Effectiveness and cost-effectiveness of the adherence improving self-management strategy (AIMS) in HIV care in the Netherlands: a multi-site randomised controlled trial

Jan Prins
Afd. Infectieziekten
AMC
Amsterdam

Marijn de Bruin
Professor of Health Psychology
Institute of Applied Health Sciences
University of Aberdeen

Disclosure belangen spreker

(potentiële) belangenverstrengeling	Geen / Zie hieronder
Voor bijeenkomst mogelijk relevante relaties met bedrijven	Bedrijfsnamen
• Sponsoring of onderzoeksgeld • Honorarium of andere (financiële) vergoeding • Aandeelhouder • Andere relatie, namelijk …	• • • •

Background

- Importance adherence known & non-adherence common
- Effect adherence interventions[1]
  - 5/17 low RoB RCTs improved adherence & outcomes
  - Complex interventions and small/medium size effects
- Cost-effectiveness adherence interventions[2]
  - 14 RCTs, narrow perspectives
  - 2 RCTs report ICERS QALY with parameter uncertainty
  - One of these gave some clue to intervention content

1- Nieuwlaat, Cochrane 2014, 11:CD00001; 2- Oberje, de Bruin et al, 2013

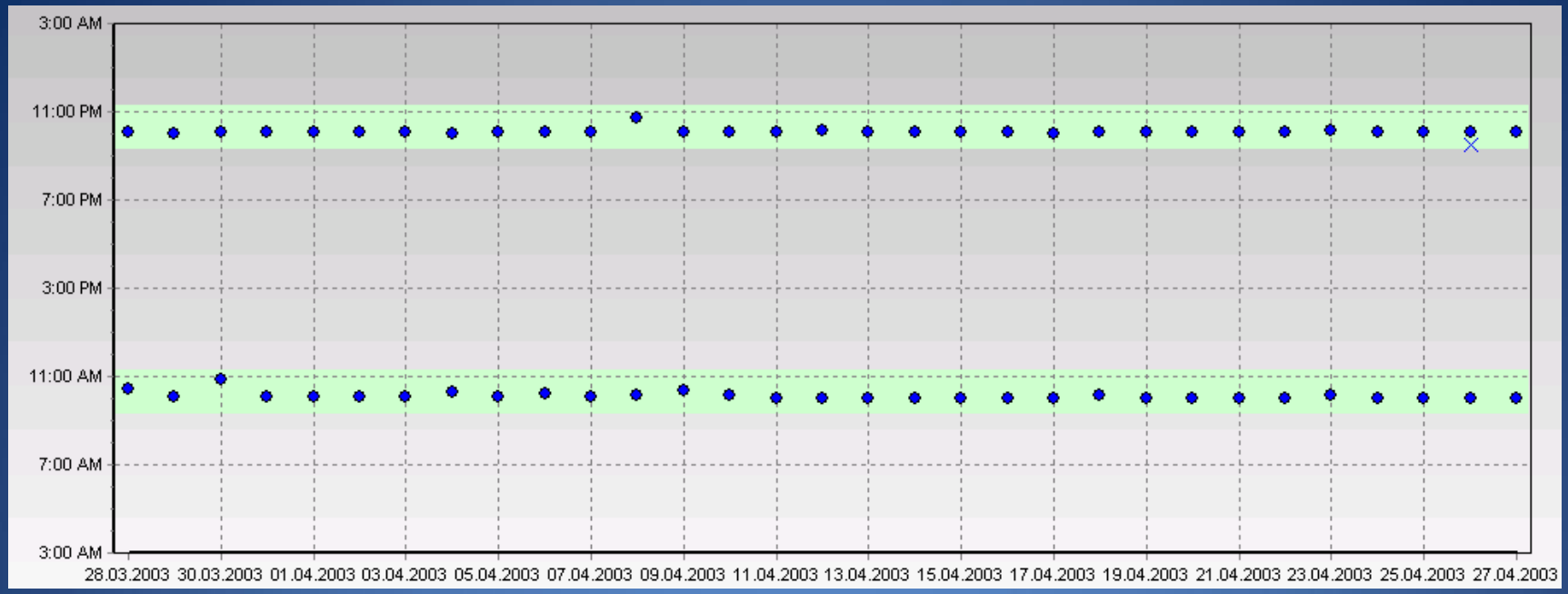
Objectives (anno 2003)

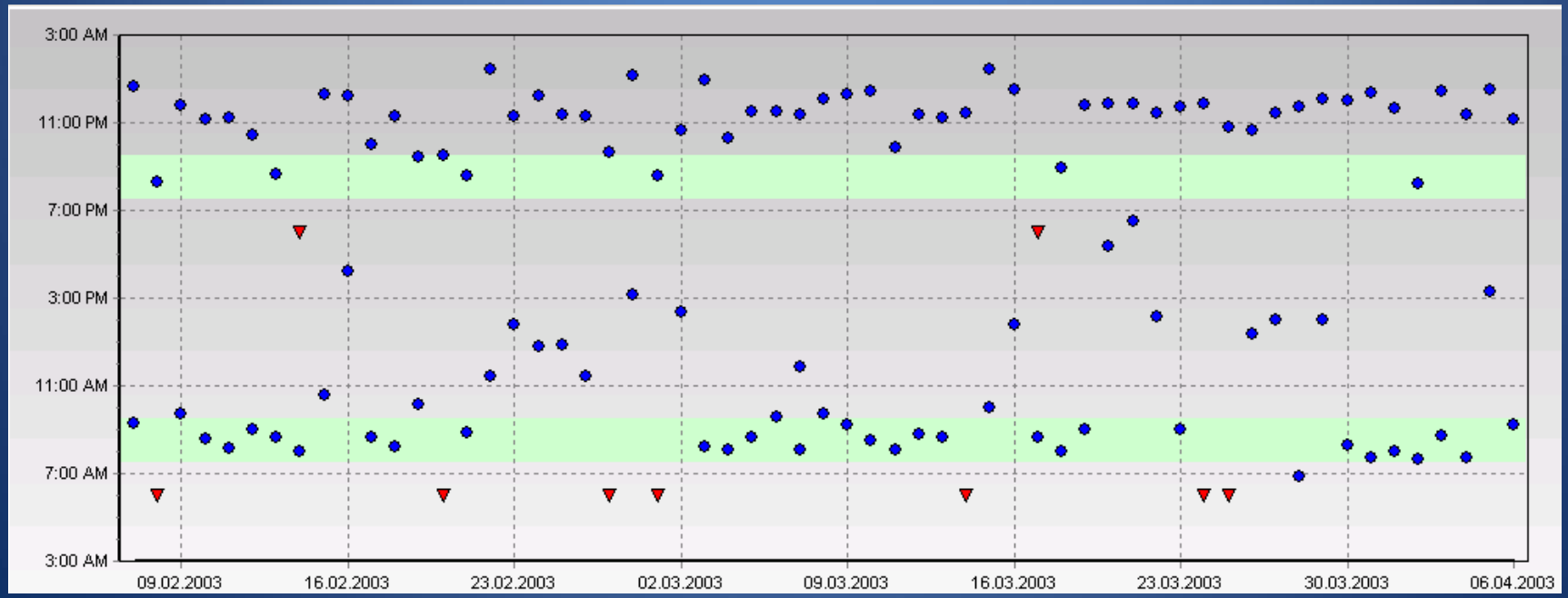
- Develop an intervention that can be delivered by nurses during routine clinical care

- Intervention content based on:[1,2,3]
  - Comprehensive literature review
  - Integration behavior (change) theory
  - Input professionals & patients
  - Use of MEMS-data

- Nurses deliver the intervention after 3-day training

1- de Bruin et al. Aids Patient Care & STDS, 2005;19(6):284-94; 2- de Bruin et al., Health Psychology, 2010;29(4):421-8; 3- Oberje, de Bruin et al., BMC HSR, 2013; 13:274


3:00 AM
11:00 PM
7:00 PM
3:00 PM
11:00 AM
7:00 AM
3:00 AM
28.03.2003 30.03.2003 01.04.2003 03.04.2003 05.04.2003 07.04.2003 09.04.2003 11.04.2003 13.04.2003 15.04.2003 17.04.2003 19.04.2003 21.04.2003 23.04.2003 25.04.2003 27.04.2003


3:00 AM
11:00 PM
7:00 PM
3:00 PM
11:00 AM
7:00 AM
3:00 AM
09.02.2003 16.02.2003 23.02.2003 02.03.2003 09.03.2003 16.03.2003 23.03.2003 30.03.2003 06.04.2003

Previous studies of AIMS

- Pilot-study (within-subject)[1]
  - N = 26
  - Feasible, acceptable, effects on adherence
- Single center RCT [2]
  - N = 133
  - Powered on adherence
  - Effects on adherence (taking and timing) & viral load

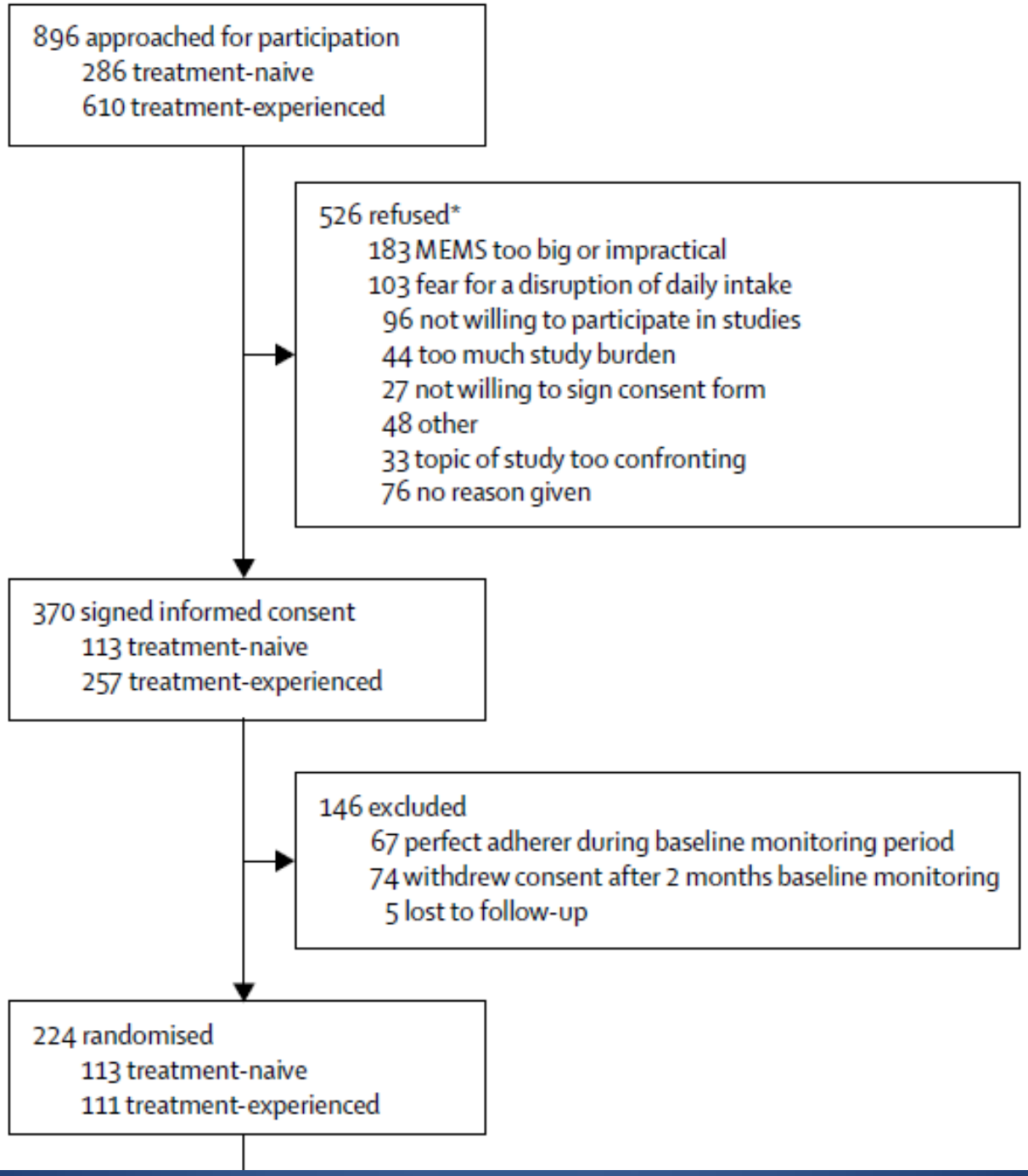
1- de Bruin, Aids Pat Care STDs, 2005;19:384; 2- de Bruin, Health Psychology, 2010;29:421.

Objectives & Design GGG project

- To evaluate the effectiveness and cost-effectiveness of AIMS in a heterogeneous group of clinics and patients
- 7 clinics, 21 nurses trained to deliver the intervention
- Primary outcomes over 3 time points/visits (M5, 10, 15):
  - Viral load, Cost-effectiveness, Cost-utility
- Individual patient randomisation (N = 223)
- All naïve patients and ‘at-risk’ treatment-experienced

  ‘At risk’: Detectable viral load in last 3 year & missed doses during baseline monitoring

1- Oberje, de Bruin, BMC HSR, 2013;13:274; de Bruin, Psych & Health, 2015;30:8; ID NCT01429142


896 approached for participation
286 treatment-naive
610 treatment-experienced
526 refused*
183 MEMS too big or impractical
103 fear for a disruption of daily intake
96 not willing to participate in studies
44 too much study burden
27 not willing to sign consent form
48 other
33 topic of study too confronting
76 no reason given
370 signed informed consent
113 treatment-naive
257 treatment-experienced
146 excluded
67 perfect adherer during baseline monitoring period
74 withdrew consent after 2 months baseline monitoring
5 lost to follow-up
224 randomised
113 treatment-naive
111 treatment-experienced

	AIMS group (n=109)	Treatment-as-usual group (n=112)
Female	14 (13%)	22 (20%)
Age (years; mean [SD])	45·4 (11·0)	43·3 (10·8)
Ethnic origin		
White	81 (74%)	62 (55%)
Sub-Saharan African	16 (15%)	21 (19%)
Caribbean*	9 (8%)	21 (19%)
Other	3 (3%)	8 (7%)
Education†		
Less than or equivalent of primary education, lower secondary education	47 (43%)	45 (40%)
Higher secondary education, lower vocational education	40 (37%)	39 (35%)
Higher vocational education, university	22 (20%)	28 (25%)
Sexual orientation		
Homosexual	56 (51%)	63 (56%)
Bisexual	11 (10%)	11 (10%)
Heterosexual	42 (39%)	38 (34%)
Treatment status		
Treatment-experienced	52 (48%)	57 (51%)
Treatment-naive	57 (53%)	55 (49%)
CD4 cell count (cells per μL)		
Treatment-experienced patients	520·6 (212·9)	535·1 (226·4)
Treatment-naive patients	379·1 (239·5)	431·8 (200·5)
Plasma HIV-RNA (copies per mL; $mean_{log}$ [SD])		
Treatment-experienced patients	1·74 (0·61)	1·83 (0·83)
Treatment-naive patients	4·83 (0·71)	4·30 (1·01)

Data are n (%) unless otherwise specified. AIMS=Adherence Improving self-Management Strategy. *Surinamese, Latin American, and Antillean. †Categorisation based on the Dutch education system.

***Table 1*: Baseline characteristics of the intention-to-treat population**

Results

- 0% missing VL data at baseline and 4% at 3 points
- Health care consumption questionnaires: 25% missing at baseline and follow-up, 50% at intermediate points
- Completeness & fidelity AIMS delivery:
  - 85% of intervention visits attended
  - 60% of intervention elements delivered
  - Moderate quality of delivery of intervention elements

Results: effectiveness

- Primary effects on viral load across 3 time points:
  - Control group had 1.28 [1.04-1.52] times higher log viral load (p = .012)
- Secondary effects on viral load accross 3 time points:
  - Intervention group had 1.89 [0.98-3.65] higher odds of being undetectable (p = .056)
  - Control group had 2.99 [1.21-7.38] higher odds of treatment failure (17% versus 7%), (p = .012)
- Effect sizes similar for ethnic groups & exp/naive pats

Results: cost-effectiveness

- Cost AIMS per patient per year: 83 euros

Data Stichting HIV Monitoring

Table 2: Costs and utilities per health state

Health State		Health care cost	Productivity loss	Transmission costs	Total costs	Utilities
1	CD4 >500; viral load 0-50	€4014	€810	€1470	€6294	0.954
2	CD4 >500; viral load 51-200	€4180	€771	€2490	€7441	0.954
3	CD4 >500; viral load 201-1000	€3770	€55	€4680	€8505	0.954
4	CD4 >500; viral load >1000	€2995	€2140	€15000	€20135	0.954
5	CD4 >201-500; viral load 0-50	€4169	€682	€1470	€6321	0.929
6	CD4 >201-500; viral load 51-200	€4372	€157	€2490	€7019	0.929
7	CD4 >201-500; viral load 201-1000	€3899	€2149	€4680	€10728	0.929
8	CD4 >201-500; viral load >1000	€2913	€2186	€15000	€20099	0.929
9	CD4 >0-200; viral load 0-50	€4647	€0	€1470	€6117	0.863
10	CD4 >0-200; viral load 51-200	€4459	€307	€2490	€7256	0.863
11	CD4 >0-200; viral load 201-1000	€4267	€0	€4680	€8947	0.863
12	CD4 >0-200; viral load >1000	€3576	€1348	€15000	€19924	0.863
13	Dead	€0	€0	€0	€0	0

Note: 6-month intervention costs were based on the costs of training nurses, time of AIMS delivery, and MEMS-caps, and were estimated at €41,50.

	Lifetime costs	Lifetime QALYs	ICERs
Offset: linear decrease of AIMS effect over 18 months			
Scenario 1 (base case)	€–592	0·034	AIMS dominant
Scenario 2	€–843	0·036	AIMS dominant
Scenario 3	€–412	0·025	AIMS dominant
Offset: effect of AIMS maintained over another 18 months			
Scenario 1	€–793	0·046	AIMS dominant
Scenario 2	€–1117	0·049	AIMS dominant
Scenario 3	€–599	0·035	AIMS dominant
Offset: no effect after stopping AIMS			
Scenario 1	€–375	0·023	AIMS dominant
Scenario 2	€–546	0·024	AIMS dominant
Scenario 3	€–221	0·016	AIMS dominant
Sensitivity analyses (base case)			
Healthcare perspective	€–597	0·034	AIMS dominant
10-year time horizon	€–643	0·028	AIMS dominant

Data from base case analyses and sensitivity analyses. Scenario 1: all relative risks where at least five transitions occurred. Scenario 2: all available transition probabilities irrespective of the number of transitions. Scenario 3: only relative risks with at least ten transitions in total. QALY=costs per quality-adjusted life-years. AIMS=Adherence Improving self-Management Strategy. ICER=incremental cost-effectiveness ratio.

Table 3: Lifetime costs per patient, QALYS, and incremental cost-effectiveness ratios of AIMS compared with treatment as usual

Conclusions

- Effects on adherence (pilot and single centre RCT) and on viral load (single and multi-centre RCT) replicated
- Seems to also translate in higher CD4 at follow-up
- Decreased costs
- Increased QUALY's

Limitations and Recommendations

- Limitations:
  - Delivery AIMS could be better
  - Inclusion rates could be higher
  - Missing data cost-utility for full trial period
  - Trial based CU analysis ignores transmission risk

- Recommendations:
  - Consider adopting AIMS in routine care

- ZonMw : implemention study: 'Implementatie van AIMS: een effectieve en kosteneffectieve interventie om therapietrouw met HIV-med icatie te verbeteren'

Effectiveness and cost-effectiveness of a nurse-delivered intervention to improve adherence to treatment for HIV: a pragmatic, multicentre, open-label, randomised clinical trial

Marijn de Bruin, Edwin J M Oberjé, Wolfgang Viechtbauer, Hans-Erik Nobel, Mickaël Hiligsmann, Cees van Nieuwkoop, Jan Veenstra, Frank J Pijnappel, Frank P Kroon, Laura van Zonneveld, Paul H P Groeneveld, Marjolein van Broekhuizen, Silvia M A A Evers, Jan M Prins

Lancet Infect Dis 2017

Published Online
March 2, 2017
http://dx.doi.org/10.1016/

Summary

Background No high-quality trials have provided evidence of effectiveness and cost-effectiveness of HIV treatment adherence intervention strategies. We therefore examined the effectiveness and cost-effectiveness of the Adherence Improving self-Management Strategy (AIMS) compared with treatment as usual.