Adherence research in adolescents with kidney disease: *The past, the present and the future*

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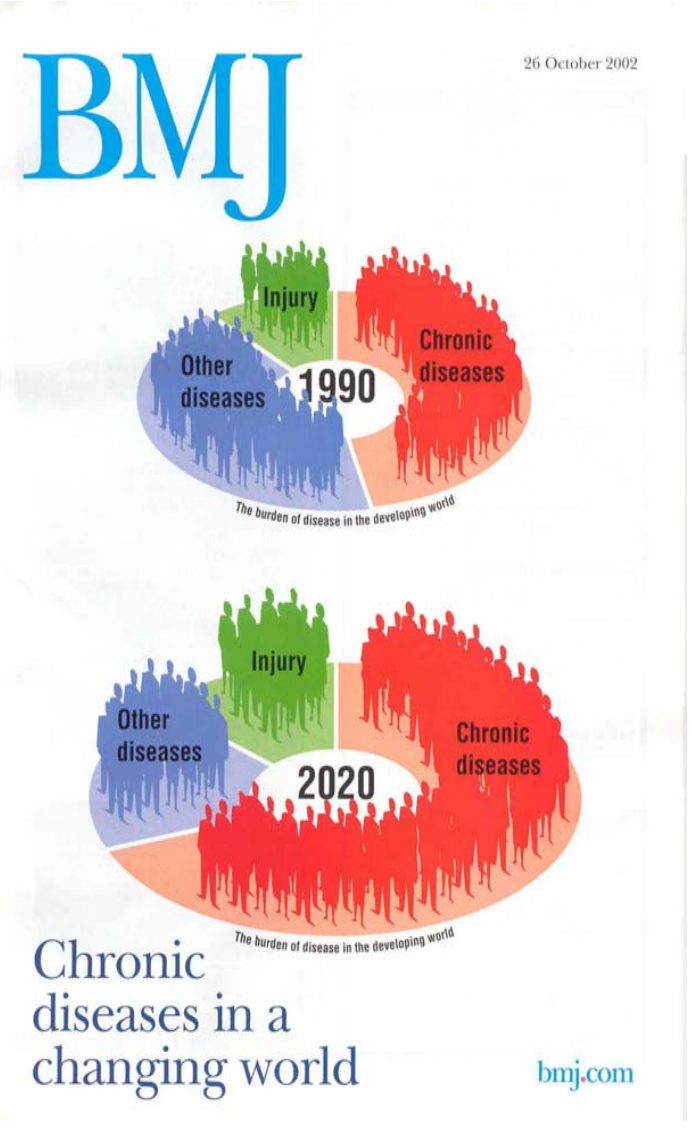
The rising burden of chronic diseases

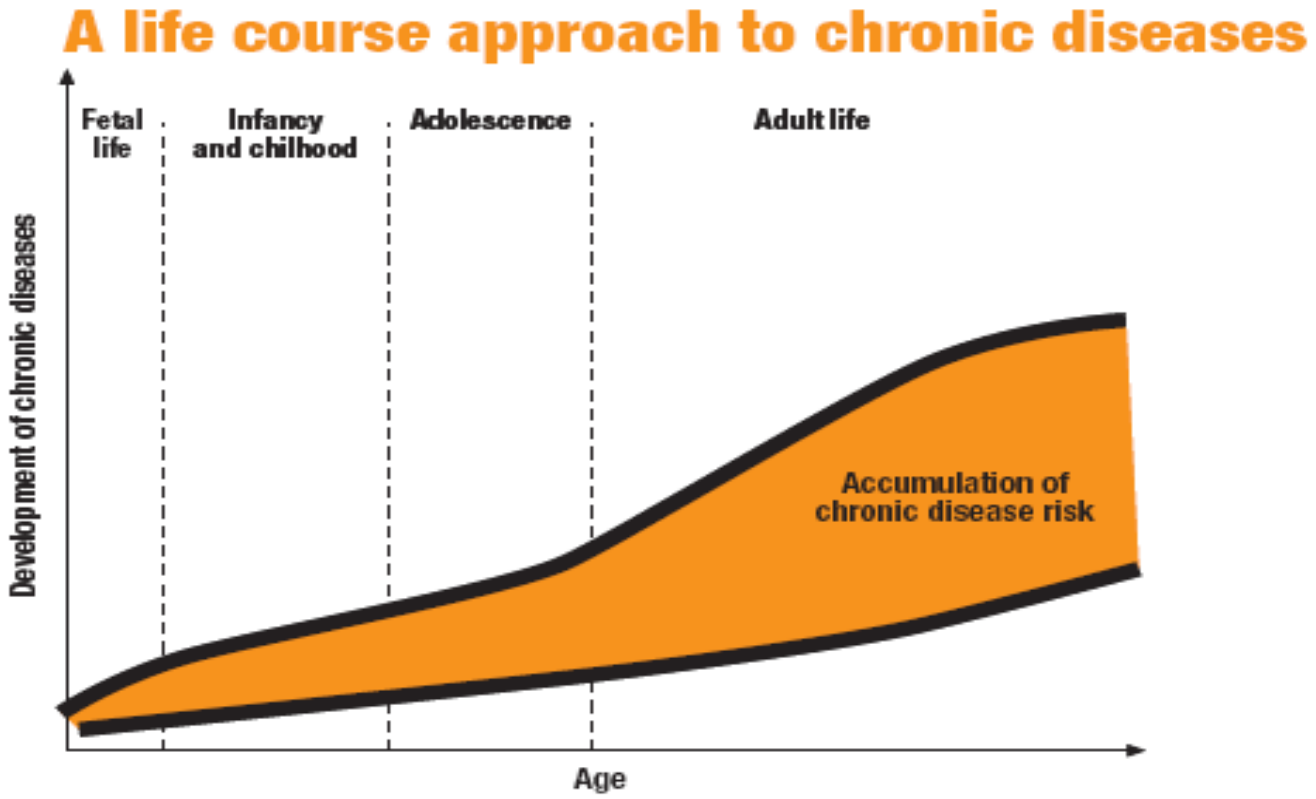


- Require ongoing management over a period of years
- Cannot be cured
- May lead to disability, or the short- or long-term reduction of a person's activity
- Goal of treatment:

  = to improve patients' ability to live a productive and pain free life

  ≠ to get rid of the disease!!!

The risk of chronic disease increases over the life course



(WHO report 2005: preventing chronic disease: A vital investment

Prevalence of chronic disease in adolescents

- Difficult to assess due to:
  - lack of quality data specifically in this age group
  - diversity in methodology
  - issues involved in the definition of chronic disease
    - duration, age at onset, congenital/acquired
    - visibility, course, impact on outcome, uncertainty,…

Surveys among in-school adolescents: 7 - 12%

Inclusion of mild conditions: ± 15%

(Suris et al. Arch Dis Child 2004; 89: 938

Adolescence and chronic disease: a complex interplay

‘Adolescere’= facing the challenges of growing up

- Independence from the parents
- Accepting bodily changes
- developing value system
- achieving responsible behavio

+

Growing up in the light of having chronic disease

- Complex drug treatment
- Execution of health behaviors
- Follow-up

Reciprocal effect of chronic condition and adolescent development

Table 1 Reciprocal effects of chronic illness or disability and adolescent development[68–72]

Effects of chronic illness or disability on development	Effects of developmental issues on chronic illness or disability
Biological	**Biologically**
Delayed/impaired puberty	Increased caloric requirement for growth may negatively impact on disease parameters
Short stature	Pubertal hormones may impact on disease parameters (e.g. growth hormone impairs metabolic control in diabetes)
Reduced bone mass accretion	
Psychological	**Poor adherence and poor disease control due to:**
Infantilisation	Poorly developed abstract thinking and planning (reduced ability to plan and prepare using abstract concepts)
Adoption of sick role as personal identifier	Difficulty in imagining the future; self-concept as being "bullet proof"
Egocentricity persists into late adolescence	Rejection of medical professionals as part of separation from parents
Impaired development of sense of sexual or attractive self	Exploratory (risk taking) behaviours
Impaired development of cognitive functions and information processing	
Social	**Associated health risk behaviours**
Reduced independence at a time of when independence is normally developing	Chaotic eating habits may result in poor nutrition
Failure of peer relationships then intimate (couple) relationships	Smoking, alcohol and drug use often in excess of normal population rates
Social isolation	Sexual risk taking, possibly in view of realisation of limited life span
Educational failure and then vocational failure; failure of development of independent living ability	

(Suris et al. Arch Dis Child 2004; 89: 938

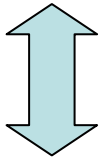
Nonadherence research: the past, the present and the future

- Conceptual definition
- Operational definition and prevalence of NA
- Measurement
- Clinical and economic consequences

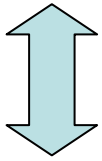
Focus on (medication) nonadherence in adolescents with chronic illnesses

Using transplantation as an example

THEORETICAL FRAMEWORK

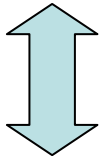


CONCEPTUAL DEFINITION



Refers to the meaning of a concept

OPERATIONAL DEFINITION



Indicates how the concept will be measured and how patients will be classified

ADEQUATE MEASUREMENT

Conceptual definition: the past and the present

Compliance = adherence = concordance

= "The extent to which a person's behavior corresponds with the ***agreed*** recommendations from a healthcare provider"

(Sabate. WHO report 2003)

= "Is a behavioral process, strongly ***influenced by the environment*** in which the patient lives, including the healthcare practices and system.
Adherence assumes that a ***patient has the knowledge, motivation, skills and resources*** required to follow the recommendations of a healthcare professional.

(AHA expert panel. Miller et al. 1997)

NA to the medication regimen: its different dimensions

- Primary versus secondary nonadherence?
- Intensity of nonadherence: total or partial?
- Problem of taking and/or timing?

Goal of PF-7 ABC project (www.ABCproject.eu) is to develop a universally accepted taxonomy on medication adherence (across diseases)

Prevalence of nonadherence

Treatment regimen (N= 520 studies)	Number of studies	% of studies	Average % adherence	95% CI
Medication	328	63%	79.4	[77.4; 81.4]
Screening	9	1.7%	72.8	[49.9; 90.4]
Exercise	13	2.5%	72.0	[60.5; 82.3]
Health behavior	88	16.9%	69.7	[65.5; 73.5]
Appointment	57	11%	65.9	[60.8; 70.7]
Diet	25	4.8%	59.3	[49.6; 70.3]

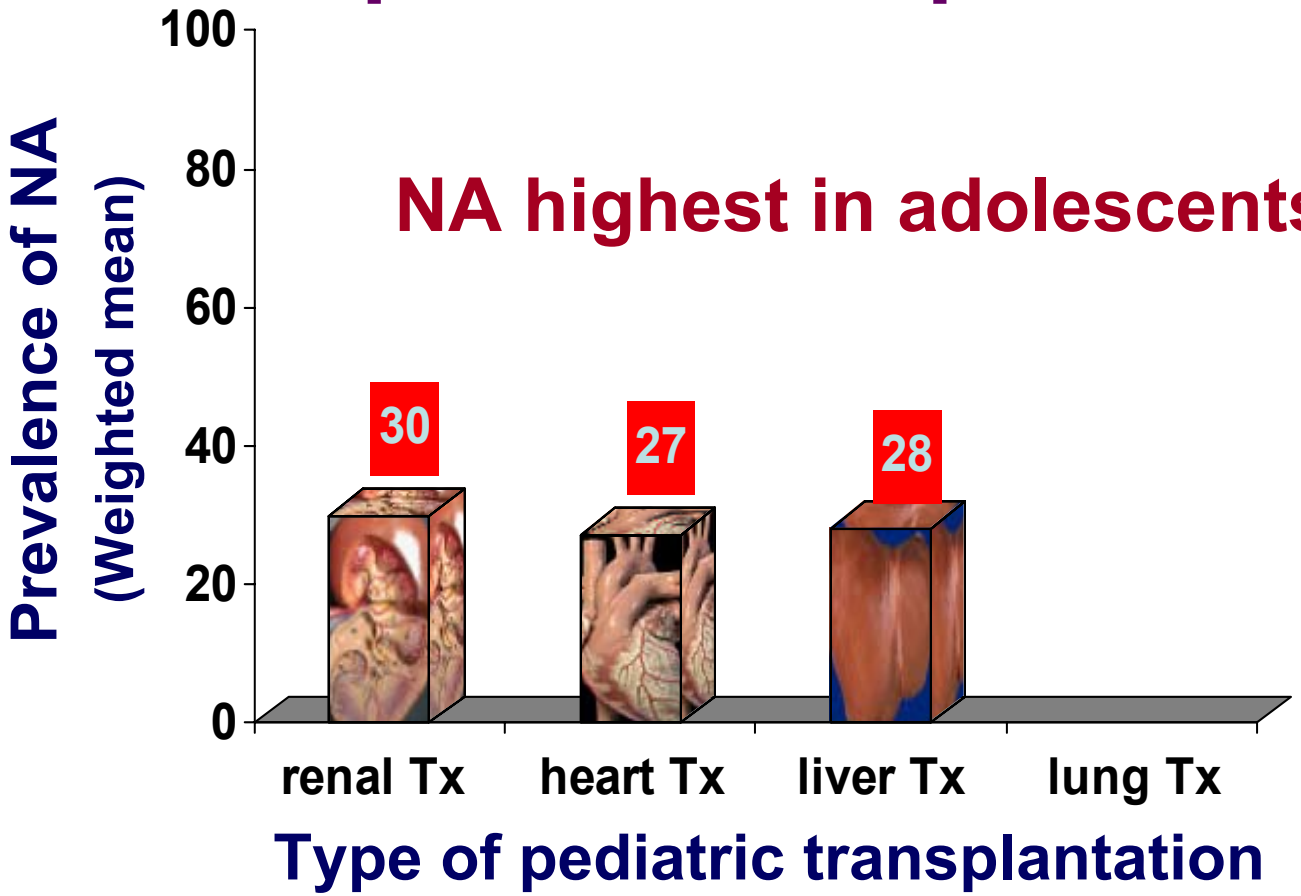
AVERAGE NA= 24.8%:

Pediatric patients > adults

Adolescents > pediatric patients (trend)

(DiMatteo RM, Med Care 2004; 42: 200

Prevalence of nonadherence in pediatric Tx patients



NA highest in adolescents: ≥ 50 %

Need for more studies in adolescents

(Dobbels et al. Pediatric Transplant 2005; 9(3): 381-390

Conceptual implications and their impact on operational definition of NA

Quantification of medication nonadherence

All or nothing conceptualization???

- Following the prescription to the letter= adherence
- Any deviation from the prescription= nonadherence

Rule of 80% taking adherence???

From conceptual to operational definition: the use of % under fire

50% adherence: *a hypothetical example*

	Day 1		*Day 2*		*Day 3*		*Day 4*		*Day 5*	
PT 1:	+	+	+	+	+	-	-	-	-	-
PT 2:	-	-	-	-	-	+	+	+	+	+
PT 3:	+	-	+	-	+	-	+	-	+	-
PT 4:	+	+	-	-	-	+	+	+	-	-

⇨ **Different adherence patterns may yield similar results**

⇨ **Adherence may change over time**

Plea for a more continuous or repeated assessment

Which measurement options do we have?

CLINICAL NONADHERENCE

SUB-CLINICAL NONADHERENCE

A. Direct methods
- observation
- assay

B. Indirect methods
- pill count
- prescription refill
- clinical judgement
- electronic monitoring
- self-report

Electronic monitoring (EM)

- Often promoted as the gold standard
  - Measures both taking and timing of medication intake
  - The only tool assessing adherence continuously
  - Superior reliability and validity compared to other methods




- Prerequisites:
  - Electronic equipment functions correctly
  - Registration (e.g. opening of the bottle) corresponds with actual medication intake
  - All patients are willing to use the monitor in daily life

(Denhaerynck et al. BMC Med Research Method 2008)

Is EM feasible in pediatric Tx?

59 pediatric kidney Tx patients eligible

- 9 patients used pill boxes and did not want to disrupt their medication taking routine
- 15 younger patients on liquid drugs

35 recruited for the study

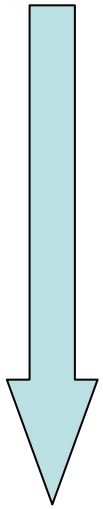
- 9 patients dropped out
  - not wanting to use the MEMS cap
  - not having enough time
  - health reasons

27 participating in the study

- difficult to transfer medication in bottle (41%)
- using MEMS extra burden (25.9%)
- MEMS interferes with routine, risk of forgetting (22.2%)

Self-report as an alternative…

…But underreporting may occur



Triangulation to be recommended!

> *" Although certain methods of measuring adherence may be preferred in specific clinical or research settings, a combination of measures maximizes accuracy"*

(Osterberg et al. N Eng J Med 2005; 353: 487-497)

Triangulation in renal TX patients improves sensitivity and specificity

	Sensitivity (%)*	Specificity (%)
Self-report + clinician	28.6%	90.1%
Self-report + clinician + assay	80.0%	42.5%

***EM as reference standard**

A composite measure of self-report, clinician's report, and blood assay best diagnostic value to identify NA, if EM not possible

Further research needed to determine which combination has best diagnostic value in adolescent populations

Conclusion

- Universally accepted definition of adherence does not exist, which has consequences for research on prevalence and measurement
- Future research should determine which combination of measurement techniques has the best diagnostic accuracy, based on a validated operational definition of NA
- NA in adolescents results in poor clinical outcomes
    - Evidence is limited
    - Room for methodological improvement
- NA may result in poor economical outcomes
    - Evidence is not existing in adolescent population
    - Room for methodological improvement