

CLINICAL REPORT

Basal Cell Carcinoma is as Common as the Sum of all Other Cancers: Implications for Treatment Capacity

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Reliable estimates of disease incidence are fundamental to planning future healthcare services. However, in many countries registration of basal cell carcinoma (BCC) is often non-existent. This study examines how many BCC treatments were carried out in Denmark in 2013. The Danish Cancer Registry and the Danish Pathology Registry were used to examine how many BCC treatments were registered, and a test sample was taken from Bispebjerg Hospital to examine the number treated but not registered. The study showed that 21.7% of BCC treatments were performed solely on a clinical diagnosis. Furthermore, some records are inadequate in relation to BCC registration, as BCCs treated are 3 times the number of individuals in the Danish Cancer Registry, and there are nearly as many BCCs as the sum of all other cancers. The increasing BCC incidence will result in difficulties in ensuring treatment capacity. *Key words: BCC; treatment capacity; incidence; cancer registry.*

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The incidence of basal cell carcinoma (BCC) has been increasing rapidly over recent decades, both in Denmark and worldwide (1–6). There is a logarithmic relationship between age and BCC development (7), and with an ever-increasing elderly population the incidence of BCC is expected to continue to rise in the future. Although mortality from BCC is low, the increasing incidence is responsible for considerable morbidity, thus placing a huge burden on healthcare services (1, 2, 5, 8, 9). In addition, a study has shown that skin cancer is among the most costly of all cancer types to treat (10). Hence, in addition to classifying types of cancer by number of deaths, the financial impact of treatment could be used to prioritize different malignancies, whereby skin cancer will rank much higher. The rapidly increasing incidence of BCC also entails a problem in relation to treatment capacity and thus in order to organize and optimize the future healthcare system it is fundamental to have reliable

estimates of BCC incidence, by identifying how many BCCs are currently treated.

In many countries the registration of BCC is non-existent and only a few cancer registries routinely collect data on BCC. Consequently, BCC is usually excluded from statistics (1, 4) making it difficult to estimate its incidence. In the UK registration is equally inadequate, yet some sources indicate that the number of BCCs treated is between 53,000 and 91,200 annually (11, 12), corresponding to 87–145 per 100,000 individuals each year (13).

In Denmark BCC is registered in 2 nationwide population-based registries: the Danish Cancer Registry and the Danish Pathology Registry (Patobank). These records also have shortcomings, and BCC is still usually excluded from statistics.

In light of the above, the aim of the present study is to examine how many BCC treatments were carried out in Denmark in 2013. The numbers provided in the Danish Cancer Registry and Patobank, and corresponding numbers of actual treatments according to medical records were used, counting both treatments based on a histologically verified sample and those based solely on a clinical diagnosis (1, 14, 15).

METHODS

The 2 Danish registries that carry out cancer registration, which was made mandatory in Denmark by administrative order in 1987 (16) are, as mentioned, the Danish Cancer Registry and Patobank. The Danish Cancer Registry is a nationwide registry that, since 1943, has registered all new cancer patients. Reporting is mandatory for public as well as private healthcare services, and additionally Patobank acts as a data source for the Danish Cancer Registry. The registry contains information on type of cancer and anatomical site. The purpose of the registry is to collect and process data in order to generate statistics on cancer in Denmark, to provide information for the planning of the Danish healthcare services for health professionals, for administrative, economic and political decisions, and to provide a basis for research, for which purpose it is used intensively. In the Danish Cancer Registry only the first incidence of BCC is recorded. After 1978 the coding process is programmed not to accept more than one tumour within the same histology group within one organ, even if the tumours are located in different regions (the skin is considered as a single organ). A special code indicates whether a person has multiple skin cancers (1, 14–17). Patobank is a nationwide registry that, since 1978, has recorded all histological diagnoses including BCC. Patobank

contains data on all pathology tests from all pathology departments and clinics in Denmark. The purpose of Patobank is to function as a daily tool for diagnostics and quality control and, as mentioned, to be a data source for the Cancer Registry. All registrations are the subject of error tracing and all diagnostic statements are approved by a pathologist (1, 18, 19). Data from the Danish Cancer Registry and Patobank for the present study were retrieved on 26 January 2015.

All diagnoses in Patobank and in the Danish Cancer Registry are linked to a unique personal 10-digit personal identification number (CPR), which is assigned to all Danish citizens. The CPR number ensures identification of the patient's test results across different registries and records, and was thus used as a key identifier.

To examine how many BCCs were treated without being registered, a test sample was taken from the Department of Dermatology at Bispebjerg Hospital from 2013. Thereby, the study moves from a national level to a more local level. Medical records for 2013 were reviewed for all patients with the diagnosis code of BCC (C440–C448) using World Health Organization (WHO) "International Statistical Classification of Diseases and Related Health Problems" (ICD-10). For the entire year of 2013 every visit to Bispebjerg Hospital was verified and every treatment of both histologically confirmed BCCs and BCCs treated based on a clinical diagnosis were reviewed. If the treatment occurred in 2013, but was based on a biopsy from 2012 the treatment was not included in the study. Conversely, if a biopsy was collected in 2013 and the treatment occurred in 2014, the tumour was included in the study. In this way a full year of treatments was included and the basis for a comparison with Patobank and the Danish Cancer Registry was established.

The development of the number of tumours and individuals with a BCC diagnosis from 1997 to 2013 and the difference between the different registries were analysed with linear regression.

RESULTS

In 2013, 12,018 patients were registered with BCC in the Danish Cancer Registry and 23,291 patients in Patobank. Thus, almost twice as many (194%) individuals were registered in Patobank as in the Danish Cancer Registry. Each individual in Patobank had a mean of 1.5 histologically verified BCCs in 2013, corresponding to 35,463 tumours.

Medical records for all patients treated for BCC at Bispebjerg Hospital in 2013 were reviewed. These covered 670 patients (315 men and 355 women) and 1,365 BCC treatments. Of these treatments 21.7% were performed based on a clinical diagnosis, while the remaining 78.3% were based on histology. The different treatment methods used included *inter alia* surgical excision, photodynamic therapy (PDT), radiation therapy and cryotherapy. A total of 1,326 of the BCC treatments in the test sample were found in Patobank. However, many BCC treatments were registered twice, or even up to 12 times, in Patobank, since, for example, both a biopsy and excision of the same tumour can appear. When adjusting for this multiple registration, only 82.2% of the BCC treatments in Bispebjerg Hospital in 2013 were found in Patobank (Table I). As the calcula-

Table I. Total number of tumours and individuals treated in 2013 according to the test sample and calculations for the entire country

Frame of reference	Sources	n (%)
Test sample – Bispebjerg Hospital	BCCs treated according to the medical records	1,365 (100 (ref))
	BCCs according to Patobank	1,326 (97.1)*
	BCCs according to Patobank adjusted for multiple registration	1,122 (82.2)*
Danish Cancer Registry	Patient with BCC in the Danish Cancer Registry	12,018 (100 (ref))
	BCCs according to Patobank	35,463 (295)
	BCCs according to Patobank adjusted for multiple registration	30,002** (250)
	Tumours treated according to the medical records	36,506** (304)

*Percentage of the 1,365 basal cell carcinomas (BCCs).

**Calculated based on review of medical records from Bispebjerg Hospital and the corresponding review of Patobank.

tions in Table I show, there are potentially 30,002 BCCs in Patobank after adjustment for multiple reporting, and, as mentioned, the number of BCCs actually treated is 36,506. Thus, when comparing these numbers with the number of patient in the Danish Cancer Registry 2.5 times and more than 3 times as many tumours are treated according to Patobank and the medical records, respectively.

According to the test sample and by including only the treatments of histologically verified BCCs, close to 80% occurred on the head or neck, approximately 14% occurred on the body, and 4.5% occurred on the extremities. When counting only the treatments performed based on a clinical diagnosis the majority occurred on the body (57%). By counting both the histologically verified treatments and the treatments carried out on clinical diagnosis the distribution is approximately 70% on the head or neck, 22% on the body, and 7% on the extremities (Table II).

As appears from Fig. 1 that the number of both BCC tumours and patients with BCC increased in both registries from 1997 to 2013 ($p < 0.001$). The difference between the Danish Cancer Registry (individuals) and Patobank (individuals) is significant from 2005 and onwards ($p = 0.012$). If the Danish Cancer Registry records all new patients with BCC, this necessarily

Table II. Localization on the body and its percentage distribution of basal cell carcinoma (BCC) identified in the test sample

Localization of BCC	Histologically verified treatments, %	Treatments based solely on clinical diagnosis, %	Histologically verified and treatments based on clinical diagnosis, %
Head and neck	79.1	27.2	70.3
Body	13.9	56.8	21.6
Upper and lower extremities	4.5	16.1	6.6
Several regions	2.5	–	1.5
In total	100	100	100

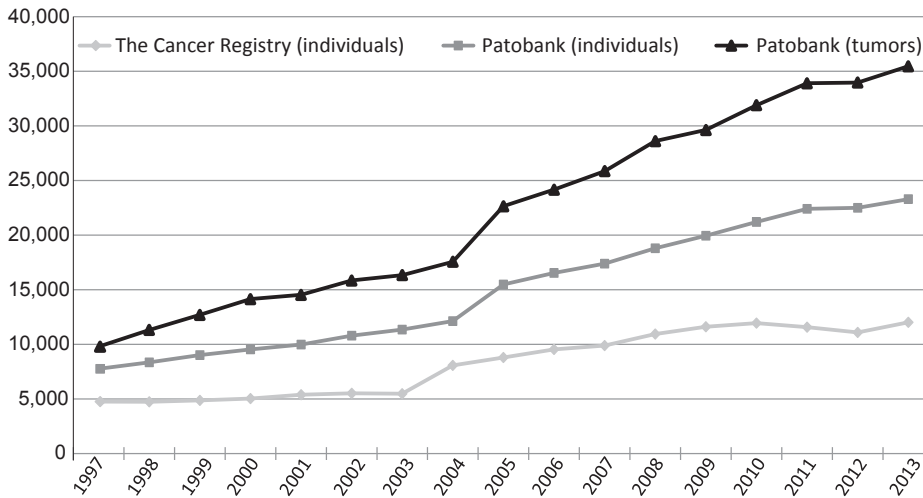


Fig. 1. Development of the number of tumours and individuals with a diagnosis of basal cell carcinoma from 1997 to 2013, illustrating that the difference between the different registries has increased throughout the years.

means that more and more people develop more and more BCCs. Equally, the difference between Patobank (tumours) and Patobank (individuals) increased significantly from 1997 to 2013 ($p < 0.001$), similarly illustrating that patients increasingly develop multiple BCCs. Moreover, the difference between the Danish Cancer Registry (individuals) and Patobank (tumours) increased significantly from 1997 to 2013 ($p = 0.035$). Overall, these findings show that the difference between the different registries, both with regard to the number of BCCs and the number of individuals with BCC, has not only increased in absolute terms, but also in relative terms. Similarly, the upper part of Table III specifies the large percentage increase from 1997 to 2013, both for individuals with BCCs and for the number of BCCs. The largest increase is for Patobank (tumours) with more than 3.5 times as many BCCs in 2013 as in 1997, while the smallest is seen for the Danish Cancer Registry with more 2.5 times as many patients with BCCs in 2013 as in 1997. The lower part of Table III shows that the difference between the registries increased from 1997 to 2013. With the Danish Cancer Registry as a benchmark, the number of individuals in Patobank was 163% in 1997, whereas in 2013 the difference had increased to 194%. Furthermore, in 1997 each individual in Patobank had a mean of 1.2 histologically verified BCC tumours, while this had increased to 1.5 in 2013 ($p < 0.001$). Overall, these results show that the

discrepancy between the reported numbers of BCCs between the 2 registries has increased over the years.

DISCUSSION

The present study shows that in 2013 nearly twice as many BCC patients were registered in Patobank as in the Danish Cancer Registry. In addition, each individual registered in Patobank had a mean of 1.5 histologically verified BCC tumours. After adjustment for multiple registration a total of 30,002 BCCs were registered in Patobank. However, based on the review of medical records it was estimated that 36,506 BCCs were actually treated in 2013. Hence, 3 times as many BCCs were treated as the number of individuals with BCC specified in the Danish Cancer Registry. Approximately 20% were treated based solely on a clinical diagnosis, which is higher than in a Dutch study (7%) examining the number of treated subsequent BCCs that were not histologically verified (20).

In 2013 there were 37,075 cases of all cancers combined, with the exception of BCCs (21). Comparing this number with the number of BCC treatments calculated in the present study (36,506) this corresponds to almost as many BCC cases as there are cases of the sum of all other cancers. It is plausible that the percentage that is treated solely on a clinical diagnosis will increase in the future, since, in addition to more people developing BCC, each patient also develops more and more BCCs, assuming that the increase will continue in the next 2 decades, as in the last 2 decades. Thus, BCC incidence will, in the near future, most likely be higher than that of the sum of all other cancers. Furthermore, the number of BCCs is equivalent to 650 BCC per 100,000 individuals each year. By comparison, if assuming the same rate per 100,000 individuals as in the Danish population, this corresponds to 416,631 BCC cases in the UK each year compared with the expected 53,000–91,200 (13). Table IV shows comparisons with some other countries.

Table III. Percentage difference in the number of tumours and individuals treated in 1997, 2005 and 2013 illustrating the discrepancy between the reported numbers of basal cell carcinomas according to the 2 registries

Source	1997	2005	2013
Danish Cancer Registry	100	185	253
Patobank (individuals)	100	200	300
Patobank (tumours)	100	231	362
Danish Cancer Registry	100	100	100
Patobank (individuals)	163	176	194
Patobank (tumours)	206	257	295

Table IV. The prevalence of basal cell carcinomas (BCCs) in different countries

Country	Number according to various available sources	Number according to calculations*	Total population in 2013, millions (13)
Denmark	–	36,506	5.6
UK	53,000–91,200 (11, 12)	416,631	64.1
Germany	160,000 (26)	524,042	80.6
The Netherlands	22,332–44,172 (27, 28)	109,227	16.8
Sweden	36,560 (29)	62,352	9.6

*Assuming the same rate of BCCs as in Denmark (650/100,000 individuals), the prevalence of BCCs in the listed countries are calculated based on the numbers in the first column.

BCC arises on areas exposed to the sun, and approximately 80% of BCCs are located on the head and neck (4, 5, 22). This is more or less consistent with the findings in the present study of the treatments performed based on histologically verification, which showed that close to 80% were located on the head or neck. As stated in the results section, when both the histologically verified tumours and the treatments carried out based on clinical diagnosis are included, 70% of the BCCs occur on the head or neck. The majority of BCCs treated solely on clinical diagnosis were on the body (56.8%). BCCs on the head or neck are most frequently nodular and solitary, while BCCs on the body are often superficial and there are more often multiple elements. Thus, BCCs on the body are, in general, easier to treat. The majority of individuals who had BCCs treated based on clinical diagnosis had currently or previously had other BCCs that were histologically verified.

Furthermore, the test sample showed that 20% of the treatments were recurrences of previous BCCs. However, the final figure is most likely much higher, since a tumour is registered to be a recurrence of a previous BCC only if this were specified in the patient's medical record or in Patobank. In relation to determining the number of tumours in a population this distinction is of importance, as the recurrent tumour will not be counted as a new tumour. In relation to treatment capacity, however, this distinction is not relevant.

If among the test sample there were BCC diagnoses in Patobank that had only been examined, but not treated, at Bispebjerg Hospital, this would nonetheless count as a single treatment in the estimate. However, if in addition to the examined BCC several other BCCs ended up being treated as well, the number of BCCs treated solely on a clinical diagnosis may have been even higher than the number stated in the present study.

In Fig. 1, which shows incidence trends over the years, a steep increase is seen between 2003 and 2004 for the Danish Cancer Registry. This is probably due to a shift from manual coding to mostly automatic coding and from paper forms to electronic forms. Similarly, there is a steep increase between 2004 and 2005 for Patobank. Despite the fact that the coverage of Patobank

is almost 100% today, partly because the registration is performed electronically and reporting of data from the public pathology departments has been nationwide from the mid-1990s, some private pathology specialists reported non-melanoma skin cancer data to the registry only from 2004 onwards (1, 18).

In a Danish report, which covers the modernization of the Danish Cancer Registry (17), it is stated that the Danish Cancer Registry is an incidence registry, which means that it only provides information about new cases of cancer (patients) within the past year. However, in order for this to be true, it should register every case within that year, even if it is within the same "organ", and not just new cases if the individual had never had skin cancer before. All histological samples are registered in Patobank. Thus, the data from Patobank has the disadvantage that there are numerous double registrations of the same tumour, for which excision material has been examined as well as pre-excision biopsy. This is problematic when used in relation to statements regarding number of tumours or diagnoses of a particular disease. Even though the BCC mortality rate is low, it is still highly relevant to obtain the correct number of treated BCCs as it is used in, for instance, allocation of resources. Moreover, numerous researchers use the Danish Cancer Registry as a source of numbers of tumours (1, 17, 23–25), but if the data do not reflect the actual number of BCC treatments, this could result in incorrect conclusions. It is not the intent of the present study to question the perfectly acceptable approach to treat BCCs based on the clinical picture and dermoscopy. The positive predictive value is very high with this approach and, as a consequence, preoperative biopsies are seldom needed, which benefits the patient. Rather, one of the intentions of this article is to make readers aware that there are some records that do not provide the full picture of BCC treatments and, from a research perspective, knowledge is lost. And with 650 BCC cases per 100,000 individuals each year and almost as many BCC cases as there are cases of the sum of all other cancers, which is also more than 3 times the number provided by the Danish Cancer Registry, it is clear that there is a need for this information to become known.

The unprecedented high number of BCCs additionally raises questions as to whether the healthcare system will be able to cope with this increasing workload and ensure treatment capacity without allocating more resources or changing treatment principles. In addition, new treatment methods may be required and may call for treatment centres that have all existing treatment modalities available. If BCC treatment is allocated solely to dermatologists, the risk of recurrences may be reduced, and it is likely that fewer false-positive tumours will be treated. However, this strategy is expensive for the healthcare system, taking the burden of the disease into consideration. Thus, specialized treatment centres need to be combined with other alternative approaches,

such as better training of GPs. In any case, it is vital to consider new treatment options in order to overcome the large and continuously growing quantity of BCCs.

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REFERENCES

- Birch-Johansen F, Jensen A, Mortensen L, Olesen AB, Kjær SK. Trends in the incidence of nonmelanoma skin cancer in Denmark 1978–2007: Rapid incidence increase among young Danish women. *Int J Cancer* 2010; 127: 2190–2198.
- Lomas A, Leonardi-Bee J, Bath-Hextall F. A systematic review of worldwide incidence of nonmelanoma skin cancer. *Br J Dermatol* 2012; 166: 1069–1080.
- Olesen AB, Hædersdal M, Wulf HC, Gniadecki R, Benfeldt E. [Growing challenges vs. improved therapies for skin cancer.] *Ugeskr Laeger* 2014; Jun 2, 176 (in Danish).
- Rubin AI, Chen EH, Ratner D. Basal-cell carcinoma. *N Engl J Med* 2005; 353: 2262–2269.
- Wong CSM, Strange RC, Lear JT. Basal cell carcinoma. *BMJ* 2003; 327: 794–798.
- World Health Organization. Ultraviolet radiation and the INTERSUN Programme – how common is skin cancer? [Cited 2015 Apr 29] Available from: <http://www.who.int/uv/faq/skincancer/en/index1.html>. 2010.
- Engholm G, Ferlay J, Christensen N, Johannesen TB, Khan S, Kötum JE, et al. NORDCAN: Cancer incidence, mortality, prevalence and survival in the Nordic countries, Version 6.1 (25.04.2014). Association of the Nordic Cancer Registries. Danish Cancer Society. [Cited 2015 Apr 29] Available from: <http://www.ancr.nu>. 2014.
- Bentzen J, Kjellberg J, Thorgaard C, Engholm G, Phillip A, Storm HH. Costs of illness for melanoma and nonmelanoma skin cancer in Denmark. *Eur J Cancer Prev* 2013; 22: 569–576.
- Roozeboom MH, Arits AHM, Nelemans PJ, Kelleners-Smeets NWJ. Overall treatment success after treatment of primary superficial basal cell carcinoma: a systematic review and meta-analysis of randomized and nonrandomized trials. *Br J Dermatol* 2012; 167: 733–756.
- Housman TS, Feldman SR, Williford PM, Fleischer Jr AB, Goldman ND, Acostamadiedo JM, et al. Skin cancer is among the most costly of all cancers to treat for the Medicare population. *J Am Acad Dermatol* 2003; 48: 425–429.
- Levell NJ, Igali L, Wright KA, Greenberg DC. Basal cell carcinoma epidemiology in the UK: the elephant in the room. *Clin Exp Dermatol* 2013; 38: 367–369.
- Bath-Hextall F, Leonardi-Bee J, Smith C, Meal A, Hubbard R. Trends in incidence of skin basal cell carcinoma. Additional evidence from a UK primary care database study. *Int J Cancer* 2007; 121: 2105–2108.
- The World Bank. Population, total. 2015. [Cited 2015 Apr 29] Available from: <http://data.worldbank.org/indicator/SP.POP.TOTL>.
- Gjerstorff ML. The Danish Cancer Registry. *Scand J Public Health* 2011; 39: 42–45.
- Storm HH, Lyng E, Østerlind A, Jensen OM. Multiple primary cancers in Denmark 1943–80; influence of possible underreporting and suggested risk factors. *Yale J Biol Med* 1986: 547–559.
- Storm HH, Michelsen EV, Clemmensen IH, Pihl J. The Danish Cancer Registry – history, content, quality and use. *Dan Med Bull* 1997; 44: 535–539.
- [The modernised Cancer Registry - method and quality Danish health and medicines authority.] 2009 [Cited 2015 Apr 29]; Available from: <http://www.ssi.dk/~media/Indhold/DK%20-%20dansk/Sundhedsdata%20og%20it/NSF/Registre/Cancerregisteret/Det%20moderniserede%20Cancerregister%20%20metode%20og%20kvalitet.aspx> (in Danish).
- Bjerregaard B, Larsen OB. The Danish Pathology Register. *Scand J Public Health* 2011; 39: 72–74.
- The Danish Registry of Pathology. [Cited 2015 Apr 29] Available from: <http://www.patobank.dk>. 2014 (in Danish).
- Flohil SC, Van Tiel S, Koljenovic S, Jaanen-van der Sanden G, Overbeek LIH, de Vries E, et al. Frequency of non-histologically diagnosed basal cell carcinomas in daily Dutch practice. *J Eur Acad Dermatol Venereol* 2013; 27: 907–911.
- Statens Serum Institut. The Cancer Registry. [Numbers and analysis.] *Cancerregistry* 2013. [Cited 2015 Apr 29]; Available from: <http://www.ssi.dk/~media/Indhold/DK%20-%20dansk/Sundhedsdata%20og%20it/NSF/Registre%20og%20kliniske%20databaser/Registre/Cancerregisteret/Cancerregisteret%202013.aspx> (in Danish).
- Bath-Hextall F, Perkins W, Bong J, Williams HC. Interventions for basal cell carcinoma of the skin. *Cochrane Database Syst Rev* 2007; 1.
- Carøe TK, Ebbenhøj NE, Wulf HC, Agner T. Occupational skin cancer may be underreported. *Dan Med J* 2013; 60: A4624.
- Carøe TK, Ebbenhøj NE, Wulf HC, Agner T. Recognized occupational skin cancer in Denmark – data from the last ten years. *Acta Derm Venereol* 2013; 93: 369–371.
- Lock-Andersen J, Drzewiecki KT, Wulf HC. Naevi as a risk factor for basal cell carcinoma in Caucasians: a Danish case-control study. *Acta Derm Venereol* 1999; 79: 314–319.
- Eisemann N, Waldmann A, Geller AC, Weinstock MA, Volkmer B, Greinert R, et al. Non-melanoma skin cancer incidence and impact of skin cancer screening on incidence. *J Invest Dermatol* 2014; 134: 43–50.
- de Vries E, Poll-Franse LV, Louwman WJ, De Gruijl FR, Coebergh JWW. Predictions of skin cancer incidence in the Netherlands up to 2015. *Br J Dermatol* 2005; 152: 481–488.
- Flohil SC, de Vries E, Neumann M, Coebergh J-W, Nijsten T. Incidence, prevalence and future trends of primary basal cell carcinoma in the Netherlands. *Acta Derm Venereol* 2011; 91: 24–30.
- Socialstyrelsen. Basal cell carcinoma in Sweden 2004–2008. 2009. [Cited 2015 Apr 29] Available from: <http://www.socialstyrelsen.se/Lists/Artikelkatalog/Attachments/17863/2009-12-12.pdf>.