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Twelve years of breast cancer screening in Flemish-Brabant and Limburg

by

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Abstract

The Leuven University Centre for Cancer Prevention (LUCK) has been involved in breast cancer screening since 1993. It participates in the Flemish breast cancer screening programme that started in June 2001 and provides a biennial mammography to women aged 50 to 69 years.

This paper presents early surrogate indicators from 1993 to 15 June 2001 (BS) and from 15 June 2001 to 2004 (AS) in the provinces Flemish-Brabant and Limburg and examines whether the recommended European standards have been achieved.

Methods: *Early quality indicators, according to The European Guidelines for Mammographic Screening (14) were calculated for initial as well for subsequent screens.*

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Results: *In this period 194,118 women have been screened, 64,503 before and 129,615 after the starting of the Flemish programme. The coverage in the first period ranged from 14.3% to 32.7% whereas the coverage AS varied between 34.6% and 44.4%.*

The corresponding recall rates were 3.1% (BS) and 2.5% (AS). Per 1000 women screened 6.6 (BS) and 6.5 (AS) breast cancers were detected. Of these cancers 81.2% (BS) and 80.1% (AS) were invasive. Of the invasive cancers 29.7% (BS) and 43.5% (AS) were less than 10 mm and 76.5% (BS) and 71.6% (AS) have no nodal involvement.

Conclusions: *The performance parameters corresponding to these two periods fulfilled the European standards for the most part.*

Keywords: *mass screening, mammography, predictive value of test, programme evaluation.*

Introduction

The Flemish experience with population-based breast screening programmes dates back 17 years when the first pilot programme in the north-eastern part of the country was organized in 1989 by the University of Leuven in the framework of the “Europe against Cancer” (EAC) programme (1).

On 15 June 2001 the Flemish Screening programme was launched. The programme offers biennial mammography to women resident in Flanders aged 50-69 years and is organized by five screening centres. One of them is the Leuven University Centre for Cancer prevention (LUCK) in charge of the programme in the provinces of Flemish-Brabant and Limburg. The LUCK has been involved in breast cancer screening since 1993. Its screening activity until June 2001 was limited to pilot population-based projects performed in different municipalities from Northern Limburg, Antwerp and Flemish-Brabant also within the framework of the EAC programme.

There is not much information on the performance of the Flemish programme (1, 2). The aim of this study is to evaluate early outcome parameters in the screening area corresponding to the LUCK before (BS) and after the starting (AS) of the programme in order to see whether they fulfil the screening criteria established by the European guidelines on breast cancer screening (14).

Methods

Women aged 50-69 years from the provinces Flemish-Brabant and Limburg are invited every 2 years. Before the starting of the programme the screening was limited to some municipalities in Northern Limburg, Antwerp and Flemish-Brabant and took place in a semi-mobile (SMU) or, since 1997, a mobile (MU) unit. Since 15 June 2001 the screening takes place either at accredited radiology units (Limburg and Flemish-Brabant) or in a MU (53 municipalities in Flemish-Brabant).

The personal data from women qualifying for screening are provided by the national population register. Women from the target population receive a personal invitation with specified appointment times accompanied by an information leaflet. The invitations are issued by the local authorities. Since the start of the programme women also have the possibility to make an appointment via the general practitioner or the gynaecologist.

Two view mammograms are taken for the initial screening as well as for subsequent screens. Mammograms are sent to the LUCK for a blind second reading with arbitrations by a third reader when the two readers disagree. All women receive a letter with the results as does the general practitioner or the medical doctor of choice.

Women who do not intend to participate are asked to inform the LUCK and to give the reasons why they do not want to participate by sending back a short questionnaire enclosed with the invitation or, since 1997, by using a toll-free number. Women with breast cancer are excluded for 5 rounds. For our programme it is not possible to identify any category of potential exclusion prior to invitation.

Performance parameters were calculated according to the European Screening guidelines (14). Invitation data corresponding to this study were not stored. Given that in Flanders women can not only be invited by the screening centre but can also be referred by their physician to accredited radiologists for a screening mammogram, we have chosen to calculate the participation rate as a coverage, i.e. the number of screened women divided by the target population during the screening period in the provinces of Flemish-Brabant and Limburg instead of as a proportion of all women who were invited to attend for screening.

During the period preceding the implementation of the screening programme women from the target population of the municipalities

participating in population-based pilot projects were invited for screening. In this case the whole target population was invited in the corresponding year and we calculated the coverage as the number of women screened in that year divided by the target population. From the time the programme started, the screening of the target population took place in a two-year interval. The coverage in a particular year was thus calculated as the number of women screened that year plus the number of women screened the year that followed divided by the target population corresponding to that particular year.

In presenting the screening results a distinction is made between initial and subsequent screening and two screening periods: before (BS) and after the start of the programme (AS) in June 15 2001.

Results

Between 1993 and 2004 a total of 194,118 women were screened, 64,503 before the starting of the Flemish programme and 129,615 AS, resulting in a coverage ranging from 14.3% to 32.7% (BS) and from 34.6% to 44.4% (AS) (table 1 and 2).

While 129,819 women had a mammogram for the first time (45,925 BS and 83,894 AS) 64,299 were screened more than once (18,578 BS and 45,721 AS) (table 2).

Women aged 50-54 represent the age-group most frequently screened for the first time (30.0% BS and 38.0% AS). The other 3 age-groups are similarly distributed in initial as well as in subsequent screens in both screening periods (table 3 and 4).

As seen in table 2, 5,212 women (2.7%) were referred for further assessment. Of these 1,982 (3.1%) were screened during the first period and 3,230 (2.5%) from the moment that the screening programme started. The recall rate (RR) for women initially screened was 3.6% (BS) and slightly lower, 3.0% after the implementation of the programme.

The corresponding values for incident screening examinations were lower, as expected for not prevalent screening examinations: 1.9% (BS) and 1.5% (AS).

Women between 50-54 years (table 3) were the most often referred for further assessment during the period preceding the implementation of the programme for the first screening examination as well as for repeated examinations, while the cancer detection rate (CDR) was higher for women aged 60-69, who had recall rates that were among the lowest.

TABLE 1.
Breast cancer screening coverage in Flemish-Brabant and Limburg 1993-2004

	1993-14/06/2001 (BS)				15/06/2001-2004 (AS)		
Year	Target population	Screenings (n)	Coverage (%)	year	Target population	Screenings (n)	Coverage (%)
1993	16,363	2,343	14.3	15/06/01 december 2001	51,937*	17,959	34.6
1994	19,353	3,919	20.3	2002	209,576	42,942	34.9
1995	24,600	4,431	18.0	2003	183,982	30,106	37.4
1996	14,474	4,726	32.7	2004	185,423	38,608	44.4
1997	38,775	7,717	19.9				
1998	61,023	14,937	24.5				
1999	42,446	10,911	25.7				
2000	41,727	9,748	23.4				
January 14/06/01	23,053	5,771	25.0				

*Target population 2001/4.

TABLE 2.
Performance of the Mammography Screening Programme in Flemish-Brabant and Limburg 1993-2004

	1993-14/06/2001 (BS)			15/06/2001-2004 (AS)			All
	Initial	Subsequent	Total	Initial	Subsequent	Total	
No. of participants	45,925	18,578	64,503	83,894	45,721	129,615	194,118
No. of recalls	1,638	344	1,982	2,553	677	3,230	5,212
Recall rate (%)	3.6	1.9	3.1	3.0	1.5	2.5	2.7
No. biopsies	436	108	544	775	269	1,044	1,588
Biopsy rate (‰)	9.0	5.8	8.4	9.2	5.9	8.1	8.2
B:M biopsy rate	0.06	0.02	0.05	0.01	0.005	0.004	0.02
No. of cancers	339	86	425	605	239	844	1,269
% invasive	80.2	84.9	81.2	78.0	85.4	80.1	80.5
% in situ	19.8	15.1	18.8	22.00	14.6	19.9	19.5
CDR * (‰)	7.4	4.6	6.6	7.2	5.2	6.5	6.5
% inv ≤ 10 mm †	26.2	42.5	29.7	43.2	44.1	43.5	38.9
Node-negative (%)‡	76.1	78.1	76.5	70.6	73.8	71.6	73.3

*Cancer detection rate. † Those with diameter unknown excluded. ‡ Those with no axillary dissection excluded.

TABLE 3.
Performance of the Mammography Screening Programme BS
in Flemish-Brabant and Limburg 1993-2004 by age-group

	Initial Screening				Subsequent Screening				
	50-54	55-59	60-64	65-69	50-54	55-59	60-64	65-69	total
No. of participants	13,763	11,044	11,088	10,030	2,517	5,165	5,593	5,303	64,503
No. of recalls	530	389	367	352	54	105	101	84	1982
Recall rate (%)	3.89	3.5	3.3	3.5	2.2	2.0	1.8	1.6	3.1
No. biopsies	124	94	105	113	14	22	39	33	544
Biopsy rate ()	8.1	8.1	9.4	10.6	5.6	4.3	7.0	6.2	8.4
B/M biopsy rate	0.110.06	0.01	0.07	0.08	0.05	0.00	0.00	0.05	
No. of cancers	80	70	83	106	10	14	33	29	425
% invasive	70.0	82.9	88.0	80.2	70.0	71.4	87.9	93.1	81.2
% in situ	30.0	17.1	12.1	19.8	30.0	28.6	12.1	6.9	18.8
CDR * ()	5.8	6.3	7.5	10.6	4.0	2.7	5.9	5.5	6.6
% inv ≤ 10 mm †	29.1	31.6	18.6	27.1	14.3	30.0	44.8	51.9	29.7
Node-negative (%)‡	76.8	70.7	74.3	81.0	85.7	70.0	75.9	81.5	76.5

*Cancer detection rate. † Those with diameter unknown excluded. ‡ Those with no axillary dissection excluded.

TABLE 4.
Performance of the Mammography Screening Programme AS in Flemish-Brabant and Limburg 1993-2004 by age-group

	Initial Screening				Subsequent Screening				
	50-54	55-59	60-64	65-69	50-54	55-59	60-64	65-69	total
No of participants	32,047	20,030	16,298	15,519	5,663	12,860	13,014	14,184	129,615
No of recalls	969	629	480	475	77	178	198	224	3,230
Recall rate (%)	3.0	3.1	3.0	3.1	1.4	1.4	1.5	1.6	2.5
No. biopsies	248	186	165	176	20	72	81	96	1,044
Biopsy rate (‰)	7.7	9.3	10.1	11.3	3.5	5.6	6.2	6.8	8.1
B/M biopsy rate	0.00	0.01	0.00	0.01	0.00	0.00	0.00	0.00	0.00
No. of cancers	181	144	142	138	14	64	74	87	844
% invasive	75.1	77.8	78.9	81.2	64.3	82.8	87.8	88.5	80.1
% in situ	24.9	22.2	21.1	18.8	35.7	17.2	12.2	11.5	19.9
CDR * (‰)	5.7	7.2	8.7	8.9	2.5	5.0	5.7	6.1	6.5
% inv $\leq$ 10 mm †	43.4	48.2	42.9	38.4	55.6	47.2	40.0	44.2	43.5
Node-negative (%)‡	65.4	73.0	76.6	68.8	87.5	71.7	67.7	79.0	71.6

*Cancer detection rate. †Those with diameter unknown excluded. ‡ Those with no axillary dissection excluded.

By contrast, from 15/06/2001 to 2004 the RR of the youngest women was similar to that of the other age-groups for first screens and the lowest for subsequent screens (table 4). CDR in this period was still the lowest amongst women aged 50-54 (5.7‰ for initial and 2.5‰ for subsequent screens) and the highest in women aged 65-69 (8.9‰ and 6.1‰ for initial and subsequent screens respectively). Overall, CDR was similar in both periods: 6.6‰ before the start of the programme and 6.5‰ after the programme began, with higher CDR for initial screens (7.4‰ BS and 7.2‰ AS) than for subsequent screens (4.6‰ and 5.2‰ for the periods BS and AS respectively) (table 2). The biopsy rate was similar in both periods with higher values for initial than for subsequent screens: those for initial were 9.0‰ BS vs. 9.2‰ AS and those for subsequent were 5.8‰ BS vs. 5.9‰ AS (Table 2). As seen in tables 3 and 4, women aged 50-54 had the lowest biopsy rates or among the lowest, as well before the start of the programme when they had the highest recall rate, as thereafter.

The number of cancers detected, tumour size and nodal status are presented in table 5.

In the period preceding the start of the programme 425 cancers were detected, 345 (81.8%) invasive and 80 (18.8%) in situ. In initial screens 19.8% of the cancers were in situ and 80.2% invasive. Of the invasive cancers 25.7% were 10 mm or less in size (pT1ab) and 75.0% had no nodal involvement. In subsequent screens the proportion of in situ cancers slightly decreased (15.1%). The proportion of invasive cancers which were 10 mm or less in size increased (42.5% subsequent vs. 25.7% initial) as well as the proportion of node-negative invasive cancers (78.1% subsequent vs. 75.0% initial).

Concerning the proportion of in situ cancers, the same trend was observed from the start of the programme. In this period 22.0% of the cancers detected in initial screens were in situ versus 14.6% in situ cancers detected in subsequent screens. The proportion of pT1ab was similar to that found in subsequent screens before the start of the programme: 43.2% for initial and 44.1% for subsequent screens.

Tables 6 and 7 represent a summary of early outcome parameters from service screening programmes in The Netherlands and the LUCK compared with the desirable reference values recommended by the European guidelines (14). The performance parameters in the whole period (1993-2004) met or exceeded the desirable levels (RR, CDR/IR, % carcinoma in situ, pT1ab, B:M biopsy ratio) as well for initial as for subsequent screens, while the proportion of node-negative invasive

TABLE 5.
Characteristics of cancers detected in Flemish-Brabant and Limburg 1993-2004

Screening period	Cancers detected (%)		Tumour size (%)					Nodal status (%)		
	Invasive	In situ	pT1	pT1ab	pT1c	pT2+	pTx	N-	N+	Nx
1993-14/06/2001 (BS)										
Initial	272 (80.2)	67 (19.8)	4.8	25.7	45.6	22.1	1.8	75.0	23.5	1.5
Subsequent	73 (84.9)	13 (15.1)	0.9	42.5	28.8	24.7	0.0	78.1	21.9	0.0
Total	345 (81.2)	80 (18.8)	4.6	29.3	42.0	22.6	1.5	75.7	23.2	1.2
15/06/2001-2004 (AS)										
Initial	472 (78.0)	133 (22.0)	2.8	43.2	23.9	30.1	0.0	70.3	29.2	0.4
Subsequent	204 (85.4)	35 (14.6)	6.4	44.1	25.0	24.5	0.0	73.0	26.0	1.0
Total	676 (80.1)	168 (19.9)	3.9	43.5	24.3	28.4	0.0	71.2	28.3	0.6

TABLE 6.
Results from screening programmes in the Netherlands and the LUCK compared with the standards set by the European guidelines (14)

	Desirable level	LUCK 1993-2004	Netherlands 1990-1995
Initial screening			
Recall rate (%)	< 5	3.2	1.3
CDR/IR*	> 3 X IR	3.62 x IR	2.95 x IR
% Carcinoma in situ	10-20	21.2	14
% Invasive cancers ≤ 10 mm	? 25	37.1	24
% Node-negative invasive cancers	> 70	72.6	67
B:M biopsy ratio	< 0.5:1	0.02:1	0.5:1

* IR: Background incidence rate 1992 = 2.01 (10).

TABLE 7.
Results from screening programmes in the Netherlands and the LUCK compared with the standards set by the European guidelines (14)

	Desirable level	LUCK 1993-2004	Netherlands 1990-1995
Subsequent screening			
Recall rate (%)	< 3	1.6	0.7
CDR/IR*	> 1.5 x IR	2.51 x IR	1.44 x IR
% Carcinoma in situ	10-20	14.8	14
% Invasive cancers Ş 10 mm	? 30	43.7	29
% Node-negative invasive cancers	> 75	74.9	71
B:M biopsy ratio	< 0.2:1	0.01:1	0.3:1

* IR: Background incidence rate 1992 = 2.01 (10).

cancers exceeded the desirable levels in initial screens and nearly met the acceptable levels in subsequent screens (74.9% vs. 75.0%).

Discussion

The results as described here give an insight into the performance of the organized screening in the provinces of Flemish-Brabant and Limburg for which the LUCK is in charge, in the periods before (1993-

14/06/2001) and after the introduction of the Flemish screening programme (15/06/2001-31/12/2004).

In the first period, before the implementation of the programme, the screening activity in Flemish-Brabant and Limburg was limited to pilot population-based screening projects.

When we look at the performance of the screening activity during this period we did not find much differences from observed parameters after the introduction of the programme.

The screening coverage was low in both periods. Even if there was an increasing trend since the beginning of the programme the level was still low in comparison with the standard levels set by the European guidelines (14). It should be remembered that these figures do not take into account that some women were undergoing current treatment for breast cancer or going for regular check-ups following breast cancer and more importantly, the presence in Belgium of an intense opportunistic screening activity. In countries with a decentralized or liberal health care system like Belgium, participation rates in organized screening mammography rarely exceed 50% of the target population whereas higher participation rates are more often seen in countries with centrally organized health care systems (3, 4).

The recall rates of both periods (3.1% BS and 2.5% AS) were lower than the desirable European standards and the referral rates found in most other programmes (4, 5).

The Netherlands may be the sole exception. The Dutch screening programme has reported recall rates as low as 1.1% for the period 1990-1995 (6) while our RR of all women screened in this period was 2.7%. Our low recall rate can be explained by the systematic 2nd reading, in practice since 1989 (1) with a third reading in cases of disagreement. Duijm et al. (7) found that if all the cases in which the two screening radiologists disagreed had been referred for diagnostic assessment without having reached a consensus the referral rate would almost have doubled.

Double reading has also been shown to increase the sensitivity of breast-screening programmes with an increase in the cancer detection rate (8-9). Our CDRs, 6.5̣ overall with 7.3̣ and 5.1̣ for initial and subsequent screens respectively, are in line with those observed in Luxembourg, a country with a liberal health care system, higher RRs and a background incidence (IR) similar to that in Belgium (4, 10). We observed an adjusted CDR for initial screens of 3.6 x IR compared to CDRs

ranging from 3.1 x IR to 4.7 x IR in Luxembourg. In subsequent screens the adjusted CDR was 2.5 x IR compared to 2.9 x IR in Luxembourg (4). By contrast, in The Netherlands the CDR for initial screens was 2.8 x IR and the outcomes of subsequent screening examinations (CDR, interval cancer rate and stage distribution) were less favourable than expected (6, 11) probably attributable to the very low recall rate.

In both periods, the adjusted CDRs exceeded the desirable reference levels: more than 3 times the IR for initial screens (3.7 x IR, BS and 3.6 x IR, AS) and more than 1.5 times the IR for subsequent screens (2.3 x IR, BS and 2.6 x IR, AS).

The ultimate goal of screening is to reduce the occurrence of advanced cancers in order to reduce the breast cancer mortality. The tumour size distribution of cancers detected at subsequent screenings might be expected to be more favourable than that of cancers detected at the initial screening. That was the case during the pilot-projects period where the proportion of invasive cancers 10 mm or less in size increased by nearly 65% from the initial to the subsequent screens. By contrast, after the start of the programme the proportion of pT1ab invasive cancers in initial and subsequent screens were similar and exceeded both the European standards established for subsequent screens ($\geqslant$ 30%). The proportion of T2+ tumours clearly decreased in incident screens in the period after the introduction of the programme whereas similar figures were observed in prevalent and incident screens during the first period of the study.

The percentage of node-negative invasive cancers was slightly higher in subsequent screens before as well as after the beginning of the programme, although it decreased slightly after the start of the programme clearly fulfilling the quality criteria in the first period. In the second period this parameter nearly achieved the desirable standards in subsequent screens (73.0% vs > 75% EU standards). A possible explanation for the similarity of breast cancers detected at initial and subsequent screens, and the similarity of cancers detected in subsequent screens in the first period and cancers detected at initial screens during the second period is the long screening interval (12). In the LUCK area between 1995-2000, 23.3% of the subsequent screens took place 30 or more months after the first screening examinations (3). A second reason could be a misclassification of screens as “initial” because previous screens had not been reported or took place before the programme started (1, 13). On the other hand, it has been reported that, in many screening studies, tumours detected in subsequent rounds had no better stage distribution than tumours detected in the first round or that the differences were very small (11).

The B:M biopsy ratio was low for initial screening (0.02:1) as well as for subsequent screening (0.01:1) compared with the European Standard (0.5:1 vs 0.3:1). There are several possible explanations: the low recall rate as reported earlier and the great expertise of the second readers in combination with the fact that the last years more core biopsies are taken before surgical biopsy.

Conclusions

The performance of the screening activity in both periods had a high quality despite the low participation, which was within the ranges expected in a country with a decentralized health care system.

The performance parameters in both periods clearly fulfilled the desirable reference values recommended by the European guidelines (14) except for the proportion of node-negative invasive cancers in subsequent screens during the second period, which nearly met the acceptable level.

The results obtained in the first period before the introduction of the Flemish programme can be seen as a translation of the knowledge and expertise acquired in the first pilot project in the provinces of Antwerp and Limburg in 1989.

It is possible to transfer the knowhow from an experimental situation to a service programme as the results during the second period demonstrate.

There is still room for improvement in the participation. Efforts have to be made to keep promoting breast cancer screening and to encourage the compliance of attenders.

Résumé

Le Centre Universitaire pour le dépistage du cancer de Leuven (LUCK) participe dans le dépistage du cancer du sein depuis 1993.
Le programme de dépistage dans la région Flamande a commencé le 15 juin 2001. Le LUCK participe dans ce programme avec un dépistage biennal pour les femmes de 50 jusqu'à 69 ans.

Ce document présente les résultats des projets pilotes de 1993 - 14/06/2001 (BS) et les résultats du 15 juin 2001 jusqu'à 2004 (AS) dans les provinces de Brabant-Flamand et Limbourg. Ces résultats sont comparés avec les standards européens recommandés.

Méthodes: *Les indications précoces de qualité, selon les 'The European Guidelines for Mammographic Screening' étaient calculés, et cela non seulement pour les premiers tours, mais aussi pour les autres tours de dépistage.*

Résultats: *dans cette période 194.118 femmes ont reçu un dépistage, 64.503 avant, et 129.615 après le début du programme Flamande. La couverture dans la première période était entre 14,3% et 32,7% (BS), la couverture AS était variable entre 34,6% et 44,4%. Le nombre des femmes rappelées était entre 3,1% (BS) et 2,5% (AS).*

Par mille femmes dépistées 6,6 (BS) et 6,5 (AS) cancers du sein étaient détectés. De ces cancers 81,2% (BS) et 80,1% (AS) étaient invasifs. Des cancers invasifs 29,7% (BS) et 43,5% (AS) étaient moins que 10 mm, et 76,5% (BS) et 71,6% (AS) n'avaient pas de ganglions positives.

Conclusions: *les paramètres de performances dans ces deux périodes correspondent dans la plupart des cas avec les standards Européens.*

Samenvatting

Het Leuvens Universitair Centrum voor Kankerpreventie (LUCK) is al sinds 1993 betrokken bij de borstkankerpreventie. Het LUCK werkt mee aan het screeningsprogramma van de Vlaamse Overheid dat gestart is op 15 juni 2001. Dit programma voorziet in een tweejaarlijkse mammografie voor vrouwen tussen 50 en 69 jaar.

Dit document stelt de surrogaatindicatoren voor vanaf 1993 tot 14 juni 2001 (BS) en vanaf 15 juni 2001 tot 2004 (AS) in de provincies Vlaams-Brabant en Limburg en onderzoekt of de Europese standaardnormen al of niet gehaald werden.

Methoden: *Vroegere kwaliteitsnormen, overeenkomstig de Europese richtlijnen voor mammografische screening, zijn zowel voor de initiële als voor de vervolgscreenings berekend.*

Resultaten: *In deze periode werden 194 118 vrouwen gescreend: 64.503 voor en 129.615 na de start van het Vlaamse programma. De dekkingsgraad in de 1ste periode liep van 14,3 % tot 32,7 % terwijl de dekkingsgraad na de start van het Vlaamse programma varieerde tussen 34,6 % en 44,4 %.*

De overeenkomstige heroproepen zijn 3,1% (BS) en 2,5% (AS). Per 1.000 gescreende vrouwen werden er 6,6 % (BS) en 6,5% (AS) borstkankers ontdekt. Bij de invasieve kankers waren er 29,7% (BS) en 43,5 % (AS) kleiner dan 10 mm. en 76,5% (BS) en 71,6% (AS) hebben geen positieve lymfeklieren.

Besluit: *De voorgestelde parameters betreffende deze 2 periodes voldoen in de meeste gevallen aan de Europese normen.*

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