Key points

Spirometry is:

- An integrative measurement: of volume and flow.
- A reliable measurement (when done properly): effort-independent in large measure.
- A responsive measurement.
- A clinically valuable measurement.

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The clinical usefulness of spirometric information

Summary

Spirometry is a remarkably versatile and informative measurement with known between-test reproducibility. It can be used reliably by a range of practitioners and technologists and changes in spirometry indicate important changes in the patient's clinical condition, although the significance of a given change has to be calibrated against the disease context in which it occurs. Community-based spirometry can identify a range of diseases and exclude others while promoting significant changes in treatment.

Spirometry is a key part of bronchial challenge testing, which can be said to diagnose and monitor progress in asthma. Reductions in forced expiratory volume in one second (FEV_1) are prognostically relevant in chronic obstructive pulmonary disease (COPD) as are decreases in vital capacity in neuromuscular disease. Determining disease progression as the rate of decline in FEV_1 is not practical at an individual patient level, but documenting the loss of lung function over time is still a valuable outcome to monitor. Used together with other clinical features, spirometry can substantially improve our assessment of the patient and their long-term management [1].

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What is spirometry?

Spirometry represents an integrative measurement of volume (forced vital capacity (FVC)) and flow (FEV_1) and the relationship between the two (FEV_1/FVC ratio). For a very simple measurement, when it is made properly, spirometry provides a great deal of information. Some of the skill in applying it to clinical medicine lies in understanding what that information might mean in a particular setting.

The really good thing about spirometry is that it is a reliable measurement when carried out properly. It is in many senses effort-independent, providing the subject makes a reasonable attempt. It is also quite acceptably reproducible from day to day and between individuals. That makes it very helpful, because observed changes represent biological differences, although it is still necessary to interpret what they might be.

Spirometry is also a responsive measurement: treatment, either short- or long-term, can change the results. The very fact that it responds to change is the whole basis of bronchial challenge testing.

Finally, spirometry is a clinically valuable measurement, although it will not provide an answer entirely by itself. It doesn't replace the process of thinking, but it greatly adds to the information on which that thinking can be based.

An integrative measurement

The two components of spirometric data are measurements of volume and flow, and it is remarkable how much information is contained in each. Generally speaking, FVC is thought of as the primary measurement of volume, but slow VC measurements can also be produced, and in some settings these can be extremely helpful. FEV_1, meanwhile, tends to be thought of as a flow measurement, but it also represents a volume change. In many patients with COPD, for instance, bronchodilator (BD) administration will produce proportionately similar changes in FEV_1 and FVC

HERMES syllabus link: modules D1.1, D1.5, B1.1, B1.4

because the operating lung volume is affected.

The volume component in spirometry reflects the size of the lungs. It particularly reflects the elastic properties of the respiratory system: those of the lung, the chest wall and sometimes, in the cases of people with airway closure severe airflow limitation, the elastic properties of the gas trapped within the lungs. Many disease processes may produce a change in volume.

In terms of flow, FEV_1 is related to airflow resistance under maximal conditions. FEV_1 reflects both large and small airway components. Much of the resistance in the respiratory system resides in the large airways, but even peripheral airways diseases make a significant contribution to overall airways resistance and thus decrease FEV_1. Rather than finding a brand new test for small airways disease, it is perhaps better to understand how this might influence FEV_1, which is at least as reliable a measurement as many of the small airways disease tests that have been proposed.

Another common piece of data is the flow-volume loop. There are situations where this can be quite helpful diagnostically. A marked collapse pattern of reduced mid-expiratory *versus* peak flows, for instance, would suggest at least a possibility that a patient has resting airflow limitation under tidal breathing conditions. A more amputated pattern in inspiration and expiration suggests extrathoracic obstruction.

A reliable measurement

The short-term reproducibility of FEV_1 is ~130 mL. Between-day repoducibility varies from series to series but is ~180 mL in most healthy people. This is commonly approximated to 200 mL, which is why the American Thoracic Society (ATS)/European Respiratory Society reproducibility and reversibility criteria incorporate this number [1].

In general, mean FEV_1 remains constant in a population, as does the variance, but there is individual variability, probably reflecting changes in resting airway smooth muscle (ASM) tone. This is important when interpreting data – they must be treated according to whether the population or the individual is being examined. Figure 1 illustrates this: a large number of COPD patients were categorised on three occasions over a 2-month period according to their reversibility with ipratropium and salbutamol [2]. On the first occasion, just over half the subjects were reversible using the ATS criteria [3]. However, the next time, of the people who had been reversible the first, almost 100 would now be re-classified. Of those, a further 50 would be changed when tested a third time. On the other side, many of those who were considered irreversible were reversible when tested again. The chance of being re-classified in this scheme (although it does not matter what scheme is used) depends on starting FEV_1. The higher the starting FEV_1, the lower the chances of being classed as reversible. A low starting FEV_1, *i.e.* greater ASM tone, leaves the BD more scope to work.

Again, average reversibility in the population is surprisingly constant, but individuals vary. This is relevant when interpreting reversibility or other day-to-day changes in FEV_1 in clinical practice. It is not true only for severe disease and it does not seem to relate to the presence of structural abnormality. It appears to be related to ASM tone and it may be present in healthy people too.

A responsive measurement

Lung function is a responsive mechanism: if patients (for instance asthmatics) are given inhaled steroids over time, dramatic improvements in FEV_1 will be seen in some of them. The difficulty for COPD patients is that the changes in absolute terms are very low, but a 5% change in a group of people with a higher starting FEV_1 really does start to matter. It is a responsive measurement and provides an idea of treatment efficacy, but confidence in the results depends on how much the measured improvement exceeds spontaneous day-to-day variability.

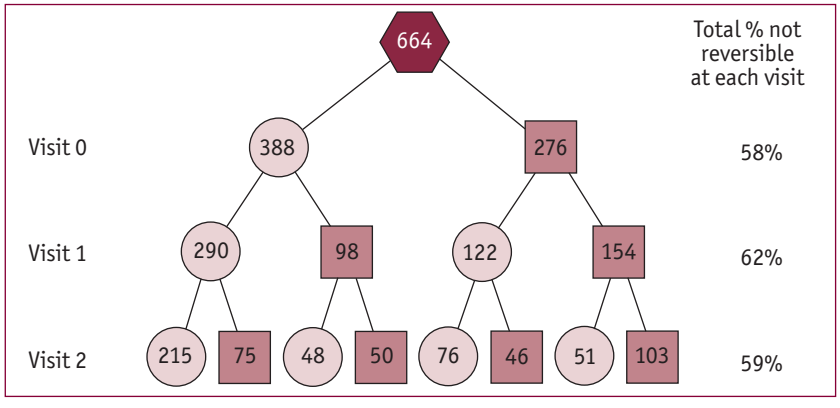


Figure 1
The number of patients with reversibility to ipratropium and salbutamol on successive visits, according to ATS criteria. Reproduced from [2], with permission from the publisher

Spirometry and diagnosis

When using spirometry in clinical practice, the big question is about where the measurement should be made. The simpler a measurement is, and the easier it is to collect, the more likely it is to be incorporated in day-to-day clinical practice. It's clear that it is now possible to produce very

good spirometry in a primary care setting. General practitioners can be trained, and seem to retain the ability, to make the measurement provided they do it frequently. Some issues have been raised, however, about long-term quality control in primary care. Data from Tasmania [4] suggests it is not particularly good and there may be better ways of obtaining reliable spirometry.

Traditionally, spirometry was carried out in the hospital laboratory, where there is good inter-laboratory quality control and systems to check the technical accuracy of the measurements. But from the patient's point of view (and often the clinician's) it is often inconvenient to have spirometry measured in the hospital. This makes it less likely that diseases will be spotted early in their natural history or be confirmed at an early stage. This will certainly have an impact in COPD and asthma, the two conditions more than any others where spirometry has been used clinically. Several papers published recently from all around the world have looked at this [4, 5], showing that nurse-led services achieved a much higher percentage reach of smokers at risk. A similar open-access service has been established at the Charing Cross Hospital in London, UK [6]. In Liverpool, UK, we have been able to move out into the community and develop stand-alone but hospital-supported spirometry services (see Box) [7].

The point is not that one method of provision is bad and another good, but that the model must be fitted to the circumstances. A number of factors influence this, such as reimbursement for spirometry services: in the UK, for instance there is a strong emphasis on reimbursement in primary care, but not necessarily to the doctor for doing it. In other systems, the doctor is more likely to be reimbursed.

It is essential to choose a system that works for the practitioner, but crucially that allows easy access for patients, reducing some of the barriers to getting spirometry done.

Challenge testing

Challenge testing, usually in clinical practice using a nonspecific challenge such as methacholine or histamine, can be used to monitor progress in asthma. It is also particularly helpful in occupational asthma, where specific challenges are used to establish whether something in the workplace is causing a problem. Caution should be exercised here: the risks of a significant late reaction must be taken into account. This is not a procedure where the patient should just attend, have an inhalation and be sent away with instructions to return to the clinic a week later.

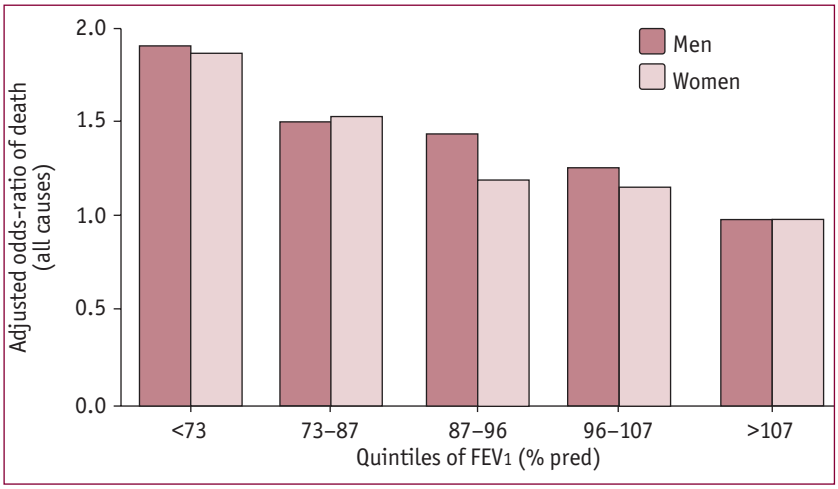
There are standardised, robust methods of carrying out challenge testing. When used regularly [8], compared with normal clinical care, maximising treatment to decrease airway hyperresponsiveness will lead to fewer exacerbations of asthma over a 2-year follow up. Although many practitioners feel that an airway hyperresponsiveness strategy is too time-consuming, it is probably not much more so than measuring exhaled nitric oxide, and it may be less time-consuming and perhaps cheaper than monitoring sputum. Each of these strategies has its proponents, but in all of them spirometric measurement plays a significant role either in identifying the disease, as a safety feature or as the key outcome variable.

Spirometry and prognosis

In a general population sample, all-cause mortality risk is related to lung function impairment (figure 2) [9]. The odds ratio almost doubled for people whose FEV_1 is <73% predicted. An almost identical pattern can be shown for the risk of cardiovascular death. In the HOLE *et al*. [9] study, a large proportion of total deaths were due to cardiovascular disease, and spirometry predicted the risks of this. It has long been known that impaired spirometry is one of the major risk factors for cardiovascular disease, suggesting a usefulness beyond COPD for spirometry-based population screening. This is really a message for primary care physicians, perhaps, rather than respiratory specialists – most of the people who come to specialist clinics have FEV_1s in the lowest quintile of the population, with a clear risk of dying.

Spirometry plays a role in the prognosis of COPD. Data from the body mass index (BMI),

Figure 2
The relationship between lung function impairment and mortality. Adapted from [9].



Using spirometry in the community - a practical example from Liverpool

Just over 1,500 patients were referred for spirometry and attended an outreach clinic [7]. Almost half did not have airflow obstruction before BD, although the referring doctors all thought they might. After reversibility testing, it was clear that there were some people whose airflow obstruction reversed so much that it was completely abolished after BD.

Unlike in COPD, where for most patients a BD reversibility test is not very important, when dealing with an unselected group of patients, reversibility testing is essential. Here, it identified a sizeable number of patients who reverse completely. Abolishing obstruction is a categorical way of showing someone is likely to have asthma. Of the people with residual airflow obstruction after BD, the researchers followed up two-thirds, in most cases obtaining medical notes and attributing diagnosis, usually asthma or COPD (table 1).

Table 1 Diagnosis from primary-care notes before spirometry testing and changes made to the diagnosis as a result of testing

Diagnosis before spirometry	Diagnosis after spirometry	Patients n
No diagnosis	Asthma	22
	COPD	60
	Other	2
Asthma	Asthma	34
	COPD	31
COPD	Asthma	15
	COPD	48
Bronchiectasis	Bronchiectasis	5
All diagnoses	Asthma	71
	COPD	139
	Bronchiectasis	5
	Other	2

Diagnostic lessons

Some diagnostic lessons can be drawn from this. It's clear that some conditions, such as COPD, need spirometry to confirm the diagnosis. It may not provide more information, or give much idea about severity, but it is necessary. In asthma, of course, spirometry can be normal; that is where challenge testing may be relevant. When spirometry is not normal, as in the people who responded to BD, there can be no doubt that we are dealing with asthma.

Even a normal result is a valuable piece of information. Many of those patients with normal spirometry were referred because of unexplained breathlessness. Where spirometry is normal, other causes should be sought. This may merely be general deconditioning and lack of fitness, but it may also be important diseases such as cardiac disease.

The results of the study were striking: 22 patients were newly diagnosed with asthma, and 60 with COPD. Almost half of "asthmatics" turned out to have COPD when the spirometry data and case notes were examined, and a significant proportion of people previously diagnosed with COPD turned out to have asthma.

The downside is that when general practitioners were told the diagnosis, it didn't necessarily change things. Table 2 gives data on 132 COPD cases. It is unsurprising that there was no large increase in short-acting β-agonist use, and encouraging that more patients were given anticholinergic drugs, but this was still only 37% of the total. Few patients received long-acting β-agonists. About half received inhaled corticosteroids (ICS), but almost a quarter of those with low FEV_1 and >1 exacerbation per year were still not receiving ICS treatment. Doctors do not always follow guidelines, even when they have the necessary information.

Table 2 Changes to pharmacological therapy in 132 COPD patients within 3 months of spirometry testing

Treatment	Patients	Patients prescribed treatment before spirometry	Patients prescribed treatment after spirometry	p-value
Short-acting β-agonists	132	104 (79%)	128 (97%)	
Anticholinergics	132	24 (18%)	49 (37%)	0.003
Long-acting β-agonists	132	10 (3%)	33 (25%)	<0.001
Inhaled corticosteroids	132	69 (52%)	94 (71%)	0.05
Inhaled corticosteroids in patients with FEV_1 <50% predicted and >1 exacerbation per year	36	23 (64%)	29 (78%)	

The other main lesson from this study is that spirometry must be accompanied by advice to doctors about how to respond to the results.

airway obstruction, dyspnoea and exercise capacity (BODE) Index paper of CELLI *et al*. [10] shows that people whose FEV_1 is <50% pred had a significant risk of death over a 4-year follow-up. But again, spirometry on its own is not enough. When exercise performance (6-min walking test), breathlessness from a simple grading scale and (BMI) were taken into account, it was possible to state a more specific risk, at least in the medium term, of death. The BODE Index (and various derivatives) is still being explored, and while spirometry is undoubtedly a key component, without which the other variables could not work as well, its unsefulness can be improved when added to other measurements. How this works in clinical practice, *i.e.* the sensitivity and specificity, is still being examined.

Looking beyond COPD, spirometry can have prognostic value in neuromuscular disease. A large number of Duchenne muscular dystrophy (DMD) patients were studied retrospectively [11]. Most of them died before age 25 years and many were dead by age 22 years. Until recently, this was the usual picture in DMD. This study looks at the relationship between the age at which vital capacity (VC) fell to <1 L and the age at death. The great majority of the boys died within 3.5 years of the time VC fell to 1 L. In this instance, vital capacity reflected the global respiratory muscle strength, rather than anything wrong with the lungs themselves. Spirometry thus produced valuable prognostic information, many centres are now using it as a guide to the stage at which night-time noninvasive ventilation should be introduced.

Spirometry and disease progression/severity

Spirometry, both FEV_1 and VC, can provide very useful prognostic information. How does it fare in telling us how severe the disease is and how big an impact it has on the patient's life? This is rather difficult. As an example, take the famous study of FLETCHER and PETO [12] into age-related decline of FEV_1. This showed that the FEV_1 of people who started at the age of 25 years with as-normal predicted spirometry slowly declined, provided they didn't smoke, whereas the lung function of people who smoked deteriorated much more rapidly. The rate at which smokers' lungs deteriorate returns to normal if they stop smoking, but they cannot regain what they have lost and so later on in life, even though they might have stopped smoking many years previously, they still may develop symptoms. The problem with these data is that they are normalised at a particular age, and it is very hard to say at what stage an individual patient may be. In fact, the picture is even more complex. Lung growth may continue until early in the third decade, and thereafter, the decline in lung function depends greatly on what happens to the patient. Certain patients may be prone to exacerbations, while in others lung function decline may be low and stable over time.

Again, while the rates of decline in FEV_1 in smokers, COPD patients and healthy people may differ, the absolute numbers in each case are likely to be considerably <100 mL per year, a figure that is appreciably smaller than the natural day-to-day variability of the measurement. The only way around this problem is to measure decline over long periods, which in itself adds difficulty.

For the most part, recording change in lung function is fine in a population, but not in individuals. Complex modelling may be required, too, to allow for comorbidities. This is something that is very difficult to take into account when trying to read studies and turn them into clinical practice.

Assessing disease severity using spirometry is also difficult. Spirometry can be very useful for detecting the onset of obliterative bronchiolitis in patients post-transplant. However, in general terms, there are other parameters that might be more useful: in asthma, monitoring peak flows will pick up intermittent events, particularly nocturnal ones; when assessing the impact of ILD, gas transfer factor or structural changes will be a much better guide to what is going on in the lungs, and particularly whether treatment will reverse it.

FEV_1, meanwhile, predicts the peak ventilation of COPD patients, but not their overall health status. This is shown by data from the ISOLDE study [13], which plots % predicted FEV_1 against St George's Respiratory Questionnaire (SGRQ) score for about 450 COPD patients (figure 3). There is a good correlation, but for any individual patient the health status measurement is only poorly related to FEV_1.

Pitfalls

There are some pitfalls to be aware of when interpreting spirometry. First, mixed pathologies cause difficulties: patients who have been smokers who develop ILD, for instance, can have a normal FEV_1/FVC ratio, as the effects of airflow obstruc-

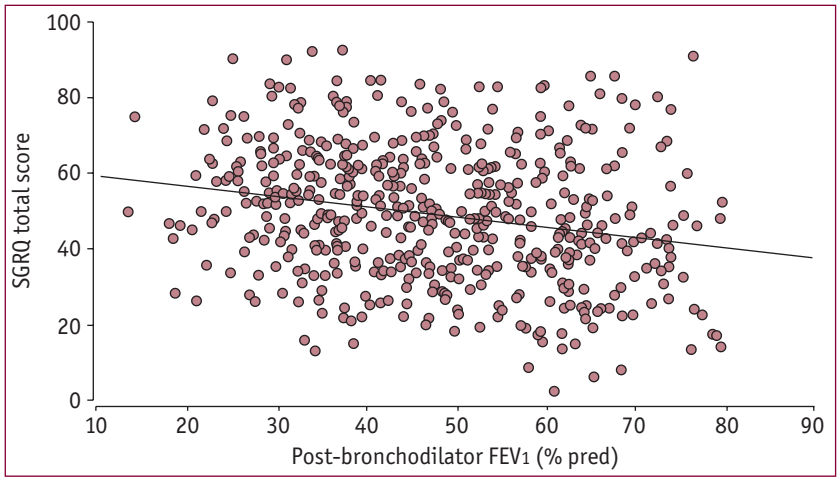


Figure 3
Data from the ISOLDE study [13] showing the relationship between FEV1 and SGRQ score.

tion are traded off against the increased elastic recoil that happens when parts of the lungs become stiffer.

Secondly, variability means the signal can be missed when making one-off measurements. This is evident in asthmatics, who may breathe badly in the morning, but by the time they come to the clinic may have normal spirometry. It's not such a problem for chronic asthmatics with some degree of fixed airflow obstruction, but in primary care it can be very misleading.

Thirdly, the change in FEV1 or in FVC may not capture the real parameter of interest: for instance, inspiratory capacity change is probably what matters in determining post-BD exercise tolerance in COPD, and likewise a rehabilitation programme that improves maximal oxygen consumption will not necessarily affect spirometry.

Finally, the way in which the patient performs the test can also vary, in a manner that is influenced by their mental state. An elderly patient who is beginning to develop some mental infirmity or early dementia may become progressively worse at performing spirometry without having anything wrong with the lungs.

Final thoughts

Despite its limitations, spirometry remains the easiest and most accurate way to assess abnormalities in lung mechanics. It is crucial that spirometry is performed properly, so that any information is not contaminated by a badly performed test. As clinicians, we make use of it as a qualitative guide to diagnosis, and in most settings it doesn't matter if FEV1 is 2.25 or 2.5 L. It probably does matter if FEV1 is 1.25 L. So spirometry is really a general guide to diagnosis and treatment, and although it is measured with great accuracy, it must be interpreted as part of the overall management of the patient. It must be accompanied by a good history with careful physical examination, which will tell the physician whether the result of the spirometry makes sense. A result that does not quite fit the clinical information is an important clue to the underlying pathology. The person whose spirometry is very poor but who complains of no symptoms needs further investigation, perhaps just to make sure they are doing the test properly, but also to find out why this is happening. Equally, the person who says they have terrible wheezing and breathlessness but has normal spirometry perhaps has another condition.

Finally, spirometry really should be used more widely, and we should not be apologetic about the information it provides. There is a lot of very solid science behind spirometry, and it can be an extremely valuable tool to improve clinical practice.

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