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

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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
- Very little promising evidence on (cost)effectiveness

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

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

- 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)
- Mixed-effects VL analyses, controlling for COVs
- Study protocol [1]; RATIONALE Table [2]; Clinicaltrials.gov[3]

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

Sample & Context

- All naïve patients and ‘at-risk’ treatment-experienced
  - ‘At risk’: Detectable viral load in last 3 year & missed doses during baseline monitoring

- Netherlands:
  - Free health care
  - Infection route sexual; intravenous drug use rare
  - Visit physician and nurse every 5-6 months
  - Caucasian, Caribbean, and SS African patients
  - 90-95% viral suppression at given time point
  - Fairly high-quality adherence support (de Bruin et al., 2009; 2010; Oberje, de Bruin, 2015)

Characteristic	Intervention group (N = 110)	Control group (N = 113)
Female, *n* (%)	14 (12.7%)	22 (19.5%)
Age, years, mean (*SD*)	45.4 (11.0)	43.4 (10.8)
Ethnicity, *n* (%)		
Caucasian	81 (73.6%)	63 (55.8%)
African	16 (14.5%)	21 (18.6%)
Caribbean[a]	7 (6.4%)	19 (16.8%)
Other	6 (5.5%)	10 (8.8%)
Education,[b] *n* (%)		
Low	48 (43.6%)	46 (40.7%)
Medium	40 (36.4%)	39 (34.5%)
High	22 (20.0%)	28 (24.8%)
Treatment-experienced	52 (47.3%)	58 (52.7%)
Treatment-initiating	58 (52.3%)	55 (48.7%)
CD_4+ cell count, cells/mm^3, mean (*SD*)		
Treatment-experienced	519.0 (222.3)	553.6 (233.8)
Treatment-initiating	379.3 (246.9)	411.8 (204.3)
Plasma HIV-RNA, $mean_{log}$ (*SD*)		
Treatment-experienced	1.74 (0.61)	1.83 (0.82)
Treatment-initiating	4.83 (0.70)	4.30 (1.01)

Results

- 40% consented, no differences Y/N participants
- 5 people died

- 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

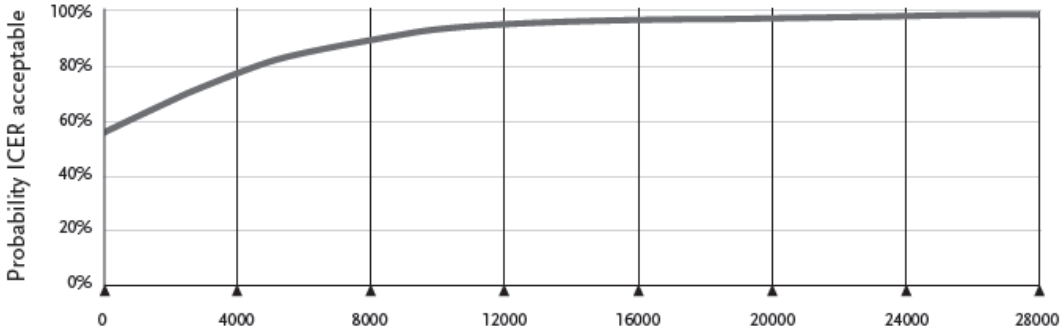
- Primary effects on viral load across 3 time points:
  - Control group had 1.28 [1.04-1.52] times higher log viral load ($F(1,196) = 6.40$, $p = .012$)
- Secondary effects on viral load accross 3 time points:
  - Intervention group had 1.89 [0.98-3.65] higher odds of being undetectable ($\chi^2(df = 1) = 3.66$, $p = .056$)
  - Control group had 3.08 [1.30-7.88] higher odds of 2 consecutive detectable VLs (17% versus 7%), ($\chi2(df = 1) = 6.39$, $p = .012$)
- Effect sizes similar for ethnic groups & exp/naive pats

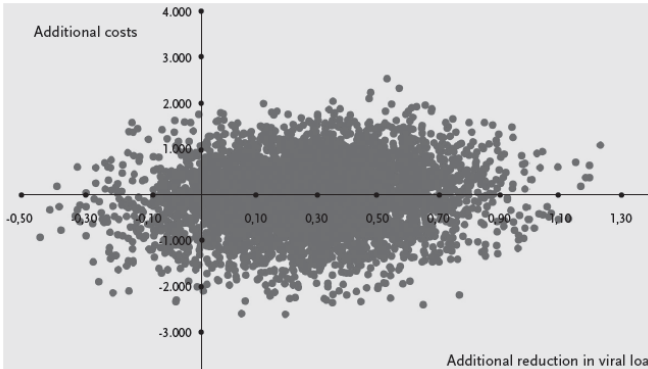
Results: cost-effectiveness

- Cost AIMS per patient per year: 83 euros

- Trial-based cost-effectiveness analysis
  - Costs/1 log reduction VL
  - 88% @ €2000, 75% @ €1000, 55% @ €0

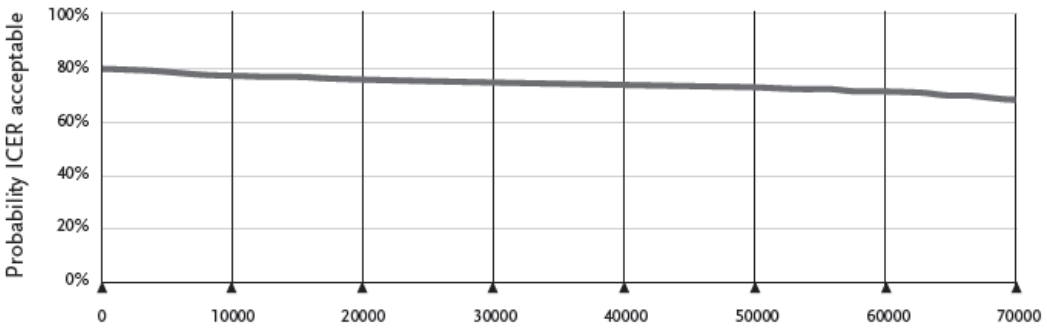
  - Costs/1 viral load ‘failure’ avoided
  - 90% @ €8000, 80% @ €4000, 58% @ €0

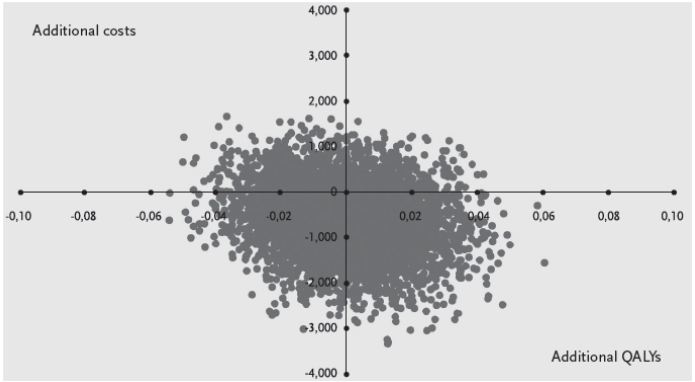




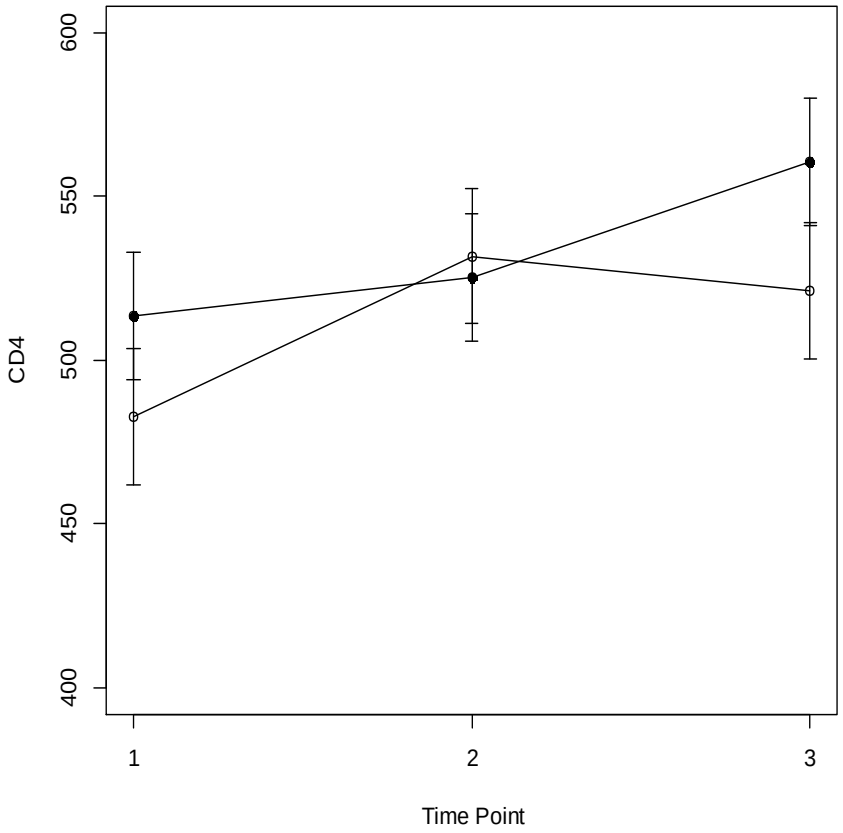
Results: cost-effectiveness

- Trial-based cost-utility analysis (societal perspective)
  - Costs/QALY full trial period (50% data imputed at intermediate measures): 54% probability CE
  - Bias with 25% imputation acceptable, at 50% high (Gomes, Med Decis Making, 2013;33:1051)
  - QoL baseline & follow-up only (25% data imputed): 80% probability CE





Additional analysis: CD4



Treatment*time interaction (contrary to viral loads), hence per time point analysis

M5: 31.0 [-8.4 to 70.4]

M10: 6.6 [-46.0 to 33.0]

M15: 40.4 [0.1 to 78.7]

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

- Trial-based cost-effectiveness analysis:
  - Viral load: strong but depends on willingness to pay
  - QALY: tricky with missing data, but positive trends

- Trial-based cost-utility: did not expect strong effects
- Markov model almost finished incl. HIV transmission[1]
- Available model Goldie [2]: High probability CE

1-Zaric, Med Decis Making, 2008;28:359; 2-Goldie, AM J Med, 2003;115:632

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
  - Need more high-quality, large scale adherence trials evaluating clinical and cost-effectiveness
  - Need more replication of successful interventions rather than testing e.g., 60 different ones in single trials

Acknowledgements

Prof. J.M. Prins
Prof. H.J. Hospers
Prof. GJ van breukelen

Prof. G Kok
Dr. EJM Oberje
Dr. Viechtbauer

Prof. S. Evers

Patients, nurses, and physicians in the Netherlands

ZonMw

Thanks

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