-58.

Lorig, K. R., & Holman, H. (2003). Self-management education: history, definition, outcomes, and mechanisms. *Annals of Behavioral Medicine, 26*(1), 1-7.

Martin, J. S., Frei, I. A., Suter-Hofmann, F., Fierz, K., Schubert, M., & Spirig, R. (in press, 2009). Evaluation der Pflege- und Führungskompetenz - eine Ausgangslage für die weitere Praxisentwicklung. *Pflege*.

Mathews, W. C., McCutchan, J. A., Asch, S., Turner, B. J., Gifford, A. L., Kuromiya, K., et al. (2000). National estimates of HIV-related symptom prevalence from the HIV cost and sevices utilization study. *Medical Care, 38*(7), 750-762.

McCoy, L. (2005). HIV-positive patients and the doctor-patient relationship: perspectives from the margins. *Qualitative Health Research, 15*(6), 791-806.

Miller, L. G., Liu, H., Hays, R. D., Golin, C. E., Beck, C. K., Asch, S. M., et al. (2002). How well do clinicians estimate patients' adherence to combination antiretroviral therapy? *Journal of General Internal Medicine, 17*(1), 1-11.

Nicca, D., Fehr, J., Battegay, M., & Spirig, R. (2005). [Ready for antiretroviral therapy? Therapy decision making experiences of persons living with HIV]. *Pflege, 18*(5), 289-298.

Peretti-Watel, P., Spire, B., Pierret, J., Lert, F., & Obadia, Y. (2006). Management of HIV-related stigma and adherence to HAART: evidence from a large representative sample of outpatients attending French hospitals (ANRS-EN12-VESPA 2003). *AIDS Care, 18*(3), 254-261.

Reilly, C. A., Holzemer, W. L., Henry, S. B., Slaughter, R. E., & Portillo, C. J. (1997). A comparison of patient and nurse ratings of human immunodeficiency virus-related signs and symptoms. *Nursing Research, 46*(6), 318-323.

Schneider, J., Kaplan, S. H., Greenfield, S., Li, W., & Wilson, I. B. (2004). Better physician-patient relationships are associated with higher reported adherence to antiretroviral therapy in patients with HIV infection. *Journal of General Internal Medicine, 19*(11), 1096-1103.

Schoen, C., Osborn, R., How, S. K., Doty, M. M., & Peugh, J. (2009). In chronic condition: experiences of patients with complex health care needs, in eight countries, 2008. *Health Affairs (Millwood), 28*(1), 1-16.

Schuster, M. A., Collins, R., Cunningham, W. E., Morton, S. C., Zierler, S., Wong, M., et al. (2005). Perceived discrimination in clinical care in a nationally representative sample of HIV-infected adults receiving health care. *Journal of General Internal Medicine, 20*(9), 807-813.

Silverberg, M. J., Gore, M. E., French, A. L., Gandhi, M., Glesby, M. J., Kovacs, A., et al. (2005). Prevalence of clinical symptoms associated with highly active antiretroviral therapy in Women's Interagancy HIV Study. *Clinical Infectious Disease, 39*(5), 717-724.

Simoni, J. M., Pearson, C. R., Pantalone, D. W., Marks, G., & Crepaz, N. (2006). Efficacy of interventions in improving highly active antiretroviral therapy adherence and HIV-1 RNA viral load. A meta-analytic review of randomized controlled trials. *Journal of Acquired Immune Deficiency Syndromes, 43 Suppl 1*, S23-35.

Spirig, R. (2002). In invisibility and isolation: The experiences of HIV affected families in German-speaking Switzerland. *Qualitative Health Research, 12*(10), 1323-1337.

Spirig, R., Moody, K., Battegay, M., & De Geest, S. (2005). Symptom management in HIV/AIDS: Advancing the conceptualization. *Advances in Nursing Science, 28*(4), 333-344.

Sterne, J. A., Hernan, M. A., Ledergerber, B., Tilling, K., Weber, R., Sendi, P., et al. (2005). Long-term effectiveness of potent antiretroviral therapy in preventing AIDS and death: a prospective cohort study. *Lancet, 366*(9483), 378-384.

Thorne, S., Paterson, B., & Russell, C. (2003). The structure of everyday self-care decision making in chronic illness. *Qualitative Health Research, 13*(10), 1337-1352.

Vervoort, S. C., Borleffs, J. C., Hoepelman, A. I., & Grypdonck, M. H. (2007). Adherence in antiretroviral therapy: a review of qualitative studies. *AIDS, 21*(3), 271-281.

Wantland, D. J., Holzemer, W. L., Moezzi, S., Willard, S. S., Arudo, J., Kirksey, K. M., et al. (2008). A randomized controlled trial testing the efficacy of an HIV/AIDS symptom management manual. *Journal of Pain and Symptom Management, 36*(3), 235-246.

Wiener, C. (1989). Untrained, unpaid, and unacknowledged: the patient as worker. *Arthritis Care and Research, 2*(1), 16-21.

Wilson, H. S., Hutchinson, S. A., & Holzemer, W. L. (2002). Reconciling incompatibilities: a grounded theory of HIV medication adherence and symptom management. *Qualitative Health Research, 12*(10), 1309-1322.

Wong, W. K., & Ussher, J. (2008). How do subjectively-constructed meanings ascribed to anti-HIV treatments affect treatment-adherent practice? *Qualitative Health Research, 18*(4), 458-468.

World Health Organization. (2003). *Adherence to long-term therapies: Evidence for action*. Geneva: WHO.

WHO. (2002). *Innovative Care for Chronic Conditions*. Geneva: WHO library Cataloging-in-Publication.

Young, J., De Geest, S., Spirig, R., Flepp, M., Rickenbach, M., Furrer, H., et al. (2004). Stable partnership and progression to AIDS or death in HIV infected patients receiving highly active antiretroviral therapy: Swiss HIV cohort study. *BMJ, 328*(7430), 15.

Chapter 6

Symptom management in HIV/AIDS: A mixed methods approach to describe collaboration and concordance between persons living with HIV and their close support persons

Dunja Nicca [1,2], Katharina Fierz [1], Mary Beth Happ [4], Kimberly Moody [5], Rebecca Spirig [1]

[1] Institute of Nursing Science, University of Basel and Department of Clinical Nursing Science, University Hospital Basel, Switzerland

[2] Division of Infectious Diseases and Hospital Epidemiology, Cantonal Hospital of St. Gallen, Switzerland

[3] Department of Clinical Nursing Science, University Hospital Basel, Switzerland

[4] School of Nursing, University of Pittsburgh, USA

[5] University of Southern Maine, Portland, Maine, USA

Corresponding author, e-mail: dunja.nicca@kssg.ch

Submitted to: Journal of Mixed Methods Research

Abstract

For persons living with HIV (PLWH) effective symptom management, on a daily basis, is crucial for good health outcomes and usually involves close support persons (CSP). This sequential exploratory mixed methods study investigated the collaboration of PLWH and their CSP within the process of symptom management, including symptom experience reports of the two players. Qualitative results revealed that collaboration is constituted by distinct but integrative positions of manager and partner which are reflected in diverse themes of daily symptom management and confirmed in the quantitatively assessed symptom experience reports. In conclusion the collaboration of the two players, in particular symptom communication in specific areas, such as neurocognitive problems, should be further supported by better integrating CSP into clinical services.

Introduction

Despite significantly improved survival prospects due to long term antiretroviral therapy, many persons living with HIV (PLWH) continue to experience a wide range of symptoms related to the disease as well as comorbidities, opportunistic infections, and medication side effects [1, 10-12]. Effective symptom management is essential for such people and usually involves collaborating with others, in particular close support persons (CSPs), since the chronic condition is mainly managed in the home setting with hospital care services provided in outpatient settings mainly. Symptom management is important since a high number of symptoms have been shown to negatively impact health-related quality of life and antiretroviral treatment adherence [9, 116, 177]. A high antiretroviral treatment adherence is key as even small irregularities can lead to insufficient plasma drug levels, which increases the risk of drug resistant mutations, cross-resistance, and ultimately, ineffectiveness of the medications used for treatment [20]. Despite this, PLWH conducted daily adherence decisions based on their symptom management [22].

PLWH symptom management is complex. It encompasses day-to-day decisions about dealing with symptoms, such as when to contact a health care provider, whether or not to alter exercise or diet, and when or when not to take certain medications [16]. These processes are likely to be influenced by the social contexts in which they take place. PLWH are part of diverse families, partnerships and friendships. In Switzerland, it has been shown that these diverse relations are influenced by the continuing social stigmatization of the condition and those affected by it. In a qualitative investigation, only a small subgroup of family members were willing to assume caregiving tasks for PLWH. They performed these very privately in order to prevent being rejected or judged by others. Nevertheless the presence of at least one close and informed support person seemed to be important for a PLWH’s health [33]. A prospective cohort study demonstrated that stable partnerships were associated with slower rates of disease progression in PLWH receiving antiretroviral therapy [122]. Other investigations found that for PLWH, high levels of social support were associated with fewer depressive symptoms and enhanced treatment adherence [124, 125]. In sum, research clearly demonstrates the importance of relationships with close support persons for PLWH health. Yet the collaboration process between PLWH and CSPs for symptom management remains unclear, even though a better understanding of this is important if health care providers are to guide tailored symptom management interventions.

The first step in the process of symptom management is the symptom experience of PLWH. This process involves a cognitive component, where the frequency and severity of a symptom is recognized, and an emotional component, where the distress caused by the symptom is felt [28]. The negative influence of high symptom frequency, severity and in particular of high distress levels on health outcomes such as adherence and quality of life has been documented [28, 71]. Taking the PLWH symptom experience as the starting point for symptom management, it would seem that concordance between symptom reports by PLWH and CSPs is crucial if they are to collaborate in the symptom management process. Insufficiently managed symptoms have been shown to cause distress not only for patients with chronic conditions but also for their CSPs. Furthermore, such distress seems to hinder effective symptom communication between the two players [178]. To our knowledge, concordance in symptom experience has not been investigated in the HIV population. In cancer patients, Kurth and colleagues found a high agreement of 71% in symptom reports between patients and their CSPs [34]. However, in a more recent study of cancer patients and their CSPs, agreement levels for single symptoms were diverse and ranged from poor to excellent with a general trend for CSPs to overestimate symptom experience [35]. An understanding of the concordance or discordance in the perception of symptoms between PLWH and their CSPs and the role this plays in the overall symptom management process would appear to be important for health care providers. For example, they might need to educate patients and support persons about symptom communication or educate support persons in symptom distress presentation, in order to improve health outcomes for PLWH.

The purpose of this mixed methods research study was therefore to explore the collaboration between PLWH and their CSPs within the process of symptom management, including the concordance of symptom reports of the two players.

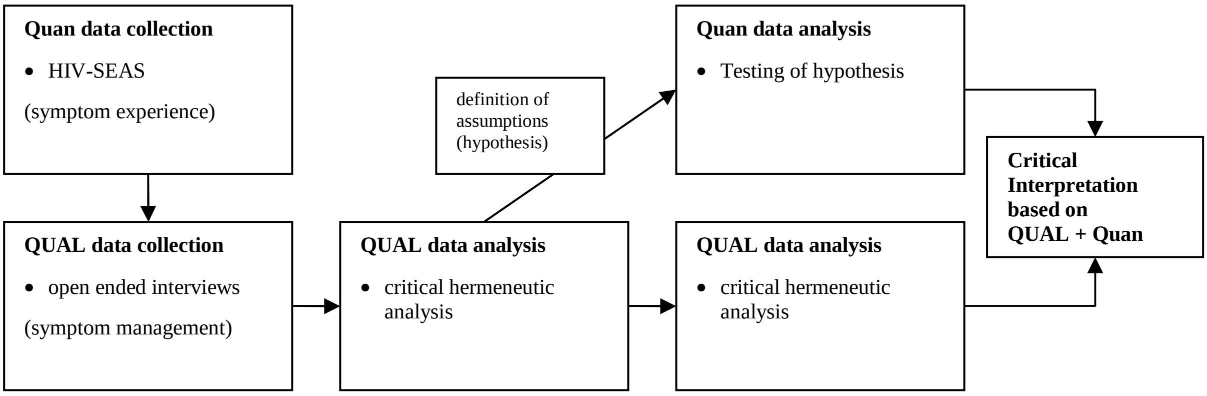
The first phase of the study involved a qualitative exploration of how PLWH and their CSPs experienced collaboration on symptom management. The second phase analyzed participants' narratives recorded during the first qualitative phase to construct three hypotheses for a quantitative exploration about concordance of symptom reports: 1) PLWH report on more symptoms than their CSPs do; 2) There are specific symptoms that are more often reported by CSPs; and 3) In the case of symptoms being reported as very distressing by PLWH, symptom reports by PLWH and CSPs do not differ.

Methodology and Methods

A mixed methods approach featuring a combination of qualitative and quantitative investigations was chosen to expand existing knowledge about how PLWH and their CSPs collaborate on the management of symptoms. More specifically, a sequential exploratory design was used with a greater emphasis on the qualitative investigation [47]. The project started with a qualitative phase designed to explore the phenomena of collaboration in symptom management. The data gathered during this phase were used to form hypotheses which were then tested with data drawn from a larger sample (Figure 1). The quantitative follow-up study was used to complement, validate, and extend the qualitative findings.

From a methodological point of view, the study was guided by a critical hermeneutical approach. This thinking tradition is grounded in critical theory and oriented toward critiquing and changing society, in contrast to traditional theories which are oriented only toward understanding or explaining phenomena [179]. A major critique within critical theory has been that scientific knowledge can not only be generated by the careful testing of clearly observable propositions, but also through understanding revealed by conversations. Therefore both approaches to knowledge generation - that is, qualitative and quantitative approaches - can be viewed as equally relevant and valid ways of exploring specific questions, as long as the results are reflected upon with respect to the social contexts in which they exist and in light of power issues [180]. At the method level, the process included shifting between the qualitative and subjective data and the use of inductive reasoning and quantitative numeric data using deductive reasoning [181]. This process is further depicted in an overview shown in Figure 1. The studies were conducted by a team of researchers with complementary expertise in qualitative and quantitative research.

Figure 1: Overview of Exploratory Sequential Design



Setting and Sample

This study was conducted within the framework of a larger multicenter investigation exploring the relationships between symptom experience, symptom manageability, adherence, health related quality of life, and disease progression in PLWH from the perspective of patients and their CSPs (Spirig 2002b). The investigation was implemented in collaboration with the Swiss HIV Cohort Study (SHCS) in four of their seven centers. The relevant ethics committees granted approval.

PLWH and their CSPs were consecutively recruited for this study at medical appointments. To be eligible for study participation, PLWH had to be on antiretroviral therapy, over eighteen years of age, able to read and speak German and able to participate together with a CSP. A CSP was defined as an individual who by birth, marriage, friendship or declared commitment shared deep and personal connections with the PLWH and provided various types of support in times of need [121]. PLWH decided whether or not they had someone who met this definition. With the consent of the PLWH, their CSP was then contacted and asked to participate in the study. From this final sample, a smaller sample was purposefully selected for interviews, in order to achieve variation according to centers, gender of the PLWH, and diversity in relationships with CSPs.

Data collection and measurement

Data collection of quantitative and qualitative data occurred independently of each other, since the granting agency required the completion of data collection within a specific timeframe.

Participants who consented to this study were given a set of structured study questionnaires, which they completed and returned by mail. Demographics were assessed with the SHCS Questionnaire. The HIV Symptom Experience Assessment Scale (HIV-SEAS) was used to assess occurrence and distress of symptoms. This consists of 73 items (symptoms) to be rated across three dimensions: frequency and severity (representing symptom occurrence) and distress. PLWH filled in the questionnaire for themselves, whereas their CSPs rated the PLWH symptom experience from their perspective. Participants were asked to indicate if a symptom had occurred during the past week (yes/no). If it had occured, they were asked to rate how often it had occured on a 4-point Likert scale (1 = rarely, 2 = occasionally, 3 = frequently, 4 = almost constantly), how severe it usually was (1 = slight, 2 = moderate, 3 = severe, 4 = very severe) and how much it distressed or bothered the PLWH (0 = not at all, 1 = a little bit, 2 = quite a bit, 3 = very much). The HIV-SEAS was developed and tested by within the larger study (Vincenzi, Moody, Spirig, 2009).

For this study, qualitative interviews took place in the participants' homes or in a private room of the HIV outpatient clinic, according to preference. PLWH and CSPs were interviewed separately. An interview guide suggesting open-ended questions was used to facilitate dialogues on participants' perspectives of symptom management and their collaboration. Interviews lasted between 50 and 90 minutes. They were recorded and later transcribed verbatim.

Data analysis

The mixed method analysis was done in a sequential but integrated fashion with periodic exchange between the preliminary results of the two parts of the study. We began by analyzing qualitative data, using the critical hermeneutic approach suggested by Diekelmann and Allen [182]. This involves multiple steps such as a) developing an overall understanding of the texts; b) defining categories for each interview; c) developing relational themes (themes that cut across all texts); and d) building constitutive patterns (patterns present in all documents expressing the relationships of the relational themes). Atlas software was used to support this process (Atlas.ti 5.2 Scientific Software Development, Berlin, Germany). Finalized descriptions of results were translated into English.

After the first two steps of the qualitative analysis (a and b above) were carried out, the preliminary results were discussed by the research team. Based on three themes that cut across all narratives, tentative hypotheses for the quantitative analysis were built and tested. Descriptive data were calculated for demographic variables as follows: medians for non-normally distributed data and frequencies for categorical data. To test the differences in the numbers of reported symptoms between PLWH and CSPs (H1), the Wilcoxon signed rank test was used. To explore discordant and concordant symptom reports (H2 and H3), the Mc Nemar paired samples test was employed. To account for multiple testing, q-values were calculated as suggested by Benjamini and Hochberg: i.e., the expected number of type I - errors was kept below 5% [108]. The adapted p-values were denoted as q-values. Symptom distress across the PLWH sample was defined by averaging individual symptom distress ratings. The presence of the twenty most 'distressing' recorded symptoms by PLWH was compared against those given by CSPs. All analyses were performed using SPSS® version 16.0 (SPSS Inc., Chicago, IL, USA).

The final steps of the qualitative analysis (c and d) were conducted concurrently with the quantitative analysis. After qualitative and quantitative analysis, data combination occurred at the level of data interpretation with a critical social perspective that is outlined in the discussion section.

Results

At medical consultation, 220 PLWH agreed to participate. Subsequently, 34 of their CSPs did not agree to participate. Of the remaining 184 dyads, 64 were lost to follow-up, mainly due to unreturned questionnaires. The final sample consisted of 122 PLWH and their 122 CSPs.

Description of samples and participants

The characteristics of the overall sample (CSPs and PLWH), those not included due to CSP refusal, and those lost to follow-up are shown in Table 1. On average the sample was middle-aged with almost no age differences between PLWH and CSPs. Participants were predominantly white Swiss men, with males accounting for 75% of PLWH and 59% of CSPs. Whereas the PLWH mostly only had a basic education, many CSPs had a higher level of education: 20% of PLWH and 40% of CSP had a bachelor's degree or higher. The median plasma CD4 cell count for the PLWH was 455 (IQR 294-590) cells/mm^3 and the majority (90%) had plasma HIV-1 RNA below 400 copies/mL.

Table 1: Characteristics of participating PLWH and CSP and non participating PLWH

Variable	**PLWH**	**CSP**	**PLWH lost to follow-up**	**PLWH whose CSPs refused participation**
Total – N	122	122	64	34
Male gender - %	75.4	59.2	84.4	76.5
Age – median (IQR)	44.5 (40-51)	45 (39-55)	43.0 (39-48)	44 (40-52)
Highest completed educational degree -%				
No completed school or educational degree	1.6	0.8	4.7	-
Mandatory schooling (9 years)	11.5	11.6	9.4	23.5
Completed apprenticeship	63.1	43.8	54.7	55.9
Bachelor degree / higher professional education	9.9	15.7	7.8	8.8
Graduate degree	10.7	24	15.6	5.9
No information / other	3.3	4.1	7.8	5.9
Swiss nationality - %	92.6	87.3	No information	75.8
White ethnicity - %	97.5	95.9	No information	97
Transmission group - %				
MSM[1]	50.8		42.2	35.3
MSF / FSM[2]	27		26.6	20.6
IV drug use	8.2		18.8	26.5
Other	14		12.5	17.6
AIDS - %	27		29.7	38.2
CD 4 cell count (mmol/L) - median (IQR)	454.5 (305.5-630.0)		369.5 (299.3-634.5)	440 (255.0-601.0)
HIV-1 RNA (copies/ml) - %				
<50	77.9		67.2	85.3
50 – 399	13.1		17.2	8.8
≥400	9		15.6	5.9

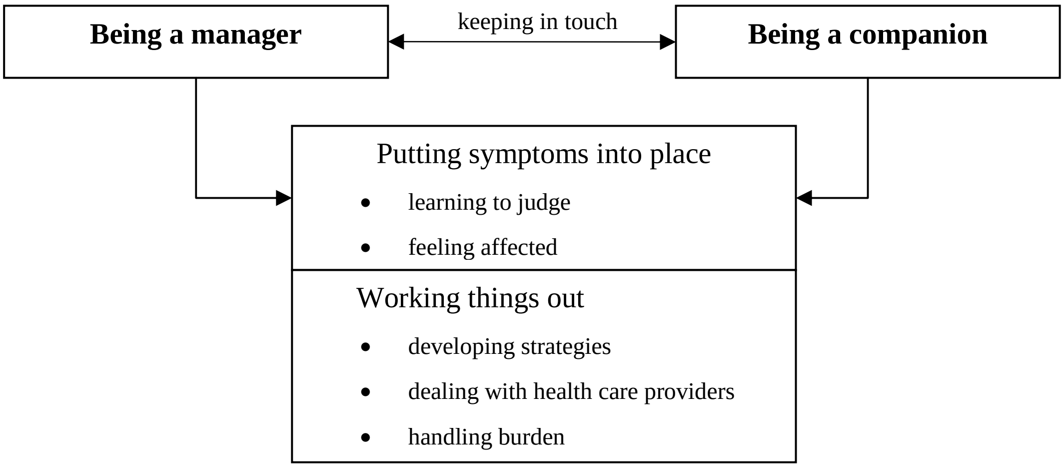
IQR = interquartile range

The qualitative sample derived from the larger sample consisted of 26 participants - 13 PLWH and their 13 CSPs. Compared to the larger sample, there were no major differences in age, CD4 cell count, HIV-1 RNA copies/mL or median of prevalent symptoms. The group of PLWH consisted of 7 males and 5 females, four of whom had a history of intravenous drug use. Their CSPs were made up of 10 males and 3 females. All the PLWH had been living with HIV for many years and their narratives revealed a broad range of experiences in managing symptoms. Their living circumstances in rural and urban areas of Switzerland were diverse: some lived in homo- or heterosexual partnerships, others in families with children, others by themselves with close contact to friends and family members. Reflecting this diversity, the CSPs consisted of partners, close friends, brothers, or sisters. All of the CSPs had had a close relationship with the PLWH for more than 2 years. The broad experiences of participants of collaboratively managing symptoms are described below.

Collaboration on Symptom Management

Narratives revealed that even small changes in the symptom experience of PLWH could severely impact their daily lives. In order to handle these changes, both PLWH and CSPs reported participating actively in the symptom management process. Constitutive across all interviews were the two distinct positions of the two players. PLWH seemed to be the managers taking a clear leadership role, whereas their CSPs appeared to be their companions who supported them in specific areas of symptom management. The positions of '*being a manager'* and *'being a companion'* were closely connected, which is portrayed by the theme *'keeping in touch.'* Two other themes, *'putting symptoms into place' and 'working things out',* each with diverse sub themes, further reveal the collaboration in symptom management as Figure 2 shows:

Figure 2: Constitutive pattern of collaboration in symptom management



Being a Manager

Interviews showed that PLWH made a clear decision to not only manage their symptoms but actively manage the entire chronic condition. The feeling of having a grip on HIV rather than being controlled by it seemed most important for them. Their narratives revealed broad medical knowledge and expertise related to their own health and wellbeing. PLWH seemed to purposefully integrate the expertise of health care providers and CSPs in their management. A female participant shared her experiences:

> *The virus is not a problem, it is quiet. My lab parameters are fine and I don't have any problems with my meds. I am so pernickety; I always take them every morning in the same order. But the fatigue is something I have to get a grip on again. I really have to discuss it with my doc next week.*

Being a companion

CSPs emphasized a strong commitment to stay in the relationship despite HIV. With a strong focus on PLWH illness management, CSPs talked about finding their own responsibilities in the process according to their own resources. For instance, CSPs talked about supporting medication management, general health behaviors such as exercise and nutrition, and symptom management. A CSP finding his own responsibility in symptom management reported:

> *Well, if he has a cold or any kind of infection, I feel a little responsible to evaluate if it's necessary for him to see his doc. You know, since I kind of have a professional background.*

Keeping in touch

Despite a broad diversity in lifestyles, participants highlighted the importance of close and ongoing contact with one another. PLWH wanted to know about the wellbeing of their CSPs and whether they felt burdened by anything. This seemed important, since a struggling partner together with their own difficulties could make PLWH feel like they were losing their grip on HIV. They mentioned that CSPs made it possible for them to live meaningfully and actively manage their condition. In addition, CSPs wanted to know about the wellbeing of the PLWH in order to better understand behaviors and provide adequate support. Knowing about a PLWH's health status seemed to help them overcome fears of losing their loved ones. Ongoing exchanges about clinic visits, medication scheduling, or symptoms were integrated into daily routines. Nevertheless both parties reported taking special efforts to enable exchanges, illustrated through the example of a male CSP:

> *I drive her to the clinic, because I think it's easier for her and on the way back we have time to talk, you know we drive for more than an hour and that's time to talk about it.*

Participants also revealed that exchanges had to be carefully balanced in order not to overburden each other. For many of them, other discussion partners were rare or not available, since they carefully balanced their need to talk with others against possible negative consequences of HIV status disclosure.

Putting symptoms into place

Participants explained the importance of watching out for new or changing symptoms and putting them into a known frame of reference. PLWH revealed a constant monitoring of their own state of health and occurring symptoms, whereas their CSPs did not seem to observe the situation constantly. However, they were attentive and listened to PLWH in their daily exchanges. The following three sub themes '*learning to judge*,' '*feeling affected*,' and '*not talking about it*' explore this process further.

Learning to judge. Participants described a learning process, which made it easier for them to put symptoms into a known frame of reference. PLWH explained how they improved their knowledge about possible treatment side effects and HIV related symptoms, learned to interpret their lab parameters, and learned to be sensitive to small body reactions. They learned from their own experiences and from health care providers. Health care providers were described as important partners, especially at the beginning. A male PLWH said:

> *Nowadays I take symptoms in a more relaxed way, if I have a rash or something like that, I recognize it but I am not scared anymore. In the beginning I went to see the doc immediately in order to get decision making support. Today I tell the doc to wait with examinations. I just know it could be this or that, I wait and I realize if it's something more serious. In such a case I don't put it off for long.*

There was more variation among the CSPs' stories. Some explained that knowing about possible symptoms and side effects helped them to overcome fears. They mostly learned about HIV from PLWH or from the media. Others favored a kind of "naive" view on symptoms. They explained that they did not want to learn anything about HIV since it helped them to interpret symptoms on an everyday level. They experienced this as complementary to PLWH symptom interpretation. Another group of CSPs had some sort of professional background which they used for basic knowledge. They mentioned how they expanded their knowledge through professional on-line searches or by asking knowledgeable colleagues. This group most often expressed fear of a misjudgment related to symptoms. One CSP revealed:

> *In the case of infections, I feel responsible to help him to evaluate if he has to see the physician. But it is difficult sometimes, since I don't want to blame myself for waiting too long or giving the wrong advice.*

Feeling affected. All participants described many similar stories about the course of certain symptoms. PLWH talked about the most difficult symptoms, which could not be sufficiently managed over time and caused uncertainty, fear and loss of morale. CSPs discussed how they recognized a PLWH's suffering and expressed empathy and understanding. They stated that they were not as affected by the symptom as the PLWH was and did not feel stressed or bothered by the problem itself. In spite of this, they felt bothered by symptoms that influenced their relationship and common activities. One CSP said:

> *I got the impression that his meds make him incredibly tired and this really troubles me. If we watch a movie together or we want to discuss something, after ten minutes he starts snoring, this really gets on my nerves. I really do not know if it is connected to the medications, the illness, or whether it would have been like this anyway.*
>
> His partner with HIV explained:
>
> *The fatigue got worse and worse. In our relationship this was a huge disturbing factor, since my partner just can't handle it. I still work full time, but in the evenings I let go and then I fall asleep when I sit down. For him it's very negative; for me it's more positive.*

Not talking about it. Participants explained that symptoms which PLWH felt they had a grip on were almost never discussed in daily life. Yet there also appeared to be reasons for not talking about new symptoms or old ones which were still distressing. Some PLWH reported dealing with all of their symptoms on their own or including health care providers as primary discussion partners. Other PLWH explained that they tried to not overburden their CSP by carefully balancing discussions about distressing symptoms. They also withheld symptoms if the CSP seemed to be very fearful. One PLWH explained:

> *There are certain things I don't tell him. If I have headaches again, I don't tell him, because otherwise he concludes it's something because of the illness.*

CSPs mentioned situations where they felt the PLWH was suffering from symptoms but did not talk about them. This seemed to cause feelings of powerlessness for some of them. CSPs also revealed that they sometimes observed symptoms which they did not share with the PLWH. They mentioned symptoms like memory loss and concentration problems, which, they assumed, might be very stressful for the PLWH. One CSP reported:

> *Well, sometimes I realize that she stops in the middle of a sentence and then starts talking again about something else. She had these gaps and she doesn't realize it. But I've never discussed it with her. I think it would be very distressing for her.*

Working things out

Participants described how they worked out strategies with the aim of curing symptoms or integrating them into daily life and reducing stress. Sometimes symptoms could be dealt with quickly and easily. In such cases the PLWH dealt with the symptoms on their own and they did not appear as major issues in the corresponding CSP narratives.

The situation was however different in the case of distressing symptoms. Here, both PLWH and CSPs described how they each had to handle their emotions and how they sometimes worked out strategies either collaboratively or on their own. This process is further described by the following sub themes: '*developing strategies*,' '*dealing with health care providers*', and '*handling burden*.'

Developing strategies. Participants revealed that very individualized strategies had to be worked out in order to manage PLWH's distressing symptoms efficiently. PLWH reported a process of testing different ways to deal with symptoms in which they integrated recommendations from health care providers, friends, and peers as well as from diverse media sources such as the internet. One female PLWH explained:

> *I have this diarrhea and the doc gave me Imodium (Loperamide). But over time I learned to better manage it. I used Bioflorin which rebuilds the intestinal mucosa. It works for me now. I have also tried managing (the diarrhea) with food. For a while I ate bananas.*

There were varying accounts of the collaboration between PLWH and CSPs. Some CSPs reported being actively integrated in the testing of different ways to manage symptoms. Others said that they mainly listened to the PLWH's stories and encouraged them to reflect on their symptoms. They also brought their own suggestions into these discussions. Some CSPs mentioned that they were not integrated into the development of strategies. In situations where PLWH were struggling with management, CSP often seemed to experience a sense of being excluded. As one male CSP revealed:

> *I would like to be more involved with his problem solving, since it's difficult for him. I still have resources and would be able to mobilize strengths to support him, in order to make him feel better and make both of us feel better.*

Dealing with health care providers. Participants' narratives revealed health care providers to be important partners for working out symptom management strategies. PLWH emphasized the importance of a close participative relationship with health care providers. They actively asked questions and developed strategies collaboratively. Yet providers were not always experienced as helpful partners. PLWH talked about providers who did not seem to listen and appeared to push their own agenda. If PLWH experienced such behaviors while struggling with symptoms, they expressed *feelings of insecurity, distress, and desperation. A male PLWH reported:*

> *All went well for years. I had the impression they [physicians] appreciated how well I managed besides a full time job. Now I have this fatigue and everything has changed. I sometimes think my lab results are still too good to be taken seriously. My last physician for example, in every consultation he told me that he wants to take me off the antibiotics and have me go back to work. He really scared me, I almost panicked. I always wanted to work, that's not it, but now I think they don't take my problems seriously.*

Their CSP did not appear to be directly involved in the collaboration with health care providers even though some had accompanied PLWH on clinical visits. Nevertheless CSPs reported discussing PLWH's clinical consultations and relationships regularly with health care providers. Accordingly they provided emotional or decision making support and sometimes encouraged the PLWH to contact a health care provider. Knowing about a positive PLWH-provider relationship seemed to relieve their own fears and sense of burden. As one male CSP put it:

> *I'm not stressed, I know she goes to see her doc every three months and also goes there in between if necessary. If something comes up, I just tell her to call the doc and ask him if it's something normal or not.*

Handling burden. Difficulties in the management of symptoms over time were shown to cause stress and be a burden for participants. PLWH emphasized that their CSP were important partners to share feelings of fear, sadness, and desperation related to unsuccessful symptom management. At the same time they revealed how they had to focus strongly on their own needs. Even though they sometimes talked about feeling guilty toward their CSPs, they described this process as important in stabilizing their situation and recovering their strength. A male PLWH explained:

> *They [friends] have to accept it. I sometimes tell my partner that I can't go out that day, I don't feel well and I just can't. For me, rest is most important, and over the years I have arranged my life according to the rest I need, it works out that way.*

CSPs seemed sometimes torn between arguing with PLWH about their own needs and being understanding toward PLWH. Due to the restrictive disclosure of HIV status, other support persons were limited. CSPs who seemed to cope well with the burden reporting escaping briefly, doing recreational things on their own, and organizing their needs around those of PLWH. A male CSP reported:

> *There are situations that are how they are, one has to accept it. And I've now learned to organize my free time (space) according to her symptoms and not the other way around. We just have to be at home by 3 pm, in order for her to relax; otherwise the evening is a mess.*

Concordance in symptom experience reports

Participants' narratives provided an in-depth insight into their collaborative management of symptoms. Based on those insights we further explored their concordance in symptom experience reports. Three hypotheses drawn from participants' narratives and tested in the larger sample of 122 dyads are described below.

The first hypothesis was that PLWH reported more symptoms than their CSPs did. Participants' stories often circled around similar symptoms. Nevertheless PLWH used very straightforward and clear language whereas their CSPs use of language often reflected some insecurity about the symptom reports, for example: "I think he had diarrhea at that time." There were statistically significant differences in symptom reports over the last week, with PLWH and CSPs reporting a median of 16 (Q_1= 9; Q_3= 24) and 12 (Q_1= 5; Q_3= 17) symptoms respectively ($p < 0.001$).

The second hypothesis was that there were specific symptoms that were more often reported by CSPs than by PLWH. CSPs' stories revealed that they did not talk to the PLWH about certain symptoms such as memory loss or forgetfulness in order not to hurt or offend them. Results revealed significant differences in symptom reports for 16 out of 73 assessed symptoms as shown in Table 2. All 16 symptoms were reported more often by PLWH.

Table 2: concordance / discordance of PLWH's and their CSPs' reports on presence of symptoms

Symptom (in order of appearance in questionnaire)	Appraisal of symptom by PLWH and CSPs **N=122**				Ho=1
	yes by PLWH	yes by CSP	Mc Nemar (paired test)		
	n	n	Chi-square	p-value (2-tailed)	q-value
muscle cramps	18	6		0.0231	0.088
weakness	23	13	2.25	0.1342	0.245
painful joints	16	17	0.01	1	1
fatigue	24	9	5.94	0.015	0.064
muscle aches	16	7		0.0931	0.2
fever	6	10		0.4541	0.603
chills	11	15	0.35	0.5562	0.712
flushing	19	18	0	1.0002	1
night sweats	20	11	2.07	0.151	0.262
day sweats	12	3		0.0351	0.116
sensitivity to insect bites	7	5		0.7741	0.869
increased sensitivity to hematoma	3	5		0.7271	0.842
weight gain	12	9		0.6641	0.822
weight loss	8	14		0.2861	0.426
weight gain in stomach area	19	21	0.025	0.8742	0.967
hump on back of neck / shoulders	2	4		0.6871	0.836
skinny arms and legs	13	5		0.0961	0.2
swollen feet / legs	8	3		0.2271	0.365
prominent leg veins	17	7		0.0641	0.146
fear / worries	**30**	**12**	**6.88**	**0.0092**	**0.041**
anxious	**31**	**12**	**7.54**	**0.0062**	**0.037**
decreased ability to withstand psychological distress	26	13	3.69	0.0552	0.146
depressed mood	23	11	3.56	0.0592	0.146
dizziness	**25**	**7**	**9.03**	**0.0032**	**0.024**
seizures / tremors	4	3		1.0001	1
difficulty concentrating	**35**	**9**	**14.21**	**2.00E-42**	**0.003**

memory loss	**21**	**6**	**7.26**	**0.0072**	**0.039**
forgetfulness	**27**	**10**	**6.92**	**0.0092**	**0.041**
insomnia / can't sleep	21	10	3.23	0.0722	0.159
vivid dreams	21	13	1.44	0.2302	0.365
headaches	19	13	0.78	0.3772	0.54
nose bleeds	8	4		0.3881	0.545
dry mouth	24	11	4.11	0.0432	0.121
mouth ulcers	14	6		0.1151	0.221
white patches in mouth	3	1		0.6251	0.787
sore, bleeding gums	**21**	**4**		**0.0011**	**0.009**
blood in spittle /sputum	3	0		0.2501	0.388
caries / brittle teeth	15	5		0.0411	0.12
swollen glands	14	6		0.1151	0.221
sore throat / painful swallowing	14	5		0.0641	0.146
tingling in head area	**14**	**1**		**0.0011**	**0.009**
blurred vision	**22**	**3**		**2.00E-41**	**0.003**
shortness of breath at rest	6	5		1.0001	1
shortness of breath with activity	17	6		0.0351	0.116
coughing	20	13	1.09	0.2962	0.432
heart racing	13	3		0.0211	0.085
chest pain	7	2		0.1801	0.306
feeling of restriction in chest	**18**	**4**		**0.0041**	**0.029**
heartburn	20	11	2.07	0.1512	0.262
abdominal pain	16	11	0.59	0.4412	0.596
lack of appetite	12	12		1.0001	1
increased appetite	9	5		0.4241	0.584
thirst	16	9		0.2301	0.365
nausea	14	5		0.0641	0.146
vomiting	6	4		0.7541	0.86
gas / bloating	28	13	4.78	0.0292	0.106
constipation	11	3		0.0571	0.146
diarrhea	23	10	4.36	0.0372	0.117
Rectal itching	**22**	**0**		**1.00E-71**	**0**
Rectal bleeding	10	2		0.0391	0.119
numbness / tingling in arms, hands, fingers	**18**	**1**		**8.00E-51**	**0.003**
numbness / tingling in legs, feet, toes	**23**	**3**	**13.89**	**2.00E-42**	**0.003**
dry skin	**25**	**8**	**7.76**	**0.0052**	**0.033**
itchy skin	20	10	2.7	0.1002	0.203
reddening skin	10	11		1.0001	1
increased rashes	14	10		0.5411	0.705

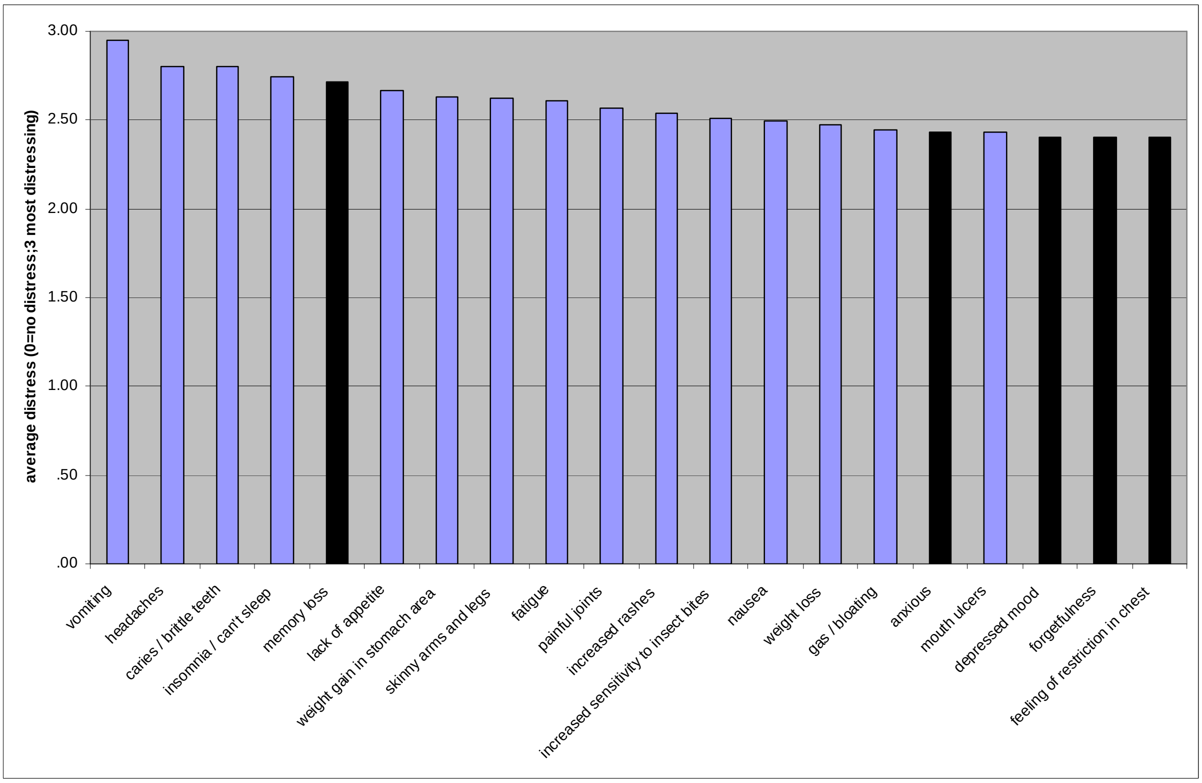
hair loss	9	4	0.2671	0.406
splitting finger nails	**15**	**1**	**0.0011**	**0.009**
change in body hair	5	3	0.7271	0.842
nipple discharge	2	1	1.0001	1
breast pain / breast changes	7	1	0.7001	0.838
Sores or lumps on genitals	4	0	0.1251	0.234
Burning with urination	**8**	**0**	**0.0081**	**0.041**

[1] exact significance, two-tailed; binomial distribution

[2] asymptotic significance, two-tailed; continuity corrected

The third hypothesis was there was no discordance between CSPs and PLWH for symptoms reported as being very stressful by PLWH. When participants talked about their most distressing stories, dyads often used almost the same wording. From the 73 assessed symptoms, 55 were reported as being ‘distressing’ by PLWH, with average distress levels ranging from 1.52 to 2.95 on a scale of 1 to 3. The 20 most distressing symptoms as rated by PLWH are shown in Figure 3. Of these 20 symptoms, there was discordance among the reports on four of the symptoms, which were also most often named by PLWH: memory loss, anxious, forgetfulness, and feeling restriction in chest (symptoms shown in Table 2)

Figure 3: The twenty most distressing symptoms for PLWH



■ *Marked black: discordant reports of symptom presence by PLWH and CSP*

Discussion

Participants’ narratives provided insights into a collaborative process of managing symptoms. This collaboration has been shown to be constituted by distinct but integrative positions. The positions, in particular the clear leadership of PLWH, seemed to be reflected in the descriptions of daily symptom management issues and also in symptom experience reports. The latter revealed that PLWH reported on more symptoms overall, that no symptoms were reported more often by CSPs, and that there was discordance among the two players’ reports for some of the most distressing symptoms for PLWH .

Consistent with earlier research, our results highlight a complex process of managing symptoms in everyday life and shed light on PLWH taking a clear position to actively manage such challenges [18, 22]. Compared to these earlier investigations, this study highlights symptom management as a collaborative task between PLWH and CSPs and provides insight into this process. So far, involvement of CSPs into symptom management has mostly been described as 'informal care giving' with support flowing in a unidirectional manner from caregiver to care recipient [183]. A few qualitative studies have added the relational and often reciprocal dynamics of informal care giving [184, 185]. Lingler et al. recently pointed out the shortcoming of those perspectives: On the basis of three case examples they highlighted the diversity in care giving relationships and the need for a broader understanding of informal care giving, in order to yield findings and develop interventions that carry greater clinical relevance [126]. The different but connected positions of PLWH and CSPs, with the clear leadership of PLWH in symptom management and strong partnerships between both players, add an additional dimension to the debate, yet to our knowledge, prior discussions have not taken account of this perspective. This seems especially important in the field of HIV/AIDS, where most publications on informal care giving described situations before highly active antiretroviral treatments became well established and helped to reduce morbidity. In those early studies the importance of non stigmatizing and reciprocal caring partnerships was emphasized, yet the active lead of PLWH in the management process was not described [32, 186, 187].

In accordance with previous studies, PLWH experienced a fair number of symptoms. For example, this study revealed an average of 16 symptoms per person during the previous week, whereas an earlier study for the same time period found an average of 14 symptoms for PLWH also on cART [10]. In contrast to a recent investigation into cancer patients and their CSPs, where a small to moderate trend for CSPs to overestimate symptoms was described [35], CSPs in this study reported on significantly less symptoms than PLWH. Not one single symptom was reported more often by CSPs. This might be explained by the different positions of PLWH and CSPs in the management process, with PLWH taking overall responsibility and integrating their CSP into different aspects of the management process. The different positions in the management process could also be influenced by health care systems that strongly focus on the individual and do not routinely integrate CSPs into their services.

Describing the collaboration in symptom management from a qualitative and quantitative perspective has broadened understanding of the issue. For example, the intense monitoring described by PLWH but not by CSPs, described as 'putting symptoms into place' could also be reflected in the quantitative survey results, illustrating that PLWH report on more symptoms than CSPs do. Yet the mixed method approach also provided unexpected results which were not easy to interpret. For example the sub theme 'not talking about it' illustrated that participants withheld symptoms in order to protect each other. CSPs in particular mentioned diverse neurocognitive problems they recognized but did not want to talk about with PLWH in order not to hurt them. This led to the hypothesis that some symptoms were reported more often by CSPs. Interestingly however this could not be proved. Symptoms such as ‘difficulty concentrating,’ ‘memory loss,’ and ‘forgetfulness’ were reported discordantly but more often named by PLWH. Further research is needed to shed light on this situation. One explanation for the somewhat unexpected results might be that in our society, cognitive impairments are highly stigmatized, especially in a middle aged population as was involved in this study. Goffman explained stigma as an attribute that is deeply discrediting and separates people with an undesired differentness from others [188]. To protect themselves from shame and social rejection, the affected persons continuously struggle with the decision of whether or not to talk about their stigmatizing attributes [92]. Even though the PLWH in this study had disclosed a stigmatized attribute such as their HIV infection to their CSP, it could be the case that they still struggled to talk about possible neurocognitive problems. The qualitative results clearly revealed such difficulties in communication for the CSPs. During the past few years, neurocognitive deficits in PLWH have received growing attention. However, the discourse has remained mostly on an epidemiological and biomedical level, describing the aging HIV population and neurocognitive deficits, the influence of cART on neurocognitive deficits, and associations of biological processes such as chronic infections on neurocognitive deficits [189, 190]. Health care providers should broaden this discussion and include patient perspectives in order to provide everyday symptom management support for PLWH and their CSPs. This seems highly important since it has been shown that neurocognitive deficits in PLWH influence activities of daily living and work performance [115, 191].

Overall the exploratory mixed method approach moved the two described phenomena of symptom experience and symptom management, which have previously often been treated as distinct, closer together. This provided new insights into the collaboration between PLWH and CSPs on both tasks. The described active and leading position of PLWH in the symptom management process and the active companionship (support) of CSPs appears to be a prerequisite for successful symptom management. Nevertheless this collaboration and in particular symptom communication should be supported by health care providers in order to improve health outcomes for PLWH. This requires a more family or dyad oriented approach with the integration of CSPs into some of the clinical services.

References

Albert, S. M., Marder, K., Dooneief, G., Bell, K., Sano, M., Todak, G., et al. (1995). Neuropsychologic impairment in early HIV infection. A risk factor for work disability. *Arch Neurol, 52*(5), 525-530.

Allen, D. G. (1995). Hermeneutics: philosophical traditions and nursing practice research. *Nurs Sci Q, 8*(4), 174-182.

Ammassari, A., Murri, R., Pezzotti, P., Trotta, M. P., Ravasio, L., De Longis, P., et al. (2001). Self-reported symptoms and medication side effects influence adherence to highly active antiretroviral therapy in persons with HIV infection. *J Acquir Immune Defic Syndr*, *28*(5), 445-449.

Bairan, A., Taylor, G. A., Blake, B. J., Akers, T., Sowell, R., & Mendiola, R., Jr. (2007). A model of HIV disclosure: disclosure and types of social relationships. *J Am Acad Nurse Pract, 19*(5), 242-250.

Benedict, R. H., Mezhir, J. J., Walsh, K., & Hewitt, R. G. (2000). Impact of human immunodeficiency virus type-1-associated cognitive dysfunction on activities of daily living and quality of life. *Arch Clin Neuropsychol, 15*(6), 535-544.

Benjamini, Y. H., Y. (1995). Controlling the false discovery rate: A practical and powerful approach to multiple testing. Journal of the Royal Statistical Society. *Series B, 57,* 289-300.

Brown, M. A., & Powell-Cope, G. M. (1991). AIDS family caregiving: transitions through uncertainty. *Nurs Res, 40*(6), 338-345.

Bunting, S. M. (2001). Sustaining the relationship: women's caregiving in the context of HIV disease. *Health Care Women Int, 22*(1-2), 131-148.

Creswell, J. W. P. C., V.L. (2007). *Designing and Conducting Mixed Methods Research*. Thousand Oaks: Sage Publications.

Diekelmann, N., & Allen, D. (1989). *A hermeneutic analysis of the NLA criteria for the appraisal of baccalaureate progams*. New York: National League for Nursing.

DiMatteo, M. R. (2004). Social support and patient adherence to medical treatment: a meta-analysis. *Health Psychol, 23*(2), 207-218.

Gifford, A. L., & Sengupta, S. (1999). Self-management health education for chronic HIV infection. *AIDS Care, 11*(1), 115-130.

Goffman, E. (1963). *Stigma: Notes on the management of spoiled identity*. New York: Simon & Schuster.

Harding, R., Molloy, T., Easterbrook, P., Frame, K., & Higginson, I. J. (2006). Is antiretroviral therapy associated with symptom prevalence and burden? *Int J STD AIDS, 17*(6), 400-405.

Harrigan, P. R., Hogg, R. S., Dong, W. W., Yip, B., Wynhoven, B., Woodward, J., et al. (2005). Predictors of HIV drug-resistance mutations in a large antiretroviral-naive cohort initiating triple antiretroviral therapy. *J Infect Dis, 191*(3), 339-347.

Ingram, K. M., Jones, D. A., Fass, R. J., Neidig, J. L., & Song, Y. S. (1999). Social support and unsupportive social interactions: their association with depression among people living with HIV. *AIDS Care, 11*(3), 313-329.

Karus, D., Raveis, V. H., Alexander, C., Hanna, B., Selwyn, P., Marconi, K., et al. (2005). Patient reports of symptoms and their treatment at three palliative care projects servicing individuals with HIV/AIDS. *J Pain Symptom Manage, 30*(5), 408-417.

Koch, T. (1996). Implementation of a hermeneutic inquiry in nursing: philosophy, rigour and representation. *J Adv Nurs, 24*(1), 174-184.

Kurtz, M. E., Kurtz, J. C., Given, C. C., & Given, B. (1996). Concordance of cancer patient and caregiver symptom reports. *Cancer Pract, 4*(4), 185-190.

Levine, C. (1990). AIDS and changing concepts of family. *Milbank Quarterly, 68*(1), 33-58.

Lingler, J. H., Sherwood, P. R., Crighton, M. H., Song, M. K., & Happ, M. B. (2008). Conceptual challenges in the study of caregiver-care recipient relationships. *Nurs Res, 57*(5), 367-372.

Lobchuk, M. M., & Degner, L. F. (2002). Symptom experiences: perceptual accuracy between advanced-stage cancer patients and family caregivers in the home care setting. *J Clin Oncol, 20*(16), 3495-3507.

Lorenz, K. A., Cunningham, W. E., Spritzer, K. L., & Hays, R. D. (2006). Changes in symptoms and health-related quality of life in a nationally representative sample of adults in treatment for HIV. *Qual Life Res, 15*(6), 951-958.

McGraw, L. A., & Walker, A. J. (2004). Negotiating care: ties between aging mothers and their caregiving daughters. *J Gerontol B Psychol Sci Soc Sci, 59*(6), S324-332.

McPherson, C. J., Wilson, K. G., Lobchuk, M. M., & Brajtman, S. (2008). Family caregivers' assessment of symptoms in patients with advanced cancer: concordance with patients and factors affecting accuracy. *J Pain Symptom Manage, 35*(1), 70-82.

Mendlinger, S., & Cwikel, J. (2008). Spiraling between qualitative and quantitative data on women's health behaviors: a double helix model for mixed methods. *Qual Health Res, 18*(2), 280-293.

Pinquart, M., & Sorensen, S. (2007). Correlates of physical health of informal caregivers: a meta-analysis. *J Gerontol B Psychol Sci Soc Sci, 62*(2), P126-137.

Powell-Cope, G. M. (1996). HIV disease symptom management in the context of committed relationships. *J Assoc Nurses AIDS Care, 7*(3), 19-28.

Reynolds, N. R., Eller, L. S., Nicholas, P. K., Corless, I. B., Kirksey, K., Hamilton, M. J., et al. (2009). HIV illness representation as a predictor of self-care management and health outcomes: a multi-site, cross-cultural study. *AIDS Behav, 13*(2), 258-267.

Rivero-Mendez, M., Portillo, C., Solis-Baez, S. S., Wantland, D., & Holzemer, W. L. (2009). Symptoms and quality of life of people living with HIV infection in Puerto Rico. *P R Health Sci J, 28*(1), 54-59.

Robertson, K. R., Nakasujja, N., Wong, M., Musisi, S., Katabira, E., Parsons, T. D., et al. (2007). Pattern of neuropsychological performance among HIV positive patients in Uganda. *BMC Neurol, 7,* 8.

Sacktor, N. (2002). The epidemiology of human immunodeficiency virus-associated neurological disease in the era of highly active antiretroviral therapy. *J Neurovirol, 8 Suppl 2,* 115-121.

Silverberg, M. J., Gore, M. E., French, A. L., Gandhi, M., Glesby, M. J., Kovacs, A., et al. (2004). Prevalence of clinical symptoms associated with highly active antiretroviral therapy in the Women's Interagency HIV Study. *Clin Infect Dis, 39*(5), 717-724.

Spirig, R. (1999). [Becoming partners: the meaning of caring for patients with HIV and AIDS]. *Pflege*, *12*(4), 230-237.

Spirig, R. (2002a). In invisibility and isolation: the experience of HIV-affected families in German-speaking Switzerland. *Qual Health Res, 12*(10), 1323-1337.

Spirig, R., Battegay, M., Moody, K., & De Geest, S. (2002b). Exploring the relationship of symptom experience, symptom manageability, adherence, health-related quality of life, and disease progression in people living with HIV/AIDS: perceptions of patients and primary family caregivers. Swiss National Research Foundation Grant SNF: Nr. 3346-100884.

Spirig, R., Moody, K., Battegay, M., & De Geest, S. (2005). Symptom management in HIV/AIDS: advancing the conceptualization. *ANS Adv Nurs Sci, 28*(4), 333-344.

Sterne, J. A., Hernan, M. A., Ledergerber, B., Tilling, K., Weber, R., Sendi, P., et al. (2005). Long-term effectiveness of potent antiretroviral therapy in preventing AIDS and death: a prospective cohort study. *Lancet*, *366*(9483), 378-384.

Thorne, S., Paterson, B., & Russell, C. (2003). The structure of everyday self-care decision making in chronic illness. *Qual Health Res, 13*(10), 1337-1352.

Vincenzi, Ch. B., Moody, K., Spirig, R. (2009). Development and pretesting of a set of symptom assessment tools in HIV: The HIV Symptom Experience Assessment Scale and the HIV Symptom Manageability Scale. Applied Nursing Research, in press.

Wilson, H. S., Hutchinson, S. A., & Holzemer, W. L. (2002). Reconciling incompatibilities: a grounded theory of HIV medication adherence and symptom management. *Qual Health Res, 12*(10), 1309-1322.

Young, J., De Geest, S., Spirig, R., Flepp, M., Rickenbach, M., Furrer, H., et al. (2004). Stable partnership and progression to AIDS or death in HIV infected patients receiving highly active antiretroviral therapy: Swiss HIV cohort study. *Bmj, 328*(7430), 15.

Chapter 7

Discussion

Patient self-management and the collaboration of patients, close support persons and health care providers have been strongly linked with improved health outcomes in chronically ill populations [19, 58]. The research presented above contributes to improving chronic care services for the population affected by HIV by improving understanding of PLWH's self-management and the various collaborations this process entails.

Six main areas have been covered: a) The different tasks of HIV self-management described in the literature have been summarized and categorized; b) The complexity of evidence based HIV specific self-management support in clinical care has been described, with a case report presented in Chapter Three; c) Evidence on interventions to enhance adherence of PLWH has been reviewed and presented, in Chapter Four; d) Insights into the tasks of medication and symptom management have been provided, from the perspectives of PLWH and CSPs, in Chapters Five and Six. One key finding was the aim of PLWH to maintain a grip on their HIV and of the dynamics that could lead to the loss – or the sense of loss – of that grip; e) Collaborations between PLWH, CSPs and HCPs regarding medication and symptom management – thus so far the focus of little attention – have been described in depth in Chapters Five and Six. This underscored the importance for PLWH of building working relationships with CSPs and HCPs to better manage their condition, and provided insights into the different roles PLWH and CSPs assume regarding collaboration. f) The symptom management experiences of PLWH and CSP have also been tested for concordance with symptom experience reports as presented in Chapter Six. This isolated a cluster of neurocognitive symptoms that some CSPs recognized but did not wish to discuss with their PLWH, whereas, in a larger sample assessment of the concordance between symptom reports revealed that all symptoms were reported more often by PLWH.

Several findings of this research program have already been discussed in the presented articles. This discussion will focus on a broader discussion of key findings across articles and on the discussion of methodological issues. Implications for further research and suggestions for clinical implementations will also be presented.

Discussion of key findings

The discussion of the key findings across the research program has been structured into three key points: the complexity of HIV self-management, PLWH as active self-managers and collaborations within self-management.

The complexity of HIV self-management

Growing evidence suggests that HIV self-management is a phenomenon incorporating diverse tasks and numerous interactive dimensions; nevertheless, this phenomenon has not yet been well described

[18, 22]. This research program casts light on the complexity of this phenomenon by integrating and contrasting perspectives on HIV medication and symptom management from the perspectives of different players and by reviewing the literature on HIV specific self-management. These two aspects, i.e., the different perspectives on HIV self-management and the literature review on HIV self-management, will be further discussed below.

Self-management of chronic conditions is influenced both by the characteristics of the respective conditions and by characteristics of the social and political context in which self-management takes place. This is especially relevant for a chronic condition such as HIV/AIDS, which bears a stigma [96]. Despite efforts to educate the public, this stigma persists, alongside false beliefs that HIV/AIDS is a highly contagious disease leading inevitably to great suffering and death. Further, the stigma and its connected assumptions discount the condition as a consequence of socially devalued behavior, such as homo- or bi- sexuality, promiscuity and illicit drug use [93, 96]. Thus, when speaking about experiences with HIV self-management, different players such as policy makers, HCPs, PLWH and their CSPs construe different discourses about these experiences [192]. Whether in the form of written texts or conversations, such discourses always inherit social norms that shape the involved relationships and therefore produce meaning [180]. This research program provides insights into the discourses of PLWH and CSPs, and a limited description of HCP perspectives.

The perspective of HCPs was, however, integrated in the description of a published clinical case report. The presentation of such texts is influenced by explanatory models and language used in the medical community and therefore also provides insights into this group’s dominant perspective on HIV self-management [192]. However, critiquing medical texts on HIV self-management has not been a focus of this research program and its depiction of the medical perspective is therefore limited.

Körner and Treloar conducted an analysis of discourses in medical journal editorials regarding their representations of people with HIV as opposed to those with hepatitis C. They noted that the discourse on Hepatitis C patients remained almost exclusively on a biomedical level, whereas, in HIV editorials, after the biomedical aspects had been accounted for, PLWH were described as active participants that belonged to cultures and subcultures and had a diversity of needs [192]. We agree with Körner and Treloar that such diverse discourse is important for the development of the medical field, adding that it is also crucial for developments on a policy level. By giving voice to the experiences of PLWH and in particular CSPs actively managing medications and symptoms, this paper expands the diversity of perspectives discussed in the medical setting.

The complexity of HIV self-management is also constituted by the challenges of the condition itself. Despite descriptions of many issues relevant to HIV specific self-management, including adherence, transmission risk or symptom management, to our knowledge, HIV self-management has been neither described comprehensively nor fully summarized. Based on a literature search including publications until June 2009, and on the Lorig and Holman’s self-management conceptualization, we summarized and categorized HIV specific self-management tasks and skills [17]. The result was a comprehensive description of HIV self-management tasks and skills usable as a guiding framework to plan both clinical self-management support interventions and HIV self-management oriented research projects. Both aspects will be further elaborated below.

Respecting clinical care, the complexity of self-management support is highlighted in the clinical case report in chapter three. Based on a comprehensive assessment of self-management support needs, health care providers had to implement a range of evidence based and individualized intervention strategies to improve health outcomes for the described patient. These strategies focused on multiple self-management tasks combining such categories as adherence, symptom management and substance use. To structure and plan these interventions, we used the self-regulatory HIV/AIDS Symptom management model (SSMM-HIV) developed by our team [28].

However the strong focus of this research model on one self-management task (symptom management) might have hindered the assessment of self-management support needs in other areas. For example, the model includes symptom management, adherence and social support, yet such a close concentration on that model may have led researchers to neglect self-management deficits relating to transmission risk management. We therefore propose that in clinical care a more comprehensive framework, centered, for example, on the described self-management tasks and skills, would be helpful to form an overview of deficits in self-management tasks; we additionally propose that models developed for research focusing on one or two self-management tasks, such as the SSMM-HIV, might be employed to explore the respective tasks in depth [28].

Regarding research, the description of HIV self-management tasks and skills might also serve as a guiding framework to better plan intervention programs focusing on combinations of self-management tasks and skills. To serve as a research model, the description will require further refinement regarding those tasks and skills. Later, the completeness and distinctness of the various tasks should be evaluated and relations between them worked out more clearly.

Additionally, the relational components of HIV-self-management should be integrated into the framework. Our own results show that PLWH actively collaborate with CSPs and HCPs to manage medications and symptoms, and that these collaborations clearly reinforce PLWH's self-management. The influences of HCPs' communication skills and other specific aspects of collaboration on PLWH's self-management have been documented elsewhere [36, 38, 193]. As proposed above, based on a comprehensive literature review, a relational component could be integrated by describing the tasks and skills of HCPs and CSPs – parallel to those of PLWH – for self-management support.

PLWH as active self-managers

PLWH narratives provide rich descriptions of active medication and symptom management strategies. They describe, for example, how PLWH develop expertise, constantly monitor and evaluate their condition, and learn from different sources to improve their medication and symptom management.

These findings are consistent with the mostly qualitative existing research describing chronically ill participants who perceive themselves as actively managing and drawing on a range of support in doing the long and often hard work [18, 194, 195]. In this study, PLWH additionally illustrated active self-management through their collaborative roles with their CSPs. Whereas PLWH felt responsible for the overall management of their condition, their CSP felt responsible to support defined aspects of that management.

This study replicated an important result described by Thorne et al., who showed that, at some point, participants with diverse chronic conditions (diabetes, multiple sclerosis, HIV/AIDS) decided unequivocally to assume control over their conditions. This development presented a shift in their relationships to their diseases and their management. “Being in control” meant being able to mediate the effects of the disease so that they could live as normally as possible [18]. With the constitutive pattern described in the qualitative results of Chapter Five (‘I have a grip on HIV - HIV has a grip on me’) PLWH in this study described a similar phenomenon.

However, our findings additionally reveal a dynamic process with two interchanging conditions. At one pole, PLWH felt fully able to manage the difficulties of their condition and keep up a meaningful life; at the other, they felt overwhelmed by difficulties and unable to manage. If changes in health and treatment were not sufficiently manageable, participants described changes in their ability to ‘keep a grip on HIV’. Such changes were described by all participants, regardless of their experiences and self-management competencies, throughout the course of the illness. This phenomenon of a constantly changing condition that can not always be successfully managed might results largely from the unpredictability of HIV infection compared to other chronic conditions [45]. Thus, with regard to self-management support for PLWH, the perceptual shift between ‘I have a grip on HIV’ and ‘HIV has a grip on me’ is a matter of considerable concern: participants who perceived that they were losing their grip on HIV described feelings of uncertainty, fear, and loss of morale. This can have serious repercussions: a range of studies have indicated that symptoms of depression can hinder effective self-management. For example, evidence indicates that depressive symptoms influence readiness to initiate cART, adherence to cART and health improving behaviors, and overall quality of life [6, 21, 27, 30, 46].

Individual behaviors, including those involved in self-management of a chronic condition, are further influenced by social norms and values [180]. In western societies, health and related productivity are a dominant expression of quality of life: physical wellbeing has become achievable for virtually everyone. With improvements in diet and medical care, social expectations have grown, so that even the chronically ill assume a responsibility to actively monitor and maintain their health [196]. Therefore, the high priority of maintaining a chronic condition, as illustrated by our results, which concur with those of other investigations, might be influenced by such values.

However, the findings of this study do not allow for broad generalization, as there could be differences across subgroups of PLWH. For example, a qualitative investigation in Australia described differences between an English speaking test group and their Arabic / Turkish speaking counterparts regarding their emotional reactions to diabetes: whereas the English speaking group emphasized the need to control the condition, the Arabic / Turkish speaking group emphasized the need to minimize the stress it caused [37].

Nevertheless, across a broad range of chronically ill populations the often challenging work that lies beyond self-management does not seem well recognized, whether in society at large or in the healthcare community [17, 195, 197]. For PLWH in particular, society’s under-valuing of their contribution to their own health is exacerbated partly by their condition’s general lack of visibility, and partly because a fear of stigmatization means PLWH generally inform only a close circle of persons about their condition [33].

The stigma of HIV, a social context where individuals are expected to maintain optimal health, and professionals’ frequent under-recognition of self-management support needs could increase PLWH’s risk of negative health outcomes.

Self-management collaboration

As with previous research, this study’s PLWH’s narratives described purposeful integration of close support persons and health care providers to better manage their condition (Thorne, Furler, Chenard). HCPs, for example, were consistently described as important sources of information [18, 37, 93], whereas CSPs were recognized as providers of various kinds of functional and emotional support on an everyday level [31, 33, 187].

However, the integration of persons from one’s social network into the process of self-management is clearly influenced by HIV related stigma [33]. In this study, PLWH described how carefully they weighed HIV disclosure to family members and friends related to their self-management. For example, in order to avoid complications with medication intake, they might disclose HIV status to friends before spending vacations together.

Concordant with such behavior, Thorne et al. pointed out that disclosure decisions were relevant to PLWH’s participation in group based self-management education programs [18], while Chenard described that gay men used various disclosure management strategies to build up a social support system [93]. An earlier qualitative investigation, also conducted in Switzerland, revealed that HIV disclosure prompted family members to adopt stances of closeness, ambivalence, or distance regarding PLWH and that few close family caregivers were willing to assume care-giving tasks [33].

Altogether, these findings highlight that HIV related stigma still shapes the social networks of PLWH, the support they receive from others and, therefore, their ability to manage their condition. Healthcare providers should therefore always consider stigma associated issues when planning clinical interventions or research.

A particularly important outcome of this research program is the deepening of our understanding of the collaboration of PLWH and CSPs. The description of the different roles these two groups adopt in the management of symptoms provides new insights into informal care interactions, which, to our knowledge, had not previously been described. In the current literature, collaboration between PLWH and CSPs has received considerable attention regarding populations subject to age-related dysfunction, Alzheimers disease and other chronic conditions such as cancer [126, 185].

Much of this literature focused on caregiving and care receiving as distinct constructs, suggesting that informal support flows unidirectionally from caregiver to care recipient [126]. Few qualitative studies added the relational and often reciprocal dynamics of informal caregiving [184, 185]. Regarding HIV/AIDS most literature on informal caregiving was conducted before cART became widely available and reduced HIV related morbidity significantly. In those early studies, CSPs revealed uncertainty about the timing and meaning of PLWH's deaths, symptoms and disclosure of HIV status as their main social and psychological issues [198]. Further non stigmatizing and reciprocal partnerships were also described [33, 186, 187, 198].

Concordant with the pre-cART reports, the PLWH and CSP narratives presented in chapter six revealed that the two groups collaborated closely to manage the condition. Yet, in contrast to earlier investigations, this collaboration was characterized by distinct roles, in which the PLWH typically assumed clear leadership roles regarding the overall management of the condition, whereas their CSP, as 'companions', tried to recognize and support aspects of self-management where they could. This reflects partnership to an extent; compared to the earlier investigations, though, the PLWH have emerged much more as the drivers of the care process. This insight into the collaborative dynamics of PLWH and CSPs is fundamental to any plans to integrate CSPs into research based clinical interventions.

To our knowledge, concordance between patient and CSP symptom reports has not been analyzed for the PLWH population; we therefore provide the first insights into the issue. A recent study of cancer patients and their CSPs detected a small to moderate tendency among CSPs to overestimate the presence of symptoms [35]. In contrast, the current study's CSPs reported significantly fewer symptoms than the PLWH they supported. Not a single symptom was reported more often by CSPs.

This difference regarding symptom perceptions in the cancer population's CSPs compared to those of the HIV population may result, to some extant, from the different roles of PLWH and CSPs in the management process, as described above in this study's qualitative results. Nevertheless, until further research is conducted to clarify such matters, no conclusions can be drawn.

Additionally, two of our hypotheses based on participants' narratives could not be proved in the quantitative analysis. The first was that some symptoms would be reported more often by CSP; the second was that the most distressing symptoms would be reported concordantly. Several content based explanations are included in the discussion section of the article presented in Chapter Six.

A more method oriented discussion is presented in the following section. However, one issue might still be highlighted at this point. CSP narratives revealed that they specifically did not wish to discuss a range of neurocognitive symptoms with the PLWHs. In the quantitative analysis, two such symptoms – memory loss and forgetfulness – which were reported as most distressing by PLWH, were also reported significantly more often by PLWH.

Despite any inter-method inconsistencies, the fact that CSPs cite difficulties talking about such symptoms, while PLWHs report some of the same symptoms as most distressing, highlights the need for increased attention to self-management support regarding neurocognitive symptoms. So far, neurocognitive symptoms have mainly been discussed on a biomedical level, with management approaches focusing on antiretroviral regimens offering better cerebrospinal fluid penetration [199]. However our results point out the need to integrate PLWH and CSP perspectives into the medical discourse in order to reinforce their self-management collaboration.

From the perspectives of PLWH in this study, health care providers are important partners in ‘keeping a grip on HIV’. This is congruent with the observations other investigations on the importance of HCPs to PLWH in gathering information, gaining confidence and developing a sense of control [18, 37, 38].

The current study adds to the existing knowledge not only by describing the PLWH-HCP collaboration but by giving insights into collaboration with a third player: CSPs. To our knowledge, research on the collaboration between CSPs and HCPs has focused only marginally in HIV research. A qualitative study conducted before cART was available revealed that CSP’s actively negotiated partnerships with HCPs in order to provide the best possible care to PLWH [198].

In contrast, our study’s PLWH and CSP narratives revealed almost no CSP interaction with HCP’s. Further, PLWH often passed on information they had received from health care providers to their CSPs: PLWH educated their CSPs with the goal of establishing partnerships to maintain their grip on HIV. We therefore assume that improvements in medical management of HIV have led to changes not only to the collaboration between PLWH and CSPs, but to the overall involvement of CSPs in the health care system.

However CSPs have proved an important source of support for PLWH regarding self-management [18, 123, 124]; it can be proposed that better prepared CSP’s will be able to provide better support. We therefore propose that neglecting CSPs’ contributions to self-management support represents a missed opportunity to strengthen self-management for PLWH and therefore to improve health outcomes.

Discussion of methods

The presented research program was guided by an exploratory mixed method design with priority on the qualitative elements [47]. This design is particularly useful to explore issues where very limited knowledge is available, such as, in this case, the collaboration of PLWH, CSP and HCP on medication and symptom management [200]. It also clearly helped to broaden the existing understanding of the various players' collaborations in symptom and medication management, and to gauge the concordance between reports of experienced versus observed symptoms. Most importantly, though, this design helped connect the concepts of symptom management and symptom experience (e.g, occurence, intensity, bothersomeness or distress of symptoms).

This study has three methodical limitations, all of which will be further discussed below. The first is the concurrent collection of qualitative and quantitative data, whereas sequential data collection strategies are general recommended for exploratory mixed method designs, with the goal of using results of the first phase to determine data collection strategies for the second phase [47].

In this case, though, the recommended sequential data collection was impossible: by the time the associated research program was approved, the quantitative data collection, which was connected to the Solexa Study (see introduction), had already been started. Therefore, the presented research program's qualitative findings could not influence quantitative data collection. Nevertheless, the hypotheses that guided the quantitative investigation were built on findings from the previous qualitative data analysis.

The chief limitation this entailed was that the scope of hypotheses was restricted to the data available for testing. In practice, participants' narratives were rich and the process of qualitative data interpretation revealed diverse themes that could be transformed into hypotheses, which could then be answered with the available quantitative data. This very likely also reflects the close relations (similarities) between the investigated concepts of symptom management and symptom experience.

The second limitation is that data collection occurred separately for PLWH and CSPs. In particular, for the qualitative exploration, pair based interviews might have helped to uncover some of the dynamics and interactions between the two players that were not shown in the individual based interviews. Nevertheless, findings from the qualitative study section revealed that separate interviews had advantages: both PLWH and CSPs mentioned issues such as symptoms or feelings they did not talk about with their counterparts. It can be assumed that those themes, which were also integrated into the hypothesis and therefore also guided the second quantitative research phase, would not have arisen in pair based interviews. Nevertheless, pair interviews might have provided further insights into the processes of collaborative management of symptoms and medications.

The third limitation is the sampling strategy used for the quantitative study. Normally the second phase of an exploratory mixed method design, this step's goal is to generalize the findings from the first, qualitative study sample to a population [47]. Due to the convenience sampling strategy used for this study's quantitative sample, findings can not be generalized for the Swiss population or be applied globally. According to the qualitative priority of our research program the sampling strategy is stronger in the qualitative study part: the purposive sampling strategy, screening according to gender, transmission category and health care center, ensured that perspectives of participants with known differences were integrated. Nevertheless, both study samples were restricted to a German speaking group of PLWH/CSP, which probably led to the exclusion of a sub-sample with backgrounds of migration and limited German language skills.

We consider the sequential and hypothetically (i.e., through our hypothesis) connected process of data analysis as strengths of the study. First, the qualitative interviews provided rich narratives, conveying, from the perspectives of PLWH and CSPs, a broad understanding of symptom and medication management and the related collaborations, along with insights into hitherto undescribed aspects, such as the roles assumed in collaboration or the dynamics behind the phenomenon of keeping a grip on HIV. Second, despite the limited evidence on symptom management collaborations between PLWH and CSPs, we were able to formulate informed hypotheses based on the two players' narratives. These allowed a focused quantitative investigation on the concordance of symptom reports. Overall, this approach allowed us to combine the strengths of qualitative and qualitative research: the qualitative phase allowed an open, in-depth assessment and extensive interpretation; the quantitative phase produced a focused, clearly defined analysis.

Further, regarding the two unconfirmed hypotheses, unexpected results were generated raising further questions and demanding further interpretation. We propose that such questions and interpretations, which result from inter-method inconsistencies, are instrumental to the development of knowledge about the phenomena at hand, and would not have arisen from an approach that was either purely qualitative or purely quantitative. For example, the hypothesis that some symptoms would be reported more often by CSP than by PLWH was not supported. In fact, without exception, all symptoms were reported more often by PLWH; and, interestingly, while CSPs mentioned symptoms such as 'difficulty concentrating', 'memory loss' and 'forgetfulness' in their qualitative interviews, all were reported significantly more often by PLWH. And only a qualitative approach could have revealed such narratives as those fitting the theme of "not talking about symptoms".

On the other hand, only a quantitative approach could have provided statistics on concordances between PLWH's and their CSPs' symptom reports. Since very little HIV literature exists on the topic, it is unlikely that our results could otherwise either have arisen or been tested as fully as a mixed methods approach permitted. Only an approach that combined the narratives, statistics, and especially the inconsistencies of findings could raise the types of questions raised here, which demand interpretation, leading to still more research questions.

Previously, inter-method inconsistencies in mixed method designs have been explained by the confounding complexity either of the phenomena studied or of the method combination [201]. Chapter Six of this study includes a discussion on the possibility that the studied phenomena (i.e., collaborations between PLWH and their CSPs regarding medication and symptom self-management) might be influenced by the stigmatization of neurocognitive problems in a relatively young population. As described in the first study phase, individual experiences of a small group of participants do not necessarily reflect the experiences of a larger population, as many unspecified variables influence the experiences of the individuals and pairs studied. Our knowledge of the characteristics of PLWH/CSP pairs is particularly limited. Additionally, the quantitative analysis used is not particularly sensitive to possibly diverse 'symptom concordance patterns' in specific pairs. Still, focusing on such patterns with case oriented analyses, however limited the generalizeability of the results, would nevertheless offer further insights and understanding [202].

Implications for future research and clinical practice

The descriptive/explorative character of this research program does not lend itself to final conclusions. However, the information obtained provides a basis for insightful questions, possibilities for further research, and suggestions regarding clinical implications.

Future research

HIV self-management has consistently been acknowledged as a complex phenomenon. This study provides an initial description of HIV self-management tasks and skills, which we offer as a guiding framework for research and clinical practice. As proposed above, HIV self-management should also be further conceptualized to integrate the dimension of collaboration.

A range of qualitative studies focusing on chronically ill persons' perspectives of self-management report on the phenomenon of patients 'taking and maintaining control', or, in the parlance of our study, of 'having and keeping a grip" on their diseases. A meta–synthesis (i.e., a qualitatively oriented aggregation of qualitative findings developed to accommodate the distinctive features of qualitative survey by extraction, grouping and formatting of findings [203, 204]) of qualitative studies describing aspects of this phenomenon could help develop further insights.

The presented research program integrated the perspectives of PLWH and their CSPs. However, HCPs' perspectives were only integrated via case reports; no specific, systematic reports yet exist on HCPs' self-management roles in relation to PLWH. We therefore propose that a study focused directly on gathering and interpreting HCPs' narratives of their collaboration in the processes of managing medication and symptoms would provide further insights. In particular, the emotions connected with such experiences cannot be shown through medical reports. Therefore, our plans include to integrate and contrast already conducted data from HCP narratives with those of PLWH and CSPs.

This study described, for the first time, aspects of the concordance between PLWH's and their CSPs symptom reports. However the quantitative description was very limited and a range of aspects, e.g., concordance across all dimensions of the symptom experience, remain to be investigated. Additionally, as discussed above in the context of study limitations, longitudinal research and case oriented techniques of analysis might provide further insights.

In accordance with previous research, our findings clearly illustrated that PLWH's collaborations with HCPs and CSPs are part of their self-management process [18, 37, 38, 193]. Further, these collaborations have been shown to either enable or hinder PLWH’s self-management [18, 193]. We therefore propose that future research on self-management support for PLWH should also focus more strongly on the collaborations inherent in the process.

For example, knowledge is needed on how to effectively access and integrate close support persons in intervention programs or clinical care. In this direction, the Swiss HIV Cohort study has approved a pilot study to test the feasibility of integrating CSP into clinical care services focusing on transmission prevention (SHCS project No 518). If successful, that study’s results will inform the development of intervention studies that focus not only on PLWH but on their CSPs to improve self-management and therefore health outcomes. Additionally, since pairs or groups of self-management tasks have been closely connected, and since many single task oriented interventions such as adherence or transmission risk management have used similar approaches, such intervention programs should focus on multiple self-management tasks, including skill building activities [88].

Previous researchers have successfully conducted self-management education in group programs [16, 23, 65, 130]. Nevertheless, such approaches do not reach all patients and long term success appears to require a combination of program based and clinic based interventions [136, 205, 206]. We propose that studies are needed to test the best combination of both approaches for various sub-groups of PLWH. For example, a group based program could provide basic self-management education, followed by individual clinical follow up interventions. Alternatively, a program could begin with structured interventions for individuals in clinical care who were hesitant or unable to join a group, followed by other, e.g., pair based (PLWH and CSP), interventions.

Our findings match those of other researchers that HCPs’ combination of communication skills and medical experience is a key issue related regarding their influence on PLWH’s self-management [38, 205]. In the general care setting, teaching specific patient centered communication techniques has been shown to improve patients’ satisfaction with care, along with health care providers’ confidence in their skills [207, 208]. However, overall self-management support requires a much broader range of communication and behavioral change strategies. Some evidence suggests that teams of health care providers with strong skill mixes can manage such challenges most effectively [209]. However, regarding HIV specific care, such programs also call for development and testing specific to the needs and capabilities of their health care organizations.

Implications for clinical practice

Ongoing implementation of research findings into clinical practice drives improvement in health care services. And while the explorative character of this research program does not allow definite recommendations regarding practice, it does provide in-depth descriptions, helping to develop a clearer understanding of PLWH’s self-management processes, including the related collaborations. Combined with an extensive literature review, assessing PLWH’s and CSPs’ perspectives has indicated the following key points for clinicians that guided the following suggestions.

Key points:

- HIV self-management includes diverse tasks and skills.
- The feeling either of 'having a grip on HIV' or that 'HIV has a grip on me' reflected PLWH's perceptions of their current ability to manage medications and symptoms.
- A PLWH with the feeling of losing his/her grip on HIV might react with feelings of anxiety and symptoms of depression.
- Changes from 'having a grip on HIV' toward losing control were described by all PLWH interviewed and can occur quickly.
- Collaboration with close support persons influences PLWH's ability to manage medications and symptoms.
- The collaboration of PLWH and CSP appears to involve the assumption of different roles (managers/companions).
- CSPs reported learning about HIV from PLWH, while experiencing almost no integration into clinical care.
- HCPs were recognized by PLWH as important players who either enabled or hindered self-management.

These key points guided the following suggestions for HIV self-management support in clinical practice. These suggestions are not immediately applicable to every situation or every patient. On the contrary, their implications require careful reflection and adaptation to the respective context and individual patient.

As discussed above, PLWH's self-management is complex, incorporating diverse tasks and skills. Our results illustrate that for some PLWH learning the skills necessary to manage medications and symptoms requires a process of trial and error (Chapter Five; theme: 'find out what works with symptoms'). Health care providers should therefore ensure that every patient receives basic self-management education, covering the most important information across all of the described self-management tasks, and integrating skill building activities as described by Lorig and colleague [17].

Due to the limited counseling time available in the clinical care setting, such basic self-management education should be considered in community based group programs or with internet based education systems, as research has shown positive results with both approaches [210]. Naturally, such approaches would have to be adapted and evaluated systematically in the context of each specific target group.

In cases where such programs are for any reason unworkable, health care providers can either set agendas for self-management education via routine consultations or plan additional counseling time to focus on self-management education. One project, which integrated self-management support regarding transmission risk management into routine clinical care, illustrated that such interventions were feasible but required extra education of health care providers [211].

Evidence supports social support as an important factor related to PLWH's health [122, 124, 211]. The current study's results revealed the importance of collaboration between PLWH and CSPs in the management of medications and symptoms, and highlighted the different roles CSPs and PLWH play to facilitate that collaboration.

Based on these insights we propose that it would be helpful to encourage PLWH to bring their CSPs to clinical consultations on basic self-management. Integrating a discussion of self-management roles, for example, using open ended and circular questions, could be helpful to build an understanding of the PLWH/CSP partnership's needs [212].

However, examples of how to reach and integrate CSPs into clinical services are very scarce [132, 213]. Regarding the current study, our own experiences recruiting PLWH and their CSP in HIV outpatient clinics revealed that many PLWH welcomed the opportunity to bring their CSPs to the clinic. PLWH who did not wish to do so cited time constraints, the clinic's opening hours (closed evenings), fear of HIV disclosure and relationship problems.

Apart from PLWH and CSPs' willingness to participate, other barriers also hinder CSPs' integration into clinical services. One is the additional expense to the clinic, to participants or both. In most countries, health care systems focus on the individual patient and only reimburse services at the individual health care level. Nevertheless, experiences of health care providers who have integrated PLWH and CSPs into paired self-management support and clinical consultations are vital to the development of projects that aim to do the same, and can also influence health care policy.

After basic self-management education, ongoing self-management support appears to be necessary, since longitudinal research has revealed changing patterns in PLWH's cART adherence, symptom clusters and transmission risk behavior [21, 89, 131]. Additionally, qualitative research has illustrated that self-management decisions are made on an everyday level [18, 22]. Continuous monitoring of self-management support needs across the full range of self-management tasks should therefore be integrated into clinical care services.

To our knowledge there is no tool that monitors PLWHs' self-management across all tasks. Based on the constitutive pattern 'I have a grip on HIV - HIV as a grip on me', developed from PLWH's narratives, we suggest to use an open ended question about PLWH's perception of having a grip on HIV. This could be helpful to build an understanding of their perceived ability to manage and the problems they see as related to self-management.

After such an open and patient centered opening, a structured interview regarding the performance of self-management tasks, using evaluated assessment tools, could be conducted. Instruments have been developed and tested for a range of self-management tasks, e.g., adherence to cART [6, 7, 129], symptom assessment [21, 109, 214], substance use, and depression and lifestyle [215, 216]. In the current investigation, PLWH narratives revealed that the impression of loosing one's grip on HIV provoked fear and a loss of morale. Checking for symptoms of depression, followed, if necessary, by effective treatment, is a potentially valuable issue related self management support that has probably in many settings not yet been integrated systematically into routine clinical care [29].

Once problems with PLWH's self-management have been identified, effective support should be provided. Intervention strategies always need to focus on the problems perceived by the individual patient [17], but not exclusively. Health care providers might identify problems such as insufficient adherence or smoking, often not perceived as such by the PLWH. Conversely, the PLWH might consider the cART associated side effects such as nausea and bloating his/her major problem. Self-management support therefore has to be focused on those symptoms to be effective. This does not mean prevent self-management support from integrating interventions to raise awareness to other problematic issues [217, 218]. Stage based approaches that raise awareness and support PLWH to overcome ambivalences have proved effective across a range of self-management behaviors [217], even if such changes demand considerable time, motivation, and effort from patients.

In planning interventions, setting priorities is therefore important [17, 218]. For several HIV self-management tasks, health care providers have to begin this prioritizing while selecting the most appropriate strategy for each PLWH from the range available. To name a few of the choices available:

Adherence interventions are summarized in Chapter Two of this study; a recent review by Simoni and colleagues summarizes adherence support strategies [23]; a proposal for cART treatment decision making support described by our team has been integrated into the European antiretorviral treatment guidelines ; symptom management support and self-care strategies have been explored extensively by Holzemer and group and a description is provided on their homepage (http://hivinsite.ucsf.edu); transmission risk management interventions have been summarized in a meta-analytic review by Crepaz and colleagues [65]; clinical based transmission risk interventions are described by Richardson and colleagues [211]; interventions related to disclosure management, role management, emotional management and lifestyle management are less well summarized and have to rely on individual studies [37, 92, 211]. Substance use management is described according to the substance(s) used. A nicotine cessation intervention for PLWH and an alcohol reduction intervention has been described by our team and can be well integrated into HIV specific care [73, 76, 219, 220]. Other substance use interventions might require referrals to specialized services.

However, even with a range of interventions at our disposal, behavioral change remains a complex issue. Support in self-management tasks often requires more than one intervention, followed by an evaluation of the effect. Our own qualitative results provide an example of an HCP who provided a patient with information related to symptom management but did not follow up, and the strategies did not work. Follow-up by health care providers is essential across all self-management interventions; even if they have been delegated to community based external programs in order to provide care continuity [221].

The evidence that can inform individualized clinical intervention approaches comes from clinical trials performed with carefully selected populations. This situation is often not comparable to real life conditions, where HCPs may find themselves caring, for example, for a PLWH with psychiatric comorbidities, who shows up for consultations infrequently and presents a range of self-management problems. Still, evidence based interventions – or their applicable elements – are such a patient’s best hope.

Naturally, health care providers working in the clinical setting have to adapt their strategies to individual patients and contexts. And while every situation is different, learning and exchanging about intervention strategies that worked or did not work in specific clinical situations remains imperative. Case reports that integrate biomedical perspectives and self-management support, as presented in Chapter Two above, also offer valuable learning opportunities for professionals across diverse health care settings. And even if the number of case reports that focusing on self-management support is limited, what reports exist are certainly worth reading and further reports focusing on self management support success of failure in clinical care should be written.

To return to the current study, findings illustrated that despite PLWH’s commitment to building working partnerships with health care providers, the relationship was sometimes described as non-supportive regarding medication and symptom management. Unsupportive health care providers were described as disinterested, inattentive, not taking symptom reports seriously, and even not medically competent (Chapter Five; theme ‘work with providers’).

These results highlight the need for a patient centered communication approach in the clinical care setting. Studies in chronic disease populations including diabetics and hypertensives have convincingly linked patient centered communication with improved health outcomes and patient satisfaction [36, 39]. We propose that basic skills in patient oriented communication techniques are indispensable for all health care providers caring for PLWH.

Nevertheless, in some cases, self-management support calls for either more advanced communication skills or a range of communication techniques. For example, motivational interviewing techniques for patients with problems in behavioral change; or if, for example, the collaboration of PLWH and CSP requires attention, a more family oriented systemic approach, as described by Wright and Leahey, might be most appropriate [212].

Extensive self-management support cannot, therefore, be provided by an individual provider. Rather, a team of HCPs with a broad mix of individual skills and orchestrated teamwork, also ensuring continuity of care, is needed [221]. Bodenheimer, for example described a “teamlet” model that addressed the inadequate resources of short consultations by changing health care providers from a lone physician to a two-person team for patients needing support for self-management. This team, whose second member was normally an advanced practice nurse, collaborated closely within defined functions to provide medical care and self-management support [222].

Self-management support of chronically ill patients is influenced not only by individual providers or teams but also by the structure of the health care organization and the social values incorporated in it, as described in the Chronic Care Model [15, 60]. The above-described self-management support has to be strongly supported by leaders of the organizantion, has to be integrated into a health care system that provides decision support and education for health care providers, that is based on a care delivery system that allows regular follow up visits and support by practice teams, and finally, that provides information systems that allow documentation of all important medical and self-management information, including clinical reminders [209, 222]

Within such a system three levels of continuity of care for PLWH are generally considered most important: 1) informational continuity, i.e., formally documented information, including patients' preferences and values; 2) management continuity, i.e., management plans, follow ups and coordination of services; and 3) relationship continuity, i.e., the accumulation of knowledge of patient preferences and interpersonal trust based on experiences with patient /provider collaboration. The importance of continuity is also reflected in our own results. PLWH described their outpatient clinic as a place where they are known, where they don't have to continually repeat their health stories, and where they can talk about HIV openly.

This last point illustrates the fear of stigmatization in the health care system, which patients maintain remains widespread. For example, in a nationally representative US sample, 26% of PLWH receiving health care reported perceiving discrimination among health care providers. In a French national survey, 24% of PLWH reported experiences of discrimination in their close social environments (relatives, friends and colleagues). In the subgroup of PLWH with a history of intravenous drug use, 32% reported discrimination in their close social environment (Peretti, 2007). It is widely agreed that HIV stigma remains a major barrier to effective care and responses to the epidemic in general. Careful reflection on stigmatizing behavior and policies should therefore be integrated into the clinical care of PLWH [96].

Conclusion

In order to provide HIV specific self-management support in clinical care or research settings the focus should be broadened from single tasks (e.g. adherence) to include pairs and groups of reciprocally influencing self-management tasks, as well as other relational components of the process. The ongoing changes in PLWH's perceptions of having or losing their grip on HIV highlights the need for continuous monitoring of self-management support needs and individualized support interventions. This phenomenon should be further investigated across diverse chronic conditions.

Enabling self management support by health care providers encompasses a patient centred communication approach, HIV specific medical competence, assistance in decision making, assessment of symptom experience, collaborative development of strategies, ongoing patient education, and support in coordination of care. Particularly in teaching hospitals, this requires a broad skill mix among individual providers, and well-coordinated teamwork.

Close support persons have proved themselves valuable partners for PLWH in self-management; however, their integration into research programs or clinical care has been marginal and should be improved. In doing so the distinct PLWH/CSP collaborative roles i.e., the clear leadership of the PLWH revealed here, should be considered.

References

1. Sterne, J.A., et al., *Long-term effectiveness of potent antiretroviral therapy in preventing AIDS and death: a prospective cohort study*. Lancet, 2005. **366**(9483): p. 378-84.
2. Hogg, R.S.S., J. A.; Graber, S.; Battegay, M.; Bonarek, M.; D'Arminio Monforte, A.; Esteve, A.; Harris, R.; Justice, A.; Hayden, A.; Lampe, F.; Mocroft, A.; Mugavero, M. J.; Staszewski, S.; Wasmuth, J.C.; van Sighem, A.; Kitahata, M.; Guest, J.; Egger, M.; May, M., *Life expectancy of individuals on combination antiretroviral therapy in high-income countries: a collaborative analysis of 14 cohort studies*. Lancet, 2008. **372**(9635): p. 293-9.
3. Unaids, *2008 Report on the global Epidemic*. 2008, WHO Library Cataloguing-in-Publication Data.
4. Mocroft, A., et al., *Decline in the AIDS and death rates in the EuroSIDA study: an observational study*. Lancet, 2003. **362**(9377): p. 22-9.
5. Burman, W., et al., *Episodic antiretroviral therapy increases HIV transmission risk compared with continuous therapy: results of a randomized controlled trial*. J Acquir Immune Defic Syndr, 2008. **49**(2): p. 142-50.
6. Deschamps, A.E., et al., *Prevalence and correlates of nonadherence to antiretroviral therapy in a population of HIV patients using Medication Event Monitoring System*. AIDS Patient Care STDS, 2004. **18**(11): p. 644-57.
7. Simoni, J.M., et al., *Self-report measures of antiretroviral therapy adherence: A review with recommendations for HIV research and clinical management*. AIDS Behav, 2006. **10**(3): p. 227-45.
8. Sitta, R., et al., *No Variability Across Centers in Adherence and Response to HAART in French Hospitals: Results From the ANRS-EN12-VESPA Study*. J Acquir Immune Defic Syndr, 2009.
9. Ammassari, A., et al., *Self-reported symptoms and medication side effects influence adherence to highly active antiretroviral therapy in persons with HIV infection*. J Acquir Immune Defic Syndr, 2001. **28**(5): p. 445-9.
10. Harding, R., et al., *Is antiretroviral therapy associated with symptom prevalence and burden?* Int J STD AIDS, 2006. **17**(6): p. 400-5.
11. Karus, D., et al., *Patient reports of symptoms and their treatment at three palliative care projects servicing individuals with HIV/AIDS*. J Pain Symptom Manage, 2005. **30**(5): p. 408-17.
12. Silverberg, M.J., et al., *Prevalence of clinical symptoms associated with highly active antiretroviral therapy in the Women's Interagency HIV Study*. Clin Infect Dis, 2004. **39**(5): p. 717-24.
13. Handford, C.D., et al., *Setting and organization of care for persons living with HIV/AIDS*. Cochrane Database Syst Rev, 2006. **3**: p. CD004348.
14. Schoen, C., et al., *In chronic condition: experiences of patients with complex health care needs, in eight countries, 2008*. Health Aff (Millwood), 2009. **28**(1): p. w1-16.
15. WHO, *Innovative Care for Chronic Conditions*. 2002, Geneva: WHO library Cataloging-in-Publication.
16. Gifford, A.L. and S. Sengupta, *Self-management health education for chronic HIV infection*. AIDS Care, 1999. **11**(1): p. 115-30.
17. Lorig, K.R. and H. Holman, *Self-management education: history, definition, outcomes, and mechanisms*. Ann Behav Med, 2003. **26**(1): p. 1-7.
18. Thorne, S., B. Paterson, and C. Russell, *The structure of everyday self-care decision making in chronic illness*. Qual Health Res, 2003. **13**(10): p. 1337-52.
19. Epping-Jordan, J.E., et al., *Improving the quality of health care for chronic conditions*. Qual Saf Health Care, 2004. **13**(4): p. 299-305.
20. Harrigan, P.R., et al., *Predictors of HIV drug-resistance mutations in a large antiretroviral-naive cohort initiating triple antiretroviral therapy*. J Infect Dis, 2005. **191**(3): p. 339-47.
21. Portillo, C.J., W.L. Holzemer, and F.Y. Chou, *HIV symptoms*. Annu Rev Nurs Res, 2007. **25**: p. 259-91.

22. Wilson, H.S., S.A. Hutchinson, and W.L. Holzemer, *Reconciling incompatibilities: a grounded theory of HIV medication adherence and symptom management.* Qual Health Res, 2002. **12**(10): p. 1309-22.
23. Simoni, J.M., et al., *Efficacy of interventions in improving highly active antiretroviral therapy adherence and HIV-1 RNA viral load. A meta-analytic review of randomized controlled trials.* J Acquir Immune Defic Syndr, 2006. **43 Suppl 1**: p. S23-35.
24. Enriquez, M., et al., *Assessment of readiness for adherence by HIV-positive males who had previously failed treatment.* J Assoc Nurses AIDS Care, 2004. **15**(1): p. 42-9.
25. Nicca, D., et al., *[Ready for antiretroviral therapy? Therapy decision making experiences of persons living with HIV].* Pflege, 2005. **18**(5): p. 289-98.
26. Nordqvist, O., et al., *Assessing and achieving readiness to initiate HIV medication.* Patient Educ Couns, 2006. **62**(1): p. 21-30.
27. Vervoort, S.C., et al., *Adherence in antiretroviral therapy: a review of qualitative studies.* Aids, 2007. **21**(3): p. 271-81.
28. Spirig, R., et al., *Symptom management in HIV/AIDS: advancing the conceptualization.* ANS Adv Nurs Sci, 2005. **28**(4): p. 333-44.
29. Eller, L.S., *Depressive symptoms in HIV disease.* Nurs Clin North Am, 2006. **41**(3): p. 437-53, vii.
30. Fehr, J.S., et al., *Starting or changing therapy - a prospective study exploring antiretroviral decision-making.* Infection, 2005. **33**(4): p. 249-56.
31. Bischofberger, I. and R. Spirig, *[The work profile of family caregivers of persons affected by HIV/AIDS].* Pflege, 2004. **17**(3): p. 176-86.
32. Powell-Cope, G.M., *HIV disease symptom management in the context of committed relationships.* J Assoc Nurses AIDS Care, 1996. **7**(3): p. 19-28.
33. Spirig, R., *In invisibility and isolation: the experience of HIV-affected families in German-speaking Switzerland.* Qual Health Res, 2002. **12**(10): p. 1323-37.
34. Kurtz, M.E., et al., *Concordance of cancer patient and caregiver symptom reports.* Cancer Pract, 1996. **4**(4): p. 185-90.
35. McPherson, C.J., et al., *Family caregivers' assessment of symptoms in patients with advanced cancer: concordance with patients and factors affecting accuracy.* J Pain Symptom Manage, 2008. **35**(1): p. 70-82.
36. Beach, M.C., J. Keruly, and R.D. Moore, *Is the quality of the patient-provider relationship associated with better adherence and health outcomes for patients with HIV?* J Gen Intern Med, 2006. **21**(6): p. 661-5.
37. Furler, J., et al., *The emotional context of self-management in chronic illness: A qualitative study of the role of health professional support in the self-management of type 2 diabetes.* BMC Health Serv Res, 2008. **8**: p. 214.
38. McCoy, L., *HIV-positive patients and the doctor-patient relationship: perspectives from the margins.* Qual Health Res, 2005. **15**(6): p. 791-806.
39. Beach, M.C. and T. Inui, *Relationship-centered care. A constructive reframing.* J Gen Intern Med, 2006. **21 Suppl 1**: p. S3-8.
40. Schneider, J., et al., *Better physician-patient relationships are associated with higher reported adherence to antiretroviral therapy in patients with HIV infection.* J Gen Intern Med, 2004. **19**(11): p. 1096-103.
41. Bodenheimer, T., E.H. Wagner, and K. Grumbach, *Improving primary care for patients with chronic illness.* Jama, 2002. **288**(14): p. 1775-9.
42. Sochalski, J., et al., *What works in chronic care management: the case of heart failure.* Health Aff (Millwood), 2009. **28**(1): p. 179-89.
43. Bangsberg, D.R., D.L. Kroetz, and S.G. Deeks, *Adherence-resistance relationships to combination HIV antiretroviral therapy.* Curr HIV/AIDS Rep, 2007. **4**(2): p. 65-72.
44. King, M.S., S.C. Brun, and D.J. Kempf, *Relationship between adherence and the development of resistance in antiretroviral-naive, HIV-1-infected patients receiving lopinavir/ritonavir or nelfinavir.* J Infect Dis, 2005. **191**(12): p. 2046-52.
45. Badia, X., et al., *Evaluating changes in health status in HIV-infected patients: Medical Outcomes Study-HIV and Multidimensional Quality of Life-HIV quality of life questionnaires. Spanish MOS-HIV and MQOL-HIV Validation Group.* Aids, 2000. **14**(10): p. 1439-47.

46. Hudson, A., K. Kirksey, and W. Holzemer, *The influence of symptoms on quality of life among HIV-infected women.* West J Nurs Res, 2004. **26**(1): p. 9-23; discussion 24-30.
47. Creswell, J.W.P.C., V.L, *Designing and Conducting Mixed Methods Research*. 2007, Thousand Oaks: Sage Publications.
48. Keiser, O., et al., *Public-health and individual approaches to antiretroviral therapy: township South Africa and Switzerland compared.* PLoS Med, 2008. **5**(7): p. e148.
49. WHO, *Antiretroviral Therapy for HIV Infection in Adults and Adolescents: Recommendations for public health approach*. 2006, WHO Library Cataloguing-in-Publication Data: Geneva.
50. Hammer, S.M., et al., *Antiretroviral treatment of adult HIV infection: 2008 recommendations of the International AIDS Society-USA panel.* Jama, 2008. **300**(5): p. 555-70.
51. Marsden, M.D. and J.A. Zack, *Eradication of HIV: current challenges and new directions.* J Antimicrob Chemother, 2009. **63**(1): p. 7-10.
52. Shen, L., et al., *Dose-response curve slope sets class-specific limits on inhibitory potential of anti-HIV drugs.* Nat Med, 2008. **14**(7): p. 762-6.
53. Whitney, J.B., et al., *T cell vaccination reduces SIV in semen.* J Virol, 2009.
54. Fellay, J., et al., *Prevalence of adverse events associated with potent antiretroviral treatment: Swiss HIV Cohort Study.* Lancet, 2001. **358**(9290): p. 1322-7.
55. Brooks, J.T., J.E. Kaplan, and H. Masur, *What's New in the 2009 US Guidelines for Prevention and Treatment of Opportunistic Infections Among Adults and Adolescents with HIV?* Top HIV Med, 2009. **17**(3): p. 109-14.
56. French, A.L., et al., *Trends in mortality and causes of death among women with HIV in the United States: a 10-year study.* J Acquir Immune Defic Syndr, 2009. **51**(4): p. 399-406.
57. Marin, B., et al., *Non-AIDS-defining deaths and immunodeficiency in the era of combination antiretroviral therapy.* Aids, 2009.
58. Beaglehole, R., et al., *Improving the prevention and management of chronic disease in low-income and middle-income countries: a priority for primary health care.* Lancet, 2008. **372**(9642): p. 940-9.
59. Thorne, S. and B. Paterson, *Shifting images of chronic illness.* Image J Nurs Sch, 1998. **30**(2): p. 173-8.
60. Wagner, E.H., et al., *Improving chronic illness care: translating evidence into action.* Health Aff (Millwood), 2001. **20**(6): p. 64-78.
61. Wagner, E.H., et al., *Quality improvement in chronic illness care: a collaborative approach.* Jt Comm J Qual Improv, 2001. **27**(2): p. 63-80.
62. Tsai, A.C., et al., *A meta-analysis of interventions to improve care for chronic illnesses.* Am J Manag Care, 2005. **11**(8): p. 478-88.
63. Coleman, K., et al., *Evidence on the Chronic Care Model in the new millennium.* Health Aff (Millwood), 2009. **28**(1): p. 75-85.
64. Singh, D., *How can chronic disease management programmes operate across care settings and providers?* 2008, Copenhagen: WHO, European Observatory of Health Systems.
65. Crepaz, N., et al., *Do prevention interventions reduce HIV risk behaviours among people living with HIV? A meta-analytic review of controlled trials.* Aids, 2006. **20**(2): p. 143-57.
66. Corbin, J. and A. Strauss, *Unending Work and Care: Managing Chronic Illness at Home.* 1988, San Francisco: Jossey-Bass.
67. Wikipedia, *Collaboration*. 2009.
68. Bodenheimer, T., E.H. Wagner, and K. Grumbach, *Improving primary care for patients with chronic illness: the chronic care model, Part 2.* Jama, 2002. **288**(15): p. 1909-14.
69. Gray, J., *Becoming adherent: experiences of persons living with HIV/AIDS.* J Assoc Nurses AIDS Care, 2006. **17**(3): p. 47-54.
70. Chou, F.Y., *Testing a predictive model of the use of HIV/AIDS symptom self-care strategies.* AIDS Patient Care STDS, 2004. **18**(2): p. 109-17.
71. Reynolds, N.R., et al., *HIV illness representation as a predictor of self-care management and health outcomes: a multi-site, cross-cultural study.* AIDS Behav, 2009. **13**(2): p. 258-67.
72. Wantland, D.J., et al., *A randomized controlled trial testing the efficacy of an HIV/AIDS symptom management manual.* J Pain Symptom Manage, 2008. **36**(3): p. 235-46.
73. Elzi, L., et al., *A smoking cessation programme in HIV-infected individuals: a pilot study.* Antivir Ther, 2006. **11**(6): p. 787-95.

74. Nijhawan, A., S. Kim, and J.D. Rich, *Management of HIV Infection in Patients With Substance Use Problems.* Curr Infect Dis Rep, 2008. **10**(5): p. 432-8.
75. Reynolds, N.R., *Cigarette smoking and HIV: more evidence for action.* AIDS Educ Prev, 2009. **21**(3 Suppl): p. 106-21.
76. Voggensperger, J., et al., *[Smoking cessation for HIV infected patients].* Pflege, 2003. **16**(5): p. 283-8.
77. Conen, A., et al., *Self-reported alcohol consumption and its association with adherence and outcome of antiretroviral therapy in the Swiss HIV Cohort Study.* Antivir Ther, 2009. **14**(3): p. 349-57.
78. Hand, G.A., et al., *Moderate intensity exercise training reverses functional aerobic impairment in HIV-infected individuals.* AIDS Care, 2008. **20**(9): p. 1066-74.
79. Hendricks, K.M., et al., *Dietary patterns and health and nutrition outcomes in men living with HIV infection.* Am J Clin Nutr, 2008. **88**(6): p. 1584-92.
80. Coleman, C.L., et al., *Gender differences in use of prayer as a self-care strategy for managing symptoms in African Americans living with HIV/AIDS.* J Assoc Nurses AIDS Care, 2006. **17**(4): p. 16-23.
81. Fitzpatrick, A.L., et al., *Survival in HIV-1-positve adults practicing psychological or spiritual activities for one year.* Altern Ther Health Med, 2007. **13**(5): p. 18-20, 22-4.
82. Kemppainen, J.K., et al., *Strategies for self-management of HIV-related anxiety.* AIDS Care, 2006. **18**(6): p. 597-607.
83. Plattner, I.E. and N. Meiring, *Living with HIV: the psychological relevance of meaning making.* AIDS Care, 2006. **18**(3): p. 241-5.
84. Riley, T.A., et al., *Low-income HIV-infected women and the process of engaging in healthy behavior.* J Assoc Nurses AIDS Care, 2008. **19**(1): p. 3-15.
85. Braveman, B., et al., *Occupational identity, occupational competence and occupational settings (environment): influences on return to work in men living with HIV/AIDS.* Work, 2006. **27**(3): p. 267-76.
86. Davies, S.L., et al., *MOMS: formative evaluation and subsequent intervention for mothers living with HIV.* AIDS Care, 2009. **21**(5): p. 552-60.
87. Merenstein, D., et al., *Association of child care burden and household composition with adherence to highly active antiretroviral therapy in the Women's Interagency HIV Study.* AIDS Patient Care STDS, 2009. **23**(4): p. 289-96.
88. Kalichman, S.C., *Co-occurrence of treatment nonadherence and continued HIV transmission risk behaviors: implications for positive prevention interventions.* Psychosom Med, 2008. **70**(5): p. 593-7.
89. Fisher, J.D. and L. Smith, *Secondary prevention of HIV infection: the current state of prevention for positives.* Curr Opin HIV AIDS, 2009. **4**(4): p. 279-87.
90. van der Straten, A., et al., *Managing HIV among serodiscordant heterosexual couples: serostatus, stigma and sex.* AIDS Care, 1998. **10**(5): p. 533-48.
91. Fox, J., et al., *Reductions in HIV transmission risk behaviour following diagnosis of primary HIV infection: a cohort of high-risk men who have sex with men.* HIV Med, 2009. **10**(7): p. 432-8.
92. Bairan, A., et al., *A model of HIV disclosure: disclosure and types of social relationships.* J Am Acad Nurse Pract, 2007. **19**(5): p. 242-50.
93. Chenard, C., *The impact of stigma on the self-care behaviors of HIV-positive gay men striving for normalcy.* J Assoc Nurses AIDS Care, 2007. **18**(3): p. 23-32.
94. Plach, S.K., P.E. Stevens, and S. Keigher, *Self-care of women growing older with HIV and/or AIDS.* West J Nurs Res, 2005. **27**(5): p. 534-53; comment 554-8.
95. Schuster, M.A., et al., *Perceived discrimination in clinical care in a nationally representative sample of HIV-infected adults receiving health care.* J Gen Intern Med, 2005. **20**(9): p. 807-13.
96. Mahajan, A.P., et al., *Stigma in the HIV/AIDS epidemic: a review of the literature and recommendations for the way forward.* Aids, 2008. **22 Suppl 2**: p. S67-79.
97. Sodergard, B., et al., *A structural equation modeling approach to the concepts of adherence and readiness in antiretroviral treatment.* Patient Educ Couns, 2007. **67**(1-2): p. 108-16.

98. World Health Organisation, *Adherence to long term therapies: Evidence for Action.* 2003, Geneva: World Health Organisation.
99. Broyles, L.M., A.M. Colbert, and J.A. Erlen, *Medication practice and feminist thought: a theoretical and ethical response to adherence in HIV/AIDS.* Bioethics, 2005. **19**(4): p. 362-78.
100. Gross, R., et al., *A simple, dynamic measure of antiretroviral therapy adherence predicts failure to maintain HIV-1 suppression.* J Infect Dis, 2006. **194**(8): p. 1108-14.
101. Glass, T.R., et al., *Correlates of self-reported nonadherence to antiretroviral therapy in HIV-infected patients: the Swiss HIV Cohort Study.* J Acquir Immune Defic Syndr, 2006. **41**(3): p. 385-92.
102. Knobel, H., et al., *Impact of different patterns of nonadherence on the outcome of highly active antiretroviral therapy in patients with long-term follow-up.* HIV Med, 2009. **10**(6): p. 364-9.
103. Wong, W.K. and J. Ussher, *How do subjectively-constructed meanings ascribed to anti-HIV treatments affect treatment-adherent practice?* Qual Health Res, 2008. **18**(4): p. 458-68.
104. Levy, J.A., *HIV and the pathogenesis of AIDS.* 3rd ed. 2007, Washington: ASM Press.
105. Bova, C., et al., *The Symptom Experience of HIV/HCV-Coinfected Adults.* J Assoc Nurses AIDS Care, 2008. **19**(3): p. 170-80.
106. Mathews, W.C., et al., *National estimates of HIV-related symptom prevalence from the HIV Cost and Services Utilization Study.* Med Care, 2000. **38**(7): p. 750-62.
107. Newshan, G., J. Bennett, and S. Holman, *Pain and other symptoms in ambulatory HIV patients in the age of highly active antiretroviral therapy.* J Assoc Nurses AIDS Care, 2002. **13**(4): p. 78-83.
108. Benjamini, Y.H., Y., *Controlling the false discovery rate: A practical and powerful approach to multiple testing. Journal of the Royal Statistical Society.* 1995. **Series B, 57**: p. 289-300.
109. Holzemer, W.L., et al., *Validation of the Sign and Symptom Check-List for Persons with HIV Disease (SSC-HIV).* J Adv Nurs, 1999. **30**(5): p. 1041-9.
110. Nicholas, P.K., et al., *Symptom management and self-care for peripheral neuropathy in HIV/AIDS.* AIDS Care, 2007. **19**(2): p. 179-89.
111. Nicholas, P.K., et al., *Unhealthy behaviours for self-management of HIV-related peripheral neuropathy.* AIDS Care, 2007. **19**(10): p. 1266-73.
112. Dodd, M., et al., *Advancing the science of symptom management.* J Adv Nurs, 2001. **33**(5): p. 668-76.
113. Sousa, K.H., S.S. Tann, and O.M. Kwok, *Reconsidering the assessment of symptom status in HIV/AIDS care.* J Assoc Nurses AIDS Care, 2006. **17**(2): p. 36-46.
114. Bastardo, Y.M. and C.L. Kimberlin, *Relationship between quality of life, social support and disease-related factors in HIV-infected persons in Venezuela.* AIDS Care, 2000. **12**(5): p. 673-84.
115. Benedict, R.H., et al., *Impact of human immunodeficiency virus type-1-associated cognitive dysfunction on activities of daily living and quality of life.* Arch Clin Neuropsychol, 2000. **15**(6): p. 535-44.
116. Lorenz, K.A., et al., *Changes in symptoms and health-related quality of life in a nationally representative sample of adults in treatment for HIV.* Qual Life Res, 2006. **15**(6): p. 951-8.
117. Sousa, K.H., et al., *Dimensions of health-related quality of life in persons living with HIV disease.* J Adv Nurs, 1999. **29**(1): p. 178-87.
118. Burgoyne, R.W. and D.H. Tan, *Prolongation and quality of life for HIV-infected adults treated with highly active antiretroviral therapy (HAART): a balancing act.* J Antimicrob Chemother, 2008. **61**(3): p. 469-73.
119. Burgoyne, R.W., et al., *Long-term quality-of-life outcomes among adults living with HIV in the HAART era: the interplay of changes in clinical factors and symptom profile.* AIDS Behav, 2004. **8**(2): p. 151-63.
120. Holzemer, W.L., et al., *Predictors of self-reported adherence in persons living with HIV disease.* AIDS Patient Care STDS, 1999. **13**(3): p. 185-97.
121. Levine, C., *AIDS and changing concepts of family.* Milbank Quarterly, 1990. **68**(1): p. 33-58.
122. Young, J., et al., *Stable partnership and progression to AIDS or death in HIV infected patients receiving highly active antiretroviral therapy: Swiss HIV cohort study.* Bmj, 2004. **328**(7430): p. 15.

123. Burgoyne, R.W., *Exploring direction of causation between social support and clinical outcome for HIV-positive adults in the context of highly active antiretroviral therapy.* AIDS Care, 2005. **17**(1): p. 111-24.
124. DiMatteo, M.R., *Social support and patient adherence to medical treatment: a meta-analysis.* Health Psychol, 2004. **23**(2): p. 207-18.
125. Ingram, K.M., et al., *Social support and unsupportive social interactions: their association with depression among people living with HIV.* AIDS Care, 1999. **11**(3): p. 313-29.
126. Lingler, J.H., et al., *Conceptual challenges in the study of caregiver-care recipient relationships.* Nurs Res, 2008. **57**(5): p. 367-72.
127. Miller, L.G., et al., *How well do clinicians estimate patients' adherence to combination antiretroviral therapy?* J Gen Intern Med, 2002. **17**(1): p. 1-11.
128. Reilly, C.A., et al., *A comparison of patient and nurse ratings of human immunodeficiency virus-related signs and symptoms.* Nurs Res, 1997. **46**(6): p. 318-23.
129. Berg, K.M. and J.H. Arnsten, *Practical and Conceptual Challenges in Measuring Antiretroviral Adherence.* J Acquir Immune Defic Syndr, 2006. **43**: p. 79-87.
130. Chiou, P.Y., et al., *A programme of symptom management for improving quality of life and drug adherence in AIDS/HIV patients.* J Adv Nurs, 2006. **55**(2): p. 169-79.
131. Simoni, J.M., P.A. Frick, and B. Huang, *A longitudinal evaluation of a social support model of medication adherence among HIV-positive men and women on antiretroviral therapy.* Health Psychol, 2006. **25**(1): p. 74-81.
132. Remien, R.H., et al., *Couple-focused support to improve HIV medication adherence: a randomized controlled trial.* Aids, 2005. **19**(8): p. 807-14.
133. Anastasi, J.K., et al., *Symptom management of HIV-related diarrhea by using normal foods: A randomized controlled clinical trial.* J Assoc Nurses AIDS Care, 2006. **17**(2): p. 47-57.
134. Neidig, J.L., B.A. Smith, and D.E. Brashers, *Aerobic exercise training for depressive symptom management in adults living with HIV infection.* J Assoc Nurses AIDS Care, 2003. **14**(2): p. 30-40.
135. Inouye, J., L. Flannelly, and K.J. Flannelly, *The effectiveness of self-management training for individuals with HIV/AIDS.* J Assoc Nurses AIDS Care, 2001. **12**(5): p. 71-82.
136. Kennedy, A., A. Rogers, and M. Crossley, *Participation, roles, and the dynamics of change in a group-delivered self-management course for people living with HIV.* Qual Health Res, 2007. **17**(6): p. 744-58.
137. Gebhardt, M., M. Rickenbach, and M. Egger, *Impact of antiretroviral combination therapies on AIDS surveillance reports in Switzerland. Swiss HIV Cohort Study.* Aids, 1998. **12**(10): p. 1195-201.
138. Clumeck, N., A. Pozniak, and F. Raffi, *European AIDS Clinical Society (EACS) guidelines for the clinical management and treatment of HIV-infected adults.* HIV Med, 2008. **9**(2): p. 65-71.
139. Deschamps, A.E., et al., *Diagnostic value of different adherence measures using electronic monitoring and virologic failure as reference standards.* AIDS Patient Care STDS, 2008. **22**(9): p. 735-43.
140. Arnsten, J.H., et al., *Antiretroviral therapy adherence and viral suppression in HIV-infected drug users: comparison of self-report and electronic monitoring.* Clin Infect Dis, 2001. **33**(8): p. 1417-23.
141. Bangsberg, D.R., et al., *Adherence to protease inhibitors, HIV-1 viral load, and development of drug resistance in an indigent population.* Aids, 2000. **14**(4): p. 357-66.
142. WHO, *Adherence to long-term therapies. Evidence for action.* 2003.
143. Knobel, H., et al., *Validation of a simplified medication adherence questionnaire in a large cohort of HIV-infected patients: the GEEMA Study.* Aids, 2002. **16**(4): p. 605-13.
144. Walsh, J.C., S. Mandalia, and B.G. Gazzard, *Responses to a 1 month self-report on adherence to antiretroviral therapy are consistent with electronic data and virological treatment outcome.* Aids, 2002. **16**(2): p. 269-77.
145. Glass, T.R., et al., *Correlates of Self-Reported Nonadherence to Antiretroviral Therapy in HIV-Infected Patients: The Swiss HIV Cohort Study.* J Acquir Immune Defic Syndr, 2006. **41**(3): p. 385-392.
146. Fogarty, L., et al., *Patient adherence to HIV medication regimens: a review of published and abstract reports.* Patient Educ Couns, 2002. **46**(2): p. 93-108.

147. Hubbard, M., *Dealing with the obstacles in adhering to highly active antiretroviral therapy.* J Assoc Nurses AIDS Care, 2006. **17**(1): p. 18-25.
148. Murphy, D.A., et al., *Barriers to antiretroviral adherence among HIV-infected adults.* AIDS Patient Care STDS, 2000. **14**(1): p. 47-58.
149. Paterson, D.L., et al., *Adherence to protease inhibitor therapy and outcomes in patients with HIV infection.* Ann Intern Med, 2000. **133**(1): p. 21-30.
150. Ammassari, A., et al., *Self-reported symptoms and medication side effects influence adherence to highly active antiretroviral therapy in persons with HIV infection*
Patient-reported nonadherence to HAART is related to protease inhibitor levels. J Acquir Immune Defic Syndr, 2001. **28**(5): p. 445-9.
151. Duran, S., et al., *Self-reported symptoms after initiation of a protease inhibitor in HIV-infected patients and their impact on adherence to HAART.* HIV Clin Trials, 2001. **2**(1): p. 38-45.
152. Garcia, R., R.T. Schooley, and R. Badaro, *An adherence trilogy is essential for long-term HAART success.* Braz J Infect Dis, 2003. **7**(5): p. 307-14.
153. Gifford, A.L. and E.J. Groessl, *Chronic disease self-management and adherence to HIV medications.* J Acquir Immune Defic Syndr, 2002. **31 Suppl 3**: p. S163-6.
154. Wagner, G.J., *Predictors of antiretroviral adherence as measured by self-report, electronic monitoring, and medication diaries.* AIDS Patient Care STDS, 2002. **16**(12): p. 599-608.
155. Catz, S.L., et al., *Patterns, correlates, and barriers to medication adherence among persons prescribed new treatments for HIV disease.* Health Psychol, 2000. **19**(2): p. 124-33.
156. Chesney, M., *Adherence to HAART regimens.* AIDS Patient Care STDS, 2003. **17**(4): p. 169-77.
157. Simoni, J.M., et al., *Best Practices in the Behavioral Management of Chronic Disease, enhancing antiretrovial adherence: a review of published reports of RCTS and on-going NIH funded research.* Vol. Volume II, Chapter 3. 2005, Los Altos, CA: Institute for Disease Management.
158. Haddad, M., et al., *Patient support and education for promoting adherence to highly active antiretroviral therapy for HIV/AIDS.* Cochrane Database Syst Rev, 2000(3): p. CD001442.
159. Knobel, H., et al., *[Adherence to very active antiretroviral treatment: impact of individualized assessment].* Enferm Infecc Microbiol Clin, 1999. **17**(2): p. 78-81.
160. Wall, T.L., et al., *Adherence to zidovudine (AZT) among HIV-infected methadone patients: a pilot study of supervised therapy and dispensing compared to usual care.* Drug Alcohol Depend, 1995. **37**(3): p. 261-9.
161. Ickovics, J.R. and C.S. Meade, *Adherence to HAART among patients with HIV: breakthroughs and barriers.* AIDS Care, 2002. **14**(3): p. 309-18.
162. Tuldra, A., et al., *Prospective randomized two-Arm controlled study to determine the efficacy of a specific intervention to improve long-term adherence to highly active antiretroviral therapy.* J Acquir Immune Defic Syndr, 2000. **25**(3): p. 221-8.
163. Rigsby, M.O., et al., *Cue-dose training with monetary reinforcement: pilot study of an antiretroviral adherence intervention.* J Gen Intern Med, 2000. **15**(12): p. 841-7.
164. Simoni, J.M., et al., *Antiretroviral adherence interventions: a review of current literature and ongoing studies.* Top HIV Med, 2003. **11**(6): p. 185-98.
165. Safren, S.A., et al., *Two strategies to increase adherence to HIV antiretroviral medication: life-steps and medication monitoring.* Behav Res Ther, 2001. **39**(10): p. 1151-62.
166. Haubrich, R.H., et al., *A randomized study of the utility of human immunodeficiency virus RNA measurement for the management of antiretroviral therapy.* Clin Infect Dis, 2001. **33**(7): p. 1060-8.
167. Mann, T., *Effects of future writing and optimism on health behaviors in HIV-infected women.* Ann Behav Med, 2001. **23**(1): p. 26-33.
168. Smith, S.R., et al., *A medication self-management program to improve adherence to HIV therapy regimens.* Patient Educ Couns, 2003. **50**(2): p. 187-99.
169. Bandura, A., *Social foundations of thougt and action: A social cognitive theory.* 1986, NJ: Prentice Hall: Englewood Cliffs.
170. Bandura, A., *Self-efficacy: toward a unifying theory of behavioral change.* Psychol Rev, 1977. **84**(2): p. 191-215.

171. Goujard, C., et al., *Impact of a patient education program on adherence to HIV medication: a randomized clinical trial.* J Acquir Immune Defic Syndr, 2003. **34**(2): p. 191-4.
172. Rawlings, M.K., et al., *Impact of an educational program on efficacy and adherence with a twice-daily lamivudine/zidovudine/abacavir regimen in underrepresented HIV-infected patients.* J Acquir Immune Defic Syndr, 2003. **34**(2): p. 174-83.
173. Pradier, C., et al., *Efficacy of an educational and counseling intervention on adherence to highly active antiretroviral therapy: French prospective controlled study.* HIV Clin Trials, 2003. **4**(2): p. 121-31.
174. Safren, S.A., et al., *Use of an on-line pager system to increase adherence to antiretroviral medications.* AIDS Care, 2003. **15**(6): p. 787-93.
175. Jones, D.L., et al., *Influencing medication adherence among women with AIDS.* AIDS Care, 2003. **15**(4): p. 463-74.
176. Haynes, R.B., et al., *Interventions for helping patients to follow prescriptions for medications.* Cochrane Database Syst Rev, 2000(2): p. CD000011.
177. Rivero-Mendez, M., et al., *Symptoms and quality of life of people living with HIV infection in Puerto Rico.* P R Health Sci J, 2009. **28**(1): p. 54-9.
178. Lobchuk, M.M. and L.F. Degner, *Symptom experiences: perceptual accuracy between advanced-stage cancer patients and family caregivers in the home care setting.* J Clin Oncol, 2002. **20**(16): p. 3495-507.
179. Koch, T., *Implementation of a hermeneutic inquiry in nursing: philosophy, rigour and representation.* J Adv Nurs, 1996. **24**(1): p. 174-84.
180. Allen, D.G., *Hermeneutics: philosophical traditions and nursing practice research.* Nurs Sci Q, 1995. **8**(4): p. 174-82.
181. Mendlinger, S. and J. Cwikel, *Spiraling between qualitative and quantitative data on women's health behaviors: a double helix model for mixed methods.* Qual Health Res, 2008. **18**(2): p. 280-93.
182. Diekelmann, N. and D. Allen, *A hermeneutic analysis of the NLA criteria for the appraisal of baccalaureate progams*. The NLA criteria for appraisal of baccalaureate programs: A critical hermeneutic analysis, ed. N.D.D.A.C. Tanner. 1989, New York: National League for Nursing.
183. Pinquart, M. and S. Sorensen, *Correlates of physical health of informal caregivers: a meta-analysis.* J Gerontol B Psychol Sci Soc Sci, 2007. **62**(2): p. P126-37.
184. Bunting, S.M., *Sustaining the relationship: women's caregiving in the context of HIV disease.* Health Care Women Int, 2001. **22**(1-2): p. 131-48.
185. McGraw, L.A. and A.J. Walker, *Negotiating care: ties between aging mothers and their caregiving daughters.* J Gerontol B Psychol Sci Soc Sci, 2004. **59**(6): p. S324-32.
186. Brown, M.A. and G.M. Powell-Cope, *AIDS family caregiving: transitions through uncertainty.* Nurs Res, 1991. **40**(6): p. 338-45.
187. Spirig, R., *[Becoming partners: the meaning of caring for patients with HIV and AIDS].* Pflege, 1999. **12**(4): p. 230-7.
188. Goffman, E., *Stigma: Notes on the management of spoiled identity*. 1963, New York: Simon & Schuster.
189. Robertson, K.R., et al., *Pattern of neuropsychological performance among HIV positive patients in Uganda.* BMC Neurol, 2007. **7**: p. 8.
190. Sacktor, N., *The epidemiology of human immunodeficiency virus-associated neurological disease in the era of highly active antiretroviral therapy.* J Neurovirol, 2002. **8 Suppl 2**: p. 115-21.
191. Albert, S.M., et al., *Neuropsychologic impairment in early HIV infection. A risk factor for work disability.* Arch Neurol, 1995. **52**(5): p. 525-30.
192. Korner, H. and C. Treloar, *Representations of people with HIV and hepatitis C in editorials of medical journals: discourses and interdiscursive relations.* Commun Med, 2006. **3**(1): p. 15-25.
193. Greene, J. and M.J. Yedidia, *Provider behaviors contributing to patient self-management of chronic illness among underserved populations.* J Health Care Poor Underserved, 2005. **16**(4): p. 808-24.
194. May, C., *Self-management of chronic conditions: re-engineering patient-hood.* Chronic Illn, 2006. **2**(1): p. 15-6.

195. May, C., *The hard work of being ill.* Chronic Illn, 2006. **2**(3): p. 161-2.
196. Kickbusch, I., *Die Gesundheitsgesellschaft Megatrends der Gesundheit und deren Konsequenzen für Politik und Gesellschaft*. 2006, Gamburg: Verlag für Gesundheitsförderung.
197. Wiener, C., *Untrained, unpaid, and unacknowledged: the patient as worker.* Arthritis Care Res, 1989. **2**(1): p. 16-21.
198. Powell-Cope, G.M., *Family Caregivers of People with AIDS: Negotiating Partnerships with Professional Health Care Provider.* Nursing Research, 1994. **43**(6): p. 325-330.
199. Cysique, L.A. and B.J. Brew, *Neuropsychological functioning and antiretroviral treatment in HIV/AIDS: a review.* Neuropsychol Rev, 2009. **19**(2): p. 169-85.
200. Hanson, W.E., Creswell, J.W., Plano-Clark, V.L., Petska, K.S., Creswell, J.D., *Mixed Methods Research Design in Counseling Psychology.* Journal of Counseling Psychology, 2005. **52**(2): p. 224-235.
201. Slonmin-Nevo, V.N., I., *Conflicting Findings in Mixed Methods Research.* Journal of Mixed Methods Research, 2009. **3**(2): p. 109-128.
202. Brown, C.G., et al., *Visual graphical analysis: a technique to investigate symptom trajectories over time.* Nurs Res, 2007. **56**(3): p. 195-201.
203. Sandelowski, M., J. Barroso, and C.I. Voils, *Using qualitative metasummary to synthesize qualitative and quantitative descriptive findings.* Res Nurs Health, 2007. **30**(1): p. 99-111.
204. Sandelowski, M., S. Docherty, and C. Emden, *Focus on qualitative methods. Qualitative metasynthesis: issues and techniques.* Res Nurs Health, 1997. **20**(4): p. 365-71.
205. Blakeman, T., et al., *A qualitative study of GPs' attitudes to self-management of chronic disease.* Br J Gen Pract, 2006. **56**(527): p. 407-14.
206. Thomson, R., *Evidence based implementation of complex interventions.* Bmj, 2009. **339**: p. b3124.
207. Breen, G.M., et al., *Improving doctor-patient communication: examining innovative modalities vis-a-vis effective patient-centric care management technology.* J Med Syst, 2009. **33**(2): p. 155-62.
208. Moran, J., H. Bekker, and G. Latchford, *Everyday use of patient-centred, motivational techniques in routine consultations between doctors and patients with diabetes.* Patient Educ Couns, 2008. **73**(2): p. 224-31.
209. Bodenheimer, T., *Interventions to improve chronic illness care: evaluating their effectiveness.* Dis Manag, 2003. **6**(2): p. 63-71.
210. Lorig, K.R., et al., *The Expert Patients Programme online, a 1-year study of an Internet-based self-management programme for people with long-term conditions.* Chronic Illn, 2008. **4**(4): p. 247-56.
211. Richardson, J.L., et al., *Effect of brief safer-sex counseling by medical providers to HIV-1 seropositive patients: a multi-clinic assessment.* Aids, 2004. **18**(8): p. 1179-86.
212. Wright, L.M.L., M., *Nurses and families: A guide to family assessment and intervention.* 5th ed. 2009, Philadelphia: F.A. Davies.
213. Remien, R.H., et al., *Moving from theory to research to practice. Implementing an effective dyadic intervention to improve antiretroviral adherence for clinic patients.* J Acquir Immune Defic Syndr, 2006. **43 Suppl 1**: p. S69-78.
214. Vincenzi, C.B., K. Moody, and R. Spirig, *Development and pretesting of a set of symptom assessment tools in HIV: The HIV Symptom Experience Assessment Scale and the HIV Symptom Manageability Scale.* Appl Nurs Res, 2009. **22**(3): p. 204-10.
215. Arroll, B., et al., *Effect of the addition of a "help" question to two screening questions on specificity for diagnosis of depression in general practice: diagnostic validity study.* Bmj, 2005. **331**(7521): p. 884.
216. Goodyear-Smith, F., B. Arroll, and N. Coupe, *Asking for help is helpful: validation of a brief lifestyle and mood assessment tool in primary health care.* Ann Fam Med, 2009. **7**(3): p. 239-44.
217. Munro, S., et al., *A review of health behaviour theories: how useful are these for developing interventions to promote long-term medication adherence for TB and HIV/AIDS?* BMC Public Health, 2007. **7**: p. 104.
218. Noar, S.M., *An interventionist's guide to AIDS behavioral theories.* AIDS Care, 2007. **19**(3): p. 392-402.

219. Strauss, S.M., et al., *HIV care providers' implementation of routine alcohol reduction support for their patients.* AIDS Patient Care STDS, 2009. **23**(3): p. 211-8.
220. Voggensperger, J., K. Fierz, and R. Spirig, *[An evidence-based guideline to support HIV/AIDS patients with alcohol problems]*. Pflege, 2006. **19**(4): p. 223-33.
221. Guthrie, B., et al., *Continuity of care matters.* Bmj, 2008. 337: p. a867.
222. Bodenheimer, T. and B.Y. Laing, The teamlet model of primary care. Ann Fam Med, 2007. 5(5): p. 457-61.

Curriculum Vitae

Personal data

Surname / Name	Dunja Nicca
Address	St. Georgenstrasse 69
City	9000 St. Gallen
Phone	0041 79 7083400
E-Mail	dunja.nicca@unibas.ch
Date of Birth	9.2.1971
Citizenship	Swiss

Education

Graduate

2006 to present	PhD study program Institute of Nursing Science, University of Basel Head of dissertation: Prof. R. Spirig Co-Evaluator: Prof. W. Langewitz External Expert: Prof. S. Rankin Other Experts: Prof. K. Moody; Prof. M. Battegay
2001-2004	Master’s Degree in Nursing Science Institute of Nursing Science, University of Basel (Masters Thesis: Ready for antiretroviral therapy? - Experiences of people living with HIV/AIDS)

Undergraduate

1998-2001	Diploma as Clinical Nurse Specialist and Public Health Care Specialist University of Applied Sciences Aargau, Health and Social Work, Aarau. (Diploma Thesis: “You can’t just sit around, you have to start something again” – the meaning of independence in older women living alone)
1989-1992	Registered Nurse in General Nursing, Evangelische Krankenpflegeschule Chur (School of Nursing at Diploma Level), Chur

Other relevant Trainings

2005	Practice Training & Independent Study of 3 weeks at the Virology Treatment Center, Maine Medical Center and The Public Health Center, Department of Health and Human Services City of Portland, in Portland, Maine, USA
1996-1997	Diploma as Clinic Instructor Institute of Economy & Pedagogy, Morschach

1995-1996	Advanced Nursing Practice Moduls, Level I, Former: Kaderschule für die Krankenpflege, (School for Postgraduate Advanced Nursing), Aarau and Winterthur (Today: WE'G (Advanced Education Centre for Health-Care Professionals / Weiterbildungszentrum für Gesundheitsberufe), Winterthur

Professional Experience

2006 to present	Advanced practice nurse, part time (40%), Department of Infectiology, Kantonsspital St. Gallen (County Hospital)
2004 to 2006	Research Assistant, part time (10%) Institute of Nursing Science, University of Basel Spirig, R., Battegay, M., Moody, K.A., and De Geest, S., Exploring the relationship of symptom experience, symptom manageability, adherence, health-related quality of life, and disease progression in people living with HIV/AIDS, Swiss National Fund proposal: Submitted Oct. 1, 2002 to the SNF Swiss National Fund (3 year funding: 409'018 CHF, Project Nr. 3346-100884)
2003- 2004	Research Assistant, part time (50%) Institute of Nursing Science, University of Basel Spirig, R., Battegay, M., Moody, K.A., and De Geest, S., Exploring the relationship of symptom experience, symptom manageability, adherence, health-related quality of life, and disease progression in people living with HIV/AIDS, Swiss National Fund proposal: Submitted Oct. 1, 2002 to the SNF Swiss National Fund (3 year funding: 409'018 CHF, Project Nr. 3346-100884)
2001 to 2006	Advanced Practice Nurse, part time (40%) HIV Outpatient Clinic, Department of Medicine, University Hospital Basel
1999-2001	Diploma Nurse, part time (10%) SPITEX (Community Care Nursing), Schaffhausen
1994-1998	Clinical Instructor (90%), Medicine department, Kantonsspital (County Hospital) Schaffhausen
1992-1994	Diploma Nurse (100%), Medicine Department, Kantonsspital (County Hospital), Schaffhausen

Research Grant

Nicca, D., Battegay, M., Tanner, M., Spirig, R. (2006). Medication- and symptom management in persons living with HIV: Perception and collaboration of persons living with HIV, their primary support persons and health care providers. Ebnet-Stiftung, 2007: 25'000 CHF; 2008: 25'000 CHF; 2009: 25’000 CHF

Fehr, J., Nicca, D., Spirig, R., Wagels, T., Kiss, A., Bregenzer, T., Vernazza,P., Sendi, P., Jäger, H., Battegay, M., Readiness, shared decision making and perception of the HIV-treatment team for patients starting or changing HAART: The Swiss HIV Chort Study, 2003, 30’400 CHF

Practice Development Projects Grant

Vernazza, P. Nicca D. Development of an intervention program to integrate HIV secondary prevention into routine clinical care and enhance prevention behavior of people living with HIV. Swiss federal health office (Bundesamt für Gesundheit), 2007, 50’000 CHF

Vernazza, P. Nicca D. Development of an intervention program to integrate HIV secondary prevention into routine clinical care and enhance prevention behavior of people living with HIV. Swiss federal health office (Bundesamt für Gesundheit), 2006, 35’000 CHF

Nicca, D., Fehr, J., Battegay, M., Spirig, R. Development of a pocket-guide for health care providers to assess readiness and support antiretroviral decision making. Bristol-Myers Squibb, 2005, 4200 CHF

Spirig, R., Nicca, D., S., Battegay, M. Developing and Establishing an Advanced HIV-Nursing Practice (Entwicklung und Etablierung einer erweiterten und vertieften HIV/AIDS Pflegepraxis)

2002: GlaxoSmithKline GSK 20.000 CHF

2003: GlaxoSmithKline GSK 20.000 CHF

2004: GlaxoSmithKline GSK 20.000 CHF

2005: GlaxoSmithKline GSK 16'000 CHF; Roche 20.000 CHF; Merck Sharp & Dohme Chibret AG MSD 16.000 CHF

2006: GlaxoSmithKline GSK 16'000 CHF; Roche 16.000 CHF; Merck Sharp & Dohme Chibret AG MSD 16.000 CHF

Publications

Bigler S., Nicca, D., Spirig, R. (2009). Enfurvirtide in HIV Patients: A Nursing Guideline for medication management. *Pflege: Die wissenschaftliche Zeitschrift für Pflegeberufe, 22(1), 29-38.*

Nicca, D., Moody, K., Elzi, L., Spirig, R. (2007). Comprehensive clinical adherence interventions to enable antiretroviral therapy: A case report. *Journal of Nurses in AIDS Care JANAC,* 18(6), 44-53.

Bigler, S., Nicca, D. (2007). Interventions to Enhance Adherence of Patients with HIV on ART: A Literature Review (Literaturzusammenfassung zur Frage: „Welche Interventionen bewirken eine Verbesserung der Adhärenz von HIV-Patienten unter ART?“). *Pflege: Die wissenschaftliche Zeitschrift für Pflegeberufe,* 20(5), 268-77.

Elzi, L., Spoerl, D., Voggensperger, J., Nicca, D., Simcock, M., Bucher, H.C., Spirig, R., Battegay, M. and the Swiss HIV Cohort Study (2006). A smoking cessation programme in HIV-infected individuals: a pilot study. Antiretroviral Therapy, 11, 787-795.

Nicca, D., Fehr, J., Battegay, M., Spirig, R. (2005). Ready for antiretroviral therapy? Decision making from the perspective of HIV-infected people (Bereit für die antiretrovirale Terapie? Die Enscheidungsfindung aus der Sicht von HIV-Infizierten). *Pflege: Die wissenschaftliche Zeitschrift für Pflegeberufe*, 18(5), 289-298.

Fehr, J., Nicca, D., Sendi, P., Wolf, E., Wagels, T., Kiss, A., Bregenzer, T., Vernazza, P., Jäger, H., Spirig, R. and Battegay, M., and the Swiss HIV Cohort Study (2005). Starting or changing therapy - a prospective study exploring antiretroviral decision making. *Infection,* 33(4), 249-256.

Spirig, R., Nicca, D., Werder, V., Voggensperger, J., Unger, M. (2004). The Advanced Nursing Practice Team as a Model for Caregiving in HIV/AIDS. *Journal of the Association of Nurses in AIDS Care JANAC*, 15(3), 47-55.

Voggensperger, J., Nicca, D., Battegay, M., Zellweger, J.P., Spirig, R. (2003). Ein Rauchstopp-Programm für HIV-infizierte Menschen (A smoking cessation program for HIV-infected people). *Pflege: Die wissenschaftliche Zeitschrift für Pflegeberufe,* 16(5), 283-288.

Spirig, R., Nicca, D., Werder, V., Voggensperger, J., Unger, M., Bischofberger, I., Kesselring, A., Battegay, M., De Geest, S. (2002). Entwicklung und Etablierung einer erweiterten und vertieften HIV/Aids Pflegepraxis (Developing and establishing an advanced HIV-nursing practice). Pflege: *Die wissenschaftliche Zeitschrift für Pflegeberufe*, 15 (6), 293-299.

Nicca, D., & Jenni, G. (2002). “Du darfst nicht nur rumsitzen, du musst wieder etwas beginnen“ – Die Bedeutung der Selbständigkeit für betagte Frauen (“You can’t just sit around, you have to start something again” – the meaning of independence in older women living alone). Intercura: Publikation des stadtärztlichen Dienstes der Stadt Zürich,77.

Nicca, D. & Jenni, G. (2002). Die Bedeutung der Selbständigkeit für alleinlebende betagte Frauen (The meaning of independence in older women living alone). Homepage des Vereins zur Förderung der Pflegewissenschaft- und Forschung: www. vfp.ch.

Presentations

Galieva, Z. Nicca, D. Schläpfer, J. Schlegel, M., Vernazza, P. Maeschli, B.: Public acceptance of harm reduction as a major limitation for HIV prevention in Bashkortostan, Russia. Deutsch-Österreichischer-Schweizerischer AIDS-Kongress, St. Gallen, Switzerland, June 24.-27.

Nicca, D. Daneel, S., Vernazza, P.: Prevention for Positives: Sexual behavior and influencing factors. Deutsch-Österreichischer-Schweizerischer AIDS-Kongress, St. Gallen, Switzerland, June 24.-27.

Nicca, D. Fehr, J. Vernazza, P., Spirig, R. Keeping a Grip on HIV: Collaborative Medication and Symptom Management. Deutsch-Österreichischer-Schweizerischer AIDS-Kongress, St. Gallen, Switzerland, June 24.-27.

Daneel, S.; Tina, A., Schläpfer, J., Schmid, P., Vernazza, P., Nicca, D.: Development of an HIV prevention flyer for illiterate persons and individuals with functional illiteracy. Deutsch-Österreichischer-Schweizerischer AIDS-Kongress, St. Gallen, Switzerland, June 24.-27.

Nicca, D.: Antiretroviral treatment decisions making support for PLWH. 7th Innsbruck HIV Update, Kühtai, Austria, 2009, April 23-26.

Nicca, D.: Vernazza, P.: The Swiss HIV Positive Prevention Project. 6th Innsbruck HIV Update, Kühtai, Austria, 2008, April 10-13.

Nicca, D.: Ready to StART? Dynamics between Clinical Practice and Research. Invited presentation Readiness Panel:International Conference on HIV Treatment Adherence (NIMH/IAPAC). New Jersey, USA, 2008, March 17-18.

Vernazza, P. Nicca, D.: Sexual risk of HIV transmission in the HAART era: an increasing dilemma for HIV counselors. Symposium: Challenges in HIV., Zürich, Switzerland, 2007, June.

Nicca, D. Fehr, J., Battegay, M., Spirig, R.: Antiretroviral Decision Making out of the Patients Perspective. Deutscher Kongress zum Thema partizipative Entscheidungsfindung (Shared Decision Making), Heidelberg, Germany, 2006, March 30 - April 1.

Nicca, D.; Moody, K., Elzi, L., Spirig, R.: The Challenge of Comprehensive Adherence Interventions in Clinical Practice for Patients with Long-Term Adherence Problems. International Conference on HIV Treatment Adherence (NIMH/IAPAC). New Jersey, USA, 2006, March 8-10.

D. Spoerl, L. Elzi, J. Voggensperger, D. Nicca, M. Simcock, H. Bucher, R. Spirig, M. Battegay and the Swiss HIV Cohort Study: A Smoking Cessation Program in HIV-infected individuals - a pilot study.10th European AIDS Conference (EACS), Dublin, Ireland, 2005, November 17-20. (Abstract PS 5/4, oral presentation).

Spirig, R. Nicca, D.: Principles of Chronic Illness Management. Impulse presentation, University Hospital Basel, Switzerland, 2005, September 27.

Nicca, D, Elzi, L., Battegay, M.; Spirig, R.: ART Adherence and Resistances-A Clinical Case Report. Swiss Infection Conference, Basel, Switzerland, 2005, June 8-10.

Nicca, D, Fehr, J., Battegay, M.; Spirig, R.: Readiness for Antiretroviral Therapy-A Dialectical Process of Decision Making. Swiss Infection Conference, Basel, Switzerland, 2005, June 8-10.

De Geest, S., Nicca, D.: Management of chronic diseases. Symposium: Infections and Nursing Care, County Hospital St. Gallen, 2004, October, 27.

Nicca, D.: Decision making and chronic illness- an example of persons living with HIV (Entscheidungsfindungen im Leben mit chronischen Gesundheitsproblemen am Beispiel der HIV-Infektion). 2nd Swiss HIV Nurses Conference, Münchenbuchsee, Switzerland, 2004, octobre 11.

Nicca, D, Fehr, J., Battegay, M.; Spirig, R.: Antiretroviral Therapy Readiness and Decision Making: The ART Decision Making Model. 12th Biennal Conference of the Workgroup of European Nurse Researchers (WENR), Lisboa, Portugal. 2004, october 5-7.

Nicca, D, Fehr, J., Battegay, M.; Spirig, R.: Ready for Antiretroviral Therapy? Experiences of persons living with HIV in the process of therapy decision making.12th Biennal Conference of the Workgroup of European Nurse Researchers (WENR), Lisboa, Portugal. 2004, october 5-7.

Spirig, R., Nicca, D.:Advanced Nursing Practice – a future oriented concept for daily nursing practice. University Hospital Zürich, Zürich, Switzerland, 2004, September 8.

Nicca, D: Ready for therapy? HIV infected patient’s experiences of antiretroviral decision making. Master’s Theses-Presentations of students of the : WE’G Advanced Education Centre for Health-Care Professionals Aarau in collaboration with the university of Maastricht and students of the Institute for Nursing Sience, University Basel, Aarau, 2004, September 1.

Fehr, J., Nicca, D., Wolf, E., Jäger, H., Vernazza, P., Bregenzer, T., Kiss, A., Sendi, P., Spirig, R, Battegay, M.: Ready for therapy? Antiretroviral therapy readiness, shared decision making and perception in patients and health care providers. 9th European AIDS Clinical Society Conference, Warschau, 2003.

Nicca, D. Fehr, J., Battegay, M., Spririg, S.: The Ready-Project – Importance of readiness for antiretroviral therapy and decision making. First Swiss HIV Nurses Congress “Management of Adherence in HIV Healthcare”. Muri Bern, 2003, November 5.

Nicca, D: The meaning of shared decision making of patients and health care providers (Die Bedeutung der gemeinsamen Entscheidungsfindung von Patienten und dem Behandlungsteam). Third Caring Symposium (Symposium Pflegebeziehung-„Ist Beziehungsfähigkeit angeboren oder erlernt?“), Will, 2003, October, 31.

Nicca, D., Werder, V., Voggensperger, J., Unger, M., Battegay, M., Spirig, R.: Empowerment of nurses to provide an advanced HIV-nursing practice. 3rd European Nursing Congress “Vulnerable groups in society: a nursing issue. Amsterdam, 2003, October 5-8.

Nicca, D., Voggensperger, J., Spirig, R. It works without smoking: A smoking Cessation Programm. Congress “ Competent Care through Clinical Expertise: Nurses as Pacemakers in the Health Care System” of the Institute of Nursing Sience University Basel, PES Clinical Nurse Specialists, and WEG , University Hospital Bern, 2003, April 4.

Nicca, D. & Jenni, G. Nursing home as the last home: The life world of elderly women (Pflegeheim als letztes zu Hause: Die Lebenswelt betagter Frauen). Forum for long term Care (Forum für Langzeitpflege), Department of long term nursing institutions Zürich (Amt für Krankenheime der Stadt Zürich), September 11, 2002.

Spirig, R., Nicca, D. Establishing an advanced HIV nursing practice. 11th Biennal Conference of the Workgroup of European Nurse Researchers (WENR), Geneva, Switzerland. Sept. 2.-4., 2002.

Nicca, D. & Jenni, G. "You can't just sit around, you have to start something again"- The meaning of independence in older women living alone. 11th Biennal Conference of the Workgroup of European Nurse Researchers (WENR), Geneva, Switzerland. Sept. 2.-4., 2002.

Spirig, R., Werder, V., Voggensperger, J., Unger, M., Bischofberger, I., Nicca, D., De Geest,S. Developing and establishing an advanced HIV nursing practice. XIV International AIDS Conference 2002, Barcelona Spain, July 7-12, Abstract on Disk MoPeE3829.

Spirig, R., Werder, V., Voggensperger, J., Unger, M., Nicca, D.: Introducing and establishing advanced HIV-nursing practice. Conference of the Clinical Nurse Specialists, Zürich, Switzerland, June, 5., 2002.

Nicca, D. & Jenni, G. The meaning of independence for older women living in nursing homes (Die Bedeutung der Selbständigkeit für betagte im Altersheim lebende Frauen). Congress: „Having a long life in the present society" (Lange leben in der heutigen Gesellschaft). WE'G: Advanced Education Centre for Health-Care Professionals, Oktober, 27, 2000.

Awards

2. Vontobel-Award of the Centre of Gerontology, University Zurich, Dec. 12., 2001

Nicca, D. & Jenni, G. "You can't just sit around, you have to start something again" – the meaning of independence in older women living alone. Diploma thesis at the University of applied Sciences Aargau.

Lectures Academic

Nicca, D.: Mixed Methods Research Course. Lecture for master students of the Institute for Nursing Science, University of Basel, April-May, 2009

Nicca, D.: Mixed Methods Research Course. Lecture for master students of the Institute for Nursing Science, University of Basel, April-May, 2008

Nicca, D.: Prevention for people living with HIV in the HAART era. Lecture for bachelor students of the University of Applied Sciences, Social Work, Olten June 2007, 2008

Nicca, D.: Chronic Illness Management: Selfmanagement. Lectures for master students of the Institute for Nursing Science, University of Basel June, 2006, 2007, 2008

Nicca, D.: Action learning: Seminar for bachelor students of the Institute for Nursing Science, University of Basel June, 2004.

Spirig, R., Nicca, D.: Advanced Nursing Practice in HIV-Care - A Team approach. Lectures for master students of the Institute for Nursing Science, University of Basel June, 2003, 2005.

Nicca, D., Fehr, J.: Therapy decision making in the life with a chronic illness (Therapieentscheidungen im Leben mit chronischen Gesundheitsproblemen). Lectures for master students of the Institute for Nursing Science, University of Basel June, 2003, 2004, 2005, 2006, 2007, 2008.

Nicca, D. & Jenni, G. "You can't just sit around, you have to start something again"- The meaning of independence in older women living alone („Du darfst nicht nur rumsitzen, du musst wieder etwas beginnen"- Die Bedeutung der Selbständigkeit für betagte Frauen). Lectures for Bachelor students of the University for Applied Sciences, Health and Social Work Aargau,. Aarau, February, 2002, 2003.

Lectures Non-Academic

Nicca, D.: Care of people living with HIV. Lectures for nursing diploma students. School of Nursing Bethesda, April 2007, April 2008 and 2009

Nicca, D. & Jenni, G. Health and Living Conditions of Elderly Women. A family-, individual- and social- perspective. Advanced Nursing Practice Moduls, Level I (3 days). Association of Swiss Nurses, Education Center, Zürich (SBK Bildungszentrum, Zürich), April 2003.

Nicca, D.; Jenni, G.: Independence out of the perspective of older women („Im Lot bleiben"- Selbständigkeit aus Sicht betagter alleinlebender Frauen). Lectures for nursing diploma students. School for Nursing, Theodosianum, Schlieren, June, 2002 and June, 2003.

Nicca, D. & Jenni, G. Insights into elderly women's life world (Ein Einblick in die Lebenswelt betagter Frauen). Lecture for nurses of the Nursing Home Adlergarten, Winterthur, March, 2002.

Department Activities

Nicca, D.; Spirig, R.: 12 day research practica over a 2 month period for a master student of the Insitute of Nursing Science, University of Basel, 2008.

Nicca, D.; Elzi, L., Lindpainter, L.: 5 clinical tutorials, related to the clinical assessment course, with a master student of the Institute of Nursing Sience, Universtiy of Basel, 2005.

Nicca, D., Spirig, R.: 2 days of clinical workshadowing, related to the advanced nursing practice course, with a bachelor student of the Institute of Nursing Sience, Universtiy of Basel, 2005.