Measuring Health-Related Quality of Life for Patients With Diabetic Retinopathy

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- Technology Assessment Report
- Conducted by the UAEPC under contract to AHRQ
  - Contract No. HHSA 290 2007 10021 I
- Requested by the Coverage & Analysis Group at CMS

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Conflicts of Interest

- AM, JAJ, DMD - no affiliations or financial involvement related to the material presented in this report
- MT, CR are directors of & have financial interests in Secure Diagnostic Imaging Inc.
  - developed and manages teleophthalmology software for the diagnosis and followup of DR
  - No treatment is performed via the software
  - No COI related to the material presented in this report

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Overview

- Background
- Methods
- Key Questions
- Results
- Discussion
- Future research
- Conclusions

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Background: Diabetic Retinopathy

- In 2005–2008, the prevalence of DR among Americans with diabetes ≥40 years was 28.5%
- Prevalence of vision-threatening DR was 4.4%
- Prevalence of clinically significant ME was 2.7%

(Zhang et al. JAMA 2010)

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Background: DR

- Prevalence & severity of DR increases with the duration of diabetes
  - Inversely related to glycemic & blood pressure control
- Early identification & treatment of DR reduces vision loss and is cost-effective
- Treatment is aimed at reducing the risk of onset and limiting disease progression
  - Direct ocular therapy is prescribed when indicated

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Background: DR

- Patients with DR report that vision loss impacts well-being
  - independence, mobility, leisure, self-care
- DR can impair functioning and overall HRQL

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Background: HRQL

- Patient reported outcomes
  - Measure aspects of care including HRQL, patient illness perceptions, treatment satisfaction
    - Include health status, functional status, HRQL
  - Directly from the patient without interpretation by another individual

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Background: HRQL

- Health status
  - Represents the patient's evaluation of their physical & mental health
  - Identification & assessment of changes in activities and perceptions compared with normal life
- Functional status
  - Focuses on the physical capacity to complete everyday activities

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Background: HRQL

- HRQL measures the impact of disease and its treatments on the lives of patients
  - From the patient's perspective
  - Multifaceted
  - Takes into account the impact of disease & its treatment
    - Physical, psychological, social, and somatic domains of functioning and well-being

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Background: HRQL

HRQL tools can be divided into 2 categories:

- Generic HRQL tools
  - Investigate all important aspects of HRQL
  - Allow broad comparisons across all domains
  - Tend to be less sensitive to changes in HRQL
- Specific HRQL tools
  - Target a particular disease, population, or outcome
  - May be more responsive to HRQL changes

Key Questions

1. a) What HRQL measures have been used in studies of treatments for DR, including DME?
   b) What are their psychometric properties?
2. What is the evidence that HRQL is improved for any intervention for DR, including DME?
3. What is the evidence about the association between improvement in HRQL & other variables?
   - baseline visual acuity, age, race, sex, severity & type of DR

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Methods: Literature Search

- Searched 6 databases:
  - MEDLINE, EMBASE, PsychINFO, Cochrane Central Register of Controlled Trials, CINAHL Plus full text, Scopus
- ClinicalTrials.gov for recently completed or ongoing studies
- No language, date, or study design restrictions
- Searches current to January 2012

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Methods: Study Selection

- 2 reviewers independently screened titles & abstracts for 1st level screening, and full-text for 2nd level screening
- Studies of adults (≥18 years) with DR, including DME
  - KQ1: studies that used any HRQL tool
  - KQ2/3: prospective comparative studies with any intervention; HRQL outcomes using tool with reported psychometric properties

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Methods: QA and GRADE

- COSMIN checklist to evaluate the psychometric properties of HRQL tools
- Newcastle-Ottawa Scale (NOS) for cohort & before-after studies
- EPC GRADE approach to assess the overall strength of evidence for HRQL
- 2 reviewers independently applied the tools
  - disagreements resolved through consensus

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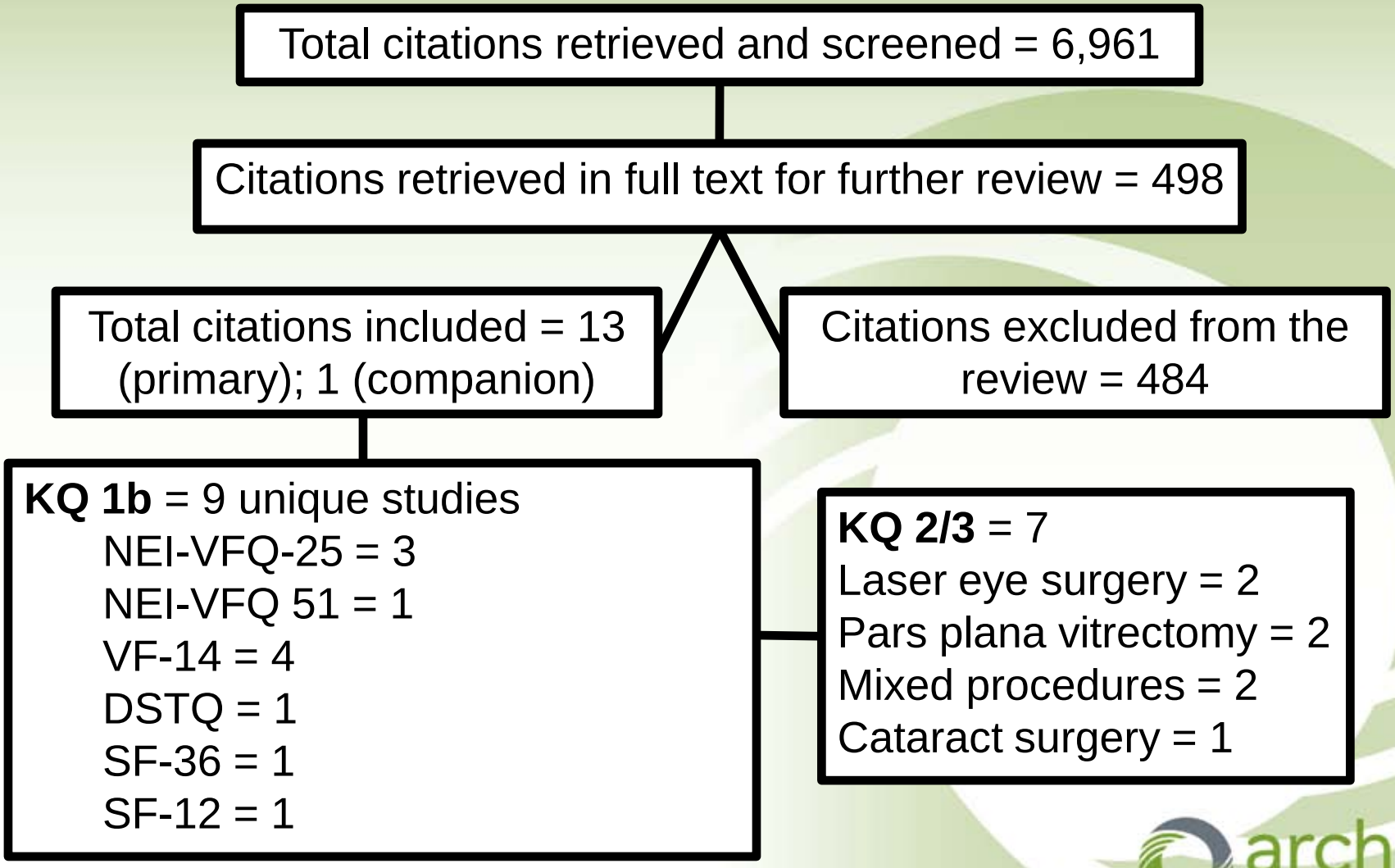
Results: Literature Selection



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Results: KQ 1a: HRQL measures

- 11 studies assessed HRQL outcomes
  - VFQ-25 + SF-36 (1 RCT)
  - VFQ-25 (2 cohort, 1 B-A)
  - VFQ-51 (1 B-A)
  - VF-14 (2 cohort)
  - VF-14 + SF-12 (1 case report)
  - VF-14 + satisfaction survey (1 cohort)
  - DTSQ (1 B-A)
  - Qualitative interviews (1 cohort)

Results: KQ 1a: HRQL measures

- RetTSQ & RetDQoL developed specifically for patients with DR
  - Not yet used to evaluate HRQL in interventions
- 7 recently completed trials reported using the VFQ–25 (Clinicaltrials.gov)
  - Results not yet published

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Results: KQ 1b: Psychometrics

Rating of the psychometric properties of health-related quality of life assessment tools used in studies of treatment of diabetic retinopathy

Measure	Content validity	Construct validity	Internal consistency	Test re-test reliability	Measurement error	Responsive-ness	Interpret-ability
SF-36	+	+	+	+	+	+	+
VFQ-25	+	+	+	+	0	?	?
VF-14	?	+	+	?	0	?	0
DTSQ	+	+	+	+	+	+	0
RetDQoL	+	+	+	0	0	0	0
RetTSQ	+	+	+	0	0	0	0

Method or result was rated as: + = high quality; ? = indeterminate; - = low quality; 0 = no data available

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Results: KQ 2&3: Changes in HRQL

- 7 observational studies addressed KQ 2&3
  - No RCTs reported HRQL outcomes
  - 4 cohort studies; 3 before-after studies
- Sample sizes ranged from 55 to 327 (IQR: 77 – 171)
- No studies conducted in North America
  - 4 studies in Europe
  - 3 studies in Japan

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Results: KQ 2&3: Patient groups

- Of the 7 studies
  - 4 reported some results for patients with DME
  - 2 included patients with DME, but results were not reported separately
  - 1 study did not report whether patients with DME were included
- 2 studies included patients with DR but the intervention was to treat cataracts

Results: KQ 2&3: Changes in HRQL

- Studies are at high risk of bias due to weak study designs (before-after or cohort studies)
- Strength of evidence was insufficient to draw conclusions about the effect of any treatment on HRQL

Results: Laser Photocoagulation

- B-A study (2004), VFQ-51
  - 55 patients with DME
  - Significant improvement in HRQL at 3 mo. post-surgery
- B-A study (2005), DTSQ
  - 105 patients with PDR and DME
    - Results not reported separately
  - Satisfaction was high for all patients at 9 mo.

Results: Vitrectomy

- Cohort study (2010), VFQ-25 [Japanese], 3 mo.
  - PDR (n=99): statistically significant improvement;
  - DME (n=38): no significant difference
- B-A study (2008), VFQ-25 [Japanese], 6 mo.
  - Vitreous hemorrhage (n=41): statistically significant improvement;
  - DME (n=28): no significant difference;
  - Fibrovascular membrane (n=18): no significant difference, except for general vision subscale

Results: Vitrectomy & Panretinal Photocoagulation

- Cohort study (2009), VFQ-25 [Japanese], 12 mo.
  - 327 patients with DR
    - Vitrectomy (n=136): statistically significant improvement;
    - Panretinal photocoagulation (n=60): no significant difference;
    - No treatment (n=131): no significant difference

Results: Phacoemulsifcation

- Cohort study (2005), VF-14, 3 mo.
  - 67 patients with DR being treated for cataracts
  - Patients with no DR/mild NPDR > improvement than patients with moderate-severe NPDR/PDR
    - statistically significant
- Cohort study (2009), VF-14, 12 mo.
  - 89 patients with DR being treated for cataracts
  - PDR & moderate/severe NPDR: no significant difference;
  - No/mild NPDR: sig. higher scores than those with severe DR

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Results: KQ3: Associated Factors

- Laser photocoagulation
  - Age <65 years, more severe level of DR, & low preoperative QOL associated with improved HRQL (multivariate, 1 study)
  - Age >65 years associated with greater satisfaction after treatment (univariate, 1 study)
- Vitrectomy:
  - Improvement in contrast sensitivity associated with changes in VFQ-25 for patients with PDR & DME (multivariate, 1 study)
- SOE is insufficient

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Discussion: HRQL Measures

- 1 generic HRQL measure: SF-36
  - SF-36 appears unresponsive to change in visual acuity in patients with DR
    - Assesses a wide range of characteristics not directly related to visual acuity
- Other generic measures that include an assessment of vision function (i.e., Health Utilities Index) may be worth consideration

Discussion: HRQL Measures

- 2 vision specific measures: VFQ-25, VF-14
  - Both have been validated and are clinically responsive
- Vision specific measures have been shown to be sensitive to differences in vision status & functioning among patients with DR & ME

Discussion: HRQL Measures

- 1 diabetes specific tool: DTSQ
  - Developed to measure patient satisfaction with treatment for diabetes
  - Not designed to measure satisfaction with other aspects of diabetes care management
  - Most useful when used with other tools to assess other important outcomes, including HRQL

Discussion: HRQL Measures

- 2 DR-specific measures have been developed: RetDQoL, RetTSQ
  - May enable patients to consider the specific impact of their diabetic eye problems & their treatment
  - Preliminary psychometric testing is promising for content validity and internal consistency
  - Additional testing is ongoing
- No DME-specific measures

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Discussion: Impact of Interventions

- No RCTs have reported HRQL outcomes
- PKC-DRS2 trial (ruboxistaurin vs. placebo) measured HRQL using the SF-36 and VFQ-25; results not yet reported
- 14 ongoing/recently completed trials investigating the impact of DR or DME interventions on HRQL have been identified

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Discussion:
Impact of Interventions

- HRQL improves following various interventions that treat DR, including DME
  - Results based on 1 or 2 observational studies for each intervention
  - SOE is insufficient to draw conclusions
- Results may not be applicable to North American patients
  - Studies conducted in Europe and Japan

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Recommendations

- RCTs are needed to assess impact of interventions for DR and DME on HRQL
- SR should be conducted in 2 years to incorporate results of ongoing RCTs
- Validated & reliable HRQL tools should be used & results reported
- Assessment of psychometric properties of DR-specific tools should continue

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Recommendations

- Patients should be followed for at least 6 months post-intervention to capture maximum improvement for visual acuity
- RCTs should be designed and conducted to minimize risk of bias
  - Blinding of patients & investigators

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Conclusions

- 4 HRQL tools have assessed the impact of treatment in patients with DR including DME
  - Psychometric properties have been adequately evaluated
- 2 DR-specific tools are currently under psychometric evaluation
- Insufficient evidence to draw conclusions about the relative effect on HRQL of 1 intervention vs. another for patients with DR or DME

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