

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

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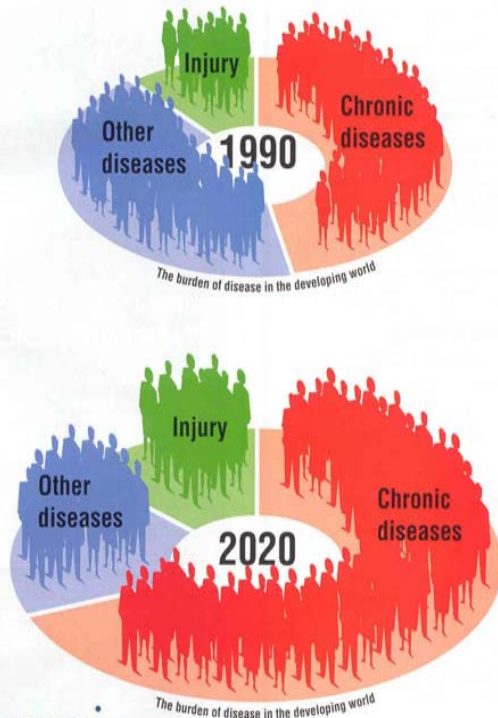
On behalf of the Leuven-Basel Compliance Research Group

Center for Health Services and Nursing Research  
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# The rising burden of chronic diseases

BMJ

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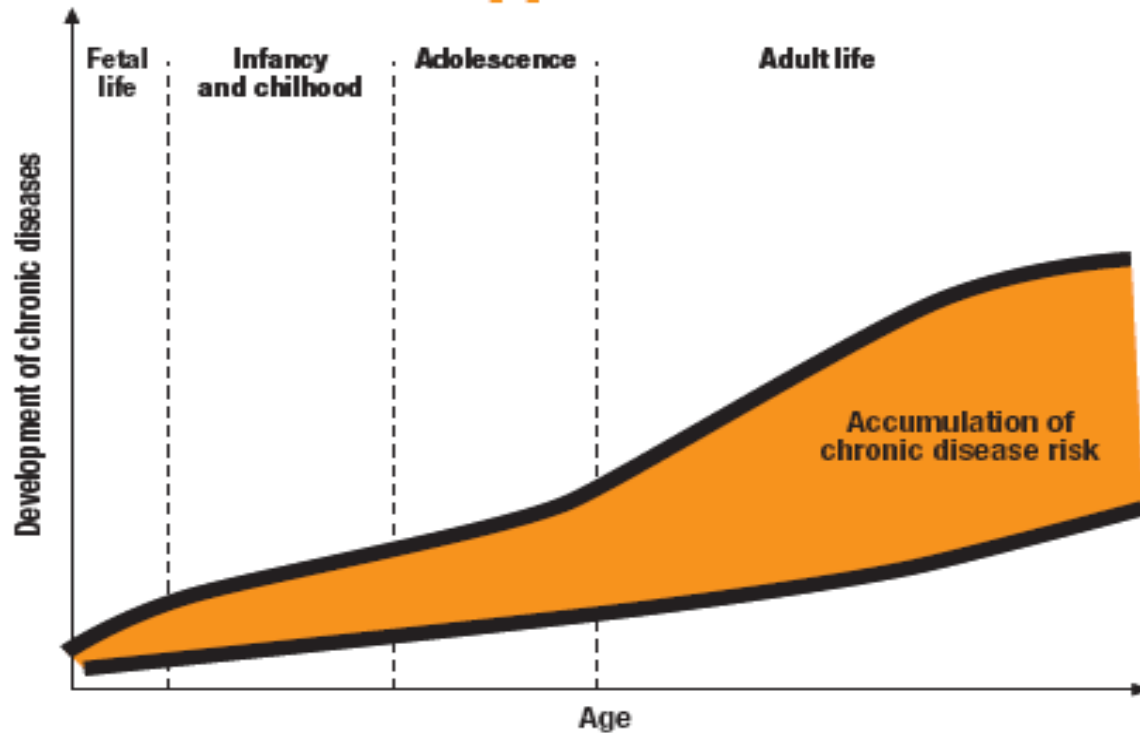
Chronic diseases in a changing world

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- 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

## A life course approach to chronic diseases



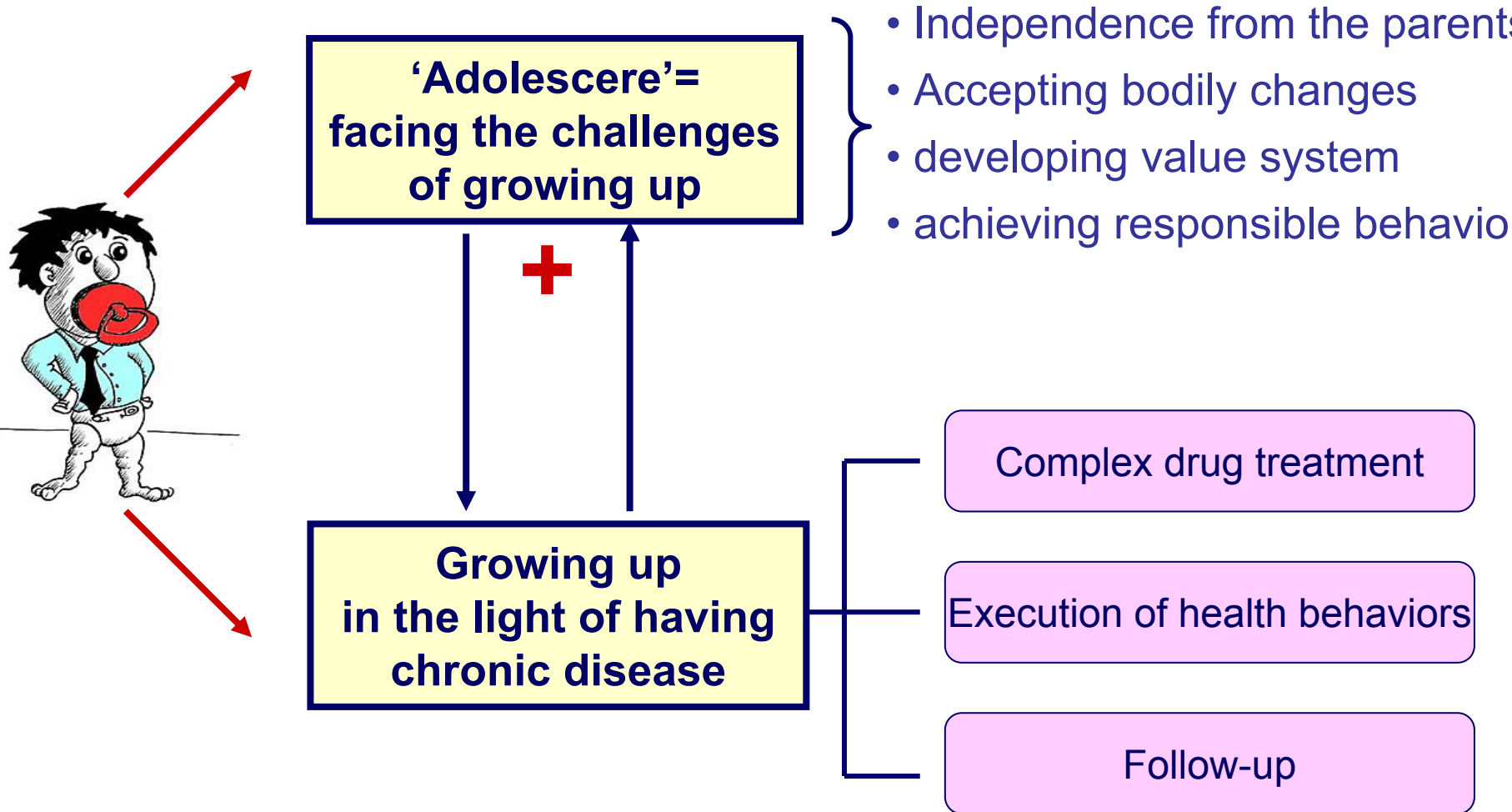
# Prevalence of chronic disease in adolescents

- 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:  $\pm$  15%**

# Adolescence and chronic disease: a complex interplay



# Reciprocal effect of chronic condition and adolescent development

**Table 1** Reciprocal effects of chronic illness or disability and adolescent development<sup>68-72</sup>

## Effects of chronic illness or disability on development

### Biological

Delayed/impaired puberty

Short stature

Reduced bone mass accretion

### Psychological

Infantilisation

Adoption of sick role as personal identifier

Egocentricity persists into late adolescence

Impaired development of sense of sexual or attractive self

Impaired development of cognitive functions and information processing

### Social

Reduced independence at a time of when independence is normally developing

Failure of peer relationships then intimate (couple) relationships

Social isolation

Educational failure and then vocational failure; failure of development of independent living ability

## Effects of developmental issues on chronic illness or disability

### Biologically

Increased caloric requirement for growth may negatively impact on disease parameters

Pubertal hormones may impact on disease parameters (e.g. growth hormone impairs metabolic control in diabetes)

### Poor adherence and poor disease control due to:

Poorly developed abstract thinking and planning (reduced ability to plan and prepare using abstract concepts)

Difficulty in imagining the future; self-concept as being "bullet proof"

Rejection of medical professionals as part of separation from parents

Exploratory (risk taking) behaviours

### Associated health risk behaviours

Chaotic eating habits may result in poor nutrition

Smoking, alcohol and drug use often in excess of normal population rates

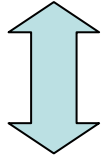
Sexual risk taking, possibly in view of realisation of limited life span

# Nonadherence research: the past, the present and the future

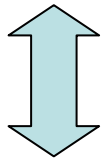
- ❖ Conceptual definition
- ❖ Operational definition and prevalence of NA
- ❖ Measurement
- ❖ Clinical and economic consequences

**Focus on (medication) nonadherence  
in adolescents with chronic illnesses**  
*Using transplantation as an example*

**THEORETICAL FRAMEWORK**

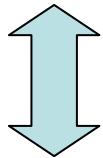


**CONCEPTUAL DEFINITION**



*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](http://www.ABCproject.eu)) is to develop a universally accepted taxonomy on medication adherence (across diseases)

# Prevalence of nonadherence

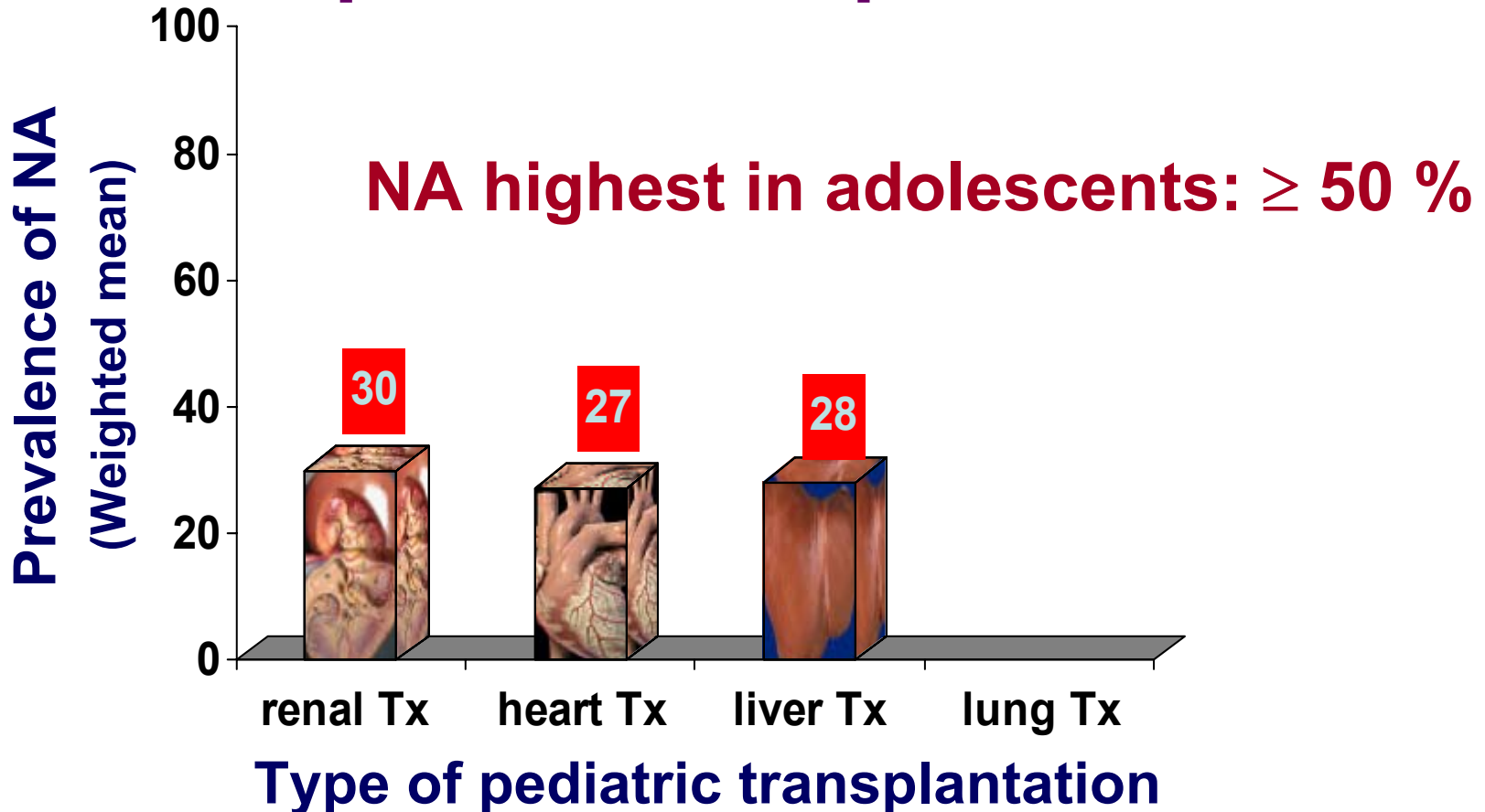
Treatment regimen (N= 520 studies)	Number of studies	% of studies	Average % adherence	95% CI
Medication	328	63%	79.4	[77.4; 81.4]
Screening	9	1.7%	72.8	[49.9; 90.4]
Exercise	13	2.5%	72.0	[60.5; 82.3]
Health behavior	88	16.9%	69.7	[65.5; 73.5]
Appointment	57	11%	65.9	[60.8; 70.7]
Diet	25	4.8%	59.3	[49.6;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

AVERAGE NA= 24.8%:

Pediatric patients > adults

Adolescents > pediatric patients (trend)

# Prevalence of nonadherence in pediatric Tx patients



**Need for more studies in adolescents**

# 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**

	<i>Day 1</i>	<i>Day 2</i>	<i>Day 3</i>	<i>Day 4</i>	<i>Day 5</i>
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



# 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

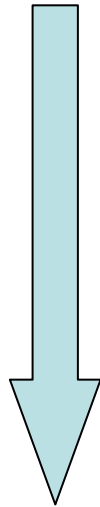
- 9 patients dropped out
  - not wanting to use the MEMS cap
  - not having enough time
  - health reasons

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**”*

# 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