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

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)
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Intervention group (N = 110)</th>
<th>Control group (N = 113)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female, n (%)</td>
<td>14 (12.7%)</td>
<td>22 (19.5%)</td>
</tr>
<tr>
<td>Age, years, mean (SD)</td>
<td>45.4 (11.0)</td>
<td>43.4 (10.8)</td>
</tr>
<tr>
<td>Ethnicity, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>81 (73.6%)</td>
<td>63 (55.8%)</td>
</tr>
<tr>
<td>African</td>
<td>16 (14.5%)</td>
<td>21 (18.6%)</td>
</tr>
<tr>
<td>Caribbean*</td>
<td>7 (6.4%)</td>
<td>19 (16.8%)</td>
</tr>
<tr>
<td>Other</td>
<td>6 (5.5%)</td>
<td>10 (8.8%)</td>
</tr>
<tr>
<td>Education, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>48 (43.6%)</td>
<td>46 (40.7%)</td>
</tr>
<tr>
<td>Medium</td>
<td>40 (36.4%)</td>
<td>39 (34.5%)</td>
</tr>
<tr>
<td>High</td>
<td>22 (20.0%)</td>
<td>28 (24.8%)</td>
</tr>
<tr>
<td>Treatment-experienced</td>
<td>52 (47.3%)</td>
<td>58 (52.7%)</td>
</tr>
<tr>
<td>Treatment-initiating</td>
<td>58 (52.3%)</td>
<td>55 (48.7%)</td>
</tr>
<tr>
<td>CD4+ cell count, cells/mm³, mean (SD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment-experienced</td>
<td>519.0 (222.3)</td>
<td>553.6 (233.8)</td>
</tr>
<tr>
<td>Treatment-initiating</td>
<td>379.3 (246.9)</td>
<td>411.8 (204.3)</td>
</tr>
<tr>
<td>Plasma HIV-RNA, mean/log (SD)</td>
<td></td>
<td></td>
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<tr>
<td>Treatment-experienced</td>
<td>1.74 (0.61)</td>
<td>1.83 (0.82)</td>
</tr>
<tr>
<td>Treatment-initiating</td>
<td>4.83 (0.70)</td>
<td>4.30 (1.01)</td>
</tr>
</tbody>
</table>
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 across 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%), \( (\chi^2(df = 1) = 6.39, p = .012) \)

- 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 transmission¹
- Available model Goldie ²: High probability CE

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
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ZonMw

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