Malocclusions and Orthodontic Treatment in a Health Perspective

A Systematic Review



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Summary and Conclusions of the SBU Report on:

Malocclusions and Orthodontic Treatment in a Health Perspective

A Systematic Review

October 2005

Project Group:

Anna-Karin Holm
(Chair)

Susanna Axelsson
(Project Director)

Lars Bondemark

Viveca Brattström

Lars-Åke Marké

Bengt Mohlin

Gunnar Paulin

Terttu Pietilä

Åsa Svensson

(Project Assistant)

Ken Hansen

Scientific Reviewers:

Maija T Laine-Alava Arild Stenvik
Maurits Persson Ingvar Westerberg

Report: Malocclusions and Orthodontic Treatment in a Health Perspective Type: Systematic Review • ISBN: 91-85413-06-2 • ISSN: 1400-1403

Report no: 176 • Publishing year: 2005

SBU's conclusions

Co	nsequences of Untreated Malocclusions
	When the patient has a large overjet and the upper lip does not protect the front teeth, the incidence of trauma to the anterior teeth of the maxilla is higher (Evidence Grade 3).
	If the maxillary canines are incorrectly positioned in the jaw bone before their eruption, the risk that they will damage the roots of the front teeth as they emerge increases (ectopic eruption) (Evidence Grade 3).
	The prevalence of caries in people with occlusal deviations is the same as in those whose bite is normal (Evidence Grade 3).
	A correlation between moderate malocclusions and negative effects on the self-image of 11–14-year-olds has not been found (Evidence Grade 3).
	Adults with untreated malocclusions express more dissatisfaction with the appearance of their bite than adults without malocclusions (Evidence Grade 3).
	Scientific evidence is insufficient for conclusions on a correlation between specific untreated malocclusions and symptomatic temporomandibular joint disorders.
Pr	iority Indices for Orthodontic Treatment
	Scientific evidence for conclusions concerning the validity (that is, if a tool measures what it is intended to measure) of morphological priority indices (indices based on deviations in the bite and the dental arch from an established norm) are lacking.

☐ Scientific evidence is insufficient for conclusions concerning the validity of esthetic indices from a societal perspective.						
 The Decision to Undergo Orthodontic Treatment □ Orthodontic treatment is initiated in most cases by the general dental practitioner (Evidence Grade 3). 						
☐ The appearance of the teeth is the patients' most important reason for seeking orthodontic treatment (Evidence Grade 3).						
Morphologic Stability and Patient Satisfaction 5 years or more after Orthodontic Treatment						
☐ Treatment of crowding aligns the dental arch. However, the length and width of the mandibular dental arch gradually shorten in the long term, and crowding of the anterior teeth can reoccur. This condition cannot be predicted at the individual level (Evidence Grade 3).						
☐ Treatment of large overjet with fixed appliances according to Herbst¹ normalizes the occlusion. Relapses occur, but cannot be predicted at the individual level (Evidence Grade 3).						
☐ Scientific evidence is insufficient for conclusions on stability after treatment of other morphological discrepancies.						
☐ Scientific evidence is insufficient for conclusions on patient satisfaction in the long term (at least 5 years) after the conclusion of orthodontic treatment.						

 $^{^{\}scriptscriptstyle 1}$ Braces that hold the mandible in a forward position via a telescoping mechanism.

Ris	ks and Complications of Orthodontic Treatment
	Orthodontic treatment with fixed appliances, as well as the application of separators and new arch wires, is painful in the beginning (Evidence Grade 2).
	Orthodontic treatment can cause a reduction of the bone level between the teeth; the scope of this reduction, however, is so small that it lacks clinical relevance (Evidence Grade 2).
	Stainless steel wires that were attached to the back of the anterior teeth of the mandible by etching (retainer) have not been found to give rise to caries in a 5-year perspective (Evidence Grade 3).
	Orthodontic treatment with fixed appliances that contain nickel have not been found to increase the incidence of nickel sensitivity (Evidence Grade 3).
	Root resorptions ² up to one-third of the length of the root occur in 11–28 percent of the patients who have undergone orthodontic treatment (Evidence Grade 3). Information on the long-term consequences of this is lacking.
	Teeth with incomplete root development are resorbed to a lesser degree than fully developed teeth (Evidence Grade 3).
	Side effects such as temporomandibular joint disorders (TMD) have not been demonstrated in connection with orthodontic treatment (Evidence Grade 3).
	Scientific evidence is insufficient for conclusions on what effect a suspension of treatment has on root resorptions during ongoing orthodontic treatment.

² Gradual dissolution of tooth roots.

SBU's Review of Praxis

- ☐ The share of orthodontic treatments that were begun per age group was on average 27 percent and varied between 21 percent and 39 percent for 20 of 21 county councils.
- ☐ The number of specialists per 10,000 children was on average 1.12 and varied between 0.82 and 1.68.

Fact box

Criteria for Evidence Grading SBU's Conclusions

Evidentiary Value and Evidence Grade

Evidentiary value concerns the scientific quality of a single study and its ability to answer a specific question in a reliable manner.

Evidence Grade expresses the combined scientific evidence for a conclusion, that is, how many high-quality studies support the conclusion.

Evidence Grade 1 - Strong scientific Evidence

A conclusion that has been assigned Evidence Grade 1 is supported by at least two studies of high evidentiary value in the body of scientific evidence. If there are also studies that seem to argue against the conclusion, however, the evidence grade may be lower.

Evidence Grade 2 – Moderately Strong Scientific Evidence

A conclusion that has been assigned Evidence Grade 2 is supported by at least one study with high evidentiary value and two studies with mediumhigh evidentiary value in the body of scientific evidence. If there are studies that appear to argue against the conclusion, however, the evidence grade may be lower.

Evidence Grade 3 - Limited Scientific Evidence

A conclusion with Evidence Grade 3 is supported by at least two studies of medium-high evidentiary value in the body of scientific evidence. If there are studies that speak against the conclusion, the scientific evidence may be considered insufficient or contradictory.

Insufficient Scientific Evidence

When no studies fulfill the demands for evidentiary value, the scientific evidence is considered insufficient to draw any conclusions.

Contradictory Scientific Evidence

When there are different studies that have the same evidentiary value but whose results diverge, the scientific evidence is considered contradictory and no conclusions can be drawn.



SBU Summary

Background

The subject field of orthodontics comprises the development and growth of the face, the jaws, and the bite. Diagnostics, preventive treatment, and treatment of congenital or acquired malocclusions are included. The term "orthodontics" comes from the Greek word "orto", which means straight, and "odous", which means tooth. The straightening of irregular teeth, or orthodontic treatment, require the use of fixed or removable orthodontic appliances to affect the jaws and their growth and to move teeth that are incorrectly positioned so that the dental arch better agrees with the "ideal" or "normal" occlusion.

Development of the Bite

The development and growth of the teeth and the jaws are essentially governed by genetic factors. During occlusal development, external factors can also have significance; for example, prolonged sucking on the fingers or use of a pacifier can cause a displacement of the teeth. The occlusion develops under a long period, from the time the first deciduous teeth emerge at 6–8 months of age to when all 28 permanent teeth have erupted at 12–14 years of age. At the same time, the jaws grow to create space, and the face increases in length. After the face ceases to grow, occlusal relationships continue to undergo minor alterations.

Malocclusions

In most cases, occlusal development results in a well-functioning and stable occlusion. In some people, however, the relation between the jaws is not what is considered to be a "normal" occlusion. The direction of tooth eruption can deviate or lack of space can arise, for example, if the jaws are small compared to the width of the teeth. These morphological discrepancies or malocclusions often have a genetic background, but there can also be other causes (see Chapter 1).

When occlusal development is unfavorable, it can be interrupted or influenced, either through preventive or through interceptive measures. An example of a preventive measure is to interrupt a sucking habit before an occlusal deviation is established. Interceptive measures are performed in the primary occlusion or the early mixed dentition and means that an unfavorable occlusal development is interrupted and that occlusal development can thereafter continue in an unobstructed manner for the individual. If malocclusions were established in the permanent occlusion, corrective treatment may be necessary. Such treatment requires removable or fixed orthodontic appliances, otherwise known as braces. Treatment with removable appliances can be done by a general dental practitioner while corrective treatment with fixed appliances is usually performed by specialists in orthodontics and requires a treatment period of 1–2 years.

Indications for Orthodontic Treatment

Most orthodontic treatment aims to move teeth into a more "normal" occlusion. Some malocclusions require a combination of surgical and orthodontic treatment. The evaluation of the need for orthodontic treatment is a delicate task. Because the "ideal" or normal bite has come to be regarded as a norm for how occlusions should look, insignificant discrepancies can also be experienced

as something that must be remedied, while in actuality they are merely an expression of individual variations in appearance. Children often desire orthodontic treatment, and their parents perhaps even more so for their child. Dentists in general practice with the patient and the parents, play the most important role in the decision process.

Orthodontic treatment usually begins at 12–14 years of age, the time in life when appearance begins to be important. The reason for beginning treatment at this age, among others, is that all permanent teeth have erupted. The individual has also reached an age when she or he is considered to have achieved autonomy and is able to desire or decline orthodontic treatment.

The organization of Orthodontic Care

Treatment need is determined by the general dental pratice team at the regular dental checkups. Certain malocclusions can be remedied with simple measures, but when the malocclusions are more complicated, the dentist may consult an orthodontic specialist. In each county council, specialists – employees of the county council or specialists in private practice – work as consultants and perform treatments. If orthodontic treatment is indicated, it can be done by a general dental practitioner under the supervision of a specialist. It is more usual, however, for the patient to be referred to specialists. The distribution between these two methods of working varies in the different county councils.

In Sweden, orthodontic treatment, subject to a means test, is part of the general dental care for children and adolescent that is free of charge for patients up to 20 years of age. Orthodontic treatment can also be performed on adults, but it is not free of charge. The actual costs for treating one patient orthodontically in Sweden can, depending on the scope of treatment and degree of severity, be as much as SEK 30,000 (USD 3,750).

Issues Addressed in the Report

- What risks or consequences does orthodontic treatment versus lack of orthodontic treatment have for the teeth and surrounding tissues, the function of the masticatory system (speech, masticatory function, jaw function), and the person's psychosocial health?
- Who initiates or decides on treatment the patient, the parents, or health-care providers?
- What devices (e.g., indices) are there to assess treatment need, and how have these indices been validated?
- Is the outcome of orthodontic treatment long lasting (at least 5 years after retention³ has ended)?
- What differences in costs can be calculated for different treatment strategies?

Qualifications and Definitions

This report is limited to clinical studies on humans and to the treatment of children and adolescents. Treatment that includes orthognathic surgery (surgical treatment of severe malocclusions) has been excluded. All types of studies, quantitative as well as qualitatative, that concern assessment of the risks of no treatment and different aspects of treatment decisions were included.

Method

Literature Search

Small work groups, working together with an information specialist sought relevant literature interactively in the Medline database from the year 1966 and forward. The reference lists obtained in the database search contained articles and abstracts and were assessed by at least two people. The full texts of the articles

³ Measures to retain the teeth in their new position.

that at least one of the assessors felt were relevant to the issues being addressed by the project were ordered. The literature was subsequently supplemented with relevant articles that had been identified in the reference lists of the articles found in the primary search, in documentation from consensus meetings, and from reference lists in review articles.

Inclusion Criteria

To be included in the next step of the review process, the purpose of the study had to be to answer one or more of the questions posed in this review, and the study had to fulfill the predetermined inclusion criteria.

The studies that were included contained healthy patients with malocclusions in which the teeth and the jaws were involved. Studies on the risk of caries and periodontitis as well as on psychological factors and factors concerning appearance were included only from 1980 forward. The reason for this late date is that it was previously common to cement metal bands on all teeth to anchor the orthodontic appliances, which may have had a great influence on the risk of caries and periodontitis. Now practice is to place orthodontic bands only on the molars. The evaluation was limited to literature on the treatment of children and adolescents. Adults could be included in studies that followed up treatment and investigated risks of not receiving treatment. For evaluation of treatment outcome after at least 5 years, randomized, controlled trials (RCTs) - prospective and retrospective comparative studies – were reviewed.

Review and Grading of the Evidentiary Value of the Studies

All types of studies were included in the review since the project's issues concerned the risks and the outcomes of measures such as the consequences of lack of treatment. The scientific efforts made to measure and compare results in a systematized manner were judged for each study. Each study was assigned an evidentiary value that summarized how reliably the study answered the questions it proposed to investigate. The evidentiary value of a study was rated as high, medium-high, or low.

Setting the Evidence Grade of the Conclusions

The scientific evidence for each summarized conclusion – the evidence grade – was rated as strong, moderately strong, limited, or insufficient depending on how many studies with different evidentiary values support the conclusion (see Fact Box 1). That the effect of a measure has insufficient or contradictory scientific support – or that scientific evidence is completely lacking – does not necessarily mean that the measure is ineffective or should not be used. If the result concerns a risk or side effect, it is not possible to guarantee in a similar manner as for other risks or side effects with a higher evidentiary value that such an outcome will not occur when the scientific evidence is insufficient or contradictory. Lack of completely clear, scientifically verified conclusions often means that additional clinical studies are needed.

Review of Praxis

Since up-to-date information on the scope of orthodontic care was lacking, the project was begun by sending a questionnaire to all county councils. The results showed that slightly more than a quarter of children and adolescents in Sweden had undergone orthodontic treatment and that variations between the county councils were significant. The annual costs per child in the ages 3–19 years (all children in Sweden) was on average 324 SEK (USD 40) with a variation between SEK 243 and SEK 456

(USD 30–57). The number of children per age group in whom treatment was initiated varied in most county councils between 21 and 39 percent, but one county council reported 86 percent. The number of specialists per 10,000 children varied between 0.82 and 1.68 with an average of 1.12.

Results of the Literature Search

Consequences of Untreated Malocclusions

Untreated deviations from a normal bite have, among other factors, been linked to a deterioration in oral health, oral function, or both in priority indices. This, together with risks of dissatisfaction with particularly visible malocclusions, were judged as important factors that motivate treatment. Untreated discrepancies were associated with higher risks of trauma, caries, and periodontitis; a deterioration in speech or masticatory function; temporomandibular joint disorders; and psychosocial problems.

Teeth that are incorrectly positioned in the jaw bone before eruption and whose direction of growth is thereby incorrect could cause defects on the roots of neighboring teeth. If this is not discovered in time, large sections of the roots of the adjacent teeth may be resorbed.

The literature review shows that there is a correlation between an incorrect positioning of the maxillary canines and resorption injuries on the roots of the lateral incisor teeth.

The scientific literature also reveals that there is a correlation between the incidence of a large overjet – where the upper lip does not protect the front teeth – and trauma to these teeth. Larger overjets are associated with more severe injuries. The results show that caries is not more common in individuals with untreated malocclusions compared with individuals with a normal occlusion. Scientific evidence is insufficient for conclusions on a correlation between periodontitis and untreated malocclusions. Scientific evidence is also insufficient for conclusions on whether

there is a correlation between untreated malocclusions and speech disorders and between untreated malocclusions and a deterioration in masticatory function.

In studies with a follow-up time of 2–5 years, people with untreated malocclusions such as a crossbite, crowding, or a large overjet have a somewhat higher frequency of signs and symptoms of temporomandibular disorders than people who have undergone treatment or who have a normal bite. But studies with longer observation times have not found a higher frequency of temporomandibular disorders among people with untreated malocclusions.

The most common reason for children to seek orthodontic treatment – or for their parents to seek treatment for their children – is dissatisfaction with the appearance of the bite, esthetics. One relevant question in connection with this is to what extent untreated malocclusions contribute to psychological problems, a

deterioration in self-esteem, or simply a deep dissatisfaction with one's appearance.

Studies where psychological tests were used have not found that untreated malocclusions negatively affect self-image in youth. Adults with malocclusions can be more dissatisfied with the appearance of their bite than those who have received orthodontic treatment or have a normal bite.

Priority Indices for Orthodontic Treatment

The wishes and needs of orthodontic patients can be satisfied as little as can those of patients in other areas of health care, since economic resources are limited. In their attempts to limit orthodontic care, county councils use different priority indices as instruments to define what care is free of charge for the patient. Such priority indices are used in many countries, independent of the reimbursement system. The components in the indices that are used can be divided into two categories:

- a grading or valuation of the morphological occlusal deviation⁴.
- an esthetic valuation of the occlusion and the appearance of the teeth.

The different priority indices therefore contain either morphological or esthetic components or a combination of these. The morphological priority indices build to a large extent on a traditional perception of the risks of malocclusions, and on the view that the more a deviation differs from a given norm (the ideal occlusion), the greater are the risks of future injuries or of pain or discomfort.

Scientific evidence to assess the validity of morphological indices is lacking. Esthetic indices were validated, but the scientific evidence was insufficient to allow any conclusions to be drawn on their validity from a societal perspective.

The Decision to Undergo Orthodontic Treatment

A decision for orthodontic treatment in countries where all or part of the costs are covered by public funds is a process of many steps. The potential patient, is often influenced by friends and parents, by the referrer (who usually is a general dental practitioner), and by the orthodontic specialist. All are influenced by esthetic conceptions, the scope of the occlusal deviation, the selection principles used (index), and the economic preconditions.

A review of the scientific evidence shows that it usually is the general dental practitioner who initiates treatment and that esthetic reasons are why the patient or the parents of the patient are seeking treatment.

⁴ Deviations of the occlusion and the dental arch from an established norm.

Morphologic Stability and Patient Satisfaction Evaluated 5 years or more after Orthodontic Treatment

Orthodontic treatment is traditionally divided into preventive, interceptive, and corrective measures. The goal of orthodontic treatment is to foster a normal or so-called "ideal" occlusion that is morphologically stable and esthetically and functionally well adjusted. While preventive or interceptive measures are performed early in life, for example, to halt an unfavorable occlusal development, corrective measures are required for the treatment of established malocclusions. Since corrective measures are frequent, extensive, and expensive, it is important to evaluate whether they are also stable in the long term.

Immediately following completed treatment, the results are usually clinically satisfactory. Long-term studies show that during a follow-up time of at least 5 years, the length and width of the mandibular dental arch shortens. Subsequent new crowding often arises in the incisor area but the extent of the changes in the mandibular dental arch and the extent of the degree of crowding which may reappear cannot be predicted on an individual basis. There is limited scientific evidence to show that treatment of a large overjet with fixed appliances according to the principles of Herbst normalizes the occlusion in the long term. It is, however, usual to find that the treatment outcome deteriorates in a number of ways after removal of retention. Whether these changes cause patients to be dissatisfied, or are indications that new treatment is necessary, is not reported.

There are few long-term follow-ups of stability (more than 5 years) after corrective and after interceptive treatment. No conclusions can be drawn on whether interceptive treatment reduces the need for later treatment.

Only a few studies on patient satisfaction after orthodontic treatment were identified, and only one of these fulfill the criteria of a 5-year follow-up. Conclusions on patient satisfaction in the long term are therefore not possible.

Risks and Complications of Orthodontic Treatment

In orthodontic treatment, forces from the appliances cause a resorption of the surrounding bone on the pressure side while new bone is formed on the tension side. In this way, the teeth can be moved to the desired position. During treatment, certain undesirable side effects that involve the teeth and the surrounding tissues can arise. Examples of such are caries, periodontitis, or hypersensitive reactions to the materials in the appliances. Pain can occur in the initial stage of tooth movement. Root resorptions and temporomandibular disorders are also possible complications.

The literature review shows that orthodontic treatment does not result in more caries than in an untreated control group, even though fixed appliances can cause plaque to accumulate. Stainless steel wire that has been bonded to the lingual surface of mandibular incisor teeth of the mandible was not found to be a cause of caries in a 5-year perspective. Orthodontic treatment can cause a reduction in the bone level between the teeth; the scope of this reduction, however, is so small that it lacks clinical relevance.

Tooth movement causes an inflammation in the tissues that surround the teeth, which can cause pain and soreness during different phases of treatment. The occurrence of pain has mainly been studied using a questionnaire. The results show that the pain begins 4 hours after the appliance has been placed, increases up to 24 hours after placement, and thereafter diminishes gradually until the seventh day. There are no clear results concerning gender differences or whether the pain is associated with age.

Orthodontic appliances usually consist of stainless steel containing chromium and nickel. Some superelastic arch wires can contain up to 50 percent nickel. Hypersensitivity to nickel is unusual and occurs more often in women than in men. A strong association between hypersensitivity to nickel and ear piercing has also been found. The literature review, however, has not shown that orthodontic treatment causes a hypersensitivity to nickel nor makes an established hypersensitivity worse. One study found

that none of the individuals who received orthodontic treatment before they pierced their ears became hypersensitive to nickel.

Root resorption is one common complication of orthodontic treatment (see Figure 1). The literature review shows that resorption occurs or is suspected to occur on at least one tooth in almost all patients. Moderate root resorption, up to one-third of the length of the root, occurs on at least one tooth of 11-28 percent of the patients. Information on the long-term consequences of this is lacking. Whether former trauma to teeth increases the risk of root resorption in subsequent orthodontic treatment has been inconclusively studied and no conclusions can be drawn, nor concerning which individuals and which teeth or groups of teeth are most subjected to root resorption. The same concerns the importance of the length of treatment and the extent of tooth movement. The need of recurrent intraoral X-ray examinations during treatment with fixed appliances, to decide whether treatment should be suspended in the case of root resorptions, was not evaluated in any study with high or medium-high evidentiary value.

The studies in the review showed that subjective findings of masticatory dysfunction (primarily pain during mandibular movements) do not seem to be more common or more severe after orthodontic treatment in the short or in the long term. Neither was an increase in the incidence of tenderness upon muscle palpation or of reduction in range of mandibular movement nor a difference in the incidence of unspecified clicking and/or popping from the temporomandibular joints after orthodontic treatment.

Economic Aspects

In the literature search, no study that met the inclusion criteria and that analyzed and compared the practical costs of orthodontic treatment was found. One model analysis that has been done is described in Chapter 3 of this report. It shows that the costs for fixed and removable appliances in the treatment of overjet (postnormal occlusion, Figure 1.3 in Chapter 1) do not differ signi-





Figure 1 Moderate root resorptions, less than one-third of the length of the root.

ficantly. Removable appliances suggest a lower cost, but since a large proportion of these patients will change to fixed appliances, the costs for those who began their treatment with fixed appliances are lower than if treatment began with removable appliances. The calculation example shows that it is important that the most suitable method for the patient is chosen from the beginning.

Ethical Aspects

The ethical aspects concerning the indices that are used in the assessment and in decisions on orthodontic treatment should be observed. Not one of the morphological treatment indices that are used in Sweden has been validated. An index value that indicates treatment need must have a solid scientific rationale. Otherwise, there is a risk that patients and health-care providers will be influenced in their decision process by alleged risks of future ill health without scientific evidence.

This review of practice found large differences in care between the different county councils. An important ethical issue is to analyze the background and the causes of these differences.

In Sweden, orthodontic care treatmentis provided free of charge to children and adolescents up to 20 years of age as part of the general children and adolescent dental care if an evaluation has determined that the patient has a treatment need. It is often initiated when the patient is 12-14 years old since the child or adolescent is then considered to have autonomy and be able to make her or his own decision. At this age, appearance is important, and esthetic indications are common. Treatment more or less always produces an outcome that the patient is satisfied with. Each patient should naturally participate in the treatment decision, but the question of whether measures that are only motivated by esthetic or cosmetic reasons should be funded at public expense needs to be discussed. The large differences between the county councils indicates that policies are different in different parts of the country - which is unsatisfied from an ethical point of view.

Future Research

This literature review shows that the need for future studies is great. There are some areas in which the review group found the need to be particularly large. Examples include indications and assessments (decisions) for orthodontic treatment, follow-up of

treatment results, the correct timing for orthodontic treatment, analysis of the factors that underlie the variations in practice between different county councils, the significance of malocclusions for quality of life, and last but not least, studies in the field of health economics.

The morphological indices that are used in the county councils today in the selection of patients for orthodontic treatment have not been validated, and consequently, no one knows if the indices measure what they are intended to measure. Primarily, an evaluation should be made of whether an index is the best aid in the decision process or if there are other ways to distribute resources. Another pressing area is to study how orthodontic specialists can best meet society's growing interest in appearance. To determine to what degree malocclusions can affect an individual's quality of life, the instrument used to select patients needs to be more than simply an index of dental and facial morphology.

Well-designed multicenter studies where the stability of the occlusion following treatment of different morphological deviations is evaluated in a long-term perspective (at least 5 years) would supply valuable knowledge, as would studies on the effect of interceptive treatment.

Today, studies that show how orthodontic resources are distributed in and between the county councils, as well as health economic studies that reflect and compare costs for different orthodontic treatments, are lacking.

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The Swedish Government has given SBU the following responsibilities:

- SBU shall evaluate the methods used in health care by systematically and critically reviewing the scientific evidence in the field.
- SBU's assessments shall cover the medical aspects and the ethical, social, and economic consequences of disseminating and applying medical and dental technologies.
- SBU's assessments shall be compiled, presented, and disseminated in such a way that all affected parties have access to the information.
- SBU shall contribute, through informational and educational initiatives, toward ensuring that the knowledge gained is used to rationally utilize available resources in health care.
- SBU shall draw on national and international experience and research findings in the field and shall serve as a focal point for health technology assessment in Sweden. This effort shall be managed in a way that secures success and respect for the organization, both domestically, and internationally.

Malocclusions and orthodontic treatment in a health perspective

The SBU report, "Malocclusions and orthodontic treatment in a health perspective", is based on a systematic and critical review of the scientific literature. It is one of a series of scientific reports published by SBU (The Swedish Council on Technology Assessment in Health Care)

The Summary and Conclusions of the report, presented in this booklet, have been approved by the SBU Board of Directors and the Scientific Advisory Committee.