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EEG as a diagnostic tool in patients with first episode psychosis

Gondinger J, Hedström A, Liljegren A, Molin C, Sjögren P, Svanberg T, Wallin A, Strandell A

EEG as a diagnostic tool in patients with first episode psychosis [EEG som ett diagnostiskt verktyg vid förstagångsinsjuknande i psykos]

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Summary of the Health Technology Assessment

Method and patient group

Electroencephalogram (EEG) has traditionally been included in the diagnostic work-up in patients with first episode psychosis. No clinical test is specific for psychosis, but it is important to detect organic and treatable conditions like tumours and nutritional deficiencies which may present with psychotic symptoms. To exclude such conditions computed tomography X-ray (CT) scans or magnetic resonance imaging (MRI) are routinely used. EEG is used as a complementary diagnostic examination in some psychiatric wards.

Question at issue

Does EEG contribute to a correct diagnosis of psychotic illness, or to exclusion of other cerebral disease, in patients with first episode of psychotic symptoms, compared to clinical evaluation and/or neuroradiologic examinations?

Studied risks and benefits

There are no studies that properly evaluate the diagnostic accuracy of EEG in patients with first episode of psychosis. Related literature comparing EEG patterns in schizophrenic patients with healthy controls describe non-specific abnormalities. The literature search identified three publications of low to moderate quality, which only partially fulfilled the PICO criteria, but still contributed with some information on diagnostic performance of EEG and CT. These studies illustrated poor diagnostic accuracy.

There is no support for EEG as a method to diagnose psychosis, or to detect organic etiology to psychotic symptoms, in patients with first episode of psychotic symptoms. Very low quality of evidence (GRADE ⊕○○○).

Ethical questions

Since EEG is a non-invasive investigation, it is not considered harmful. However, patients have to be transported to another hospital and there is a risk for delay in starting treatment. Other patient groups will benefit from having increased access to neurophysiological investigations if EEG is not performed routinely in patients with first-episode psychosis.

Economical aspects

The cost of performing EEG for one patient at the Sahlgrenska University Hospital is about 200 €. The annual cost is estimated to 18,000 €.

Concluding remarks

EEG is sometimes used as a complementary investigation in patients with first-episode psychotic symptoms. The present evaluation shows that there is an absence of appropriate literature. There is no support for EEG as a method to diagnose psychosis, or to detect an organic etiology to psychotic symptoms, in patients with first episode of psychotic symptoms. Very low quality of evidence (GRADE ⊕○○○).

Which health technology or method will be assessed?

1a **Who will lead the project?**
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1b **Who posed the question?**
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1e **Are there any conflicts of interest for the proposer or any of the participants in the work group?**
No

Disease/disorder of Interest and Present Diagnostic Procedures

2a Disease/disorder of interest and its degree of severity

The condition of interest is psychotic symptoms, occurring for the first time. Having psychotic symptoms means having a disturbed sense of reality, manifested through hallucinations, delusions or disturbed or disordered thoughts (Herlofson, 2010). Hallucinations are perceptions generated without external stimuli, such as hearing voices that do not exist. Delusions are ideas that are not real, such as believing that the police stalk one, or that others can read your mind. Disturbed or disorganised thoughts might be manifested by incoherent speech or speech that is suddenly stopped.

Psychotic symptoms may be a part of several different conditions such as intoxications, mania, severe depression, dementia, infections, nutritional deficiencies, or brain tumours. If psychotic symptoms are not secondary to a physical illness the condition is called a "non-organic" psychosis. Non-organic psychoses may become recurring or manifest, resulting in chronic psychoses such as paranoid schizophrenia. It is believed that about one third of the patients having first episode psychotic symptoms will develop schizophrenia.

Psychosis is diagnosed using a clinical interview. The most commonly used criteria are the ones presented in the Diagnostic and Statistical Manual of Mental Disorders (DSM) version IV, published by the American Psychiatric Association or in World Health Organization's International Classification of Diseases (ICD-10). No clinical test is specific for psychosis, but it is important to detect organic and treatable conditions like tumours or nutritional deficiencies. Therefore, laboratory tests and computed tomography X-ray (CT) scans of the brain are routinely used to exclude such conditions. Also, electroencephalography (EEG) is commonly used as a routine examination in psychiatric wards.

Degree of severity

- ☐ Risk of premature death
- ☑ Risk of permanent illness or damage, or reduced quality of life
- ☐ Risk of disability and health-related quality of life

2b Prevalence and incidence of the disease/disorder

It is commonly assumed that 15-20 individuals per year, in a population of 100,000, are diagnosed with psychotic illness, and eight to ten of them with schizophrenia. Schizophrenia is thus the most common psychotic disorder. These figures would mean that there are about 225-300 new patients per year, in the Region Västra Götaland, half of them with schizophrenia.

In the regional VEGA database, there were 6,462 registered visits at the psychiatric emergency wards in Göteborg, in year 2011. Among these visits, a diagnosis of psychotic symptoms was used at 686 occasions, of which 413 for the first time. There were 567 hospital admissions due to psychotic symptoms.

2c **Present diagnostic tool of the disease/disorder in the outpatient setting/ in-patient setting.**

EEG is performed at the Neurophysiology Department at the Sahlgrenska University Hospital. The procedure takes about an hour. A brain-CT scan is an x-ray scan performed locally at the Imaging Department at Sahlgrenska University Hospital Mölndal. It takes approximately 20 minutes.

2d **Number of patients per year who undergo current diagnostic examination regimen?**

Approximately 90 patients per year undergo EEG as a diagnostic tool in first episode psychosis. The use of EEG as a routine examination differs between different psychiatric wards at the Sahlgrenska University Hospital.

2e **The normal pathway of a patient through the health care system**

Patients with psychotic symptoms may either turn directly to psychiatric care through the emergency department, or be referred to a specialist clinic through primary care centres. Also, patients may be referred from other hospital wards if other symptoms were initially more pronounced, e.g. substance abuse or depression.

2f **Actual wait time in days for medical assessment**

Waiting time for EEG for admitted patients is usually about a week. For brain-CT it is usually one or two days. In case of emergency, a brain-CT scan can be performed within half an hour.

Present Health Technology

3a Name/description of the health technology at issue

EEG is a useful tool in epileptology. Other specific activities in the EEG are distinctive for wakefulness and the different sleep stages.

The EEG records the regional and summed variations of electrical fields of the brain originating from a subset of excitatory neurons, the pyramidal cells, in the cerebral cortex. If presented as time-voltage graphs the displayed waveforms, rhythms and solitary events are shown with an extremely large inter-individual variability, age-dependent development during childhood, variability due to wakefulness or depth of sleep and with reactivity to many CNS-active drugs and external stimuli.

The EEG can record the spontaneous activity of the cerebrum or as averaged responses to external stimuli. In the clinical setting, the evaluation of the EEG recording of the spontaneous activity from the individual patient is based on visual pattern recognition of qualitative features in a graphical time-voltage presentation, here called standard EEG (sEEG). The quantitative information in recorded spontaneous activity can be analyzed with computerized methods such as spectral analysis and correlation tests, here called quantitative EEG (qEEG). However, the enormous variability of the recorded activity in EEG has defied any clinically used computerized diagnostic analysis for the individual patient. qEEG are frequently used in research to find group differences between patient groups or healthy controls, but has no diagnostic value for the individual patient. Averaged responses to external stimuli, such as evoked potentials, event-related responses and cognitive responses as P300, gives latencies from the stimuli to the response and the voltage amplitude of the response. Stimulated EEG is not clinically used to detect specific features of the cerebral activity in psychiatric patients.

Galderisi and Mucci, 2009) systematically reviewed the usefulness of sEEG, increased qEEG slow waves, and reduction of P300 amplitude for improval of schizophrenia diagnostics. For sEEG, no meta-analysis could be conducted due to lack of reliable quantification methods in the included studies. Analyses of qEEG of delta or theta increase, revealed a significant effect on data heterogeneity for both delta and theta bands, with a much higher effect size in chronic patients than in first episode patients. Medication effects were significant for the theta band, but unclear since the findings for drug-naive and drug-free subjects were in different directions. A meta-analysis for P300 reduction showed an effect size of 0.93, with all studies pointing in the same direction. It was concluded that, although good candidates, the examined indices are not ready yet for improvement of present clinical diagnostic standards of schizophrenia.

3b The work group's understanding of the potential value of the health technology

For psychotic patients, it is crucial that the initiation of treatment is not delayed, since early treatment has long-term impact on the prognosis. Adequate efforts during the early years enable prevention, or reduction of harmful effects of biological, cognitive, and psychosocial kind. The patients' conditions may otherwise deteriorate markedly during the first two to five years (Regionalt vårdprogram, 2009).

The aim is to quickly achieve remission from the psychotic symptoms. Thus, in order to establish a correct diagnosis and prevent disability and development of a chronic disease it would be valuable to have an objective method, not based on observations or interviews. For diagnostic purposes, as a complement to clinical evaluation, EEG

registration is often used for patients with first episode psychotic symptoms. Although, EEG is routinely and traditionally used as a medical technology for these patients, there seems to be an absence of literature that evaluates the diagnostic accuracy of EEG in patients with first episode of psychosis.
There are descriptions of specific EEG-patterns among patients with chronic psychosis, particularly schizophrenia, in comparison with healthy controls. These patterns do not seem to be of diagnostic value in patients with first episode psychotic symptoms. In clinical practice at this hospital, no recordable electrical cerebral activity that is unique for first episode psychosis or chronic psychosis has been detected with EEG. Our clinical impression is that EEG is only of value in patients with history suspicious of temporal lobe seizures or acute encephalitis.

3c **The central question for the current HTA project in one sentence**

Does EEG contribute to a correct diagnosis of psychotic illness, or to exclusion of other cerebral disease, in patients with first episode psychotic symptoms of psychosis, compared to clinical evaluation (including routine laboratory tests) and/or CT/MRI?

3d **PICO** (P= Patients, I= Intervention, C= Comparison, O=Outcome)

P = Adult patients (>16 years) with first episode psychotic symptoms (without other specific symptomatology requiring separate examination).

I= Routine EEG scan (spontaneous brain activity, not "evoked potentials") with visual analysis.

C1 = Clinical diagnosis according to e.g. DSM-IV, ICD, or structured interview.
C2 = CT (with x-ray)/MRI.

O = Primary outcome: sensitivity/specificity for:

O1: Psychotic illness with duration of at least one month.

O2: Other pathology of organic origin (tumour, encephalitis, atrophy etc.).

Secondary outcomes:

- Mortality
- Quality of Life (QoL)
- Functional impairment
- Morbidity
- Complications to EEG

3e **Key words**

EEG, psychosis, diagnosis
EEG, psykos, diagnos

4 Search strategy, study selection and references – appendix 3

(Search strategy, Eligibility criteria, Selection process – flow diagram, References)
During December, 2011, the librarians (AL, TS) performed searches in PubMed, EMBASE, PsycInfo, the Cochrane Library, and a number of HTA-databases. Reference lists of relevant articles were also scrutinized for additional references. A total of 1,104 articles were identified after removal of duplicates, of which 1,039 abstracts were excluded by the librians. After having been read in full text, another 44 articles were excluded by the librarians. Twenty-one articles were sent to the work group for assessment. Three of these articles are included in the report, although they only partially fulfilled the PICO criteria, but still contributed with some information on diagnostic performance of EEG and CT. The appraisal of articles is based on the Swedish version (SBU) of QUADAS regarding diagnostic accuracy studies.
Search strategies, eligibility criteria and a graphic presentation of the selection process are accounted for in Appendix 3. The literature searches and exclusion of abstracts were done by the two librarians in consultation with the HTA-centre and the work group.

5a Describe briefly the present knowledge of the health technology

The optimal study design to evaluate the diagnostic accuracy of EEG among patients with first episode of psychosis would be a cross-sectional study where patients are examined with EEG and followed with clinical instruments for up to one month, during which a diagnosis of psychosis may be established or rejected. This design would allow for calculation of sensitivity and specificity for EEG in diagnosing first event psychosis. However, no such study could be located (PICO 1) in the literature searches. Neither could we find any published comparisons between EEG and CT in this patient group (PICO 2).
No studies were found assessing the specified secondary outcomes.

There is an abundance of articles describing EEG-patterns among patients with psychosis, particularly schizophrenia, in comparison with healthy controls. One systematic review of such studies has been further commented on at the end of section 3a, but it was not included among the critically appraised articles, since the design of the studies was not in agreement with the PICO and could not evaluate diagnostic accuracy (Galdersisi and Mucci, 2009).

The three included articles are not presented in tables but summarized below:

Small *et al* (1983) is a cohort study of moderate quality comprising 1,494 adults who were hospitalized in a psychiatric clinic in the US between 1965 and 1972. Admission EEG recordings were done in all patients. Among these patients, 759 received a primary diagnosis of schizophrenia, according to DSM-I and II classification of psychiatric illness. All cases were subsequently re-diagnosed with Feighner *et al.* (1972) criteria of psychiatric illness. If the Feighner criteria are considered as reference standard, the diagnostic accuracy of EEG for psychosis can be estimated at a sensitivity of 38% and a specificity of 51%.

Gschwandtner *et al.,* (2009) is a Swiss study of moderate quality, comprising three cohorts; patients with first episode psychosis (n=31), at-risk mental state patients (ARMS) defined by genetic risk, psychopathological and psychosocial changes

(n=42) and healthy controls (n=35). The main result is that transition to psychosis for ARMS patients can be predicted with increased specificity (from 59% to 73%) if EEG is added to a clinical symptom rating scale, while sensitivity was unchanged (82%). Data on patients with first episode psychosis, the group of interest for the HTA-report, were very scarce; a frequency of 23% EEG abnormalities was presented in comparison with 11% for healthy controls. ARMS patients showed significantly more EEG abnormalities than healthy controls (36% vs. 11%).

Batista *et al.,* (1995) is a cross-sectional diagnostic study, of low quality, with the main objective to search for regional blood flow abnormalities by means of single photon emission computer tomography, in adolescents from Cuba with early schizophrenia (duration 0,5 +/-0,3 years). EEG and CT were complementary tools. EEG abnormalities were noted in 12 out of 15 patients. Positive CT findings were present in two patients; cortical atrophy, and dilatation of ventricles, both of clinical significance.

From adjacent literature, summarized above, there is no support for EEG as a method to diagnose psychosis, or to detect an organic etiology to psychotic symptoms, in patients with first episode of psychotic symptoms. Very low quality of evidence (GRADE ⊕○○○).

5b **Outcome tables – appendix 1**

The literature search derived three publications. None of these publications completely fulfilled the PICO criteria, but contributed with some data to elucidate the EEG findings in first episode psychosis patients. No estimates of the pre-defined outcomes could be retrieved and presented. Instead the three articles are summarized in section 5a.

5c **Excluded articles – appendix 2**

5d **Ongoing research?**

A search in Clinicaltrials.gov (2012-02-17) using the words *(psychosis*OR *psychoses*OR *psychotic*OR *schizophrenia*OR schizophrenic) AND *(electroencephalography*OR e*lectroencephalogram*OR *EEG)*AND *(first*OR *early*OR *early-onset)*, identified 56 studies. None of these registered trials fulfilled the PICO criteria.

6 **Which medical societies or health authorities recommend the health technology?**

- ☐ **The National Board of Health and Welfare**
- ☐ **Medical societies**
- ☑ **Other health authority:**

Regionalt vårdprogram 2009, Other references, Appendix 3
http://intraprimgbg.vgregion.se/upload/ZRoot/20091030143614749.pdf

Ethical aspects

7 Ethical consequences

Since EEG is a non-invasive investigation, it is not considered harmful. However, patients have to be transported to another hospital and there is a risk for delay in starting treatment. Other patient groups would benefit from having increased access to neurophysiological investigations if EEG was not performed routinely in patients with first-episode psychosis.

Organisation

8a When can this new health technology be put into practice?

Standard EEG with visual analysis is already used in clinical practice at the Sahlgrenska University Hospital in Göteborg.
Stimulated EEG, P300, is not clinically used to detect specific features of the cerebral activity in psychiatric patients.

8b Is this technology used in other hospitals in Region Västra Götaland of Sweden?

All psychiatric clinics in VGR, except Falköping Hospital, have resources to perform EEG in patients with first episode psychosis and EEG is occasionally performed for patients with first episode psychosis.

8c According to the work group, will there be any consequences for personnel?

Increased demand in personnel resources or changed priorities will be required if EEG is to be used as a standard screening technology for all patients with first episode psychotic symptoms. If the method is to be discontinued, personnel will be available for other prioritized groups.

8d Will there be any consequences for other clinics or supporting functions at the hospital or in the whole Region Västra Götaland of Sweden?

Patient referrals within VGR will not be affected by any change in utilization of EEG.

Economy

9 Present costs of currently used technologies

The cost of performing electroencephalography for one patient at Sahlgrenska University Hospital, Göteborg is about 200 €. Thus, the annual cost is estimated to 18,000 €. Cost for transportation between hospitals is not included.

Unanswered Questions

10a Important gaps in scientific knowledge?

There is no literature that properly evaluates the diagnostic accuracy of EEG in patients with first episode of psychosis.

10b Is there any interest in your own clinic/research group/organisation to start studies/trials within the research field at issue?

The work group does not consider further diagnostic studies on routine EEG motivated for patients with first episode psychotic patients. However, it would be of interest to find new predictors for the progression of early psychotic symptoms, based on modern technologies.

Utlåtande och sammanfattande bedömning från Kvalitetssäkringsgruppen

EEG som ett diagnostiskt verktyg vid förstagångsinsjuknande i psykos

Metod och målgrupp:
Elektroencefalografi (EEG) har länge ingått i den diagnostiska utredningen av patienter med förstagångsinsjuknande i psykotiska symtom. Psykoser diagnostiseras genom kliniska intervjuer och det finns inget specifikt kliniskt test. Det är viktigt att kunna detektera eventuella bakomliggande organiska, behandlingsbara tillstånd såsom tumörer och bristtillstånd som kan ge psykotiska symptom. För att utesluta sådana tillstånd används rutinmässigt datortomografi röntgen (CT) eller magnetkameraundersökning (MRI). EEG används ibland vid utredningen av psykotiska patienter.

Frågeställning:
Kan EEG bidra till korrekt diagnostik av psykotisk sjukdom, eller till uteslutande av annan cerebral sjukdom, hos patienter med förstagångsinsjuknande i psykotiska symtom, i jämförelse med klinisk utvärdering och/eller neuroradiologisk undersökning?

PICO: (Patient, Intervention, Comparison, Outcome)

P = Vuxna (>16 år) med förstagångsinsjuknande i psykotiska symtom (utan annan specifik symtomatologi som kräver separat utredning).
I = Rutin EEG (spontan hjärnaktivitet, ej "evoked potentials") med visuell analys.
C_1 = Klinisk diagnos enligt tex. DSM-IV, ICD, eller strukturerad intervju.
C_2= CT/MRI
O = Primärt utfall: sensitivitet/specificitet för:
O_1: Psykotisk sjukdom med minst en månads duration.
O_2: Annan patologi av organisk genes (tumör, encefalit, atrofi, etc.).

Sekundära utfall: Mortalitet, Livskvalitet, Funktionsnedsättning, Morbiditet, Komplikationer till EEG.

Evidensläge för studerad patientnytta:
Det finns rikligt med litteratur som beskriver ospecifika EEG fynd hos psykospatienter, särskilt bland schizofrena. Det finns ingen litteratur där den diagnostiska tillförlitligheten av EEG har utvärderats bland patienter med förstagångsinsjuknande i psykotiska symtom.
Litteratursökningarna resulterade i tre publikationer av låg till medelhög kvalitet, som endast delvis uppfyllde PICO kriterierna, men som bidrog med viktig information. Dessa studier hade inkluderat liknande patientgrupper, men EEG uppvisade oacceptabelt låg diagnostisk säkerhet. Det finns inget stöd för EEG som diagnosmetod vid psykotisk sjukdom, eller för att utesluta annan cerebral sjukdom av organisk genes, hos patienter med förstagångsinsjuknande i psykotiska symtom.
Otillräckligt vetenskapligt underlag (GRADE ⊕○○○).

Etiska aspekter:
Eftersom EEG är en icke-invasiv undersökning anses den vara harmlös. Undersökningen är förknippad med vissa kostnader och resursanvändningen kan fördröja tillgänglighet till neurofysiologiska undersökningar för andra patientgrupper.

Ekonomiska aspekter
Kostnaden för en EEG undersökning på Sahlgrenska Universitetssjukhuset är ca 1800 SEK. Den årliga kostnaden har uppskattats till 160 000 SEK.

Sammanfattning och slutsats

EEG har använts som tilläggsundersökning hos patienter med förstagångsinsjuknande i psykotiska symtom. Den föreliggande rapporten visar att diagnostiska studier saknas, och närliggande litteratur indikerar inte att EEG har en diagnostisk potential vid psykossjukdom. Det finns inget stöd för EEG som diagnosmetod vid psykisk sjukdom, eller för uteslutande av annan cerebral sjukdom av organisk genes, hos patienter med förstagångsinsjuknande i psykotiska symtom. Otillräckligt vetenskapligt underlag (GRADE ⊕○○○).

HTA-kvalitetssäkringsgruppen har ett uppdrag att yttra sig över genomförda HTA i Västra Götalandsregionen. Yttrandet skall innefatta sammanfattning av frågeställning, samlat evidensläge, patientnytta, risker samt ekonomiska och etiska aspekter för den studerande teknologin.

Projektet har pågått under perioden 2011-12-06—2012-04-25.
Sista uppdatering av artikelsökning december 2011.

För HTA-kvalitetssäkringsgruppen 2012-04-25

Christina Bergh
Ordförande

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Statement from the HTA-centrum of Region Västra Götaland, Sweden

EEG as a diagnostic tool in patients with first episode psychosis

Method and patient category:
Electroencephalography (EEG) has since long, been included in the diagnostic work-up for patients with first episode psychosis. Psychosis is diagnosed by means of a clinical interview and there is no specific clinical test. It is however, important to detect organic and treatable conditions like tumours and nutritional deficiencies which may present with psychotic symptoms. To exclude such conditions computed tomography (CT) scans or magnetic resonance imaging (MRI) of the brain and laboratory tests are routinely used. EEG is sometimes used as a complement in the diagnostic work-up of psychotic patients.

Question at issue:
Does EEG contribute to a correct diagnosis of psychotic illness or to exclusion of other cerebral disease, in patients with first episode of psychotic symptoms, compared to clinical evaluation and/or neuroradiologic examinations?

PICO (Patient, Intervention, Comparison, Outcome)

P = Adult patients (>16 years) with first episode psychotic symptoms (without other specific symptomatology requiring separate examination).
I = Routine EEG scan (spontaneous brain activity, not "evoked potentials") with visual analysis.
$\mathbf{C_1}$ = Clinical diagnosis according to e.g. DSM-IV, ICD, or structured interview.
$\mathbf{C_2}$ = CT (with x-ray)/MRI.
O = Primary outcome: sensitivity/specificity for:
O_1: Psychotic illness with duration of at least one month.
O_2: Other pathology of organic origin (tumour, encephalitis, atrophy etc.).

Secondary outcomes: Mortality, Quality of Life, Functional impairment, Morbidity, Complications to EEG.

Level of evidence:
Abundant literature describes non-specific EEG-patterns among psychosis patients, particularly in patients with schizophrenia. There are no studies that properly evaluate the diagnostic accuracy of EEG in patients with first episode of psychosis. The literature search located three publications of low to moderate quality that only partially fulfilled the PICO criteria, but still contributed with some information on diagnostic performance of EEG and CT. Examining similar patient groups, these studies illustrated very poor diagnostic accuracy of EEG.
Conclusion: There is no support for EEG as a diagnostic method for psychosis, or to detect an organic etiology to psychotic symptoms, in patients with first episode of psychotic symptoms. Very low quality of evidence (GRADE ⊕◯◯◯).

Ethical aspects:
Since EEG is a non-invasive investigation, it is considered harmless. However, there is an associated cost and the use of these resources may delay access to neurophysiological investigations for other patient groups.

Economical aspects:
The present cost of one EEG at the Sahlgrenska University Hospital is about 200 €. The annual cost could is estimated to 18,000 €.

Concluding remarks:

EEG has traditionally been used as a complementary investigation in patients with first episode of psychotic symptoms. The present evaluation shows that there is an absence of diagnostic studies. Related literature indicates no diagnostic potential for EEG in first episode psychosis. There is no support for EEG as a diagnostic method for psychosis, or to detect an organic etiology to psychotic symptoms, in patients with first episode of psychotic symptoms. Very low quality of evidence (GRADE ⊕◯◯◯).

On behalf of the HTA-centrum, Region Västra Götaland, Sweden

Göteborg, Sweden, 2012-04-25

Christina Bergh, Professor, MD
Head of HTA-centrum of Region Västra Götaland, Sweden

The Regional Health Technology Assessment Centre (HTA-centrum) of Region Västra Götaland, Sweden (VGR) has the task to make statements on HTA reports carried out in VGR. The statement should summarise the question at issue, level of evidence, efficacy, risks, and economical and ethical aspects of the particular health technology that has been assessed in the report.

The HTA was accomplished during the period of 2011-12-06 –2012-04-25.
Last search updated in December 2011.

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Appendix 2 Excluded articles

Study (author, publication year)	Reason for exclusion
Clementz 1994	Wrong design and intervention (qEEG)
Gattaz 1992	Wrong design. EEG evaluated in not only first-episode schizophrenic patients and healthy controls.
Kanemoto 2001	Wrong population; epilepsia (and psychosis) was an inclusion criterum.
Khodayari-Rostamabad 2010	Wrong population; inclusion of patients with major depression disorder and chronic schizophrenia.
Manchanda 2003	Wrong design. Evaluates prognosis based on EEG.
Manchanda, 2005a	Wrong design. 2-yr follow-up of Manchanda 2003
Manchanda 2005b	Wrong design. 2-year follow-up, prediction of recovery based on EEG among other factors.
Manchanda 2008	Wrong design. 3-yr follow-up of Manchanda 2003
Norman 2007	Wrong design. Compares EEG between first-episode schizophrenia, relatives and controls.
Poulin 2008	Wrong design and intervention. REM sleep EEG evaluated in first episode schizphrenia and healthy controls.
Reeves 2003	Wrong intervention (qEEG)
Sarkar 2010	Wrong population and intervention: Not first-episode patients, sleep EEG was used.
Galderisi 2009	Wrong population, systematic review (commented upon)
Merlo 1998	Wrong design. EEG was evaluated in first-episode schizophrenic patients for prediction of early or late response to medical treatment.
Sponheim 2003	Wrong intervention (qEEG)
Sponheim 1994	Wrong Design. Compares EEG between first-episode schizophrenia, chronic schizophrenia and controls. Included in SR by Galderisi et al 2009
Zimmerman 2010	Wrong population (ARMS), intervention (qEEG) and design.
Sponheim 2001	Wrong intervention (qEEG), and design. No numbers to extract on EEG.

Appendix 3, Search strategy, study selection and references
Project: EEG as a diagnostic tool for patients with first episode psychosis

Question(s) at issue:
Does EEG contribute to a correct diagnosis of psychotic illness, or to exclusion of other cerebral disease, in patients with first episode psychotic symptoms of psychosis, compared to clinical evaluation and/or CT/MRI?

PICO: (Patient, Intervention, Comparison, Outcome)

P = Adult patients (>16 years) with first episode psychotic symptoms (without other specific symptomatology requiring separate examination).

I= Routine EEG scan (spontaneous brain activity, not "evoked potentials") with visual analysis.

C1 = Clinical diagnosis according to e.g. DSM-IV, ICD, or structured interview.
C2 = CT (with x-ray)/MRI.

O = Primary outcome: sensitivity/specificity for:
O1: Psychotic illness with duration of at least one month.

O2: Other pathology of organic origin (tumour, encephalitis, atrophy etc.).

Secondary outcomes:
- Mortality
- Quality of Life (QoL)
- Functional impairment
- Morbidity
- Complications to EEG

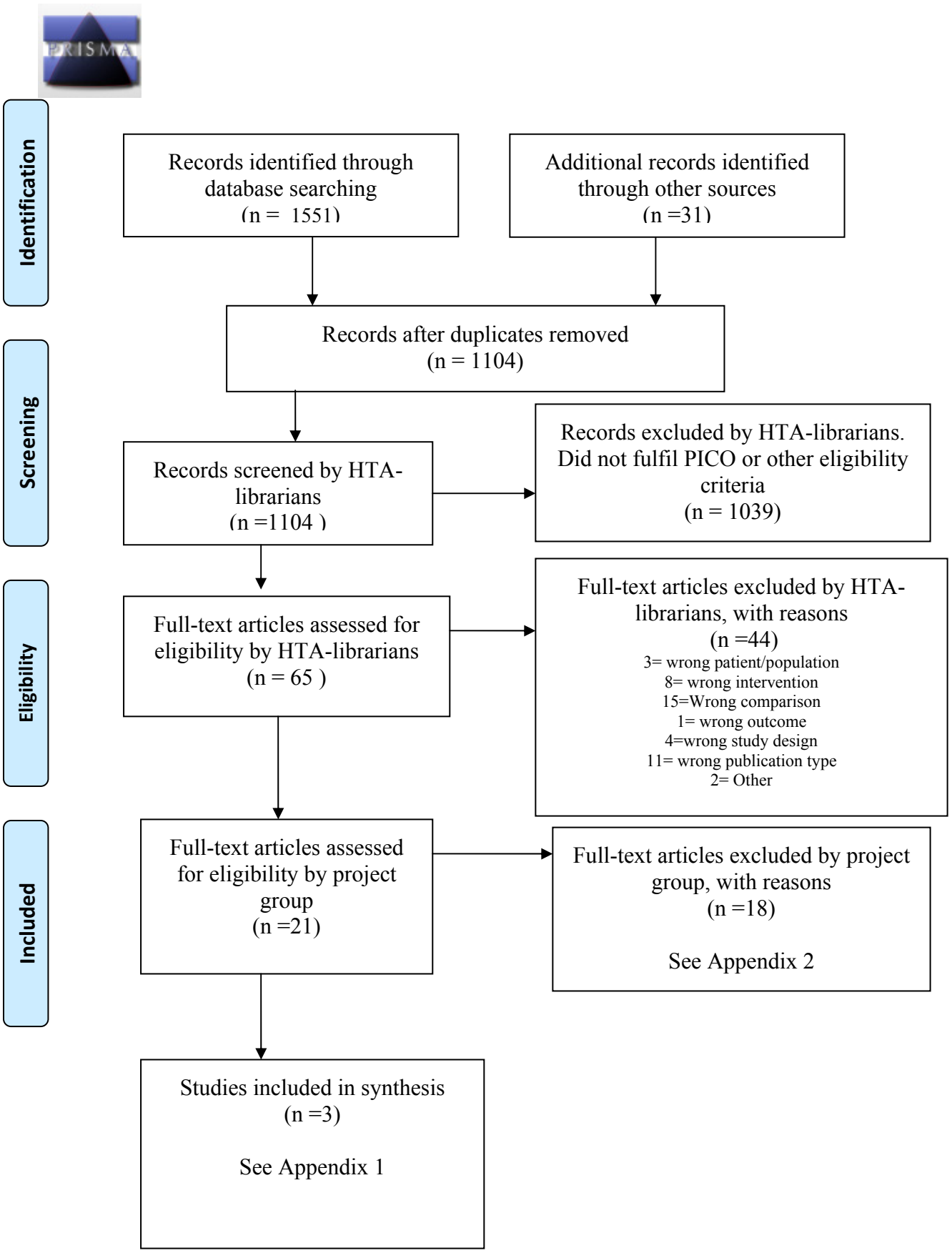
Eligibility criteria

Study design:
- Studies with some kind of control group
- ≥ 10 patient in the EEG-group
- Systematic reviews

- No review articles

Language:
English, Swedish, Norwegian, Danish

Selection process – flow diagram



Search strategies

Database: PubMed
Date: 2011-12-16
No of results: 576

Search	Query	Items found
#31	**Search #24 NOT #26 Limits: English, Danish, Norwegian, Swedish**	**576**
#27	Search #24 NOT #26	642
#26	Search Editorial[ptyp] OR Letter[ptyp] OR Comment[ptyp] OR case reports[ptyp]	2530651
#24	Search #19 AND #16 AND #23	718
#23	Search first[tiab] OR early[tiab] OR early-onset[tiab]	2156879
#19	Search #18 OR #7	137326
#18	Search psychosis[tiab] OR psychoses[tiab] OR psychotic[tiab] OR schizophrenia[tiab] OR schizophrenic[tiab]	103052
#16	Search Electroencephalography[Mesh] OR Electroencephalography[tiab] OR Electroencephalogram[tiab] OR EEG[tiab]	124001
#7	Search "Schizophrenia and Disorders with Psychotic Features"[Mesh]	104995

Database: EMBASE (OVID SP)
Date: 2011-12-16
No of results: 587

#	Searches	Results
1	exp electroencephalography/	79476
2	(Electroencephalography or Electroencephalogram or EEG).ti,ab.	65789
3	1 or 2	113965
4	exp psychosis/	180285
5	(psychosis or psychoses or psychotic or schizophrenia or schizophrenic).ti,ab.	123461
6	4 or 5	197623
7	exp electroencephalogram/	59818
8	3 or 7	141753
9	(first or early or early-onset).ti,ab.	2412247
10	6 and 8 and 9	1093
11	**limit 10 to (human and embase and (danish or english or norwegian or swedish) and (article or "review"))**	**587**

Database: PsycInfo (ProQuest)
Date: 2011-12-16
No of results: 297

Set	Search	Results
S9	**S7 AND S6 AND S3 Limits: Record type: Conference Proceedings, Journal Article Language: 4 languages searched Danish, English, Norwegian, Swedish**	**297**
S8	S7 AND S6 AND S3	392
S7	S5 OR S4	134439
S6	all(first OR early OR early-onset)	490886
S5	all(psychosis OR psychoses OR psychotic OR schizophrenia OR schizophrenic)	130987
S4	su EXACT.EXPLODE("Schizoaffective Disorder" OR "Schizoaffective Disorder") OR su EXACT.EXPLODE ("Borderline States" OR "Psychosis" OR "Paranoid Schizophrenia")	24736
S3	Su EXACT.EXPLODE ("Electroencephalography") OR all ((electroencephalography OR electroencephalogram)) OR all(EEG)	31283

Database: The Cochrane Library
Date: 2011-12-16
No of results: 79
Cochrane reviews 3
Clinical trials 76

ID	Search	Hits
#1	(psychosis OR psychoses OR psychotic OR schizophrenia OR schizophrenic):ti,ab,kw	9840
#2	(Electroencephalography OR Electroencephalogram OR EEG):ti,ab,kw	5194
#3	MeSH descriptor Electroencephalography explode all trees	3549
#4	MeSH descriptor Schizophrenia and Disorders with Psychotic Features explode all trees	4991
#5	(#1 OR #4)	9847
#6	(#2 OR #3)	5236
#7	(#5 AND #6)	233
#8	(first OR early OR early-onset):ti,ab,kw	201523
#9	**(#7 AND #8)**	**79**

Database: CRD
Date: 2011-12-16
No of results: 11

ID	Search	Hits
#1	electroencephalography OR electroencephalogram OR EEG	
#2	psychosis OR psychoses OR psychotic OR schizophrenia OR schizophrenic	
#3	**#1 AND #2**	**11**

The web-sites of **SBU, Kunnskapssenteret** and **Sundhedsstyrelsen** were visited 2011-12-16
Nothing relevant to the question at issue was found

Reference lists
13 results

Reference lists

Included studies:

Batista, J. F., M. C. Galiano, et al. (1995). "Brain single-photon emission tomography with technetium-99m hexamethylpropylene amine oxime in adolescents with initial-stage schizophrenia." Eur J Nucl Med **22**(11): 1274-7.

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Small, J. G., V. Milstein, et al. (1984). "Electroencephalographic findings in relation to diagnostic constructs in psychiatry." Biol Psychiatry **19**(4): 471-87.

Excluded studies:

Clementz, B. A., S. R. Sponheim, et al. (1994). "Resting EEG in first-episode schizophrenia patients, bipolar psychosis patients, and their first-degree relatives." Psychophysiology 31(5): 486-494.

Galderisi, S., A. Mucci, et al. (2009). "Evidence-based medicine and electrophysiology in schizophrenia." Clin EEG Neurosci 40(2): 62-77.

Gattaz, W. F., S. Mayer, et al. (1992). "Hypofrontality on topographic EEG in schizophrenia. Correlations with neuropsychological and psychopathological parameters." Eur Arch Psychiatry Clin Neurosci 241(6): 328-32.

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Khodayari-Rostamabad, A., J. P. Reilly, et al. "Diagnosis of psychiatric disorders using EEG data and employing a statistical decision model." Conf Proc IEEE Eng Med Biol Soc 2010: 4006-9.

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Norman, R. M., R. Manchanda, et al. (2007). "The significance of family history in first-episode schizophrenia spectrum disorder." J Nerv Ment Dis 195(10): 846-52.

Poulin, J., E. Stip, et al. (2008). "REM sleep EEG spectral analysis in patients with first-episode schizophrenia." Journal of Psychiatric Research 42(13): 1086-1093.

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Sarkar, S., M. Z. Katshu, et al. (2010) "Slow wave sleep deficits as a trait marker in patients with schizophrenia." Schizophr Res 124(1-3): 127-33.

Sponheim, S. R., B. A. Clementz, et al. (1994). "Resting EEG in first-episode and chronic schizophrenia." Psychophysiology 31(1): 37-43.

Sponheim, S. R., W. G. Iacono, et al. (2001). "Using biological indices to classify schizophrenia and other psychotic patients." Schizophr Res 50(3): 139-50

Sponheim, S. R., W. G. Iacono, et al. (2003). "Sensitivity and specificity of select biological indices in characterizing psychotic patients and their relatives." Schizophrenia Research 63(1-2): 27-38.

Zimmermann, R., U. Gschwandtner, et al. (2010). "EEG spectral power and negative symptoms in at-risk individuals predict transition to psychosis." Schizophr Res 123(2-3): 208-16.

Other references:

Berger H. Ueber das Elektrenkephalogramm des Menschen. Arch Psychiatr Nervenkr 1929;87:527-570.

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Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med. 2009 Jul 21;6(7):e1000097.

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Available from:
http://www.sahlgrenska.se/upload/SU/HTA-centrum/Hj%c3%a4lpmedel%20under%20projektet/B04_Granskningsmall%20f%c3%b6r%20diagnostiska%20studier%20QUADAS.doc

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http://intraprimgbg.vgregion.se/upload/ZRoot/20091030143614749.pdf

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Vårdprogram för utredning och behandling av patienter med schizofrenisjukdom och näraliggande tillstånd. Kompetenscentrum för Schizofreni. Psykossektionen, Sahlgrenska University Hospital/Psychiatry. Version 1.1, p. 6. 2005. Accessed 2012-04-03. Available from:
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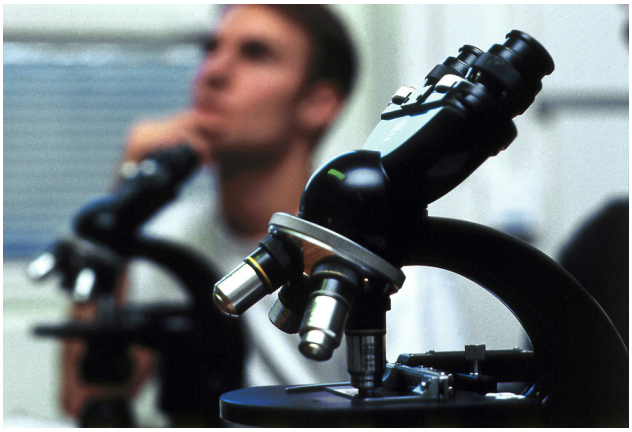
Region Västra Götaland, HTA-centre

Health Technology Assessment
Regional activity-based HTA



HTA

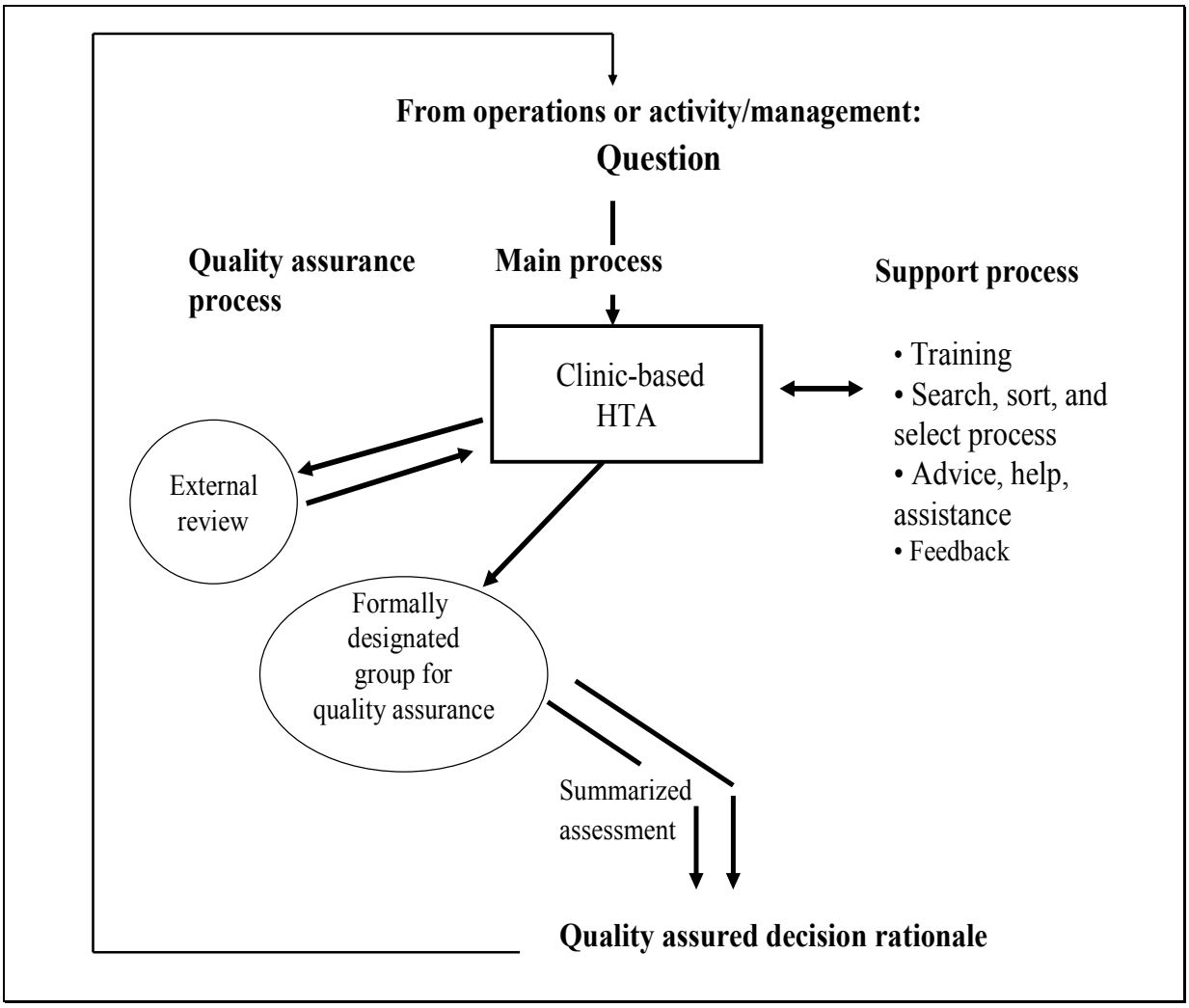
Health technology assessment (HTA) is the systematic evaluation of properties, effects, and/or impacts of health care technologies, i.e. interventions that may be used to promote health, to prevent, diagnose or treat disease or for rehabilitation or long-term care. It may address the direct, intended consequences of technologies as well as their indirect, unintended consequences. Its main purpose is to inform technology-related policymaking in health care.

To evaluate the quality of evidence the Centre of Health Technology Assessment in Region Västra Götaland is currently using the GRADE system, which has been developed by a widely representative group of international guideline developers. According to GRADE the level of evidence is graded in four categories:

High quality of evidence	= (GRADE⊕⊕⊕⊕)
Moderate quality of evidence	= (GRADE ⊕⊕⊕O)
Low quality of evidence	= (GRADE ⊕⊕OO)
Very low quality of evidence	= (GRADE ⊕OOO)

In GRADE there is also a system to rate the strength of recommendation of a technology as either “strong” or “weak”. This is presently not used by the Centre of Health Technology Assessment in Region Västra Götaland. However, the assessments still offer some guidance to decision makers in the health care system. If the level of evidence of a positive effect of a technology is of high or moderate quality it most probably qualifies to be used in routine medical care. If the level of evidence is of low quality the use of the technology may be motivated provided there is an acceptable balance between benefits and risks, cost-effectiveness and ethical considerations. Promising technologies, but a very low quality of evidence, motivate further research but should not be used in everyday routine clinical work.

Christina Bergh, Professor, MD.
Head of HTA-centre


From operations or activity/management:
Question
Quality assurance process
Main process
Support process
Clinic-based HTA
• Training
• Search, sort, and select process
• Advice, help, assistance
• Feedback
External review
Formally designated group for quality assurance
Summarized assessment
Quality assured decision rationale

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