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Impact of health care system factors on adherence in transplantation: looking beyond the horizon

EWOPA,
Leuven, Belgium, 05-06-2009

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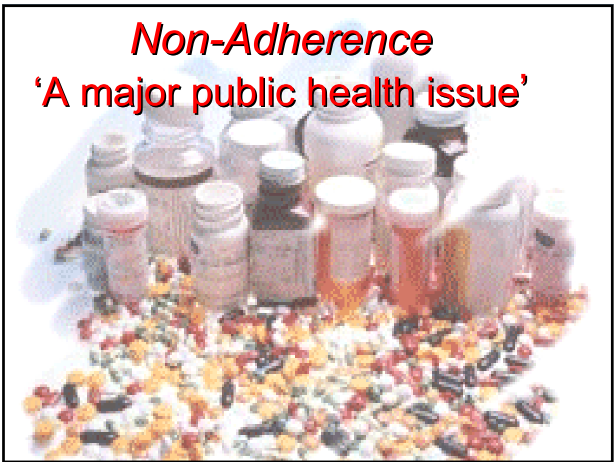

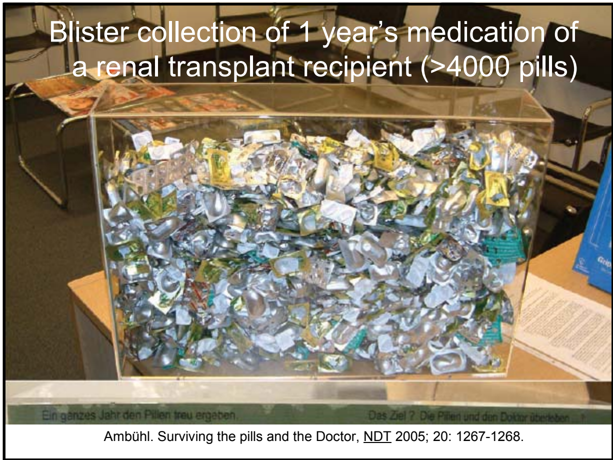

Ambühl. Surviving the pills and the Doctor, NDT 2005; 20: 1267-1268.

Looking beyond the horizon

1. System related factors:
   Adding an ecological perspective to adherence research
2. Multilevel factors associated with non-adherence

Looking beyond the horizon

1. **System related factors:**
   Adding an ecological perspective to adherence research
2. Multilevel factors associated with non-adherence

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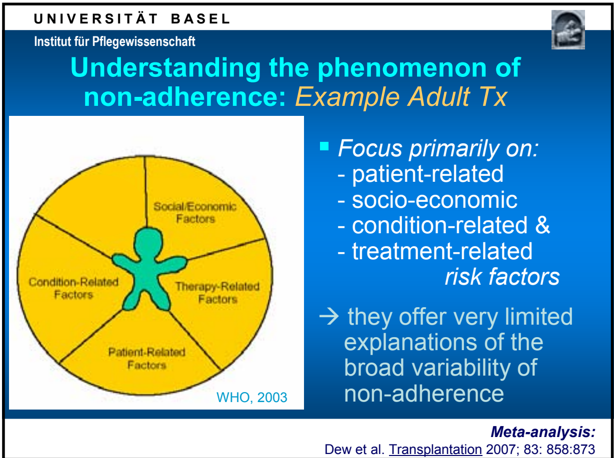
Understanding the phenomenon of non-adherence: *Example Adult Tx*



- *Focus primarily on:*
  - patient-related
  - socio-economic
  - condition-related &
  - treatment-related
  risk factors

→ they offer very limited explanations of the broad variability of non-adherence

Meta-analysis:
Dew et al. Transplantation 2007; 83: 858:873

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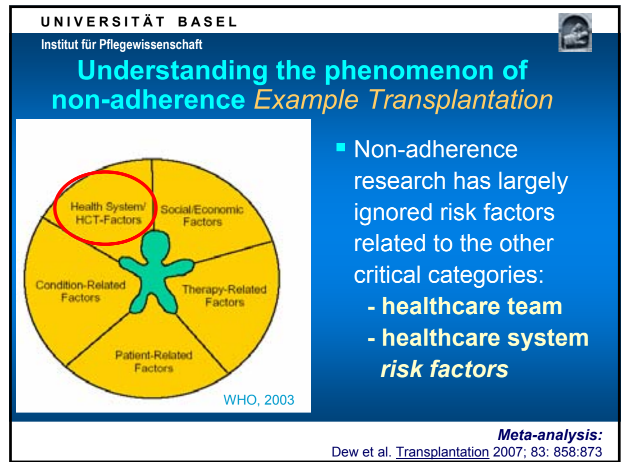
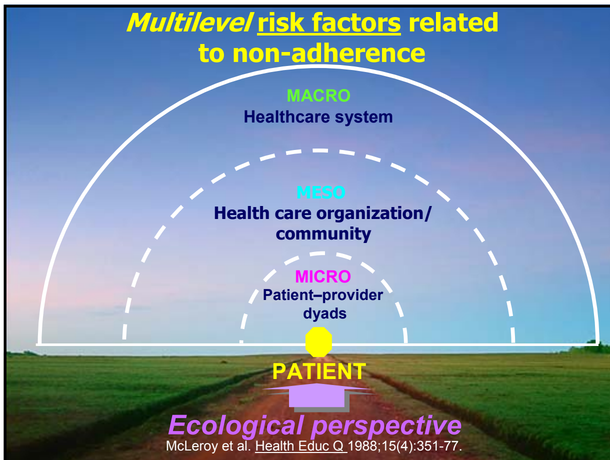
Meta-analysis of correlates non-adherence with immunosuppressive drugs (N=46 studies, 1981-2005, adults)

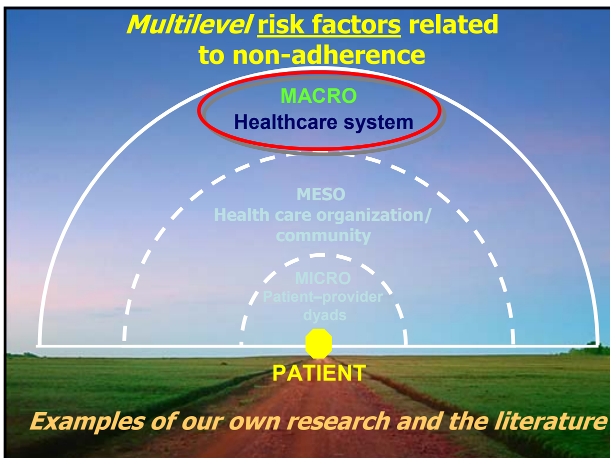
- Kidney > heart > liver
- Non white ethnicity ↑
- Poorer social support ↑
- Poorer perceived health ↑
- **North America ↑**

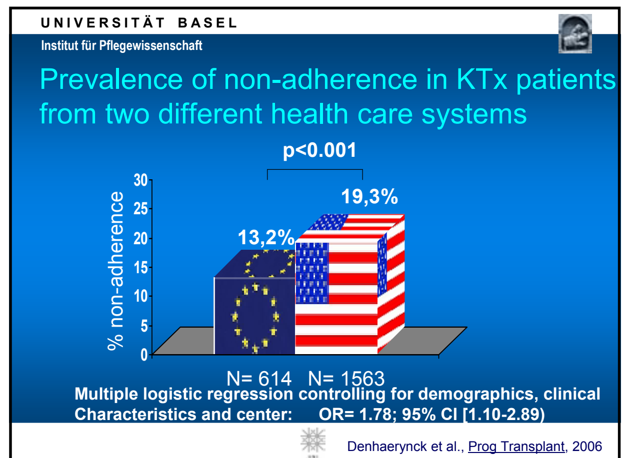
→ only small part of variance explained

Meta-analysis:
Dew et al. Transplantation 2007; 83: 858:873









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Macro level: Health care system factors

- Variability in adherence observed between different health care systems and countries

Dew et al, Transplantation, 2007; Denhaerynck et al., Progress in Transplantation, 2006

- Insurance status & reimbursement of treatment has been found to be related with nonadherence in US studies

Dew et al, Transplantation, in press; Butkus et al. N Engl J Med 1992

Hypotheses:

- Insurance coverage varies between continents and countries?
- Cultural differences?
- Variability in policy incentives for support in self-management/adherence?

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Cost related non-adherence (CRN)

- CRN primarily assessed in US
  18%-28% in those without prescription coverage

Safran et al. Health Affairs 2002; W253-W268; Piette et al. Arch Int Med 2004; 164: 1749-1755; Piette et al. Medical Care 2004; 42:102-109; Piette et al. Am J Manag Care 2004; 10 (part 2): 861-868; Wilson et al. J Gen Intern Med 2004; 20:715-720; Heisler et al. Medical Care 2004; 42; 626-634; Heisler et al. J Behav Med. 2005 28(1):43-51; Piette et al. Arch Int Med 2005; 165: 1749-1755; Piette et al. J Clin Epidemiol. 2006 Jul;59(7):739-46; Wagner et al., Health Econ Policy Law 2008; 3:51-67

- Pharmacy benefit caps / Co-payments as driver in CRN, *yet also other factors involved*

Tseng et al., JAMA 2004; 292: 952-960; Gibson et al. Am J Manag Care 2005; 11: 730-740; Hsu et al. N Eng J Med 2006; 354: 2349-59; Joyce et al. Health Affairs 2007; 26: 1333-1344; Zhang et al., J Manag Care Pharm 2007; 13: 664-676

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2008 Commonwealth Fund International Health Policy Survey of Chronicaly Ill in 8 countries (n=7,461)

	AUS	CAN	FR	GER	NETH	NZ	UK	US
Unweighted N	593	1,956	851	867	736	518	933	1,007
Access problems because of cost in past 2 years Did not fill Rx or skipped doses	20%	18%	13%	12%	3%	18%	7%	43%

Schoen et al, Health Affairs 2009;28(1):w1-16

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Cost related non-adherence (CRN)

- CRN in dialysis patients in 12 countries
  Range: 3 % Japan to 29 % US

Percentage Of Patients Reporting Having Some Out-Of-Pocket Drug Spending Versus Mean Total Monthly Spending, By Country, 2002–2004

SOURCE: Authors' calculations using data from the Dialysis Outcomes and Practice Patterns Study.
NOTES: The area of each bubble equals the percentage of patients reporting nonpurchase of medication because of cost. R^2 = 0.4372. PPP is purchasing power parity.

Hirth, Piette et al. Health Affairs 2008; 27:89-102

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Cost related non-adherence (CRN)

- Switzerland: 19% of adult Tx patients reported that they did not have the financial means to pay for their medications (CRN not assessed)

De Geest et al. Swiss Medical Weekly 2007; 137: 125S-127S

Transcultural issues as a factor related to non-adherence

- Illness cognitions
- Health beliefs

CHAPTER 5

The Center Effect in Heart Transplantation

Roger W. Evans, Frederick B. Dong, and Diane L. Manninen

Health and Population Research Center
Battelle-Seattle Research Center
Seattle, Washington

Evans et al. In: Terasaki (Ed). Clinical Transplants 1991; pp. 45-59

What is a center effect?

- Center effects are differences in outcomes among treatment that cannot be explained by identifiable differences in patients treated or specific treatments applied and are presumed to be the result from differences in the ways health care is delivered, for example, training and experience of personnel, availability of resources and characteristics of the center‘s organization

Loberiza et al. Bone Marrow Transplantation 2003; 31: 417-421

Meso level factors:

Health care organization and community

- Center effects in adherence outcomes in Tx and in other chronically ill patient populations observed
  Weng et al. , J Am Soc Nephrol, 2005;
  Glass et al., JAIDS, 2006; Saran et al. Kidney Int. 2003
- Factors in literature (limited)
  - Living a longer distance from the transplant center
    Didlake et al., Transplant Proc, 1988; Santiago-Delpin et al., Transplant Proc 1989; Rodriguez et al., Transplant Proc, 1991
  - Not being under direct supervision of a health care team
    Cooper et al., Journal Heart Transplantation 1984
  - Size dialysis center, highly trained staff, dietician part of team
    Saran et al. Kidney Int. 2003 2003

Meso level factors: *pediatric Tx*

Health System/ HCT-Factors
Social/Economic Factors
Condition-Related Factors
Therapy-Related Factors
Patient-Related Factors

WHO, 2003

- Lack of continuation of follow-up
- Interference of follow-up with school / work
- Poor accessibility of care
- Unidisciplinary care
- Transition to adult unit

Dobbels et al., Pediatr Transplant. 2005;9:381-90

Alan R. Watson

Non-compliance and transfer from paediatric to adult transplant unit

A natural experiment in „system change“

Fig. 1 Plasma creatinine before and after transfer (T) in 20 patients

Creatinine (µmol/l)

Time (months)

- N=20
  Mean age 17.9 y.
- 8/20 grafts failed
- 7 unexpected AR due to non-adherence, var. CsA levels

Watson et al., Pediatr Nephrol. 2000; 14: 469-72

Transition as risk factor for poor outcome

A natural experiment in „system change“

- OPTN/SRTR data
- Kidney N=4221; Liver N=3558
- 18 years as cut-off, 4 years follow-up
- Kidney:
  ↑ RR graft failure at age 18 compared with 17 (p=0.03)

Thomas et al., WTC, Boston, 2006

Degree of Chronic Illness Management in your center?

Chronic Illness Management

- % self-management support?
- % clinical information system?
- % Adherence monitoring and interventions?
- % HCW mastering behavioral interventions?
- % patient active partner?
- % Decision making support?
- % collaboration with community, primary care, and other?
- ,…

Bodenheimer et al., JAMA 2002; 288: 1775-9; WHO, 2002

Multilevel risk factors related to non-adherence

MACRO
Healthcare system
MESO
Health care organization/ community
MICRO
Patient–provider dyads
PATIENT

Examples of are own research and the literature

Micro level factors

- Patient's formal and informal social networks and social support systems
- Patient-provider relationship
- Health care professional's communication style
- Trust
- Language difficulties

Battaglioli-DeNero J Assoc Nurses AIDS Care 2007; Beachet al. J Gen Intern Med 2006; Stewart et al., Cancer Prev Control 1999; Hall et al. Med Care 1988; Bischoff et al. Br J Gen Pract 2003; Piette et al. Soc Sci Med 2006; Piette et al. Arch Intern Med 2005; Johnell et al. BMC Public Health 2006; 6:52-60.

Micro level factors: *pediatric Tx*

Health System/ HCT-Factors
Social/Economic Factors
Condition-Related Factors
Therapy-Related Factors
Patient-Related Factors

WHO, 2003

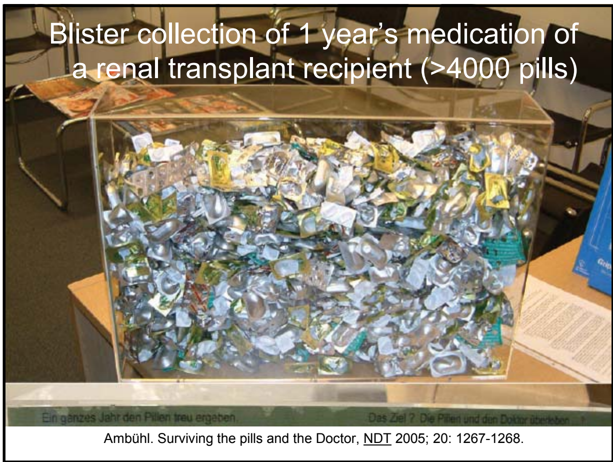
- Poor communication between HCW, family and patient
- Lack of trust
- Authoritarian communi-cation style and poor didactic skills of HCW
- Poor knowledge of NA measurement & management by HCW

Dobbels et al., Pediatr Transplant. 2005;9:381-90

How confident are you that you are up-to-date in the most effective strategies for reducing treatment non-adherence among patients with hypertension and hyperlipidemia?

- Not at all confident 20%
- Somewhat confident 59%
- Confident 17%
- Very confident 2%

Foody J. Medication adherence: America's 'Other drug problem' http://www.medscape.com/viewarticle/549907



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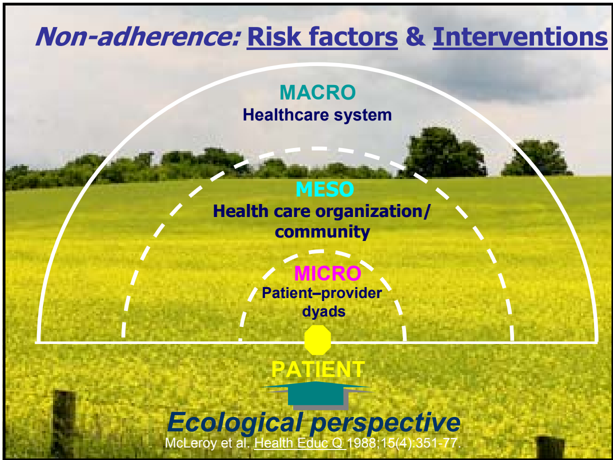
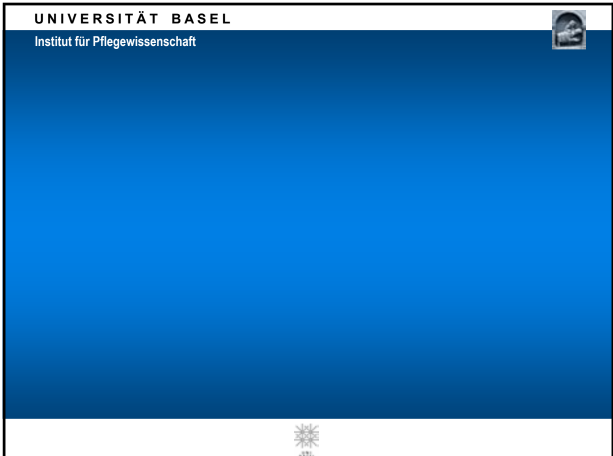
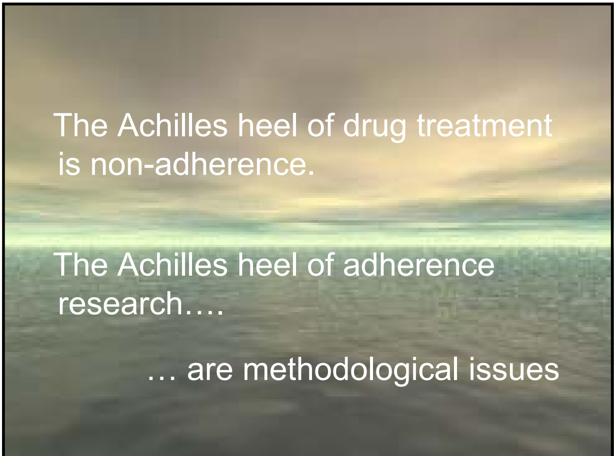






Tour de Horizon

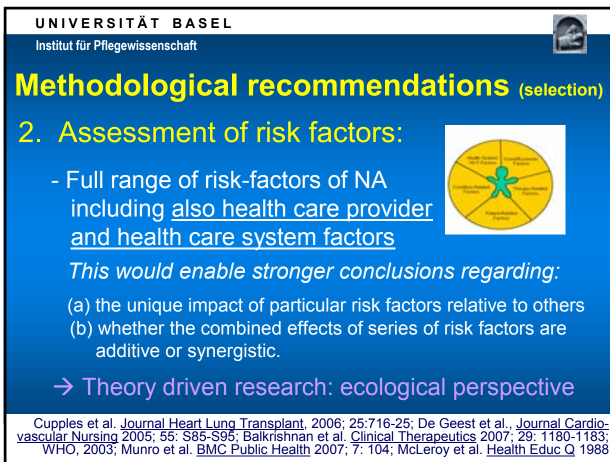
1. System related factors:
   Adding an ecological perspective to adherence research
2. Multilevel factors associated with non-adherence
3. Methodological implications

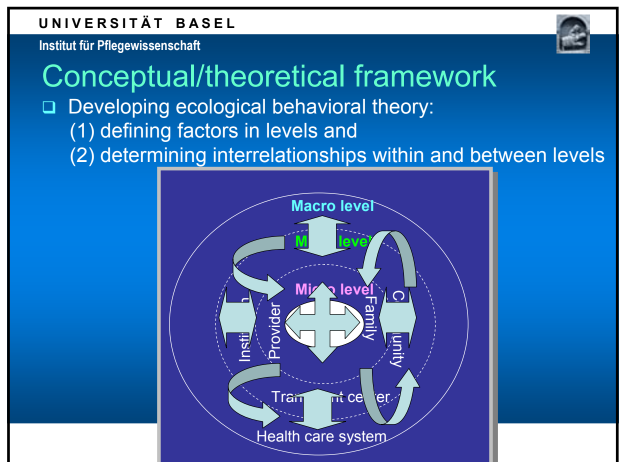
N. E

Methodological recommendations (selection)

1. Research should shift away from purely descriptive studies toward longitudinal and prospective studies that examine adherence, a comprehensive set of risk factors and outcomes simultaniously.

Cupples et al. Journal Heart Lung Transplant, 2006; 25:716-25
De Geest et al., Journal Cardiovascular Nursing 2005; 55: S85-S95.
Balkrishnan et al. Clinical Therapeutics 2007; 29: 1180-1183





Methodological recommendations (selection)

3. Sample & Setting:
   - Representativeness ~ generalizability
   - In light of research questions that address multiple levels

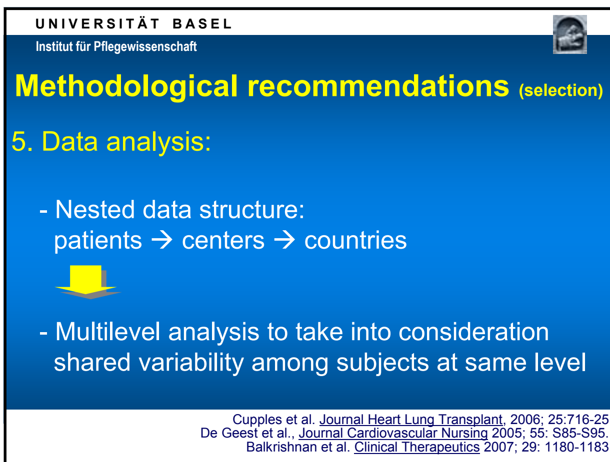
   → sampling strategy – multicenter approach must

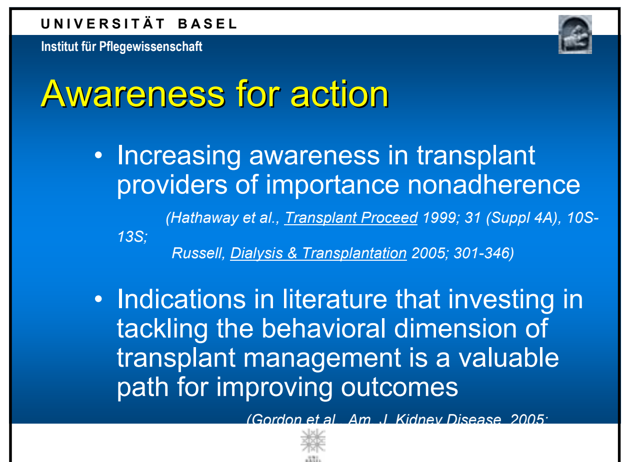
Cupples et al. Journal Heart Lung Transplant, 2006; 25:716-25
De Geest et al., Journal Cardiovascular Nursing 2005; 55: S85-S95.
Balkrishnan et al. Clinical Therapeutics 2007; 29: 1180-1183

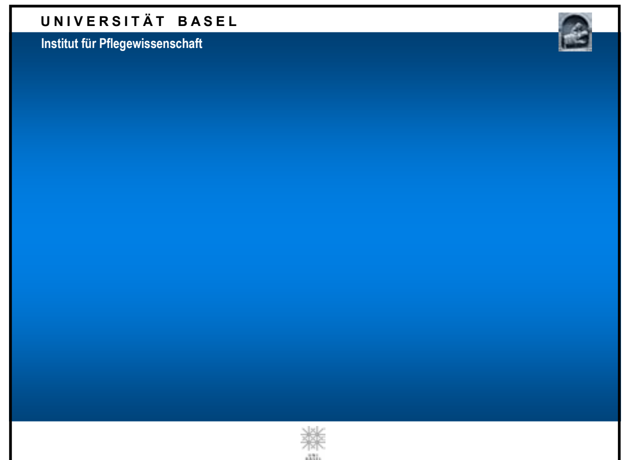
Methodological recommendations (selection)

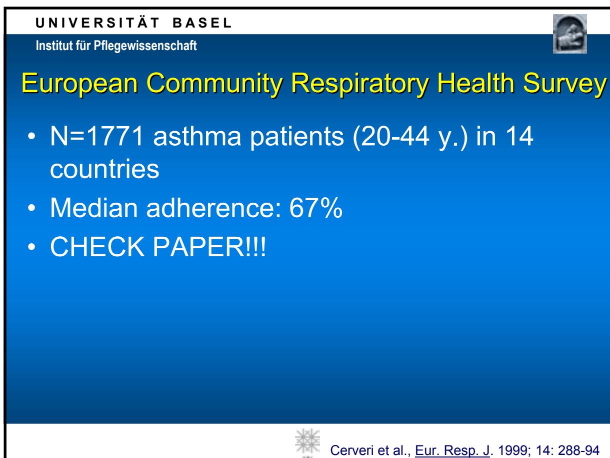
4. Intervention research → Absolute priority
   - *Content:* Multidimensional & Multilevel
     → development and testing interventions also addressing system level factors
   - *Design:*
     → Cluster randomized trials especially when testing efficacy of multilevel interventions
     → Factorial designs to disentangle effects of components of the intervention

Cupples et al. Journal Heart Lung Transplant, 2006; 25:716-25
De Geest et al., Journal Cardiovascular Nursing 2005; 55: S85-S95.
Balkrishnan et al. Clinical Therapeutics 2007; 29: 1180-1183









Dialysis Outcomes and Practice Patterns Study

- **Larger facility size (per 10 patients) was associated with the following:**
  - **Higher odds ratios (OR) of skipping (OR=1.03, *P*=0.06), shortening (OR=1.03, *P*=0.05), and IDWG (OR=1.02, *P*=0.07)**
- **An increased percentage of highly trained staff hours was associated with lower odds of skipping (OR=0.84 per 10%, *P*=0.02)**
- **Presence of a dietitian was associated with lower odds of excessive IDWG (OR=0.75, *P*=0.08)**

DOPPS

Saran R et al. *Kidney Int* 64:254-262, 2003

DOPPS
Dialysis Outcomes and Practice Patterns Study

Nonadherence Measures	Europe n=4075	Japan n=2459	United States n=8396	Overall n=14,930
Skipped ≥ 1 HD session per month[a]	0.6	0.6	7.9	3.8
Shortened session by ≥ 10 minutes[b]	9.8	5.7	19.6	13.0
IDWG > 5.7 % of dry weight	11.0	34.5	16.8	19.6
PO_4 > 7.5 g/dL	12.8	12.1	15.4	13.7
K > 6.0 mEq/L	20.0	7.6	6.3	10.8

IDWG is interdialytic weight gain; [a]One session skipped (N=136) (46.6%); two sessions skipped (N=67) (23.0%); three or more sessions skipped (N=89) (30.4%); [b]One session shortened (N=370) (37.0%); two sessions skipped

(N=231) (23.1 %); three or more sessions skipped (N=399) (39.9%)

DOPPS

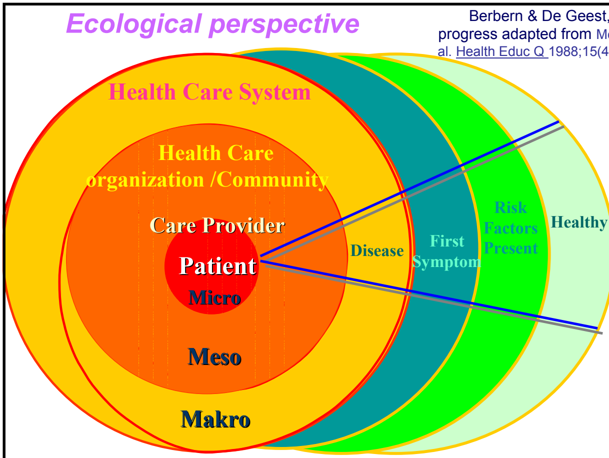
Hirth, Piette et al., Health Affairs 2008; 27:89-102
→ Out of pocket spending and medication adherence among dialysis in 12 countries

Multilevel: Health care provider (micro)
"Adherence Counselling Toolkit"

→ adaptable to different socioeconomic settings or literacy level of individual patient including:

1) knowledge (information on adherence)
2) thinking (clinical decision-making process)
3) action (behavioural tools for health professionals)

WHO, 2003; Ockene et al., JACC 2002



2008 Commonwealth Fund International Health Policy Survey of Sicker Adults in the US, Canada, UK, Australia and New Zealand (n=3,849)

Cost Barriers, Access to Physicians, And After-Hours Care Among Adults With Chronic Conditions, In Eight Countries, 2008

	AUS	CAN	FR	GER	NETH	NZ	UK	US
Unweighted N	593	1,956	851	867	736	518	933	1,007
Access problems because of cost in past 2 years								
Did not fill Rx or skipped doses	20%[c,d,e,g,h]	18%[c,d,e,g,h]	13%[e,g,h]	12%[e,f,g,h]	3%[f,g,h]	18%[g,h]	7%[h]	43%
Did not visit doctor when had a medical problem	21[b,c,d,e,g,h]	9[d,e,f,g,h]	11[d,e,f,g,h]	15[e,f,g,h]	3[f,h]	22[g,h]	4[h]	36
Did not get recommended test, treatment, or follow-up	25[b,c,d,e,f,g,h]	11[e,f,g,h]	13[e,f,g,h]	13[e,f,g,h]	3[f,h]	18[g,h]	6[h]	38
Any of the above access problems because of cost	36[b,c,d,e,g,h]	25[e,f,g,h]	23[e,f,g,h]	26[e,g,h]	7[f,g,h]	31[g,h]	13[h]	54

Schoen et al, Health Affairs 2009;28(1):w1-16

Eight Countries, 2008

	AUS	CAN	FR	GER	NETH	NZ	UK	US
Final sample of sicker adults (unweighted N)	750	2,635	1,202	1,201	1,000	751	1,200	1,205
Has any of 7 chronic conditions, doctor diagnosis	74%	72%	67%	68%	66%	64%	75%	78%
Hypertension	30	32	32	41	34	25	37	43
Heart disease, including heart attack	15	13	14	22	16	13	14	14
Diabetes	13	17	12	15	13	10	11	21
Arthritis	36	33	12	15	19	20	35	38
Lung problems (asthma, emphysema)	23	20	15	11	15	20	18	22
Depression	30	26	34	15	16	17	25	31
Cancer	11	11	10	10	9	14	9	13
Adults with any chronic condition (unweighted N)	593	1,956	851	867	736	518	933	1,007
Has 2 or more chronic conditions (out of 7)	63%[c,e,f,h]	62%[c,d,e,f,h]	53%[g,h]	56%[h]	55%[h]	51%[g,h]	61%[h]	71%
Age 50 or older	56[c,d,e,g]	57[c,d,e,g]	67[f,h]	72[f,h]	73[f,h]	58[g]	71[h]	58
Health care use in past 2 years:								
Hospitalized for other than normal pregnancy	58[b,e,g,h]	47[c,d,f,g]	57[e,g,h]	58[e,g,h]	45[f]	59[g,h]	42[h]	48
Major surgery	25[c,d,h]	29[c,d]	33[e,g]	36[e,f,g]	23[h]	29	26[h]	34
Number of doctors seen								
2 or fewer	37	40	40	24	36	42	41	37
3	23	24	27	26	31	22	25	21
4 or more	38[b,c,d,g]	32[d,h]	31[d,h]	50[e,f,g,h]	34	34	31[h]	38
Overall health system views								
Only minor changes needed, system works well	22[b,c,e,f,g]	32[c,d,e,g,h]	41[d,f,h]	21[e,f,g]	42[f,h]	29[g,h]	38[h]	20
Fundamental changes needed	57[b,c,e,f,g,h]	50[c]	33[d,e,f,g,h]	51	46	48	48	46
Rebuild completely	20[d,e,g,h]	16[c,d,e,f,g,h]	23[e,g,h]	26[e,g,h]	9[f,h]	21[g,h]	12[h]	33
Perception of ineffi... wasteful care in pa...								
Doctors recomme... treatment you t... little or no health benefit	22[c,e,g]	22[c,e,g,h]	35[d,e,f,g,h]	24[e,f,g]	14[h]	19[h]	15[h]	27
Often/sometimes felt your								

Schoen et al, Health Affairs 2009;28(1):w1-16

Nonadherence to Imatinib in CML: the Adagio study

- N=202 CML patients of 34 Belgian centers
- 33% of patients nonadherent (Self-report, collateral report, pill-count)

	Value
suboptimal response	23.20%
optimal response	7.30%

p<0.005

Y-axis: 0.00%, 5.00%, 10.00%, 15.00%, 20.00%, 25.00%

- Suboptimal response was related with non-adherence

Noens et al., Blood, under review

Glaucoma Adherence and Persistency Study (US)

- Retrospective database & chart reviews + prospective patient surveys
- 300 patients and 103 MDs
- Adherence: Medication possession ratio
- Correlates of non-adherence (multivariate analysis):
  (1) hearing all of what you know about glaucoma from your MD
  (2) not believing that reduced vision is a risk of not taking medication as recommended
  (3) having a problem paying for medications
  (4) difficulty while traveling or away from home
  (5) not acknowledging stinging and burning
  (6) being nonwhite
  (7) receiving samples
  (8) not receiving a phone call visit reminder.

Friedman et al., Ophthalmology 2008; Epub.

EXHIBIT 4
Prescription Medications And Safety Among Adults With Chronic Conditions, In Eight Countries, 2008

	AUS	CAN	FR	GER	NETH	NZ	UK	US
Unweighted N	593	1,956	851	867	736	518	933	1,007
Prescription medications								
Percent taking Rx medications regularly	78%[b,d,e,g,h]	84%[d,f]	84%[d,f]	89%[f]	85%[f]	74%[g,h]	85%	86%
Number of different Rx medications								
4 or more	33[b,g,h]	41[f,g,h]	38[g,h]	39[g,h]	39[g,h]	35[g,h]	50	48
Base: Taking Rx medications regularly, in past 2 years								
How often have any of your doctors or pharmacists reviewed and discussed all medications you are using?								
Always	34[c,e,g]	40[c,d,e,g]	18[d,e,f,g,h]	29[h]	25[f,h]	34[g]	27[h]	38
Often	21	18	10	20	11	13	22	20
Sometimes, rarely, or never	41[c,d,e]	40[c,d,e,f]	68[d,f,g,h]	49[e,h]	62[f,g,h]	48[h]	48[h]	41
Pharmacist told you the Rx you were about to fill might be harmful because of medications you were taking	30[b,c,d,e,f,g,h]	23[c,d,e,g]	12[e,f,g,h]	15[e,h]	38[f,g,h]	20	17	20
Medical and medication errors in past 2 years								
Believed a medical mistake occurred in treatment or care	17[c,d,e,g]	16[c,d,e,g]	8[f,h]	12[g]	9[f,h]	15[g]	8[h]	16
Given the wrong medicatio								
Either/both medical or med								

Schoen et al, Health Affairs 2009;28(1):w1-16

Oral chemotherapy: ***Adagio***

(Adherence Assessment with Glivec® (Imatinib): Indicators and Outcomes)

- Prospective, observational, multi-center, non-interventional study with two time points: baseline and 90 days
- 169 patients by 51 physician-investigators at 34 centers
- Adherence: multiple measures
- Patient, physician & center related factors explored
- Hierarchical modeling

Noens et al., Blood, in press

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Oral chemotherapy: ***Adagio***

- **Prevalence** non-adherence by patient's self-report: - 36.1% baseline
  - 32.7% at 90 days
- Patient self reported non-adherence:
  - 34.6% of variance accounted for by the class effect of *clinician/center*
  - 65.4% of variance remains attributable to *patients*

Noens et al., Blood, in press

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ADAGIO: Canonical correlation modeling

Determinants of Increased Nonadherence	Canonical Loading
Patient-related	
Age (being older)	0.649
Months since diagnosis of CML (longer time)	0.272
Living alone	0.246
Male gender	0.194
Months on imatinib (longer time)	0.193
Imatinib dose ≥ 600mg/daily	0.193
Quality of chronic care (higher degree)	0.125
Functional status / quality of life* (higher level)	0.117
Physician-related	
Median duration of treatment follow-up visits ???	0.237
Years of professional experience ???	0.135

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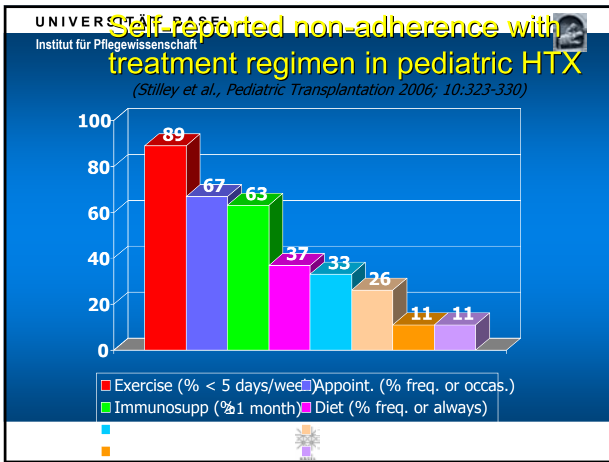
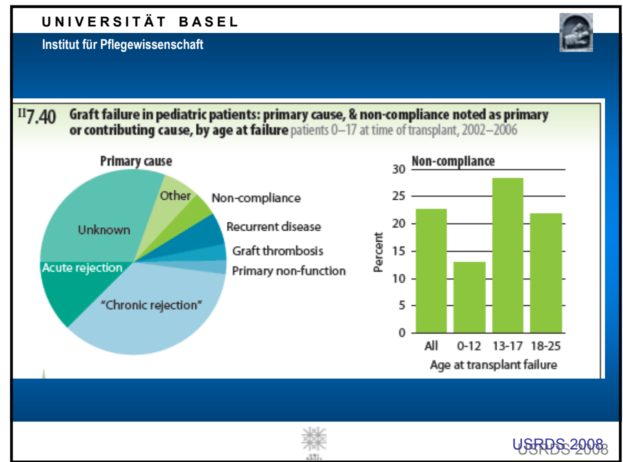
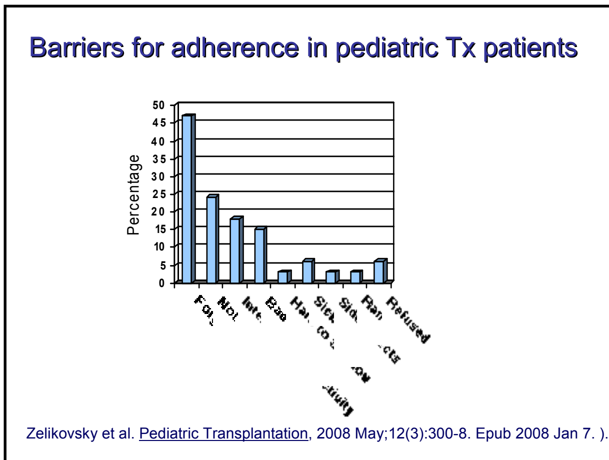
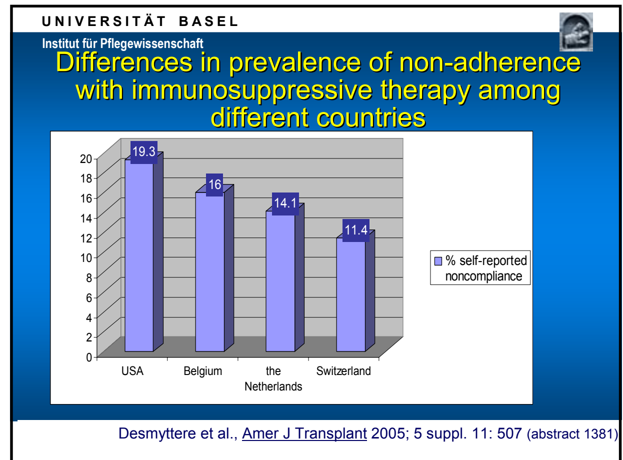
ADAGIO: Canonical correlation modeling

Determinants of Decreased Nonadherence	Canonical Loading
Patient-related	
Knowledge of disease and treatment	- 0.314
Number of medications taken per day (more)	- 0.184
Secondary school graduate or higher education	- 0.140
Long-term medication behavior self-efficacy	- 0.062
Physician-related	
Number of CML patients seen in past year	- 0. 363
Median duration of first visit with newly diagnosed CML patient	- 0.119
Practicing in university or university-affiliated hospital	- 0.003
Hematologist	- 0.002









Lifesaving Kidney Treatment, but Only to a Point

The New York Times

Margaret Oliver, a 47-year-old hairdresser in Venice, Calif., received a lifesaving kidney transplant in 2002. The government covered the costs under a special Medicare program for the hundreds of thousands of Americans with kidney failure who need either dialysis or a transplant.

Three years later, Medicare stopped paying for the expensive immunosuppressive drugs that Ms. Oliver needed to minimize the risk that her body would reject the organ. Because her kidney was functioning successfully at that point, she was no longer considered to be suffering from end-stage disease and so no longer qualified for the special coverage.

Medicare has stopped paying for the immunosuppressive drugs that Margaret Oliver needs after having a kidney transplant in 2002.

With the drugs costing about $800 a month, Ms. Oliver, who was self-employed, was able to buy them only sporadically, which endangered her transplanted organ. "It was horrifying," Ms. Oliver said. "I just didn't know what to do."

Medicare
- Cost immunosuppressants: $17,000/year
- Dialysis: $70,000/year
- (Transplant procedure: > $100,000)

http://www.nytimes.com/2009/03/13/health/13kidney.html?_r=1&emc=eta1

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The Impact of Integrated HIV Care (IHC) on viral suppression

- A retrospective cohort study of 1018 HIV patients from 5 VA facilities (2000-2006)
- IHC: care model in which specialists from multiple disciplines collaborate within a geographically and temporally constrained clinic environment to provide HIV-infected patients with onsite primary care (adherence support included)

Hoang et al., Medical Care 2009; 47 1-8

The Impact of Integrated HIV Care (IHC) on Patient Health Outcomes

TABLE 1. Four Levels of Integrated HIV Care Clinics

Components of Integrated HIV Care	Services	Levels IV	III	II	I
Nurse practitioner, physician assistant	To follow patients on HIV treatment	x	x	x	x
Clinical coordinator	To link patients to community-based programs for food, dental care, home care, etc.	x	x	x	x
HIV physician specialist	To provide diagnosis, counseling and treatment for HIV infection	x	x	x	
Dedicated pharmacist	To help patients with cART refills, side effects, food restriction, etc.	x	x	x	
Social worker	To help patients with housing, transportation, disability benefits, etc.	x	x		
Psychiatrist	To provide psychiatric diagnosis and treatment for substance abuse and mental illnesses	x	x		
Psychologist	To provide counseling for substance abuse and mental illnesses	x			

'x' indicates that the specialists are available at the HIV clinics to offer on-site services to HIV-infected patients.

Hoang et al., Medical Care 2009; 47 1-8

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The Impact of Integrated HIV Care (IHC) on viral suppression (Kaplan meier)

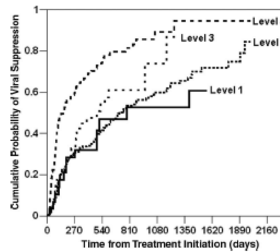

FIGURE 1. Cumulative probability of viral suppression stratified by integrated HIV care levels.

- IHC remained independent predictor after controlling for demographics and clinical variables in Cox regression analysis (HR 1.10, CI 1.09–1.11)
- IHC levels III & IV associated with best results

Hoang et al., Medical Care 2009; 47 1-8ep

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Patients escape penalties for not taking doctor's advice

Annette Tufts HEIDELBERG

Patients with chronic disease in Germany will now be penalised only if they explicitly declare that they have not taken drugs and followed their doctor's advice and will continue doing this in the future.

The government originally wanted to impose financial penalties on any patient who did not follow medical advice. But the plan was abandoned after doctors and patient groups mounted vigorous protests, saying that it would destroy the doctor-patient relationship. The legality and ethics

BMJ 2008 Jan 12;336(7635):65