IQWiG Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen

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Benefit assessment of HPV testing in primary screening for cervical cancer – update[1]

Executive Summary

[1] Translation of the executive summary of the rapid report *Nutzenbewertung eines HPV-Tests im Primärscreening des Zervixkarzinoms – Aktualisierung* (Version 1.0; Status: 14 May 2014). Please note: This translation is provided as a service by IQWiG to English-language readers. However, solely the German original text is absolutely authoritative and legally binding.

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Executive summary

On 21 October 2013, the Federal Joint Committee (G-BA) wrote to the Institute for Quality and Efficiency in Health Care (IQWiG) to commission the update of the benefit assessment of HPV testing in primary screening for cervical cancer (S10-01) with the following goal.

Research question

The goal of this research was to answer the question whether and, if any, which changes of the conclusion of the final report S10-01 have resulted from the literature on the topic of commission S10-01 published in the meantime.

Methods

In principle, the same methods were used for the present rapid report as in commission S10-01. The following deviations were specified with regard to information retrieval: According to current procedures, the search was conducted in the publicly accessible trial registries ClinicalTrials.gov and International Clinical Trials Registry Platform (ICTRP) Search Portal, and no search was conducted in conference proceedings. Randomized controlled trials (RCTs) with a minimum duration of one year were included that investigated HPV testing alone or in combination with cytology-based testing in primary screening versus a strategy that exclusively applied cytology-based testing in primary screening with regard to patient-relevant outcomes.

For this purpose, a systematic literature search was performed in the following databases: MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (Clinical Trials). In addition, a search for relevant systematic reviews took place in the databases MEDLINE and EMBASE in parallel with the search for relevant primary studies. Searches were also conducted in the databases Cochrane Database of Systematic Reviews (Cochrane Reviews), Database of Abstracts of Reviews of Effects (Other Reviews), and the Health Technology Assessment Database (Technology Assessments). The last search in bibliographical databases was conducted on 6 November 2013. Furthermore, systematic reviews and the publicly accessible trial registries ClinicalTrials.gov and ICTRP Search Portal were screened.

The selection of relevant studies was performed by 2 reviewers independently of each other for the result from the bibliographic literature search and the search in publicly accessible trial registries as well as for potentially relevant studies from systematic reviews.

Data extraction was conducted in standardized tables. To evaluate the certainty of results, the risk of bias at study and outcome level was assessed and rated as low or high respectively. The results of the individual studies were described, organized by outcomes. If the studies were comparable regarding the research question and relevant characteristics, the individual results were pooled quantitatively by means of meta-analyses.

Results

Studies that, in principle, fulfilled the criteria for inclusion in the benefit assessment (see Section 4.1 of the final report S10-01), were not necessarily suited for the assessment of the patient-relevant benefit. In accordance with the methods of the final report S10-01, data on incidence were primarily used for the benefit assessment. At the same time, the assessment of incidence could only be based on the results of a second screening round. In compliance with the methodological approach of the final report S10-01, the benefit assessment therefore primarily refers to the results of the second screening round.

No additional studies relevant for the benefit assessment were found in comparison with the 5 studies included in the final report S10-01. One new publication on the POBASCAM study considered in the final report S10-01 with new study results was identified.

The 5 studies included in the benefit assessment were population-based randomized controlled intervention studies and investigated HPV testing alone or in combination with cytology-based testing in primary screening versus a strategy that exclusively applied cytology-based testing in primary screening with regard to the patient-relevant outcomes "CIN3/CIS", "invasive cervical cancer" and "CIN3+".

For the outcome "CIN3+", there was a "substantial" (first screening round) and a "moderate" (second screening round) heterogeneity between the studies, which is why no common effect estimate was calculated. The results of the first screening round showed, with the exception of the ARTISTIC study, a higher identification rate of CIN3+ when using HPV testing alone or in combination with cytology-based testing than when using cytology-based testing alone. However, in comparison with the final report S10-01, there were no longer differences in the same direction, because the weighting of the studies with statistically significant group difference among the studies with the same direction was less than 50%. For the outcome "CIN3+", the benefit assessment provided an indication that HPV testing alone or in combination with cytology-based testing leads to a lower incidence of CIN3+ than cytology-based testing alone.

For the outcome "invasive cervical cancer", the results of the first screening round produced heterogeneous results without recognizable direction of the differences. For the outcome "invasive cervical cancer", the benefit assessment provided an indication that HPV testing alone or in combination with cytology-based testing leads to a lower incidence of cervical cancer than cytology-based testing alone.

For the outcome "CIN3/CIS", there was "considerable" heterogeneity between the studies in both screening rounds, which is why no common effect estimate was calculated. The results of the first screening round showed, with the exception of the ARTISTIC study, a higher identification rate of CIN3/CIS when using HPV testing alone or in combination with cytology-based testing than when using cytology-based testing alone. However, in comparison with the final report S10-01, there were no longer differences in the same

direction, because the difference in POBASCAM was no longer statistically significant and therefore the weighting of the studies with statistically significant group difference among the studies with the same direction was less than 50%. For the outcome "CIN3/CIS", under consideration of the new results, the benefit assessment no longer provided a "hint" of an effect of HPV testing alone or in combination with cytology-based testing in comparison with cytology-based testing alone. As under inclusion of the additional results the effect of the POBASCAM study was no longer statistically significant, there were no effects in the same direction anymore.

Conclusions

The present benefit assessment of HPV testing was based on the patient-relevant outcomes "CIN3/CIS", "invasive cervical cancer" and "CIN3+", because data were only available on these outcomes. The publications included provided no data on the following patient-relevant outcomes: overall survival, disease-specific mortality, screening-related harm and changes in health-related quality of life.

For the assessment of the outcomes "CIN3+" and "invasive cervical cancer", no change in comparison with the final report S10-01 resulted from the consideration of the publication on the POBASCAM study additionally identified.

For the outcome "CIN3+", the benefit assessment, also under consideration of the new results, produced an indication of a benefit of HPV testing alone or in combination with cytology-based testing versus a cytology-based strategy alone in primary screening for cervical cancer.

Under consideration of the additional results of the POBASCAM study, there was also an indication of benefit for the outcome "invasive cervical cancer".

In comparison with the final report S10-01, there was a change in the assessment of the outcome "CIN3/CIS". Under consideration of the new results from the POBASCAM study, the benefit assessment no longer contained a hint of an effect of HPV testing for the outcome "CIN3/CIS".

Due to the insufficient data availability, the benefit of HPV screening with regard to the patient-relevant outcomes "overall survival" and "disease-specific mortality" remained unclear. It was also not possible to conduct a comparative assessment of harm from HPV testing alone or in combination with cytology-based testing in comparison with a cytology-based strategy alone.

As in the final report S10-01, no recommendation for a specific screening strategy could be made.

Keywords: mass screening, papillomavirus infections, uterine cervical neoplasms, benefit assessment, systematic review

The full report (German version) is published under https://www.iqwig.de/de/projekte_ergebnisse/projekte/nichtmedikamentoese_verfahren/s13_03_nutzenbewertung_eines_hpv_tests_im_primarscreening_des_zervixkarzinoms_rapid_report.3753.html#overview.