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Cervical cancer screening in the Faroe Islands

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ABSTRACT

Background. The Faroe Islands have had nationally organised cervical cancer screening since 1995. Women aged 25–60 years are invited every third year. Participation is free of charge. Although several European overviews on cervical screening are available, none have included the Faroe Islands. Our aim was to provide the first description of cervical cancer screening, and to determine the screening history of women diagnosed with cervical cancer in the Faroe Islands.

Material and methods. Screening data from 1996 to 2012 were obtained from the Diagnostic Centre at the National Hospital of the Faroe Islands. They included information on cytology and HPV testing whereas information on histology was not registered consistently. Process indicators were calculated, including coverage rate, excess smears, proportion of abnormal cytological samples, and frequency of HPV testing. Data on cervical cancer cases were obtained from the Faroese Ministry of Health Affairs. The analysis of the screening history was undertaken for cases diagnosed in 2000–2010.

Results. A total of 52 457 samples were taken in 1996–2012. Coverage varied between 67% and 81% and was 71% in 2012. Excess smears decreased after 1999. At present, 7.0% of samples have abnormal cytology. Of all ASCUS samples, 76–95% were tested for HPV. A total of 58% of women diagnosed with cervical cancer did not participate in screening prior to their diagnosis, and 32% had normal cytology in the previous four years.

Conclusion. Despite the difficult geographical setting, the organised cervical cancer screening programme in the Faroe Islands has achieved a relatively high coverage rate. Nevertheless, challenges, e.g. consistent histology registration and sending reminders, still exist.

The Faroe Islands are located in the North Atlantic Ocean between Scotland, Island and Norway. They consist of 18 islands, of which 17 are inhabited on a total area of 1399 km^2. Together with Greenland, the Faroe Islands are a part of the Danish Realm and have since 1948 had home-rule administration. The population of approximately 48 000 in 2013 has a life expectancy of 84.6 years for women and 79.6 years for men. The gross domestic product per capita was 44 317 US$ in 2009 [1]. The primary healthcare system is largely financed through taxes and compulsory health insurance with some co-payment for pharmaceutical products. At present, all hospitals and general practitioners use an electronic patient record system, Cosmic.

Historically, the Faroe Islands have had a pattern of cervical cancer quite different from the other Nordic countries. Owing to the small population, the incidence rate of cervical cancer in the Faroe Islands has fluctuated tremendously. At its highest, in 1996, it reached 47 per 100 000 (ASW) [2]. In the period 2001–2010, it was on average 12 per 100 000, ranging between 0 and 24 per 100 000 [2]. Since 1995, the Faroe Islands have had a nationally organised cervical

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cancer screening programme. Invitations are sent every third year to all women aged 25–60 years. Samples are taken by general practitioners and gynaecologists who are responsible for informing the women of the test outcome. Most gynaecologists practice in the hospitals and at present, only one gynaecologist is in private practice. General practitioners are financed by the Ministry of Health Affairs and screening and follow-up samples are free of charge.

Although several comprehensive overviews of cervical screening in European countries have been published, none included the Faroe Islands [3, 4]. Furthermore, the Faroese programme has not been systematically monitored [5]. Therefore, the aim of this article was to provide the first description of cervical cancer screening in this country.

Material and methods

Cervical cancer screening in the Faroe Islands

Cervical cancer screening is the only nationally organised cancer screening programme in the Faroe Islands. The programme was announced by the Faroese health minister in 1995, and is handled by the Diagnostic Centre at the National Hospital of the Faroe Islands. Approximately 3500 invitations are sent out on a yearly basis, except for the period of 1995–1996 where an elevated number of invitations were sent. In 1995–1998, samples were evaluated at the Faroese National Hospital. Since then, no pathology laboratory has evaluated cervical samples in the Faroe Islands, and the samples have been sent to Denmark [6]; in 1998–2002, to an unidentified laboratory; in 2002–2008 to Copenhagen University Hospital Rigshospitalet; in 2008–2012 to Hillerød Hospital; and since 2012 to Copenhagen University Hospital Hvidovre. The latter two laboratories evaluated SurePath samples. The reading was assisted by FocalPoint GS Imaging System (BD Diagnostics, Burlington, NC, USA), and diagnoses were reported according to the Bethesda 2001 classification. All results are mailed to both the general practitioner and to the Diagnostic Centre. In case of an abnormal sample, the letter includes a diagnosis and a recommendation for further management according to the Danish guidelines [7]. For women above the age of 30 years, samples with a diagnosis of atypical squamous cells of undetermined significance (ASCUS) have been tested for human papillomavirus (HPV) using the Hybrid Capture 2 assay; the same is now recommended for women after treatment of cervical intraepithelial neoplasia.

Cancer registration

The Faroese Cancer Register was established in 1994 in cooperation with the Danish Cancer Society. The content of the register is directly compatible with the Danish register. An exception is the personal identification numbers (CPR). The Faroese patients are given a fictitious serial number because the original unique Faroese person-numbers (so-called p-nr, including the date of birth and a three-number code) are not compatible with the format of the Danish CPR numbers. If, however, a Faroese person has a Danish CPR number, this will be used. Cancer cases are registered in the Faroese cancer register with ICD-10 codes.

Data sources

Data for this study were retrieved in February 2013 by the Diagnostic Centre at the National Hospital of the Faroe Islands (for screening) and by the Faroese Ministry of Health Affairs (for cancers).

Screening data consisted of cytological samples registered between 1973 and 2013 (N = 107 627). Histology samples have not been registered consistently and were excluded from the analysis.

Due to incomplete data on cytology before 1996, the data used included 52 457 cervical samples registered between 1 January 1996 and 31 December 2012. These data are registered by p-nr. Cytological diagnoses and results of HPV testing were registered either with codes as defined in the official Faroese cervical screening form following the Bethesda 2001 classification system (using numerical coding), or as free text. When diagnoses were only available as part of free text descriptions, these were classified by researchers following an automated script using regular expressions. As free text, diagnoses were usually also written out in Bethesda 2001 terminology; in some cases, the diagnoses were translated into Faroese. Misspelled terms were hand-searched until all cytological samples could be assigned a diagnosis. In case several diagnoses were available, we used the highest abnormality reported for a given sample. For 822 (1.6%) samples, diagnoses could not be determined. The reasons for taking the cytological sample and for HPV testing were not registered; we assumed that HPV testing was undertaken for an ASCUS diagnosis if the two diagnoses were registered for the same sample.

Cancer data from the Ministry of Health Affairs included all women with a cervical cancer diagnosis living on the Faroe Islands, in total 150 women for the period 1963–2010. We used data from the 47 women diagnosed between 1 January 2000 and 31 December 2010, a number very close to 46 reported by NORDCAN in the same period [2]. The linkage between cancer and screening data was only possible using the date of birth, as the three-number code in the p-nr was not registered in the cancer registry.

Screening histories of 16 of 47 women with cervical cancer overlapped with screening histories of one or more other women having the same birth date; these women were excluded from further analyses. The type of linkage of screening data to cancer data via birth date only may have led to faulty linkage of 'administrative twins' [8], and consequently to an underestimation of women without prior screening.

Statistics on the female population by age group were retrieved from Statistics Faroe Islands (www.hagstova.fo).

Statistical analyses

We calculated the following screening programme indicators: coverage rate, proportion of abnormal cytological samples, number of excess smears per 1000 women, and proportion of HPV tests for samples with an ASCUS diagnosis. Additionally, we determined the screening history of women with cervical cancer.

Screening coverage was calculated as the proportion of women alive on 31 December every year who had at least one cytological sample taken in the last 3.5 years. The period of 3.5 years was chosen to allow for some delay in participation as the recommended screening interval is every third year. With the screening data complete from 1996 onwards, we calculated the screening coverage for 1999 onwards.

The number of excess smears per 1000 women in the target age group was used as an indicator of overuse of cytology after accounting for the observed coverage. It was calculated as (total yearly number of smears – number of smears needed yearly to reach the observed coverage) $\times 1000$ / number of women in the target group. The number of smears needed yearly to reach the observed coverage was calculated as (the population at risk in the target age range $\times$ observed coverage) / recommended interval [9]. This indicator includes screening samples taken within too short an interval after a previous normal screening sample, but also samples taken for follow-up after recent abnormalities, which are recommended for an effective running of the programme. For the relative risks (RR), 95% confidence intervals (CI) were calculated assuming that the logarithms of RR were approximately normally distributed.

The screening history of women with cervical cancer was analysed in four-year periods before the diagnosis, and the worst cytological diagnosis was determined based on the available screening data. Cytological samples registered in the last six months before the diagnosis of cervical cancer were excluded because those smears might have been taken for diagnostic purposes rather than screening [10].

Data were retrieved as Excel files. After cleaning, they were analysed with SPSS (IBM, Version 20). The study was approved by the Faroese Data Protection Agency, J. nr. 20120198–2 and J. nr. 20120198–11.

Results

A total of 52 457 smears were taken in 1996–2012, of which 45 206 (86.2%) were classified as normal, 2398 (4.6%) as ≥ ASCUS, 4031 (7.7%) as inadequate, and 822 (1.6%) had an unknown diagnosis (Table I). The proportion of inadequate smears decreased from 11.0% in 1996–1998 when conventional cytological samples were used, to 0.2% in 2011–2012 when liquid-based cytology was used. The relative risk of receiving an abnormal cytological test result varied but was significantly lower before 2008 compared to the period thereafter. In 2011–2012, the proportion of cytological samples with ≥ ASCUS was 7.0%. The highest number of smears

Table I. Number of cytological samples classified according to grade of cytological abnormality.

Cytological diagnosis	1996–1998 N (%)	1999–2001 N (%)	2002–2004 N (%)	2005–2007 N (%)	2008–2010 N (%)	2011–2012 N (%)	1996–2012 N (%)
Unknown	41 (0.4%)	122 (1.2%)	221 (2.4%)	126 (1.5%)	164 (1.9%)	148 (2.6%)	822 (1.6%)
Inadequate	1174 (11.0%)	836 (8.5%)	961 (10.2%)	838 (10.0%)	213 (2.5%)[a]	9 (0.2%)	4031 (7.7%)
Normal	9142 (85.6%)	8326 (84.4%)	7919 (84.6%)	7181 (85.8%)	7595 (88.4%)	5043 (90.2%)	45 206 (86.2%)
ASCUS	156 (1.5%)	391 (4.0%)	133 (1.4%)	154 (1.8%)	359 (4.2%)	179 (3.2%)	1372 (2.6%)
LSIL	75 (0.7%)	106 (1.1%)	81 (0.9%)	42 (0.5%)	86 (1.0%)	94 (1.7%)	484 (0.9%)
≥HSIL	86 (0.8%)	86 (0.9%)	47 (0.5%)	30 (0.4%)	175 (2.0%)	118 (2.1%)	542 (1.0%)
≥ASCUS	317 (3.0%)	583 (5.9%)	261 (2.8%)	226 (2.7%)	620 (7.2%)	391 (7.0%)	2398 (4.6%)
Total	10 674 (100%)	9867 (100%)	9362 (100%)	8371 (100%)	8592 (100%)	5591 (100%)	52 457 (100%)
RR of ≥ASCUS (95% CI)	0.42 (0.37–0.49)	0.84 (0.75–0.96)	0.40 (0.34–0.46)	0.39 (0.33–0.45)	1.03 (0.91–1.17)	1.00 (ref.)	

ASCUS, atypical squamous cells of undetermined significance; CI, confidence interval; HSIL, high-grade squamous intraepithelial neoplasia (including atypical squamous cells – HSIL cannot be excluded, atypical glandular cells, adenocarcinoma in situ, and squamous carcinoma); LSIL, low–grade squamous intraepithelial neoplasia; RR, relative risk.

[a]The proportion of inadequate smears was 7.2% in 2008, 0.5% in 2009 and 0.3% in 2010.

Table II. 3.5-year screening coverage rates of women aged 25–60 years on 31 December, and number of excess smears per year per 1000 women in the target age group.

Year	Coverage (%)	RR (95% CI)	Excess smears per 1000 (N)
1999	75%	1 (ref.)	164
2000	70%	0.93 (0.91–0.95)	89
2001	71%	0.95 (0.93–0.96)	44
2002	70%	0.93 (0.91–0.94)	98
2003	67%	0.89 (0.87–0.90)	90
2004	66%	0.88 (0.87–0.90)	52
2005	66%	0.88 (0.87–0.90)	53
2006	65%	0.87 (0.85–0.88)	80
2007	64%	0.86 (0.84–0.87)	23
2008	64%	0.86 (0.84–0.87)	36
2009	67%	0.89 (0.88–0.91)	100
2010	67%	0.89 (0.88–0.91)	35
2011	68%	0.91 (0.89–0.92)	45
2012	66%	0.88 (0.87–0.90)	56

was taken in the first years of the organised screening programme, around 5500 in 1996, compared to an average of around 2700 in the recent years (data not tabulated).

Overall, 3.5-year screening coverage was highest in 1999, 75%, and lowest in 2007–2008, 64% (Table II). The screening coverage was significantly lower in all years following 1999. In 1999, the coverage was lowest for women aged 25–29 years (61%), whereas the coverage was 74–84% among women aged 30–54 years. By 2012, the coverage for women aged 55–60 years had decreased from 68% in 1999 to 59%. For women aged 25–54 years, the coverage varied between 65 and 70% in 2012 (Table III).

The number of cytological samples per 1000 women aged 25–60 years decreased from 355 in 1996–1998 to 251 in 2011–2012. Hence, the number of excess smears also decreased from 1999 onwards (Table II).

The number of HPV tests before 2009 was very low (data not tabulated). In 2009–2011, the majority of HPV tests were used in women with ASCUS at age ≥ 30 years (79–92%, Table IV). However, the proportion decreased to 52% in 2012. In total, 27–28% of ASCUS samples were HPV positive in 2009–2011, but this increased to 48% in 2012 (Table IV). Of all ASCUS samples from women above 30 years, between 76% and 95% were tested for HPV (Table V).

Table III. 3.5-year cervical cancer screening coverage rates by age group on 31 December.

Age group (years)	1999 (%)	2012 (%)
25–29	61%	66%
30–34	75%	65%
35–39	82%	67%
40–44	84%	69%
45–49	77%	68%
50–54	74%	70%
55–60	68%	59%
25–60	75%	66%

Table IV. HPV tests among women screened in the Faroe Islands in the period 2009–2012.

Year	HPV tests (N)	HPV tests with ASCUS at age ≥ 30 years (N, % of HPV tests)	Positive HPV tests (N, % of HPV tests with ASCUS at age ≥ 30 years)
2009	131	121 (92%)	33 (27%)
2010	124	98 (79%)	26 (27%)
2011	98	81 (83%)	23 (28%)
2012	92	48 (52%)	23 (48%)
2009–2012	445	348 (78%)	105 (30%)

ASCUS, atypical squamous cells of undetermined significance; HPV, human papillomavirus.

Table VI shows the number of women diagnosed with cervical cancer in 2000–2010 according to their screening history. A total of 58% of patients (18/31) had no recent screening, and 32% (10/31) had screening with normal cytology in the previous four years. Although based on small numbers, women with no screening history tended to be older than women with normal cytological samples in their screening history. Likewise, there were no statistically significant differences between the women with different types of screening histories according to histological types of cancer and their stages.

Discussion

Although in the Faroe Islands, an organised cervical cancer screening programme has been running for almost 20 years, this is the first publicly available overview. Overall, the continuous running of the national Faroese cervical cancer screening programme can in itself be regarded as a success, particularly considering the scattered landscape and no pathology laboratory evaluating cervical samples

Table V. The proportion of ASCUS samples at age ≥ 30 years with HPV testing in 2009–2012.

Year	ASCUS at age ≥ 30 years (N)	ASCUS at age ≥ 30 years tested for HPV (N, %)
2009	159	121 (76%)
2010	104	98 (94%)
2011	85	81 (95%)
2012	60	48 (80%)
2009–2012	408	348 (85%)

ASCUS, atypical squamous cells of undetermined significance; HPV, human papillomavirus.

Table VI. Four-year screening history of women diagnosed with cervical cancer in 2000–2012.

	No screening (N = 18)		Screening with normal cytological samples (N = 10)		Screening with abnormal cytological samples (N = 3)	
	Number	(%)	Number	(%)	Number	(%)
Age group (years)						
0–24	0		0		0	
25–29	0		0		0	
30–34	0		0		0	
35–39	2	11%	3	30%	2	67%
40–44	3	17%	1	10%	0	
45–49	1	5%	0		1	33%
50–54	1	5%	2	20%	0	
55–60	3	17%	1	10%	0	
61+	8	45%	3	30%	0	
Histology types						
Squamous	15	83%	6	60%	2	67%
Adenocarcinomas	2	11%	2	20%	1	33%
Other & unknown	1	6%	2	20%		
Stage						
Localised	11*	61%	4	40%	2	67%
Regional metastases	3	17%	2	20%		
Distant metastases	2	11%	1	10%		
Unknown	2	11%	3	30%	1	33%
Total	18	100%	10	100%	3	100%

*One cancer case was registered as FIGO stadium 1 and one cancer case as stadium 2. No further information on sub-staging was available.

within the country. The screening coverage rate has been rather high. As elsewhere [11], the Faroese data though suggest that a further increase in the coverage could decrease the number of women developing cervical cancer.

From the 1960s onwards, the Faroese incidence rates of cervical cancer showed a slightly increasing trend, but they appear to have been decreasing since the implementation of organised screening in 1995 [2]. Due to a small population, however, these rates have fluctuated, so the trends will need to be monitored further. For Nordic countries, an association has often been shown between the patterns of organised screening and changes in the cervical cancer incidence [12]. Denmark, e.g. started with local combinations of organised cervical screening programmes and opportunistic screening in the 1960s. The incidence of cervical cancer was halved by the 1980s. Stronger decreases were seen in Sweden, Iceland, and Finland, where nationally organised screening was started in the 1960s and 1970s. In Norway, however, an increase in cervical cancer incidence continued until around 1975 when (opportunistic) screening became frequent [2].

According to the European Guidelines for Quality Assurance in Cervical Cancer Screening, evaluation and monitoring of an organised cervical cancer screening is a necessity in order to implement quality assurance [13]. Also, comparisons to other countries with organised screening programmes are important for identifying bottlenecks and thereby improving screening performance [14]. Given that the Faroe Islands are a part of the Danish Realm and the samples are evaluated in Denmark, a comparison with the Danish national organised screening programme is particularly interesting. In Denmark, the programme is evaluated yearly by the Danish Cervical Cancer Screening Quality Assurance Data Base [15].

The coverage rate on the Faroe Islands was 66% in 2012 (3.5 years for women aged 25–60 years), and 76% in Denmark (3.5 years for women aged 23–49, and 5.5 years for women aged 50–64 years). According to Danish recommendations, the rate should ideally be above 85% [15], but within Europe in 2009, Anttila et al. reported a coverage rate above 70% only for Finland, Alsace (France), Sweden, England and the Netherlands [4]. Greenland is another part of the Danish Realm with a home-rule administration. However, that vast country with a population size similar to that of the Faroe Islands, where most traffic takes place by air or water, faces very difficult logistic conditions for cervical cancer screening. Correspondingly, the current coverage rate is much lower than in the Faroe Islands, below 40% among women aged 23–65 years (unpublished data for 2008–2012 based on the Danish National Pathology Data Bank). The Faroe Islands had the highest coverage rate of 75% in 1996–1997 when yearly reminders were sent by a pathologist from the Diagnostic

Centre to all women, including those who had already participated. In keeping to a three-year recommended interval, yearly reminders (in fact, yearly invitations) are not sent anymore. The data furthermore suggested that in the Faroe Islands, particularly in the recent years, the excess use of cytological samples was relatively low compared to other countries [9,16].

Denmark recommends the proportion of inadequate samples to be below 1.5% [15]. For Faroese samples, this ranged between 0.2% and 0.5% in 2009–2012, which was similar to all samples evaluated in the Hillerød (0.8%) and the Hvidovre (0.6%) laboratories [15]. In 2011, the proportion of samples classified as ≥ ASCUS was 7% in Hvidovre laboratory [17]. On the Faroe Islands, the proportion of abnormal samples increased from the initial 3% to 7%, when the pathology laboratories from Hillerød and Hvidovre took over the evaluation. According to Rask et al., this could be ascribed to a modernisation in the technology of preparing and reading cytological samples in theses laboratories [18]. Probably this change led to an increased sensitivity for detecting high-grade cervical intraepithelial neoplasia, though this is only possible to evaluate when data on follow-up including biopsies and treatments become available. The change in the technology, however, also influenced the number of inadequate smears, which can be seen in their decreasing frequency, particularly from 2008 to 2009.

Denmark furthermore recommends that more than 95% of samples with ASCUS from women above age 30 years should be tested for HPV [15]. For the Faroe Islands, this was the case for 76–95% of the samples in 2009–2011, as compared to almost 100% for samples evaluated in the laboratories of Hillerød and Hvidovre Hospitals [15]. In 2009–2011, the majority of all HPV tests appeared to have been done for women with ASCUS above age 30 years, and the proportion testing positive was stable at just below 30%. By 2012, the proportion of HPV tests that were taken with ASCUS as the indication decreased, and the proportion of positive HPV tests results among women with ASCUS increased. These fluctuations may have been a consequence of small numbers, but they might also derive from a change in the Hvidovre laboratory (which took over the Faroese samples in August 2012), where samples with an initial diagnosis of ASCUS and a negative Hybrid Capture 2 result were reclassified as normal cytology. Finally, HPV testing as a part of follow-up after treatment of cervical intraepithelial neoplasia started in more recent years and this could perhaps explain why the proportion of HPV tests with an ASCUS diagnosis decreased. Unfortunately, the indication for HPV testing and/or treatments were not registered, so that the use of HPV testing for follow-up after treatment could not be verified.

This is the first time that the data from the Faroese screening programme have been linked to data on cervical cancer cases. These data suggested that almost 60% of women with cervical cancer were not recently screened, and about a third had had a recent normal cytological sample. This appears to be similar to data from Denmark, where for the period of 2003–2007, Dugué et al. found that 55% of Danish women with cervical cancer had not participated in the two previous screening rounds [19]. In the future, HPV self-sampling may improve the uptake of screening among non-responders. Additionally, primary HPV based screening may reduce the number of women with cervical cancer after a normal screening test result, currently estimated at 32%.

Apart from reducing the risk of cervical cancer, screening might also have a negative impact on the women, particularly by inducing anxiety. In 2009, Danielsen et al. found that Faroese women experienced anxiety when having to undergo a gynaecological examination, and thereafter wait for the screening result [20]. Furthermore, women were in general insecure due to a perception of not being invited with the correct interval and thereby being doubtful about whether they were included in the programme or not. There are two larger urban settlements in the Faroe Islands, but otherwise the country is composed of many small villages. As seen elsewhere, small communities may be challenging for preservation of confidentiality [21]. Danielsen et al. found that women regarded general practitioners as important in terms of raising the awareness of screening. In small villages, however, the general practitioner is a part of the local community and therefore a gynaecological examination, e.g. for taking screening cytology, could also be dismissed due to personal familiarity. Several foreign general practitioners have practiced in the country, and they were perceived to have both a positive and a negative effect on the participation in screening: some women reported discomfort with an unfamiliar general practitioner, whereas other women found it comforting. In the Faroe Islands, the implementation of HPV vaccination gave rise to a debate on celibacy as an alternative to vaccination, a debate not seen in the other Nordic countries [22]. Since HPV is sexually transmitted, it has been suggested that Faroese women might dismiss the gynaecological examination to not appear promiscuous [20]. Some of the above mentioned issues arising due to the small societies at the Islands could potentially be overcome by HPV self-sampling.

Despite the geographically difficult setting, the Faroe Islands have been able to run a long-

standing organised cervical cancer screening programme with a coverage rate above 70%. The programme follows the European and Danish guidelines on the target age range and the screening interval. Evaluation of cytological samples including follow-up samples has been undertaken in Danish laboratories, which follow the national guidelines – these have been evidence-based and are frequently updated. However, the scarce amount of evaluation reports on cervical cancer screening on the Faroe Islands can be considered a weakness. The programme at present faces two main challenges. First, although cytological data have been registered virtually completely, the lack of registration of histological samples poses a problem for comprehensive monitoring, particularly of the follow-up of abnormal screening samples. Effective follow-up of abnormalities is the cornerstone of any screening programme. As a result of this study, the registration of cervical cancer cases from 2011 and onwards will, starting in 2014, include the full p-nr enabling a correct linkage between the screening and the cancer databases. Second, reminders are not sent to non-participants on a regular basis. This is pending a software update when the screening data will begin to be automatically linked to the electronic patient register of the National Hospital of the Faroe Islands.

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