CHAPTER 1.

Audit of cervical cancers in a screening programme

1.1 Definition of audit in general and audit in the context of cervical screening

A **health-care audit** is defined as a quality improvement cycle or process to measure the effectiveness of health-care services against agreed, proven, evidence-based, and recognized standards to improve quality of care and outcomes [3–6]. Audit of any health-care service is considered by WHO to be a critical function of an organization, to provide objective assurance on its integrity and credibility [7].

Specifically, a cervical screening programme benefits from being audited. **Audit of a cervical screening programme** is defined as a programmatic set of measurements of quality and effectiveness of screening services using structural, process, and outcome indicators against evidence-based and realistic standards agreed upon by relevant stakeholders.

Audit of cancers in a cervical screening programme is part of the programmatic audit process and is a component of the overall evaluation of screening effectiveness. It involves an in-depth review of the screening pathway for women diagnosed with cervical cancer [8]. An audit of cancers may include any of the following categories of cancer:

- cancers that occur in women with irregular participation or non-participation in screening;
- cancers that are detected in women with abnormal screening test results; and
- cancers that are detected in women with normal screening test results.

The terms audit, quality assurance, and quality improvement are often used interchangeably, although they are not synonymous. **Quality assurance** has been defined as a systematic process that describes the achievable and the desirable levels of quality and assesses the extent to which these levels are achieved. The aim of quality assurance is to enable a level of quality to be reached [9]. Whereas quality assurance focuses on measuring compliance against quality standards, **quality improvement** is a more proactive approach that aims to improve systems and outcomes based on a systematic analysis of current performance. **Audit** is the part of the quality assurance or quality improvement process that focuses on specific issues of health-care and clinical practice.

An audit by itself will not assure quality or lead to quality improvement unless the audit outcome leads to specific recommendations to close

any quality gaps identified by the procedure and actions are taken based on those recommendations to improve quality. **Hence, audit of cancers is part of a broader quality assurance or quality improvement exercise in any cervical screening programme**.

1.2 Key objectives of an audit of cervical cancers

The overarching goal of programmatic audit in any health-care service is to discover discrepancies between actual practice and recommended standards in order to identify any changes needed in the process or the system to improve the quality of care [10]. A well-organized cervical screening programme is expected to reduce the incidence of cervical cancer significantly (but never to zero) and to ensure that incidence rates remain very low by detecting and treating the disease at a precancerous stage. Cervical screening also reduces the mortality from cervical cancer by detecting early- stage cancers before they are symptomatic and therefore when treatment is likely to be effective. For this reason, any cervical cancer that occurs in a population targeted by a screening programme needs to be audited, to understand whether it could be prevented or detected even earlier through improved quality of services.

Findings from the programmatic audit of cancers in a cervical screening programme are expected to direct further investigations of screening practice that target improvement rather than blaming an individual professional or an organizational entity for perceived lapses [8]. It is of critical importance for the audit team to ensure that the professionals involved in the screening process do not interpret audit as an inspection of their individual clinical competence, which may make them avoid participating in the audit process, either consciously or subconsciously, thus defeating the very purpose of the audit [10]. It is also important that all stakeholders – screening participants, the media, politicians, and legal teams – do not interpret audit as a process used to identify error or negligence. Rather than finding fault, an audit may identify best local practice and innovation that should be promoted and disseminated in the programme and elsewhere.

1.3 The cancer audit process – guiding principles

An audit of cervical cancers in a screening programme, like any other health-care audit, should have a documented policy and process framework. An audit process involves a cycle (Fig. 3), which consists primarily of the following phases [4, 6, 11, 12]:

1. The audit process starts with a **planning phase** to select a suitable clinical condition to be investigated (e.g. cancers detected in a cervical screening programme), to identify indicators to be used to determine performance (e.g. interval cancer rate, percentage of cytology slides reviewed that contain missed abnormalities, or percentage of cases not managed according to national guidelines), and to agree on standards of performance relevant to the selected clinical condition.
2. The next phase is systematic data collection to **measure performance against the agreed standards,** which will lead to identification of the gaps in service or some of the best practices.
3. **All stakeholders then need to review** the audit outcomes and formulate strategies to address the gaps identified, to disseminate the best practices, and to improve quality.
4. The **process needs to be continued** as a cyclical exercise.

Audit planning is key to the success of the entire exercise. It starts with the selection of an appropriate theme [10], which ensures that:

- the problem to be audited has an important impact in terms of costs, resources, or risk;
- there is strong scientific evidence available (guidelines and systematic reviews), which has been used to determine the acceptable and desirable standards; and
- the improvements to be recommended on the selected theme have important clinical or organizational consequences and can be easily measured.

Occurrence of cervical cancers in a screening programme fulfils all the above-mentioned criteria and is a suitable clinical condition to be audited.

The **objectives of the audit** should be clearly delineated in the plan. For example, the core objective of an audit of cervical cancers in a screening programme is to maximize the benefits of screening without increasing the risks to the women who are offered screening. The aims of an audit in the NHS England Cervical Screening Programme are shown in Box 2.

An **audit team** should be customized to the selected topic and should include representatives from multiple disciplines with appropriate skills (e.g. cytopathologist, colposcopist, histopathologist, and statistician for an audit of cervical cancers). The responsibility for initiating the audit process regularly according to the programme's published policy and framework lies with the managers of the organization that provides the screening services.

The indicators to measure performance and their standards (often categorized as acceptable

Fig. 3. Stages of a health-care audit. © IARC.

Box 2. Aims of an audit of cervical cancers in the NHS England Cervical Screening Programme

The aims of an audit of cervical cancers as stipulated in the NHS England Cervical Screening Programme are to:

- support the **continuous learning and development** of health professionals involved in the programme;
- **monitor the effectiveness** of the cervical screening programme by comparing the screening histories of individuals who develop cervical cancer with those who do not;
- identify **areas of good practice** and indicate where **improvements** might be made to support evidence-based policy and practice; and
- ensure that participants are given **information** about their screening history review (if they wish to receive it).

and desirable) should be listed and derived from international guidelines, the scientific literature, expert consensus, and data obtained from other health-care facilities or case studies. The threshold of acceptability for each standard (as desirable and acceptable, or as satisfactory and unsatisfactory) needs to be defined. Defining the indicators and standards requires active engagement with all stakeholders. Before proceeding with data collection, it is necessary to plan carefully how the variables will be recorded and the type of analysis to be conducted.

Data collection (from case records, review of specimens, etc.) requires an appropriate legal and ethical framework (see Chapter 2). Reviewing the results and developing action plans for quality improvement should be a multidisciplinary process that involves various levels of stakeholders. The audit process should be repeated periodically in order to document that the implementation of the suggested action plan has resulted in improvement [11].

An appropriate strategy for communication of the programmatic audit outcomes and the recommended improvements should be incorporated into audit planning. After the data have been collected and analysed, the results of the programmatic audit and the action plan should be communicated to all the stakeholders. The members of the TWGs concurred that a programmatic audit is not the same as **an individual case review** (for more details, see Section 1.4). Programmatic audit should produce aggregate (i.e. system-level) results and not pinpoint what has happened to a specific screening participant.

The audit plan needs to make provision for adequate resources (financial and logistic) to support audit planning, team building, data collection, training of health professionals (including education on audit techniques), facilitation, and data management and dissemination. The strategy for effective audits is shown in Box 3.

1.4 Audit of cancers versus individual case review in a cervical screening programme

The overarching aim of programmatic audit of cancers in cervical screening is to evaluate the effectiveness of a screening programme in reducing the incidence of cervical cancer and minimizing the risks associated with screening [13]. On the basis of the programmatic audit outcomes, rational decisions can be made about modifications in several areas of service delivery, such as the training of health professionals, the introduction of an improved screening test, the strengthening of fail-safe mechanisms, the improvement of capacity to reduce delays, and the reduction of inequalities [13–16].

As mentioned earlier, audit of cervical cancers aims to evaluate the programme (i.e. the system) and not individual health professionals or what happened to an individual participant. In any programme, some cancers will be missed. Some interval cancers are due to fast-growing tumours that could not be detected through screening at the specified interval. Also, cervical cytology was not designed to assess endocervical disease and will miss many such cases. Missing such cancers is not a deficiency of the programme. The audit looks at the extent to which cervical cancer could be further prevented in the population by avoiding human or systematic errors, and not at whether the failure to detect a cancer in a particular woman was a result of human error. This distinction is key to an understanding of the programmatic value of audit of cervical cancers. The results of a cancer audit should not appear in the medical records of an individual patient, because the results have no bearing on the patient's management or treatment outcomes.

Box 3. How to make audits work effectively

1. Engage all health-care professionals involved to use the shared commitment of the entire team working together and sharing common protocols and practice. Follow the local bottom-up approach through discussion with professionals to recognize issues of interest from their own discipline.
2. Involve relevant stakeholders (including screening participants, patients, and public advocates) in the design and communication of the audit.
3. Focus on knowledge-sharing. Make it clear to the health-care professionals that the audit is a learning opportunity. Dedicate time and attention to sharing knowledge with colleagues about the quality of care as it relates to the design of the care pathway.
4. Identify a local champion (or champions) as the driving force behind the audit. This is more likely to encourage health-care professionals to take ownership and see the audit process as worth the effort. The champion will motivate colleagues and work with them to implement changes in practice.
5. Educate all stakeholders in advance about the interpretation of results and likely actions.
6. Create an enabling environment to receive feedback. Encourage health-care professionals and other stakeholders at all levels to provide feedback on the audit process and outcomes.

It is also important to remember that no matter how high the quality of cancer screening is, it is **not possible to achieve zero-error screening** in standard practice [17]. A well-organized population-based screening programme with high quality and good coverage will significantly reduce the number of cervical cancers but will never eradicate the disease. Many of the diagnostic investigations used in cervical screening, such as cervical cytology, colposcopy, and histopathology, are subjective tests and are susceptible to interpretation errors. Although the practice standards have not been well defined in cytology, a systematic review reported that even in countries with organized screening programmes, 20–55% of women who developed cervical cancer had had false-negative smear test results within 6 years before the diagnosis [18].

The same subjectivity also applies to colposcopy and histology. Although a well-organized cervical screening programme is expected to detect and treat most disease when the risk of progression to cancer is high, and thus to be very efficient in preventing progression to invasive cancer, the **incidence of cervical cancer cannot be reduced to zero**, even in the best of circumstances. Combined data from the four randomized controlled trials in Europe demonstrated that even in such highly controlled research settings the cumulative incidence of invasive cervical carcinoma in women with negative results from human papillomavirus (HPV) testing (which is currently considered to be the most accurate test available) was 4.6 per 100 000 at 3.5 years and 8.7 per 100 000 at 5.5 years. All of these cancers were detected in subsequent rounds of screening. The corresponding values for women with negative cytology results (not screened with HPV testing) were 15.4 per 100 000 at 3.5 years and 36.0 per 100 000 at 5.5 years, which shows the inherent low sensitivity of cytology, even in a research setting [19].

An **individual case review** should be distinguished from a programmatic audit and should be planned and implemented differently, because the two processes have different objectives. An individual case review is not based on quality assurance principles of improving the programme. Instead, it is an attempt to determine how or why a specific individual developed cancer despite participating in screening. A programme may offer an individual case review to any woman who develops cancer and requests such a review. As in audit, the process involves a review of the patient's medical records, test results, pathology specimens, and care received before the diagnosis. However, in an individual case review, (i) the patient's consent is needed, and (ii) the results must be disclosed to the patient, which is not mandatory in programmatic audit of cancers. When discussing an individual case review with the patient, every attempt should be made to explain the process before the review is done. The patient should be told about:

- the likely outcomes of a review, and that such a review is very unlikely to modify the course of treatment;
- the relevance of retrospective (or hindsight) bias and how a finding of discordance between the original result and the review result is not always a proof of negligence; and
- the possible psychological impact of finding out on review that abnormal cells were present but were not reported.

An introductory meeting is key, so that the patient who is requesting such a review can outline her main areas of concern. It also gives the clinical team an opportunity to explain what the comprehensive review entails and to discuss the issues mentioned above. This helps the team to plan the schedule for delivering the review results and to plan any support to the patient that may be required.

If the patient has died or is not in a physical or mental state to provide informed consent, an individual case review may be requested by the partner, spouse, or other close relative(s) of the patient. The principles of the restorative approach to individual case review are shown in Box 4.

1.5 Cervical cancer audit practices in different countries

There is wide variability in audit practices internationally. The IARC Secretariat reviewed publications that reported the processes used for the audit of cervical cancers in various countries. Most reports were based on regional or national population-based screening programmes in European countries, such as Denmark [20–22], England [15], Finland [23], the Netherlands [24], Poland [25, 26], and Sweden [27]. The IARC Secretariat also found a report from New Zealand [28]. Some reports were based on the routine audit of screening programmes [15, 22, 28], whereas other audits were undertaken for one-time research to inform quality assurance and practice.

Audits of cervical cancers collate data from different sources, including population-based cancer registries, screening registries, routine medical records, screening invitations, cytology and histology laboratories, and colposcopy clinics. Cytology review was the most commonly described audit process across different countries, although NHS England also includes colposcopy and histology review [15] as part of an audit of cancers. In countries where cytology

Box 4. Principles of the restorative approach to individual case review

The restorative approach aims to bring all of those affected by an adverse event together in a safe and supported environment. Key principles that must be followed are to:

- prepare the patient in advance for the potential review findings;
- ensure that a support person is available for patients during the process;
- use simple language to explain the review findings; and
- ensure that post-disclosure support is available.

The approach to individual case review should contain the following elements. There should be an introductory meeting, to provide information and set expectations for the review. The case review should be followed by a discussion meeting, which should facilitate supported discussion of the review findings and the resulting clinical impact. The meeting will give an opportunity for patients to understand how discordance happens (if such discordance has been observed), and such an explanation needs to be provided in a protected and compassionate space.

This process aims to restore screening to its place in health care as a service that benefits population health but also acknowledges its limitations.

review was performed using controls, the case-to-control ratio varied; the ratios used included 1:2 [26], 1:4 [15], 1:5 [14], and 1:10 [29]. Countries also differed in who reviewed the cytology or histopathology. In some programmes, the technicians or pathologists who reviewed the slides for the audit were those who had performed the original review, in some programmes the audit review was performed by an independent panel, and in some programmes it was a mixture of these two approaches. The degree of blinding during audit also varied. On the basis of reports from the various programmes and the opinions of the members of the TWGs, some of the best practices in the audit of cervical cancers are listed in Section 1.6.

1.6 Audit of cancers in a cervical screening programme – practice issues

1.6.1 Should all cervical cancers be included in an audit?

The European guidelines recommend that all cervical cancers should be investigated, whether detected in screened women or in unscreened women [30]. **Audit of cancers in unscreened women is relevant only for population-based programmes that have a system of sending individual invitations and follow-up.** Whenever possible, screen-detected cancers should be distinguished from cancers detected in symptomatic women outside routine screening, and all interval cancers should be identified (according to the definitions given Section 1.6.2). However, such comprehensive evaluation requires robust linkage between the population-based cancer registry and the screening registry (the database that maintains individual records of the women eligible for screening) and individual medical records. As much as possible, the list of cancer cases that were diagnosed during the time period under consideration and the clinical information for each case (screening invitations, cytology results, colposcopy results, histology, and mode of detection) should be obtained from the population-based cancer registry and the clinical records.

For cancers that are diagnosed in unscreened women in a population-based programme, the process of invitation and response to invitation should be examined. A systematic audit will distinguish between a situation where there was a failure to invite the woman (Was full information available in the register? Did the woman receive an invitation or a reminder as per protocol?) and a situation where a woman was invited but did not attend screening for various reasons. The proportion of women diagnosed with cervical cancer within the eligible age group who did not receive an invitation is a key indicator and is estimated either from the case records or by interviewing the patients, or both. Feedback on this issue from the women themselves – including perceived barriers to accessing screening, and perceptions of screening and how it is delivered, whether it is culturally acceptable, and resulting inequalities – is particularly valuable and may help to develop strategies to improve the programme.

1.6.2 How are interval cervical cancers defined?

Definitions of interval cervical cancer and its reported incidence vary in the literature. Most of the programmes or studies define only those cancers that occur in screen- negative women as interval cancers and do not include cancers that occur after a negative diagnostic test result (colposcopy and/or biopsy) in screen-positive women in the definition of interval cancer. Hakama et al. considered such cases to be failures of the screening episode and that this justified including such cancers within interval cancers. Some audits

exclude microinvasive cancers [31–33] in the definition, whereas other do not. On the basis of evidence from this review [15, 16, 31–36] and from the multicountry survey [37], the members of the TWGs defined an interval cervical cancer **as any cancer (including microinvasive cancer [stage IA]) diagnosed in a woman between her most recent screening episode and her next screening round, at an interval stipulated by the programme, who had either (i) no abnormal screening test result or (ii) an abnormal screening test result but a negative triage test result or a negative diagnostic test result.**

Thus, an audit of interval cancers should consider the following:

- cancers in women with negative results from screening tests performed within an interval stipulated by the programme;
- cancers in women with positive screening test results but negative triage test results (when the protocol involves triage); and
- cancers in women with positive screening test results (and positive triage test results, depending on the protocol) but negative diagnostic test results (colposcopy and/or biopsy).

Cancers that occur during follow-up after treatment of high-grade precancers (cervical intraepithelial neoplasia grade 2 or 3 [CIN2/3]) have different follow-up protocols and risk profiles and should not be defined as interval cancers. The members of the TWGs are of the opinion that any abnormal screening tests reported within the 6-month period before diagnosis should be considered to have led to the diagnosis of cancer. Therefore, cancer cases with an abnormal screening test reported within 6 months of diagnosis should be excluded from the definition of an interval cancer.

1.6.3 Is it mandatory to obtain informed consent from the women to be included in an audit?

As Sasieni and Cuzick explain, reliable audits cannot depend on consenting women alone but must be representative of the whole population. Analyses based only on consenting women are likely to be biased and misleading [13]. The members of the TWGs concluded that **not obtaining individual informed consent at the time of a programmatic audit is justified.** This is because the public good and the responsibility to provide a high-quality screening programme outweigh the possible risks to an individual from participating in the audit. However, this means that the women who undergo screening must be informed at the time of the screening of the possibility of an audit. It also means that the auditors must make exceptionally determined efforts to ensure that the data are kept safe and confidential. Clear information about the process should be provided to women at the time of invitation to or participation in screening, so that they are adequately informed about the audit process. All personal data should be removed at the time of audit to ensure anonymization when a woman has denied consent for the use of her data. For further information on the consent requirements and process in an audit, please see Section 2.2.

1.6.4 Is ethics approval necessary for an audit?

Although an audit is designed and conducted with the sole purpose of defining or judging the quality of current service, very often an audit of cancers in cervical screening is both an audit and a research activity. However, an audit is not the same as experimental clinical research, because there is no intervention. An audit is a form of non-intervention system research. An audit protocol may be formally **reviewed by an ethics committee**, but this will be in the context of it being at most non- experimental health systems research. The use of personal data requires approval in most legal systems. For more information on the use of personal data, please see Section 2.4.

1.6.5 How to measure and compare rates of interval cancers

Interval cancers are measured in different ways. As a result, the estimated rates vary widely, which makes it difficult to compare them between programmes. The members of the TWGs observed the following different ways in which interval cancer occurrence has been measured:

1. **Interval cancer incidence as person-years at risk.** This is calculated in women with an interval cancer from the date of the entry test to the date of the next (second) routine test, the date of diagnosis of cancer, the date of emigration to a foreign country, the date of death, or the end of the period of estimation, whichever occurred first.
2. **Interval cancer rate in a screening episode.** This is defined as the number of interval cervical cancer cases detected within the interval after a single screening episode with negative cervical screening results and before the next scheduled episode, per 100 000 women.
3. **Age-standardized interval cancer incidence rate.**
4. **Percentage of women with interval cancers who had a false-negative screening test result.** This is the percentage of patients with cervical cancer who had a negative cytology test result within *X* years (where *X* = the screening

interval) of cancer diagnosis and whose slides upon review were upgraded to borderline (atypical squamous cells of undetermined significance [ASC-US]) or worse cytology.

5. **Relative risk of developing cervical cancer** in women screened in time and who had only normal test results compared with unscreened women.

The measurements are often stratified by age groups. Whatever method is used to measure the occurrence of interval cancers, the programmes need to compare interval cancer occurrence over time. It is also useful to compare the rates of newly detected cervical cancers in screened women (both screen-detected and interval cancers) and unscreened women for a particular year.

1.6.6 How to decide on the standard (benchmark) for interval cervical cancer rates

The number of cancers diagnosed in the interval between screening episodes is one of the fundamental indicators of the quality of programme performance. A low interval cancer rate usually demonstrates high effectiveness of the screening programme. This review found that in population-based screening, rates of interval cervical cancer were between 1.4 and 10.2 per 100 000 women-years in screen-negative (on cytology) women. These different rates may be due to the different denominators used. The members of the TWGs concurred that a rate of < 10 interval cervical cancers per 100 000 women-years is an acceptable rate in a cytology-based programme, but the programme should aim for < 4 interval cervical cancers per 100 000 women-years, especially for screening based on HPV testing. The programme has to take into consideration the cervical cancer incidence rate and the inclusion of stage 1A disease, which can increase the number of interval cancers.

When comparing newly detected cancers in screened women (both screen-detected and interval cancers) and unscreened women, the members of the TWGs agreed that the rate of cervical cancers (stage 1B and above) in screened women should be less than 25% of the rate in unscreened women. However, the number of screen-detected cancers is expected to be high in a programme that has recently launched screening based on HPV detection, because it is more sensitive in detecting prevalent disease.

1.6.7 How to assess cancers in unscreened or inadequately screened women

Very few details are available in the literature about the audit of cancers in unscreened or inadequately screened women. The measure used in the audit of these groups of women is cervical cancer risk associated with non-participation in screening (the relative risk of invasive cervical cancer in women who were unscreened or inadequately screened in the past two screening rounds compared with women who were screened in time).

1.6.8 What is the process of review of cytology slides?

In a cytology-based programme, the European guidelines recommend a review of the negative cytology slides preceding the detection of cancer for all cervical cancer cases [30]. For patients who develop cancer despite undergoing screening, the slides for one or two screening rounds before the diagnosis of cancer need to be retrieved from the relevant cytology laboratories; for this, documented ethical and legal guidelines are essential. Smears collected within 6 months of the date of diagnosis of cancer should be disregarded because they are most likely to have led to the cancer diagnosis.

A set of control slides for women (age-matched) without cervical cancer may be included in the review. In published studies, the number of controls per case varies from 2 to 30 [2, 7, 12–14]. It is recognized that because of retrospective (or hindsight) bias, 30–50% of slides obtained from patients with interval cancer will be found to have abnormalities when a review is performed. Adding the controls and reviewing the slides in a blinded manner help to adjust for such bias by comparing the proportion of unsatisfactory misses in cases with that in controls.

If the audit of cancers decides to include controls to verify whether the reading of slides under audit conditions increases the detected abnormality rate, slides from at least 100 controls per age group (e.g. 100 controls aged 20–49 years and 100 controls aged 50–69 years) and at least one control per case are required for the review. Obtaining slides from a sample of women with false-positive cytology reports is also recommended. Both blinded and non-blinded assessments need to be performed, to enable distinction between human error in cytological interpretation and interpretation error due to factors beyond the control of the cytology reader, such as slides that contain very few abnormalities or slides that are poorly prepared or poorly stained.

More than one (preferably three) cytopathologists or technologists should review the sample slides. Usually, the cytopathologist or technologist who examined the slides originally is included in the team. The final decision should be based on consultation with the reviewers, thereby arriving at a consensus. Each slide is first assessed for suitability for review. The review result will distinguish false-negative interpretations due to human errors from the features recognized as being at risk of being missed (e.g. few or

pale abnormal cells). In England, the programmes categorize each cytology slide according to the nature of discordance between the original result and the reviewers' interpretations into satisfactory, satisfactory with learning points, or unsatisfactory [2].

1.6.9 Should histopathology slide review be a part of an audit of cancers?

Ideally, for all cancer cases included in the audit, the previous histopathology slides (if any) should be reviewed as well. The data required for such a review include the date of specimen collection, the type of specimen, the pathological diagnosis, and the excision margins (for large loop excision of the transformation zone [LLETZ] or other excisional specimens). Multiple reviewers should be involved, just as for cytology review. In England, for example, all cervical histology slides reviewed for the audit of invasive cervical cancers are categorized, as with cytology, into satisfactory, satisfactory with learning points, or unsatisfactory.

1.6.10 Should review of colposcopy be a part of an audit of cancers?

Any colposcopic examinations that predate the index referral by up to 5 years should be reviewed, because these examinations (and associated management) may have affected the development of cervical cancer. For each case under review, colposcopy data are obtained; these include the total number of colposcopy appointments and, for each, the date of the appointment, attendance at the appointment, whether the examination was satisfactory, and information on any biopsy or treatment procedure(s) performed. Additional findings include the colposcopic impression (including cervical images, if available), the pathological diagnosis, whether the woman was pregnant, the time to the next follow-up appointment, and whether the case was managed according to existing guidelines.

1.6.11 Laboratory audit for cervical screening based on HPV detection

Most cervical cancer screening programmes in higher-resource settings either have already replaced cytology with the detection of oncogenic HPV as the primary screening test or will do so in the near future. The principles of the audit of cancers in cytology-based screening may not be applicable to screening based on HPV testing, because the cervical specimens collected during a screening interval before a cancer diagnosis may not be available for retesting. The review should include the original result, valid run data either from the analyser archive viewer or downloaded and stored on laboratory digital data storage systems (where available), and external laboratory quality assessment reports. For patients who were diagnosed with an interval cervical cancer despite a positive HPV test result, the triage cytology slides (when cytology triage is used) and downstream management must be reviewed as described in this document. The experience of such audits within a screening programme based on HPV detection is still very limited.

For example, the central cervical screening laboratory in Stockholm, Sweden, identified 2033 cases of cervical cancer or CIN3 diagnosed through an organized screening programme in 2012–2017. These cases had had a previous cervical screening test (either an HPV test or liquid-based cytology [LBC]) within 3 years of cancer diagnosis [38]. The available LBC specimens taken before diagnosis of invasive cancer and a random selection of the specimens taken before diagnosis of CIN3 were selected for auditing (a total of 1054 specimens). The histopathology slides of patients who originally had an HPV-negative test result were reviewed to confirm the diagnosis. The LBC samples from patients who were either HPV-negative on screening or did not have an HPV test were tested or retested with a validated HPV test. The LBC samples that tested negative on the HPV test were subjected to a highly sensitive HPV genotyping test and whole-genome sequencing (if the genotyping was negative). The cytology slides were also reviewed.

The key observations were as follows:

- The validated HPV test had an average sensitivity of 97.0% to detect CIN3 or worse (CIN3+).
- Cytology had an average sensitivity of 91.6% to detect CIN3+.
- The proportion of CIN3+ cases that were HPV-positive but false-negative on reflex cytology was very low.
- When the few apparently HPV-negative samples were retested with the same method, about 17% showed HPV positivity, thus proving that no detection method is 100% reproducible or 100% accurate.
- Only 0.4% of the samples had no evidence of presence of HPV by any of the tests.

Screening programmes based on HPV detection often rely on a centralized laboratory where a quality control protocol similar to the one described above may be followed. A standard operating procedure is required for archiving the samples collected for HPV detection. Audit of cytology would be required if the test is used for triage, and the principles and procedures described earlier would need to be followed.

1.7 Next steps after analysis of data from an audit of cervical cancers

Outcomes of the audit must be discussed in a multidisciplinary forum so that factors that resulted in cancers not being prevented can be put in the context of other factors, such as the stage and pathology of the cancer and whether the cancer was detected through the screening programme (screen-detected cancers also include those detected during follow-up processes). Feedback of the audit results to the health professionals concerned requires appropriate planning. Communication of an interpretation error to an individual professional in a manner suggesting blame can be counterproductive and is not the objective of an audit of cancers. The performance of all staff needs to be monitored as part of routine programme quality assurance, and any issue that is identified through an audit should not be considered as reflecting an individual's skills or abilities. A contingency plan based on the audit outcomes must be prepared to improve the quality of services (e.g. reorientation training or improving coverage in vulnerable women) and should be included in the communication.

For the principles of disclosure of audit outcomes to the screening participants, please see Section 2.6.