Thieme

Evaluations of the 2019 Annual Statistics Under the Cervical Cytology Quality Assurance Agreement

2019 Annual Statistics for Cervical Cytology from 15 608 413 Women

Auswertungen der Jahresstatistik 2019 im Rahmen der Qualitätssicherungsvereinbarung Zervix-Zytologie

Jahresstatistik Zervix-Zytologie 2019 von 15 608 413 Frauen

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Key words

cervical cancer, precancerous cervical lesions, epidemiology, cervix, quality assurance, cytology

Schlüsselwörter

Zervixkarzinom, Zervixpräkanzerose, Epidemiologie, Zervix, Qualitätssicherung, Zytologie

received 18.4.2023
accepted after revision 20.7.2023
published online 22.9.2023

Bibliography

Geburtsh Frauenheilk 2023; 83: 1235–1249
DOI 10.1055/a-2134-6740
ISSN 0016-5751

Georg Thieme Verlag KG, Rüdigerstraße 14, 70469 Stuttgart, Germany

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Deutsche Version unter: https://doi.org/10.1055/a-2134-6740.

ABSTRACT

Background

Cervical cancer screening, which was introduced into the programme of medical care covered by statutory health insurance in Germany in 1971 and has since been constantly updated through quality assurance measures, was fundamentally revised and developed in 2008 through the Cervical Cytology Quality Assurance Agreement pursuant to Section 135(2) of the German Social Code Book V [SGB V]. Since 2015 it has been mandatory for cytology facilities to record annual statistics based on the Munich Nomenclature III. The aim of this article is to present the results of the annual statistics for 2019, which was the last year before the introduction of the cervical cancer screening programme in accordance with the Federal Joint Committee's guideline on organised cancer screening programmes [1].

Materials and Methods

The annual statistics of the laboratories, including histology analyses performed up until 30 June the following year, are reported to the Regional Associations of Statutory Health Insurance Physicians. The laboratories receive benchmark reports from their Regional Associations of Statutory Health Insurance Physicians, and these statistics are transmitted anonymously to the National Association of Statutory Health Insurance Physicians (KBV).

Results

In 2019, 17 609 082 smears from 15 608 413 women were examined in Germany. Of these smears, 97.49 % were normal and 2.51 % showed atypical or suspicious changes, consisting mostly of minor squamous epithelial changes in groups II-p (0.81 %) and IIID1 (0.735 %).

Histology specimens are available for "Dysplasia findings with higher probability of regression" in group IIID1 (4.89 %

of initial IIID1 cytology findings), group IIID2 (18.60 %), "unclear or doubtful findings" in group III-p to x (20.7 %), and "immediate precursors to cervical carcinoma" in group IV (83.1 %) and group V (77.19 %).

In the cytology findings for group IVa-p, which corresponds to CIN 3 target lesions, the cytology correlated with the histology finding in 80.48 % of cases.

Lesions found in 2019: 23 463 CIN 3 lesions, 668 adenocarcinomas in situ, 3891 malignant tumours, including 2342 cervical carcinomas of which 1743 were squamous cell carcinomas and 599 were cervical adenocarcinomas (25.57 %); 1549 endometrial carcinomas and other malignancies.

Inference/Conclusion

The data demonstrate the good practicability of cervical cancer screening in 2019. Higher grade lesions were reliably clarified histologically.

ZUSAMMENFASSUNG

Hintergrund

Die Früherkennung des Zervixkarzinoms, eingeführt 1971 in die vertragsärztliche Versorgung der Bundesrepublik Deutschland und durch Maßnahmen zur Qualitätssicherung immer wieder aktualisiert, wurde 2008 durch die Qualitätssicherungsvereinbarung Zervix-Zytologie nach § 135 Absatz 2 Sozialgesetzbuch V grundlegend überarbeitet und weiterentwickelt. Die obligatorischen Jahresstatistiken sind von den zytologischen Einrichtungen seit 2015 verbindlich nach der Münchner Nomenklatur III anzufertigen. Ziel der Arbeit ist die Darstellung von Ergebnissen aus der Jahresstatistik 2019, dem letzten Jahr vor Einführung des Programms zur Früherkennung des Zervixkarzinoms nach der Richtlinie des G-BA für organisierte Krebsfrüherkennungsprogramme [1].

Material und Methoden

Die Jahresstatistiken der Laboratorien werden mit Einbeziehung der bis 30. Juni des Folgejahres erfolgten Histologien den Landes-KVen gemeldet. Die Laboratorien erhalten von ihren KVen hierzu Benchmarkberichte, diese Statistiken werden anonymisiert an die Kassenärztliche Bundesvereinigung (KBV) weitergeleitet.

Ergebnisse

2019 wurden in Deutschland 17 609 082 Abstriche von 15 608 413 Frauen untersucht. 97,49 % der Abstriche waren unverdächtig, 2,51 % auffällig, darunter überwiegend geringfügige plattenepitheliale Veränderungen der Gruppen II-p (0,81 %) und IIID1 (0,735 %).

Histologien liegen vor bei „intraepithelialen Veränderungen mit größerer Regressionsneigung" Gruppe IIID1 (4,89 % der zytologischen IIID1-Ausgangsbefunde), IIID2 (18,60 %), bei „unklaren bzw. zweifelhaften Befunde" der Gruppe III-p bis x (20,7 %), bei „unmittelbaren Vorstadien des Zervixkarzinoms" der Gruppe IV (83,1 %) und bei der Gruppe V (77,19 %).

Bei den zytologischen Befunden der Gruppe IVa-p, welche die Zielläsion einer CIN 3 abbildet, korreliert die Zytologie mit dem histologischen Befund in 80,48 % der Fälle.

2019 gefundene Läsionen: 23 463 CIN 3, 668 Adenocarcinoma in situ, 3891 maligne Tumoren, darunter 2342 Zervixkarzinome, davon 1743 Plattenepithelkarzinome sowie 599 Zervixadenokarzinome (25,57 %); 1549 Endometriumkarzinome und sonstige Malignome.

Schlussfolgerungen/Fazit

Die Daten zeigen die gute Praktikabilität der Früherkennung des Zervixkarzinoms im Jahr 2019. Höhergradige Läsionen wurden zuverlässig abgeklärt.

Introduction

Back in 1971, a screening examination using the Papanicolaou cervical smear, or Pap smear, was introduced in Germany. Since then, all women covered by statutory health insurance have been entitled to an annual cancer screening examination. In the meantime, there have been further developments in the accompanying quality assurance measures, in particular for cervical cytology.

A very important step was the fundamental revision and development of the Cervical Cytology Quality Assurance Agreement pursuant to Section 135(2) of the German Social Code Book V [SGB V], which entered into force on 1 October 2007 [2].

In addition to measures relating to the entry qualification of eligible medical groups, the qualification of cytology assistants responsible for assessing specimens, ensuring regular continuing education, QA sampling of cytology preparations, and medical documentation, the doctors designated as "physicians responsible for cytology" were now also required to compile annual statistical records of the examination results, referred to as the "annual statistics". In the context of the clinic's internal organisation, this requires the aggregation and correlation of cytology and histology findings. The annual statistics, which include a case-based listing of the cytology finding groups, are reviewed and evaluated by the Cytology Committees of the Regional Associations of Statutory Health Insurance Physicians. Any anomalies are clarified in dialogue with the physicians responsible for cytology.

The Munich Nomenclature is the diagnostic scheme used nationwide for cytodiagnosis of cervical smears. An updated version, the Munich Nomenclature III, entered into force on 1 July 2014 [3]. The Munich Nomenclature III [3] essentially corresponds to the Bethesda system [4] and is also an important basis for the S3 guideline on prevention of cervical cancer [5] and its procedural algorithms. With the introduction of the Munich Nomenclature III and the associated finding groups, the data collection form was

updated as an annex to the cytology agreement. The annual statistics of the respective Regional Associations of Statutory Health Insurance Physicians are forwarded to the National Association of Statutory Health Insurance Physicians, where they are compiled and evaluated. The aggregated and anonymised data are made available to the Federal Collective Agreement partners for further consultation at the federal level.

The data provide a unique view of a country's cervical carcinoma screening over a period of a year, based on the size of the population, the uniform nomenclature, and the three-tier categorisation of intraepithelial lesions.

Data for the years 2015 to 2016 have already been obtained and evaluated in a similar way [6]. In this article we examine the data from the 2019 reporting year.

In 2020, the organised screening programme for cervical cancer was launched with additional HPV testing for women aged 35 and over. For this reason the data from 2020 cannot easily be compared to the data from previous years, partly due to the specification of algorithms for clarifying suspicious findings.

Cervical Cytology Quality Assurance Agreement

The original "Agreement on qualification requirements for conducting cytological examinations for the diagnosis of carcinomas of the female genitals pursuant to Section 135(2) SGB V" (Cytology Agreement) dates from 1992. Amended in 1994, it only regulated the structural quality aspects of the qualification requirements for conducting and billing for cytological examinations.

In order to standardise existing regional quality assurance activities, including in terms of process and result quality, and to adapt them to be in line with international concepts, the partners of the Federal Collective Agreement substantially revised the existing cytology agreement, with effect from 1 October 2007. In the following years there were further adaptations and developments, although some of these were minor. In particular, the rules currently in force relate to the following important aspects:

Uniform entrance qualification

For pathologists and gynaecologists, in addition to successfully completing an examination on specimens, uniform entry qualifications are regulated in Section 3.

Professional qualification of cytology assistants responsible for assessing specimens

For technical assistants in cytology laboratories who are responsible for assessing specimens under the guidance and supervision of the physicians responsible for cytology, the professional qualification is defined in Section 4 of the abovementioned Quality Assurance Agreement.

Assessment of cytology specimens

The process quality requirements for cytology specimen findings set out in Section 6 of the Quality Assurance Agreement stipulate that assessment of the cytology specimen must take place on the premises of the cytology facility and in a cytology workspace. Assessment of the specimen can also be delegated by the "physician responsible for cytology" to the "cytology assistant responsible for assessing specimens". Cytology assistants working at a microscope must not assess more than 10 specimens per working hour on average. This has not been changed for thin-layer cytology.

The agreement contains further requirements for the preparation of specimens (e.g., Papanicolaou staining) and makes it mandatory for specimens to be assessed in accordance with the "Munich Nomenclature III". It also determines which specimens should be evaluated in each case by the physician responsible for cytology. Within the framework of the clinic's internal organisation (Section 10), the requirements include, among other things, re-examination of a random selection of at least 5 % of all specimens assessed as negative, and the establishment of a "recall system" for cytology and histology findings that need to be checked.

Review of specimen quality and medical documentation

The Association of Statutory Health Insurance Physicians requires physicians responsible for cytology to submit 12 specimens, each with the associated documentation and findings, every 24 months (Section 7). The submitted specimens are checked by the Quality Assurance Committee for adequate technical quality of the specimen preparation, for a correct and complete evaluation of the specimen, and for complete documentation. If the review has been passed twice in a row, the specimen quality and documentation of the physician responsible for cytology will be re-checked every 4 years (four-year review cycle).

Statistical recording of examination results

Relating conspicuous cytology findings to histology is a core element of both national and international approaches to quality assurance in cervical cytology. The physician responsible for cytology is required to compile the "annual statistics", which include a case-based listing of the cytological diagnostic groups (Section 8) for which cytology and histology findings have been combined and correlated as part of the clinic's internal organisational procedures. The Regional Association of Statutory Health Insurance Physicians provides the physician with the consolidated annual statistics ("benchmark report") for the respective area under its purview.

Materials and Methods

All data in the 2019 annual statistics were collected under the Cervical Cytology Quality Assurance Agreement. Annual statistics are compiled by all physicians who carry out preventive and curative cytological examinations, as well as cytological examinations necessary in the context of contraception. For this purpose, we determined the total number of cytological examinations performed from 1 January to 31 December of the given year. The number of technically unsatisfactory findings (Group 0) was reported. The statistics also include women with hysterectomy or neovagina. For the purpose of correlating cytology and histology, the cytology findings from the highest finding group were mapped to the results from the histology examinations performed up to 30 June of the following year.

The data collected and submitted by the physicians responsible for cytology are from cytology facilities/laboratories of different sizes. While preserving the anonymity of the participating women,

the cytology facilities forward the data to the responsible Association of Statutory Health Insurance Physicians. The Cytology Committees of the 17 Regional Associations of Statutory Health Insurance Physicians evaluate the statistics from each facility, perform an expert assessment in consultation with the respective facility, and, if necessary, provide guidance and recommendations. The aggregated statistics are then forwarded by the Regional Associations of Statutory Health Insurance Physicians to the National Association of Statutory Health Insurance Physicians.

The annual statistics for 2019 were evaluated on the basis of these statistics compiled by the National Association of Statutory Health Insurance Physicians. Without exception, this involves an approved extract of confidential data from the National Association of Statutory Health Insurance Physicians and Regional Associations of Health Insurance Physicians.

When collecting and merging such large amounts of data, errors can occur at all levels: data collection in the laboratories, compilation of statistics, transmission of data, and consolidation of data by the Regional Associations of Statutory Health Insurance Physicians (KVs). Good data quality was ensured through computational and technical plausibility checks. There are no obvious indications that the results are distorted by undetected errors.

Results of the Evaluation of the 2019 Annual Statistics

Data for the years 2017 to 2019 are currently being evaluated. The data for 2019, the last year before the start of "organised screening" [1], are presented and considered here.

Development of the number of laboratories and physicians with billing authorisation

Both the number of cytology facilities/laboratories and the number of physicians with billing authorisation (▶ **Table 1**) are continuously decreasing, continuing a previously known trend [6].

▶**Table 1** Trend in the number of cytology laboratories and physicians with billing authorisation in Germany from 2011–2019 (as of: 10 May 2021).

Year	Facilities/ Laboratories	Doctors with billing authorisation
2011	761	1025
2012	727	1017
2013	699	986
2014	667	976
2015	635	942
2016	587	898
2017	553	871
2018	524	833
2019	491	806

▶**Table 2** Number of specimens, technically unsatisfactory specimens, number of women examined, and total number of women in Germany from 2017 to 2019.

Year	Specimens	Unsatisfactory specimens	Women examined	Total number of women [7]
2017	17833170	24809 (0.14%)	15707768	41948786
2018	17783495	26781 (0.15%)	15640595	42052522
2019	17609082	25630 (0.15%)	15608413	42129098

Number of specimens, technically unsatisfactory findings, women examined

▶ **Table 2** shows the number of specimens, the number of unsatisfactory specimens, the number of women examined, and the number of women in Germany for the years 2017, 2018, and 2019. Only cases in which no diagnostically usable smear was able to be assessed, even when the woman was re-examined in the same year, are recorded as technically unsatisfactory specimens. The number of women examined, on average 15.65 million per year (approximately 37% of all women in Germany [7]), indicates that there is a good rate of participation in the cancer screening programme (see ▶ **Table 2**). Data with an age breakdown, taking into account multi-year cumulative participation rates [8], provide a more detailed view.

The cytology findings for 2019 came from 491 cytology facilities/laboratories. The average number of examinations per facility was 35863. This makes an average of 21847 examinations for each physician responsible for cytology.

The number of unsatisfactory specimens compared to the number of women examined is very low. The number of examinations per facility and by physician responsible for cytology is increasing, see ▶ **Table 1** and ▶ **Table 2**.

Cytological diagnostic groups according to the Munich Nomenclature III

Among the **Diagnostic Groups** (▶ **Fig. 1**) according to the Munich Nomenclature III, normal (negative) findings (**Groups I and II-a**) make up the vast majority at 97.49%. This includes negative cytology findings classified as II-a (0.660%) due to anomalies in the patient's medical history (▶ **Fig. 2**, row 1).

Among group II findings (**"findings with limited protective value", II-p, II-g, II-e)** [9], with a combined rate of 1.061%, marginal squamous epithelial changes (II-p ≙ ASC-US) are predominant at 0.814%.

Among the conspicuous findings, there was a predominance of cases such as groups II-p and IIID1 that did not require immediate action in 2019 other than, for example, cytology check-ups. This means that only about 1% of the findings in 2019 resulted in measures that went beyond cytology check-ups.

Coordination Conference on Cytology (KoKoZyt)
Munich Nomenclature III for gynaecological cytodiagnosis of the cervix

Group	Definition → Management	Correlate in the Bethesda system
0	**Insufficient material → repeat smear**	Unsatisfactory for evaluation
I	**Normal, no suspicious findings** → *Smears performed at normal screening interval*	NILM
II-a	**Unconspicuous findings with a conspicuous medical history** → *If applicable, repeat cytology due to abnormal medical history (cytological/histological/colposcopic/clinical finding)*	NILM
II	**Findings with limited protective value**	
II-p	Squamous epithelial cells with less severe nuclear changes than in CIN 1, also with koilocytic cytoplasm/parakeratosis → *Repeat cytology if applicable, taking into account medical history and clinical findings (e.g., after anti-inflammatory treatment and/or hormonal clarification; in special cases, additive methods and/or colposcopy)*	ASC-US
II-g	Cervical glandular cells with abnormalities beyond the spectrum of reactive changes → *Repeat cytology if applicable, taking into account medical history and clinical findings (e.g., after anti-inflammatory treatment and/or hormonal clarification; in special cases, additive methods and/or colposcopy)*	AGC endocervical NOS
II-e	Endometrial cells in women aged over 40 in the second half of the cycle → *Clinical check-up taking into account medical history and clinical finding*	Endometrial cells
III	**Unclear or doubtful findings**	
III-p	**CIN 2/CIN 3/squamous cell carcinoma cannot be excluded** → *Differential colposcopy, additive methods if applicable, possibly short-term cytological control after anti-inflammatory treatment and/or hormonal clarification*	ASC-H
III-g	Pronounced atypia of the glandular epithelium, adenocarcinoma in situ/ invasive adenocarcinoma cannot be ruled out → *Differential colposcopy, additive methods if applicable*	AGC endocervical, favour neoplastic
III-e	Abnormal endometrial cells (especially postmenopausal) → *Further clinical diagnostics, with histological clarification where applicable*	AGC endometrial
III-x	Suspicious glandular cells of uncertain origin → *Further diagnostics (e.g., fractionated abrasion; additive methods/differential colposcopy if applicable)*	AGC, favour neoplastic
IIID	**Dysplasia findings with higher probability of regression**	
IIID1	Cell image of mild dysplasia corresponding to CIN 1 → *Repeat cytology in 6 months, if it persists > 1 year: additive methods/differential colposcopy, if applicable*	LSIL
IIID2	Cell image of moderate dysplasia corresponding to CIN 2 → *Repeat cytology in 3 months, if it persists > 6 months: Differential colposcopy, additive methods, if applicable*	HSIL/CIN 2
IV	**Immediate precursors to cervical carcinoma** → *Differential colposcopy and therapy*	
IVa-p	Cell image of severe dysplasia/carcinoma in situ corresponding to CIN 3	HSIL/CIN 3
IVa-g	Cell image of adenocarcinoma in situ	AIS
IVb-p	CIN 3 cell image, invasion not excluded	HSIL with features susp. for invasion
IVb-g	Cell image of adenocarcinoma in situ, invasion not excluded	AIS with features susp. for invasion
V	Malignancies → *Further diagnostics with histology and therapy*	
V-p	Squamous cell carcinoma	Squamous cell carcinoma
V-g	Endocervical adenocarcinoma	Endocervical adenocarcinoma
V-e	Endometrial adenocarcinoma	Endometrial adenocarcinoma
V-x	Other malignancies, including those of unclear origin	Other malignant neoplasms

▶ **Fig. 1** Munich Nomenclature III: Data from the Cytology Coordination Conference [3]: Adapted here in such a way that the increasing risk is roughly illustrated in colour according to a traffic light scheme. Green: very low risk; yellow: IIID1 and IIID2, low risk for invasive carcinoma but significant risk for CIN 3; grey: significant risk of malignancy in unclear/doubtful group III; orange: immediate precursors to cervical carcinoma -a with low and -b with higher risk of invasion; red: malignancies. Very high probability of malignancy.

Initial findings (01/01–31/12) 2019	Negative		Group II			Group III				Group IIID		Group IV				Group V				Sum of all initial findings (I/II to V)
	I	II-a	II-p	II-g	II-e	III-p	III-g	III-e	III-x	IIID1	IIID2	IVa-p	IVa-g	IVb-p	IVb-g	V-p	V-g	V-e	V-x	
Number of women	15113475	103031	127037	24156	14373	18882	6295	3369	1016	114688	54797	22784	917	1157	134	1311	265	442	284	15608413
% of all initial findings	**96.83%**	**0.660%**	**0.814%**	**0.155%**	**0.092%**	**0.121%**	**0.040%**	**0.022%**	**0.007%**	**0.735%**	**0.351%**	**0.146%**	**0.006%**	**0.007%**	**0.001%**	**0.008%**	**0.002%**	**0.003%**	**0.002%**	
Cases for which histological clarification was performed by 30 June of the following year																				
No indication of carcinoma precursors or carcinoma	1650	3481	775	195	172	927	619	709	100	1354	1056	746	52	46	4	16	7	28	6	11943
CIN 1	97	208	253	20	2	322	99	10	13	2163	1290	480	25	12	4	1	1	0	0	5000
CIN 2	53	95	217	10	3	589	124	8	13	1260	3943	1787	33	43	3	7	0	1	0	8189
CIN 3	68	136	107	24	0	1686	381	12	45	799	3828	15259	327	558	26	187	9	5	6	23463
Adenocarcinoma in situ	8	4	9	4	0	34	144	10	9	9	20	143	219	14	18	11	9	2	1	668
Squamous cell carcinoma of the uterine cervix	19	7	9	4	2	202	42	11	23	3	35	450	21	207	16	627	33	12	20	1743
Adenocarcinoma of the uterine cervix	10	2	6	9	1	36	77	47	18	3	5	59	75	17	25	61	100	35	13	599
Endometrial carcinoma, other malignancies	96	31	9	16	32	107	73	377	123	15	13	35	8	25	10	110	59	273	137	1549
Total (findings with histological clarification)	**2001**	**3964**	**1385**	**282**	**212**	**3903**	**1559**	**1184**	**344**	**5606**	**10190**	**18959**	**760**	**922**	**106**	**1020**	**218**	**356**	**183**	**53154**
% of findings with histological clarification (% of initial findings)	**0.01%**	**3.85%**	**1.09%**	**1.17%**	**1.47%**	**20.7%**	**24.8%**	**35.14%**	**33.86%**	**4.89%**	**18.60%**	**83.21%**	**82.88%**	**79.69%**	**79.10%**	**77.80%**	**82.26%**	**80.54%**	**64.44%**	**0.341%**
% of total initial findings for which there was histological clarification	**0.01%**	**0.03%**	**0.01%**	**0.00%**	**0.00%**	**0.03%**	**0.01%**	**0.01%**	**0.00%**	**0.04%**	**0.07%**	**0.12%**	**0.00%**	**0.01%**	**0.00%**	**0.01%**	**0.00%**	**0.00%**	**0.00%**	**0.341%**
	15382072					**29562**				**169485**		**24992**				**2302**				
	7844					**6990**				**15796**		**20747**				**1777**				
Histological clarification	**0.051%**					**23.65%**				**9.32%**		**83.01%**				**77.19%**				

	Negative		Group II			Group III				Group IIID		Group IV				Group V				
	I	II-a	II-p	II-g	II-e	III-p	III-g	III-e	III-x	IIID1	IIID2	IVa-p	IVa-g	IVb-p	IVb-g	V-p	V-g	V-e	V-x	
No indication of carcinoma precursors or carcinoma	82.46	87.82	55.96	69.15	81.13	23.75	39.70	59.88	29.07	24.15	10.36	3.93	6.84	4.99	3.77	1.57	3.21	7.87	3.28	22.47
CIN 1	4.85	5.25	18.27	7.09	0.94	8.25	6.35	0.84	3.78	38.58	12.66	2.53	3.29	1.30	3.77	0.10	0.46	0.00	0.00	9.41
CIN 2	2.65	2.40	15.67	3.55	1.42	15.09	7.95	0.68	3.78	22.48	38.69	9.43	4.34	4.66	2.83	0.69	0.00	0.28	0.00	15.41
CIN 3	3.40	3.43	7.73	8.51	0.00	43.20	24.44	1.01	13.08	14.25	37.57	80.48	43.03	60.52	24.53	18.33	4.13	1.40	3.28	44.14
Adenocarcinoma in situ	0.40	0.10	0.65	1.42	0.00	0.87	9.24	0.84	2.62	0.16	0.20	0.75	28.82	1.52	16.98	1.08	4.13	0.56	0.55	1.26
Squamous cell carcinoma of the uterine cervix	0.95	0.18	0.65	1.42	0.94	5.18	2.69	0.93	6.69	0.05	0.34	2.37	2.76	22.45	15.09	61.47	15.14	3.37	10.93	3.28
Adenocarcinoma of the uterine cervix	0.50	0.05	0.43	3.19	0.47	0.92	4.94	3.97	5.23	0.05	0.05	0.31	9.87	1.84	23.58	5.98	45.87	9.83	7.10	1.13
Endometrial carcinoma, other malignancies	4.80	0.78	0.65	5.67	15.09	2.74	4.68	31.84	35.76	0.27	0.13	0.18	1.05	2.71	9.43	10.78	27.06	76.69	74.86	2.91

▶ **Fig. 2** Annual Statistics 2019 Cytohistological Correlation in 15 608 423 Women.

Also among the **"unclear or doubtful findings"** (**Groups III-p to III-x**), with a combined rate of 0.190%, squamous epithelial changes (III-p) were predominant at 0.121%.

The group for **"Dysplasia findings with higher probability of regression" (IIID1 and IIID2)** represents the largest group of conspicuous findings, at 1.086%. At 0.735%, IIID1 (cytology of mild dysplasia ≙ CIN 1) was more prevalent than IIID2 (cell picture of moderate dysplasia ≙ CIN 2) at 0.351%. The ratio of IIID1 to IIID2 is 2.094. IIID2 is about 2.5 times more common than IVa-p (see below). Thus, the abnormalities become less frequent as they become more severe. The image of IIID1/CIN 1 corresponds to a mostly reversible HPV-related lesion of the cervix, which is not usually considered to require treatment. For II-p, the changes are even smaller.

Group IV (0.16%) represents "immediate precursors to cervical carcinoma", severe dysplasia and *carcinoma in situ* (together corresponding to CIN 3), and *adenocarcinoma in situ* (AIS). IV-a stands for cases without evidence of invasive carcinoma, IV-b stands for cases with insufficient evidence of invasive growth. The most common finding in group IV was IVa-p, the cytology corresponding to CIN 3, at 0.146%. In other words, the most important target lesion of cervical cancer screening was assumed to be present in 22784 cases. The cytology finding IVa-g corresponding to an expectation of glandular lesions, i.e., *adenocarcinoma in situ* (AIS), was much less common, with 917 cases (0.006%). The finding groups IVb-p corresponding to CIN 3 with incomplete features of invasion, n = 1157 (0.007%), and IVb-g corresponding to the cytological expectation of an AIS with incomplete features of invasion, n = 134 (0.001%), were significantly less frequent.

Cytological suspicion of CIN 3 constitutes the largest group of cases classified among the immediate precursors to cervical carcinoma. Cytological findings corresponding to CIN 3 (IVa-p) are more than 20 times more frequent than indications of AIS (IVa-g).

Cell images with the cytology of **"Malignancies" (groups V-p to V-x)** represent only a small portion of the conspicuous cytology findings (n = 2302, 0.0147%). Squamous epithelial findings were also predominant in groups V-p to V-x (group V-p).

Proportion of histological examinations in the cytology groups

The cytology diagnostic groups based on the Munich nomenclature III (▶ **Fig. 1**) were matched to the histology findings. A total of 53154 histology findings were submitted (▶ **Fig. 2**).

The total number of histology analyses triggered by cytology is very low. The proportion of histological examinations increases with the severity of the cytology findings.

Few histological examinations have been documented for negative cytology findings (groups I and II-a). As expected, fewer histological examinations were recorded for the group I findings (group I, 0.01%) than for women with anomalies in their medical history (group II-a, 0.03%).

"Findings with limited protective value" [9]: The proportion of histological examinations for II-p to II-e ranged from 1.09% for II-p to 1.47% for II-e. For II-g, the proportion of "histological clarifications" was 1.17%.

However, there is no consistent ascending risk trend among the Munich Nomenclature III diagnostic groups I to V. Group III with the unclear/doubtful findings is arbitrarily placed ahead of the groups of findings with the expectation of clearly definable histology, i.e., before groups IIID1 to V-x. Accordingly, in ▶ **Fig. 1**, the groups of findings are marked with colours ranging from green to red according to increasing risk.

"Unclear or Doubtful Findings": In groups III-p to III-x, the rate of histological examinations ranged from 20.7% in III-p to 35.14% in III-e. The rate of histological clarification was 24.8% for III-g. The fact that histological clarification is most common in group III-e may be due to the fact that **cytology monitoring** is usually not useful in these cases, and HPV diagnostics can only make a minimal contribution to determining the likelihood of cervical versus endometrial lesions.

In case of cytological suspicion of **intraepithelial squamous epithelial lesions** (IIID1 ≙ CIN 1, IIID2 ≙ CIN 2 and IVa-p ≙ CIN 3), histology specimens were presented in 4.89% of cases for group IIID1, 18.60% for group IIID2, and 83.21% of cases for group IVa-p (▶ **Table 3**). I.e., for "Dysplasia findings with higher probability of regression", histology is predominantly not performed for **IIID1 + IIID2**, while in group **(IVa-p) "immediate precursors to cervical carcinoma"**, results from histological clarification were presented in a very high percentage of cases. The data reflect that an initial IIID1 finding (2019) typically does not involve a histological examination. The high regression rate of these lesions has been known for a long time [10]. Reasons for histological clarification may include prolonged persistence, the patient's wishes, or abnormalities during the clinical examination. For cytological and histological findings that need to be checked, laboratories have set up a "recall system" in accordance with the Cytology Agreement. However, colposcopy findings are not recorded in the cytology laboratories, so it is not possible to correlate cytology results to colposcopy results. The recall system serves to ensure the quality of cytology services and helps patients to receive appropriate care from the time of the initial suspicious finding until their condition is clearly diagnosed. Patients who had two normal follow-up findings after one or more IIID1 finding would return to the usual annual screening program without histological examination. If a patient had a group IVa-p finding in the same year after cytological control following a IIID1 finding (usually after about six months), that patient would appear under IVa-p in the statistics.

With regard to histological clarifications for groups IVb-p, IVb-g and groups V-p to V-x, in some cases fewer histological specimens were able to be submitted. The proportion of histological clarifications in group V-p was 77.80%. In principle, there is a conflict between the desire for prompt quality assurance with feedback for the laboratories and the desire for ideal data quality; in this regard, the specified submission deadlines represent a compromise. At the time of compiling the annual statistics for 2019, laboratories faced an extreme organisational burden due to the shift to "organised screening", while at the same time there were burdens due to the coronavirus pandemic. However, it can be assumed that it is very rare that organisational errors would prevent histological clarification of a group V case, as cytology laboratories have a "recall" system in place for dealing with conspicuous findings [2].

▶**Table 3** Histology results for initial cytology findings IIID1, IIID2 and IVa-p (KBV Annual Statistics 2019). Cells with optimal cytology and histology matching are marked with an *.

	2019 initial cytology findings (total n = 15 608 413)					
	IIID1		IIID2		IVa-p	
	n	%	n	%	n	%
n = number of women	114 688	**0.735**	54 797	**0.351**	22 784	**0.146**
Histological clarification performed up to 30 June of the following year	5606	**4.89**	10 190	**18.60**	18 959	**83.21**
Histology results						
No indication of carcinoma precursors or carcinoma	1354	**24.15**	1056	**10.36**	746	**3.93**
CIN 1	2163*	**38.58***	1290	**12.66**	480	**2.53**
CIN 2	1260	**22.48**	3943*	**38.69***	1787	**9.43**
CIN 3	799	**14.25**	3828	**37.57**	15 259*	**80.48***
Adenocarcinoma in situ	9	**0.16**	20	**0.20**	143	**0.75**
Squamous cell carcinoma of the uterine cervix	3	**0.05**	35	**0.34**	450	**2.37**
Adenocarcinoma of the uterine cervix	3	**0.05**	5	**0.05**	59	**0.31**
Endometrial carcinoma, other malignancies	15	**0.27**	13	**0.13**	35	**0.18**

In 2019, relatively few histological examinations appeared to be required for low-grade lesions with a high regression rate. On the other hand, for serious lesions (CIN 3+), results from histological examinations were able to be submitted in a high percentage of cases.

Cytology finding groups: histology results

Groups I and II-a

For cytology finding groups I and II-a, histological examinations are probably not triggered by cytology in most cases, but rather by additional clinical findings. Correspondingly, far more endometrial carcinomas were identified in this context than cervical squamous cell carcinomas.

Group II (II-p to II-e): Cases with limited protective value

In each of these groups, "endometrial carcinomas and other malignancies", which are located outside the cervix, made up the highest proportion of malignancies. In II-e, there was an increased number of endometrial carcinomas; this can probably be explained considering that endometrial cells occasionally lead to the detection of endometrial carcinomas in the second half of the cycle or in post-menopause even without recognisable atypia (see Bethesda system).

Groups IIID1 and IIID2, "Dysplasia findings with higher probability of regression"

When the Munich Nomenclature III was developed, the three-tiered categorisation of squamous intraepithelial lesions was retained as it appeared to be more appropriate for risk-based patient management than the two-tiered system favoured in the USA [4] and by the WHO [11]. The frequency of IIID1, IIID2 and IVa-p cytology findings decreases with severity, while the frequency of histological clarifications increases with severity (▶ **Table 3**). In 2019, immediate histological clarification is unlikely to have been performed for any IIID1 ≙ CIN 1 finding, while only in exceptional cases (e.g., pregnancy) would histology not have been promptly performed for a IVa-p ≙ CIN 3 finding. Although there are several molecular biological steps in the development of the precursors to cervical carcinoma, the cytology or histology images cannot precisely identify these steps; instead, they essentially correspond to a morphological continuum. The classification is therefore subjective both for cytology and histology [12]. Therefore, a perfect match between cytology and histology findings cannot be expected [13].

In 2019, a high proportion (24.15 %) of histological examinations of IIID1 cases showed no lesion. In contrast, in 2019, only a small proportion (3.93 %) of histological analyses of IVa-p cases showed no lesion. Causes of clinically relevant discrepancies, such as negative histology or only CIN 1 in IVa-p, are usually elucidated through collegial dialogue. A very high match rate was only found for IVa-p corresponding to CIN 3. It is unknown in which cases the histology result was based only on a biopsy or "cone biopsy".

Group III: unclear or doubtful findings

Among the group III-p to III-x findings, there is a significant proportion of malignancies (▶ **Table 4**). There were 278 squamous cell carcinomas, 178 cervical adenocarcinomas, and 680 endometrial and other carcinomas. In total, 1136 carcinomas with a group III finding were identified. Overall, the results show a very good correlation, with histology matching the corresponding epithelial type (III-p, III-g, III-e, III-x) (▶ **Table 4**).

▶**Table 4** Histology results for the initial cytology findings for group III-p, III-g, III-e and III-x (KBV Annual Statistics 2019).

	2019 initial cytology findings for group III							
	III-p		III-g		III-e		III-x	
	n	%	n	%	n	%	n	%
n = number of women	18882	**0.121**	6295	**0.040**	3369	**0.022**	1016	**0.007**
Histological clarification performed up to 30 June of the following year	3903	**20.7**	1559	**24.8**	1184	**35.14**	344	**33.86**
Histology results								
No indication of carcinoma precursors or carcinoma	927	**23.75**	619	**39.70**	709	**59.88**	100	**29.07**
CIN 1	322	**8.25**	99	**6.35**	10	**0.84**	13	**3.78**
CIN 2	589	**15.09**	124	**7.95**	8	**0.68**	13	**3.78**
CIN 3	1686	**43.20**	381	**24.44**	12	**1.01**	45	**13.08**
Adenocarcinoma in situ	34	**0.87**	144	**9.24**	10	**0.84**	9	**2.62**
Squamous cell carcinoma of the uterine cervix	202	**5.18**	42	**2.69**	11	**0.93**	23	**6.69**
Adenocarcinoma of the uterine cervix	36	**0.92**	77	**4.94**	47	**3.97**	18	**5.23**
Endometrial carcinoma, other malignancies	107	**2.74**	73	**4.68**	377	**31.84**	123	**35.76**

Clinically, a histology result of CIN 2, CIN 3, squamous cell carcinoma can be described as a very good match for group III-p. If the histology of a lesion of at least CIN 2 severity ("CIN 2+") is added, the match increases slightly. Predicting AIS and invasive adenocarcinoma of the cervix for group III-g cases is less successful. However, if the histology of a lesion of at least CIN 2 severity ("CIN 2+") is considered to match, this gives rise to a strong improvement. Among the III-e and III-x cases for which histology was performed, there is a strong increase in endometrial carcinomas, with the match for group III-x increasing more strongly when CIN 2+ or CIN 3+ is assessed as matching.

Immediate precancerous stage group (IV)

Group IVa-p is the finding group corresponding to expected CIN 3: The main target lesion in cervical cancer screening is CIN 3, as the development of invasive cervical carcinomas can be stopped by diagnosing and removing CIN 3. This corresponds to cytology finding group IVa-p, with 22784 cases. Histological clarification was performed in 83.21% of these cases (n = 18959), and CIN 3 lesions were found in 80.84%. CIN 2 was found in 9.43% of cases. Within this scope, a result of CIN 2 is quite acceptable. In systems with only a two-tier classification of intraepithelial lesions [4], these discrepancies cannot be detected; this makes it possible to avoid overdiagnosis of the often reversible lesions. Invasive squamous cell carcinomas were found in 2.37% of cases. This demonstrates an astonishingly good ability to distinguish between in situ lesions and invasive carcinomas. Negative histology findings (3.93%) or histology of only mild dysplasia (2.53%) are serious discrepancies which need to be clarified under the Cytology Agreement [2]. Overall, for IVa-p findings, negative or CIN 1 histology findings occurred in 6.46% of cases. It is unknown how many of these cases can be attributed to cytology errors or histology errors (colposcopy and histology). The potential for errors occurring in histological clarification is known. Elaborate external troubleshooting usually follows an internal review of the laboratory's own specimens [13, 14, 15].

Group IVa-g/*Adenocarcinoma in situ* (AIS): In group IVa-g, only 28.82% of cases were found to be AIS on histological examination. In contrast, for IVa-g findings, the most common histology result, at 43.03%, was CIN 3, an immediate precursor stage of squamous epithelial cancer. For IVa-g findings, there was a "CIN 3+" histology finding, i.e., at least CIN 3 or AIS, in 85.53% of cases, and in 89.87% of cases there was a CIN 2+ finding, i.e., at least moderate dysplasia. Thus, the immediate pre-cancer stages in need of therapy were very well recognised. In this context, the weakness of cytology lies in the unsatisfactory identification of the epithelial type. The inclusion of a*denocarcinoma in situ* in the Munich Nomenclature III has thus proved its worth insofar as it shows up the weaknesses in the diagnosis of these very rare lesions. Even in histology, a diagnosis of AIS is not easily reproducible [16]. To make matters worse, AIS often occurs in combination with CIN 3.

Differentiation of malignant tumours

The inclusion of differentiation of malignant tumours in the Munich Nomenclature III (▶ **Table 5**) was undoubtedly quite optimistic, especially since the possibility of clearly distinguishing between tumour types on smears is limited. One goal was to bring the new nomenclature in line with the Bethesda system. The Munich Nomenclature III has defined groups of findings which make the findings verifiable and falsifiable.

▶**Table 5** Histology results for initial group V cytology findings: V-p, V-g, V-e and V-x (KBV 2019 Annual Statistics). Fields with matching cytology and histology findings are marked with an * in the table. Other fields with histology corresponding to CIN 3+ are marked with #.

	2019 initial cytology findings (total: n = 15 608 413) Group V							
	V-p		**V-g**		**V-e**		**V-x**	
	n	**%**	**n**	**%**	**n**	**%**	**n**	**%**
n: Number of women	1311	**0.008**	265	**0.002**	442	**0.003**	284	**0.002**
Histological examination performed up to 30 June of the following year	**1020**	**77.80**	**218**	**82.26**	**356**	**80.54**	**183**	**64.44**
Histology results								
No indication of carcinoma precursors or carcinoma	16	**1.57**	7	**3.21**	28	**7.87%**	6	**3.28**
CIN 1	1	**0.10**	1	**0.46**	0	**0.00**	0	**0.00**
CIN 2	7	**0.69**	0	**0.00**	1	**0.28**	0	**0.00**
CIN 3	187#	**18.33#**	9#	**4.13#**	5#	**1.40#**	6#	**3.28#**
Adenocarcinoma in situ	11#	**1.08#**	9#	**4.13#**	2#	**0.00#**	1#	**0.55#**
Squamous cell carcinoma of the uterine cervix	627*	**61.47***	33#	**15.14#**	12#	**3.37#**	20#	**10.93#**
Adenocarcinoma of the uterine cervix	61#	**5.98#**	100*	**45.87***	35#	**9.83#**	13#	**7.10#**
Endometrial carcinoma, other malignancies	110#	**10.78#**	59#	**27.06#**	273*	**76.69***	137*	**74.86***

Group V-p: Expectation of invasive squamous cell carcinoma

V-p (n = 1311), the cytological assumption of invasive squamous cell carcinoma, was histologically confirmed in 61.47% of cases (▶ **Fig. 2**). The presence of immediate precursors or other invasive carcinomas was found in 36.17% of cases. A lesion of at least CIN 3 severity or AIS ("CIN 3+") was found in 97.64% of cases. Invasive cervical carcinoma – and not just CIN 3 – is also a target lesion for early detection of cancer, as the prognosis for cervical carcinoma is highly stage-dependent.

Group V-g: Expectation of cervical adenocarcinoma

Group V-g was found in 265 cases. Of these, 45.87% were found to be cervical adenocarcinomas on histology (▶ **Fig. 2** and ▶ **Table 5**). Changes that did not require immediate therapy (negative histology, CIN 1, CIN 2) were reported in 3.67% of cases. Accordingly, over 96% of cases had immediate precancerous stages or cancer. As expected, the ability to distinguish these from endometrial carcinomas/other malignancies is not ideal: for V-g, endometrial carcinomas and other malignancies were found in 27.06% of cases. Only a few cases of AIS (4.13%) and CIN 3 (4.13%) were found in group V-g. Differentiation from squamous cell carcinomas is also not ideal. In group V-g, squamous cell carcinomas were found in 15.14% of cases.

Group V-e

Group V-e, corresponding to an expectation of endometrial carcinoma, was assigned to 442 women. In 76.69% of cases there was histological confirmation of "endometrial carcinoma, other malignancies" (▶ **Table 6**). Over 90% of the findings corresponded to invasive carcinomas. 9.83% of patients had cervical adenocarcinoma.

Group V-x: other malignancies of unclear origin

Group V-x, which corresponds to an expectation of "other malignancies of unclear origin", was assigned in 284 women. There was histological confirmation of "endometrial carcinoma, other malignancies" in 74.86% of cases (▶ **Table 5**). Overall, malignancies were found in 92.89% of cases. Cervical carcinoma, squamous cell carcinoma, and cervical adenocarcinoma are significantly underrepresented in this group at 18.03%. Since the histology for this group is not further broken down, there is no relevant information, e.g., on the frequency of ovarian, urothelial, tubal, or rectal carcinomas, melanomas, etc.

Histologically diagnosed lesions in the 2019 annual statistics

In the 2019 annual statistics (▶ **Fig. 2**), totals for histologically diagnosed lesions are given at the end of the line. These include: 5000 CIN 1, 8189 CIN 2, 23463 CIN 3, 668 AIS, 1743 cervical squamous cell carcinomas, 599 cervical adenocarcinomas, and 1549 endometrial carcinomas and other malignancies (▶ **Fig. 2**). The total number of malignant tumours was 3891. Of the 2342 cervical carcinomas, 25.57% were cervical adenocarcinomas. In 2019, CIN 3 occurred more frequently than invasive squamous cell carcinoma by a factor of 13.46. The ratio of AIS to cervical adenocarcinoma is 1.19. The ratio of CIN 3 to AIS in 2019 was 35.12.

▶**Table 6** Histological results for initial cytology findings relating to endometrial glandular changes: II-e, III-e and V-e (▶ **Fig. 2**). Fields marked with an asterisk * are the fields that correspond to a good match.

	2019 initial cytology findings (total n = 15 608 413)					
	Group II-e		Group III-e		Group V-e	
	n	%	n	%	n	%
n = number of women	14 373	**0.092**	3369	**0.022**	442	**0.003**
Histological clarification performed up to 30 June of the following year	212	**1.47**	1184	**35.14**	356	**80.54**
Histology results						
No indication of carcinoma precursors or carcinoma	172	**81.13**	709	**59.88**	28	**7.87**
CIN 1	2	**0.94**	10	**0.84**	0	**0.00**
CIN 2	3	**1.42**	8	**0.68**	1	**0.28**
CIN 3	0	**0.00**	12	**1.01**	5	**1.40**
Adenocarcinoma in situ	0	**0.00**	10	**0.84**	2	**0.00**
Squamous cell carcinoma of the uterine cervix	2	**0.94**	11	**0.93**	12	**3.37**
Adenocarcinoma of the uterine cervix	1	**0.47**	47	**3.97**	35	**9.83**
Endometrial carcinoma, other malignancies	32*	**15.09***	377*	**31.84***	273*	**76.69***

The high number of "endometrial carcinoma and other malignancies", at 1549, is particularly striking since endometrial carcinoma is not a target lesion of the cytological screening programme for women. It is all the more gratifying that these carcinomas can be found without additional organisational effort and cost, even though the sampling site (cervical smear) is located far from the site of cancer development (the uterine body). In principle, an earlier diagnosis can be considered a clinical advantage for patients. However, the actual contribution to prevention/screening is not known.

Looking at the frequency of the various histological diagnoses can give an indication of the incidence, especially for the changes that are usually clarified through histology, and thus of the a priori probability of detecting screening-relevant diseases. These data can be correlated with the statistical data, e.g., the cancer register or the Robert Koch Institute.

Distribution of histological diagnoses correlated to initial cytology findings in the 2019 annual statistics

The rows in ▶ **Fig. 2** indicate the cytology diagnostic group in which the lesions were found, as well as which lesions are easier and which are more difficult to diagnose. For example, among the CIN 3 cases, 65.03% are in cytology group IVa-p, while among the squamous cell carcinomas, only 35.97% are in group V-p. Thus, the cell images of invasive squamous cell carcinoma are more difficult to accurately classify than those of CIN 3. The reasons for this could include: concomitant inflammation, necrosis symptoms, high heterogeneity of carcinomas, difficult classification of syncytia, etc. Approximately two thirds of histologically diagnosed CIN 3 cases were accurately predicted in group IVa-p. The most important target lesion of cervical cancer screening – CIN 3 – seems to be the most easily diagnosable. Of the histologically confirmed endometrial carcinomas, more were found in group III-e than in group V-e.

Proportion of CIN 3+ among histologically clarified cases

Among cases with documented histology (n = 53 154), the proportion with CIN 3+ findings was 52.71 % (n = 28 022). The percentage of CIN 3+ among histologically clarified cases may also depend on the more random reporting of negative histology without cytological indication (group I), as the recording of histology findings without cytological suspicion is not regulated.

11 943 women had negative histology findings, including 1650 women with normal cytology. It can be expected that this number will increase massively in the future under the organised screening programme for cervical cancer, for example if patients with persistent HPV but with negative cytology undergo colposcopy and biopsy examinations. This will have to be closely observed, especially in the context of organised screening (in place since 2020). The proportion of target lesions, such as CIN 3 and invasive cervical carcinomas, among women for whom histological analysis has been performed may be indicative of efficacy and possible overdiagnosis. Similar factors include, for example, histological clarifications performed for group IVa-p compared to group IIID1, or histology results of CIN 3 compared to histology results of CIN 1. The low thresholds currently in place (since 2020) for determining when colposcopy and biopsy are indicated include pointers on performing a risk/benefit assessment for the patient and obtaining their informed consent.

▶**Table 7** Histology results for initial cytology findings IVa-p and IVa-g (KBV annual statistics 2019). The fields with optimal matching of cytology and histology are marked here with an *.

	2019 initial cytology findings (total n = 15 608 413)			
	IVa-p		IVa-g	
	n	%	n	%
n = number of women	22 784	**0.146**	917	**0.006**
Histological clarification performed up to 30 June of the following year	18 959	**83.21**	760	**82.88**
Histology results				
No indication of carcinoma precursors or carcinoma	746	**3.93**	52	**6.84**
CIN 1	480	**2.53**	25	**3.29**
CIN 2	1787	**9.43**	33	**4.34**
CIN 3	15 259*	**80.48***	327	**43.03**
Adenocarcinoma in situ	143	**0.75**	219*	**28.82***
Squamous cell carcinoma of the uterine cervix	450	**2.3**	21	**2.76**
Adenocarcinoma of the uterine cervix	59	**0.31**	75	**9.87**
Endometrial carcinoma, other malignancies	35	**0.1**	8	**1.05**

Analysis by epithelial type

In the Munich Nomenclature III, the diagnostic groups are marked with suffixes indicating the expected epithelial type: -p for squamous epithelium, -g for endocervical glandular, -e for endometrial, and -x for unknown. The question here is around the extent to which assigned epithelial types are able to be confirmed, and the extent to which the finding groups show a risk stratification (▶ **Table 6**).

▶ **Table 6** shows that the rate of histological examinations increases in line with the finding group, and that an increase in the number of endometrial carcinomas is successfully identified.

Positive prediction and performance data from cervical cytology screening

Based on the available data, it is only possible to make a good assessment of the positive predictive power (i.e., disease is present if the test is positive) [17]. The ability of cytology to predict serious disease (CIN 3+) is so good that in these cases a histological examination is usually performed (▶ **Fig. 2**). Unlike many laboratory tests, there are usually no test repeats.

The objective of early cancer detection, in particular the aim of finding and treating the immediate precancerous stages and malignancies, means that histological examinations are almost invariably carried out in patients with group IV and V cytology findings, which correspond to CIN 3+.

However, it is not possible to calculate further performance data for cytology screening because, among other reasons, it is not known how many sick or healthy people there are among the population. Specifically, the sensitivity cannot be determined with certainty; this is true for all screening procedures. To obtain estimates of the match rate (i.e., correct findings in all finding groups) in screening clinics, it would be necessary to perform calculations based on various assumptions relating, for example, to correct or incorrect cytology or histology findings, false-negative cytology results, etc. However, this is beyond the scope of this article. While the fact that it is possible to compile the available data shows the practicability of cervical screening, this does not constitute validation of the screening program.

Cytology examinations do not only answer the question of whether or not disease is present; they also try to predict the type of disease and its severity. The histology match for IVa-p cases categorised as CIN 2+ was very good, at 93.37% (▶ **Table 7**). For IVa-p, the precise prediction of CIN 3 was 80.48%. The match for IVa-g was 89.87% for cases categorised as CIN 2+. In contrast, with an AIS finding, the rate of exact histology match was only 28.82% (▶ **Table 7**).

As shown in ▶ **Table 5**, with group V cytology findings of suspected carcinoma, there are few cases that do not lead to detection of a serious lesion, i.e., at least CIN 3+. Differential cytological matching is also good. The errors that occur in the differential diagnosis may be due to the somewhat similar morphology of different lesions, e.g., cervical adenocarcinoma and endometrial carcinoma, or invasive squamous cell carcinoma and “carcinoma in situ”.

For IIID1 findings, the positive predictive power is more difficult to determine, as histological examinations are performed in a smaller proportion of cases, and usually after a time delay.

Discussion and Outlook

The data demonstrate the practicability of cytology-based cervical cancer screening in Germany. Our evaluation shows that the screening programme reached a very large number of women (approximately 15 million). The proportion of suspicious smears was well below 3 %.

The annual statistics allow all physicians responsible for cytology to compare the distribution of findings and the correlation between cytology and histology in their own laboratories with regional and nationwide results. Benchmarking reports of this kind can be an important support tool, not only for in-house quality management.

The Munich Nomenclature III allows for risk stratification through its risk-based groups. This is also reflected in the rates of histological clarification, which vary depending on the cytology finding. Findings of CIN 3 and higher (CIN 3+) result in a high rate of histological clarification, with a good match rate.

The three-tiered classification of cervical intraepithelial neoplasia (CIN) / lesions, which is commonly used in Germany, also allows for a conservative wait-and-see approach. In the data, for the IIID1 cases for which histology is performed (4.89 % of all IIID1 cases/▶ **Table 3**), the time at which the histological examination was performed after the initial IIID1 finding remains unclear. In most cases, histology is performed one or two years after the initial IIID1 finding.

The Cancer Screening and Registration Act (KFRG), which came into effect on 9 April 2013, creates a legal framework for the ongoing development of the content and organisation of cancer screening programs. Among other things, under this law, the screening programmes previously in place (for cervical cancer, colon cancer, breast cancer, skin cancer) are to be converted into organised screening programs. The structural changes are intended to sustainably improve the effectiveness and quality of existing cancer screening services. At its meeting on 22 November 2018, the Federal Joint Committee decided to add the cervical cancer screening programme to the Guideline on Organised Cancer Screening Programmes.

Given the annual statistics provided under the 2019 Cervical Cytology Quality Assurance Agreement, the question arises as to what developments in “organised screening” can be expected for 2020 and beyond.

One key difference is a process for creating invitations. It is hoped that this will make it possible to reach women who are not yet participating. In addition to the cytology smear, various changes have been introduced, including an HPV test for women of 35 and above, an algorithm has been established to determine when histological clarification is needed. Also a new concept for data collection has been implemented. Evidence-based results to compare the effectiveness of “opportunistic” versus “organised” screening are not yet available.

Even before the launch of the new programme, important measures were proposed and implemented. These included the Munich Nomenclature III [3] and the development of new guidelines [18, 19]. Without time pressure, it would hardly have been possible to make the Munich Nomenclature III legally binding.

Also, the reorganisation of cervical cancer screening has significantly increased interest in cervical cancer and its precursor stages [20, 21].

There are currently no official data on the “organised” cervical cancer screening programme introduced in 2020. We can therefore only speculate on the effects of organised screening in Germany from 2020 onwards.

Since 2020, patients have been asked about their HPV vaccination status during screening examinations, and this information has been recorded for statistical purposes. This will facilitate future evaluations of the effect of HPV vaccination. Another positive change is the fact that colposcopy procedures performed for diagnostic clarification are now funded under the statutory health insurance scheme. However, there is a lack of process quality checks and a lack of statistics on the quality of the results.

There has always been a lack of data from cervical cancer screening; given the complexity of screening within a public healthcare system, this will never be remedied. As part of “organised screening”, data collection in 2020 was significantly improved [1]; however, the problem remained that it was not possible to evaluate the data in a timely manner. It is to be hoped that this wealth of data can be enhanced in the future. However, this may not be enough to address the massive information deficit; it is therefore to be hoped that we will also see individual initiatives from laboratories, clinics, professional societies, professional associations, health insurance companies, cancer registers, etc.

In many cases, the histology results are from biopsies in which the interpretation of the findings is similarly subjective to that of cytology. Among the methods used in cervical cancer screening, patient-based quality assurance is currently only established for cytology; there is room for improvement here. It remains to be seen whether the changes to the cervical cancer screening programme from 2020 onwards will provide additional improvements in quality assurance. In principle, the annual statistics can also provide indications of the benefits and harm from screening examinations. For example, a significant parameter is the total number of lesions found in relation to the number of additional high-grade lesions that are found, including carcinomas.

As cytology laboratories usually use specialised software tailored to their needs, data could be compiled even more effectively in the future. It is hoped that the proportion of documented histological clarifications will continue to increase. In the 2019 annual statistics, some of the organisational changes scheduled for 2020 were already noticeable in advance, as many doctors had prepared themselves, for example, for the planned introduction of an algorithm-based method for determining when colposcopy is indicated for diagnostic clarification. Developments in the data for the years 2020 and beyond is unlikely to become easier to interpret: each set of annual statistics now includes the patients who have newly reached the age threshold for the co-test (cytology + HPV test). Patients in whom the co-test was negative in the first year should be absent from the statistics in the following two years. Patients who come to light because of minor abnormalities will often only be included in the statistics in the year following the first co-test. From the fourth year onwards, there are also many women who are in the “second round” of screening with co-testing. The number of women who are receiving a co-test for the first time

will decrease over time. The year 2020 was beset with difficulties due to the Covid-19 pandemic. The start of data collection under the rules of the guideline on organised cancer screening was delayed for organisational reasons.

Regardless of the available results and data from organised cervical cancer screening, measures to maintain and improve participation in cancer prevention/screening programmes are always desirable.

Glossary

AIS	Adenocarcinoma in situ
ASC	Atypical squamous cells
CIN	Cervical intraepithelial neoplasia
CIN 1	Mild dysplasia
CIN 2	Moderate dysplasia
CIN 2+	Lesions as severe as or more severe than CIN 2 (moderate dysplasia)
CIN 3	Highest severity level of squamous epithelial cancer precursor, immediate precursor to carcinoma
CIN 3+	Lesions as severe as or more severe than CIN 3 (severe dysplasia or carcinoma in situ)
Group 0	Insufficient material
Group I	Normal, unsuspicious findings
Group II	Findings with limited protective value
Group II-a	Normal findings with a conspicuous medical history
Group II-p	Squamous epithelial cells with nuclear changes less severe than CIN 1, including koilocytic cytoplasm/parakeratosis
Group IIID2	Cell image of moderate dysplasia corresponding to CIN 2
Group IIID1	Cell image of mild dysplasia corresponding to CIN 1
Group III-p	CIN 2/3/squamous cell carcinoma cannot be excluded
Group III-x	Dubious glandular cells of uncertain origin
Group IV	Immediate precursors to cervical carcinoma
Group IVa-p	Cell image of severe dysplasia/carcinoma in situ corresponding to CIN 3
Group V	Malignancies
HPV	Human papillomavirus
KBV	National Association of Statutory Health Insurance Physicians
KV	Regional Association of Statutory Health Insurance Physicians

Acknowledgement

The authors are grateful to Dr med. Jochen Möckel (†), gynaecologist and pathologist, Freiburg im Breisgau. The authors are grateful to the Associations of Statutory Health Insurance Physicians and to those responsible from the Cytology Committees for their assistance in compiling the data. We would like to thank Dr Anke Holthenrich from the Department of Digitalisation and IT at the National Association of Statutory Health Insurance Physicians, a corporation constituted under public law, for her assistance in the analysis of the data.

Conflict of Interest

The authors declare that they have no conflict of interest.

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