“Prevalence & Correlates of Incorrect Eye Drop Use: The Belgian Compliance Study in ophthalmology (BCSO)”

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ESPACOMP BANGOR
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Glaucoma

- 66 million people worldwide \(^1\)
- 3.5% in Belgium \(^2\)
- Progressive damage optic nerve \(\rightarrow\) blindness \(^3,4\)
- Symptoms only late in the disease process

- **Primary risk factors:** \(\uparrow\) intraocular pressure (IOP) & fluctuations in IOP
- **Other risk factors:** age, race, family history & diastolic perfusion pressure

\(^1\) Quigley et al, Br J Ophthalmology 1996
\(^2\) Detry-Morel et al, Eur J Ophthalmology 2004
\(^3\) Maier et al, BMJ 2005
\(^4\) American Academy of Ophthalmology 2000
State of the art treatment

Mono-or combination eye drop therapy of:
- Beta-blockers
- Alpha2-adrenergic agonists
- Carbonic anhydrase inhibitor
- Cholinergic agonist
- Prostaglandine analogues
- Fixed combination

Goals:
- Lowering & controlling intraocular pressure
- Preventing visual field loss

Eye drops do not work if patients are not administrating them correctly
Non-adherence in glaucoma

- Prevalence of NA with eye drop treatment:

  30% (range: 8%-59%) \(^1,2\)

(Depending on case finding methods, operational definitions and measurement methods used)

\(^1\) Olthoff et al, ophthalmology 2005.
Correlates of NA in glaucoma

- Patient-, treatment-, condition- and socio-economic correlates of NA studied (to a limited extent) \(^1,2,3\):
  - Knowledge on disease & treatment
  - Skill-level of eye drop administration
  - Cost
  - Forgetfullness
  - Health-related beliefs
  - Complexity of treatment
  - Younger age

\(^1\) Olthoff et al, Ophthalmology 2005.
\(^3\) Friedman et al, J Glaucoma 2008.
GAPS in NA-research in POAG

- **Samples:**
  - Often selected in one single center
  - Only a few studies exceeding 200 patients (range: 11-500) \(^1\)

- **Limited use of multi-method approach to increase sensitivity for NA-measurement** \(^2\) (e.g. combination of different adherence measures)

- **Limited number of health-care organizational correlates of NA studied** (e.g. treating ophthalmologist, frequency of follow-up)

- **No application of multi-level modeling in statistical analysis**

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\(^1\) Olthoff et al, Ophthalmology 2005

\(^2\) Osterberg et al, BMJ 2003
AIMS of BCSO-study

1) To investigate the prevalence of NA with eye drop treatment in a **large multicenter** study

2) To investigate selected **correlates** of NA
Design & Sample BCSO-study

**Design:**
- Multi-center cross-sectional survey in Belgium (i.e. Wallonia & Flanders)

**Sample & setting:**

  Staged stratified sampling:

  1) All Belgian **ophthalmologists** (n=1012) from hospitals or private practices

  2) Convenience sample of minimum 10 **patients** per ophthalmologist
In-and exclusion criteria
BSCO-study

1) Ophthalmologists:
   - No specific in-or exclusion criteria stated

2) Patients:
   **Inclusion criteria:**
   - POAG/ocular hypertension under topical treatment
   - > 18 years
   - Able to understand & fill out Dutch/French questionnaire

   **Exclusion criteria:**
   - Blind
   - Other types of glaucoma
1) Non-adherence with eye drop treatment:

<table>
<thead>
<tr>
<th>MEASURE</th>
<th>DEFINITION</th>
</tr>
</thead>
<tbody>
<tr>
<td>PATIENT SELF-REPORT</td>
<td>Patients are NA if they answer:</td>
</tr>
<tr>
<td>Single question on self-report questionnaire:</td>
<td>“seldom”, “once a week” or “every day”.</td>
</tr>
<tr>
<td>“How often did you forget to administer your</td>
<td></td>
</tr>
<tr>
<td>eye drops in the past 2 weeks?”</td>
<td></td>
</tr>
<tr>
<td>(Never, Seldom, Once a week, Every day)</td>
<td></td>
</tr>
<tr>
<td>COLLATERAL REPORT</td>
<td>Patients are NA if ophthalmologists answer:</td>
</tr>
<tr>
<td>Single question on self-report questionnaire:</td>
<td>“Yes”</td>
</tr>
<tr>
<td>“Is your patient NA?”</td>
<td></td>
</tr>
<tr>
<td>(Yes, No, Don’t know)</td>
<td></td>
</tr>
<tr>
<td>COMBINATION</td>
<td>Patients are NA if 1 of both measures rate patients as NA</td>
</tr>
<tr>
<td>Combined self-report &amp; collateral report</td>
<td></td>
</tr>
</tbody>
</table>

Alternative definition of self-reported NA to test robustness of the data: patients answering “once a week or daily”
2) Socio-demographic correlates:
- Age, gender, marital status, education & language
  (*Patient self-report questionnaire*)

3) Condition- & treatment-related correlates:
- Diagnosis, treatment, IOP, visual field loss & comorbidities
  (*Ophthalmologist self-report questionnaire*)

4) Health-care organization correlates:
- Treating ophthalmologist & frequency of follow-up (i.e. “once a year”, “every 6 months”, “every 4 months” or “every 3 months or more”)
  (*Ophthalmologist self-report questionnaire*)
Procedure BCSO-study

• Invitation send to ophthalmologists

• Ophthalmologist selected the patients

• Written informed consent was obtained

• Questionnaire completion:
  – **Patients**: independently at home (send back to coördination center)
  – **Ophthalmologists**: during or after patient visit (collected by medical representative)

• Clinical measurements performed during same visit

• Matching numbers between both questionnaires provided
1) **Prevalence of NA:**
- Frequencies for self-report, collateral report & combined measure

2) **Correlates of NA:**
   - For both definitions of NA:
   - Univariable & multivariable multi-level binary logistic regression with self-reported NA as dependent variable and variable “ophthalmologist” as random factor
     (decision level for building multivariable model: p<0.10)
**Sample BCSO-study**

<table>
<thead>
<tr>
<th>TARGET POP.:</th>
<th>Ophthalmologists</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Belgian ophthalmologists (N=1012)</td>
<td>Inclusion of minimal 10 patients per ophthalmologist</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>RETURNED QUESTIONNAIRES:</th>
<th>N=912</th>
<th>N=827</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>ATTRITION:</th>
<th>Incomplete or no corresponding patient questionnaire available (N=249)</th>
<th>Incomplete questionnaires (N=161)</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>RECORDS COMPLETE:</th>
<th>N=105</th>
<th>N=663; Median of 7 patients (range 1-17)</th>
</tr>
</thead>
</table>

AVAILABLE FOR ANALYSIS: 663 corresponding questionnaires
<table>
<thead>
<tr>
<th>CHARACTERISTIC</th>
<th>N</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female (%)</td>
<td>318</td>
<td>48.0</td>
</tr>
<tr>
<td>Flemish (%)</td>
<td>366</td>
<td>55.2</td>
</tr>
<tr>
<td>30-39 year (%)</td>
<td>1</td>
<td>0.20</td>
</tr>
<tr>
<td>40-49 year (%)</td>
<td>57</td>
<td>8.60</td>
</tr>
<tr>
<td>50-59 year (%)</td>
<td>130</td>
<td>19.6</td>
</tr>
<tr>
<td>60-69 year (%)</td>
<td>186</td>
<td>28.0</td>
</tr>
<tr>
<td>&gt;69 year (%)</td>
<td>289</td>
<td>43.6</td>
</tr>
<tr>
<td>Primary school (%)</td>
<td>141</td>
<td>21.2</td>
</tr>
<tr>
<td>Secondary school education (%)</td>
<td>330</td>
<td>49.8</td>
</tr>
<tr>
<td>Higher education (%)</td>
<td>192</td>
<td>29.0</td>
</tr>
</tbody>
</table>
## Prevalence of NA with eye drop treatment

<table>
<thead>
<tr>
<th>Measurement methods</th>
<th>Prevalence of Non-adherence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient self-report (%)</td>
<td>260 (39.2)</td>
</tr>
<tr>
<td>Ophthalmologists’ report (%)</td>
<td>14 (2.1)</td>
</tr>
<tr>
<td>Combined measures (%)</td>
<td>266 (40.1)</td>
</tr>
</tbody>
</table>

**DEFINITION NA:**

a) Patient-self-report:  
   How many times did you miss a dose during the last 2 weeks?  
   “seldom”, “once a week” or “every day”

b) Ophthalmologist-report:  
   Is your patient NA?  
   “Yes”

c) Combined measures:  
   One of both measures showing NA
<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>$\chi^2$</th>
<th>Df</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HEALTH CARE SYSTEM RELATED FACTORS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treating ophthalmologist</td>
<td>0.66</td>
<td>0.5</td>
<td>0.21</td>
</tr>
<tr>
<td>Lower frequency of follow-up</td>
<td>6.65</td>
<td>3</td>
<td><strong>0.08</strong></td>
</tr>
<tr>
<td><strong>PATIENT RELATED FACTORS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Higher frequency of dosing (&gt; 2/day)</td>
<td>14.2</td>
<td>2</td>
<td><em>0.001</em></td>
</tr>
<tr>
<td>Younger age</td>
<td>9.17</td>
<td>3</td>
<td><em>0.027</em></td>
</tr>
<tr>
<td>Male gender</td>
<td>6.30</td>
<td>1</td>
<td><em>0.01</em></td>
</tr>
</tbody>
</table>

* = p<0.05   ** = p<0.10

**Tendency to significant correlation between “frequency of follow-up & NA**

**Post-hoc analysis:** Dichotomizing “frequency of follow-up”:
“less then every 3 months” vs “every 3 months or more”
Frequency of follow-up of “every 3 months or more”: ↓ risk for NA (p=0.01)
Conclusions BCSO-study

- **Four out of ten** patients admitted to be NA with eye drop treatment

- Significant correlates of NA with eye drop treatment are: male gender, younger age and a higher frequency of dosing

- There is no significant variability in NA with eye drop treatment between the different ophthalmologists

- Patients visiting their ophthalmologist $\geq 3$ months have lower risk for NA with eye drop treatment
Frequent follow-up visits \textit{(i.e. at least every 3 months)} & easier treatment regimens \textit{(i.e. 2 doses or fewer daily doses)} are possible pathways to improve adherence.

\textbf{Role of healthcare system related factors needs more attention!}
Adherence in glaucoma

“the extent to which a person’s behavior (i.e. administering eye drops at fixed time points) corresponds with the agreed recommendations of the ophthalmologist”

(Haynes et al 1979, Sabaté et al 2003)

2 MAIN COMPONENTS:

1. **Persistence**: “length of time during which the medication is taken (i.e. the time from the first taken dose to the last taken dose)”

2. **Execution**: “multidimensional outcome of the comparison of two time series (i.e. the prescribed drug dosing regimen and the patients’ drug dosing history while the patient is still engaged in the treatment)”

(Vrijens et al 2008)