Healthcare Improvement Scotland | SHTG Advice on health technologies

SHTG Assessment

February 2025

In response to an enquiry from the Centre for Sustainable Delivery

Stability of prostate specific antigen (PSA) in blood samples

Key messages

1. In NHSScotland, total prostate specific antigen (PSA) levels are measured as a first line test for men presenting in primary care with symptoms suggestive of prostate cancer.
2. Total PSA levels in whole blood or serum are more stable over time than free PSA levels.
3. Variation in total PSA levels in samples remained below 5% change from baseline for approximately 3 days at room temperature. Changes in free PSA levels exceeded 5% within about 24 hours, even at refrigerated temperatures. A 5% change from baseline is viewed as a clinically important change that affects the accuracy of the test result.
4. Refrigerating blood or serum samples for PSA testing slows down the changes in total and free PSA levels before testing.
5. Storing serum on the clot or allowing blood to coagulate leads to larger and faster changes in total and free PSA levels.
6. A requirement to test total PSA levels within 24 hours has potential implications for NHS Boards serving people living in remote, rural and island communities in Scotland.

What were we asked to look at?

We were asked to review the evidence on the stability of PSA levels in blood and serum samples to support updating of the Scottish cancer referral guidelines on prostate cancer.

Why is this important?

PSA is a protein produced by both normal and cancerous cells in the prostate.[1] Elevated PSA levels may indicate prostate cancer.[1]

A blood test is available to measure PSA levels.[1] PSA levels in blood or serum samples consist of free PSA and PSA bound to other proteins. PSA levels vary over time for a number of physiological or pathological reasons.[2] Laboratories in NHSScotland generally test for total PSA.

Guidance in England and Belgium suggests that PSA blood samples should reach the laboratory within 16–18 hours for serum separation and testing.[2-5] Scottish cancer referral guidelines do not currently recommend a turnaround time for PSA test samples.[6]

What was our approach?

We reviewed the published literature on how long PSA levels remain stable in blood and serum samples. More information about SHTG assessments can be found on our website.

What next?

The evidence on the stability of PSA levels in blood and serum samples will be considered as part of an update of the Scottish suspected cancer referral guidelines on prostate cancer.[6]

Key points

1. The published evidence on the stability of total and free PSA levels in blood and serum samples is of limited quality. All studies reviewed were experimental studies with methodological limitations.
2. A 5% change from baseline is viewed as a clinically important change that affects the test result, for example changing the result from elevated PSA to normal levels of PSA.
3. Two studies (n=20 and n=45) found that total PSA levels varied by less than 2% over the first 24 hours when stored as serum at room temperature.[7, 8] Variation in total PSA levels remained less than 5% for up to 72 hours after blood was drawn. In the same two studies, free PSA levels changed by more than 5% within 24 hours under the same conditions.
4. One study (n=45) found that total PSA levels in serum varied by less than 1.5% over 7 days when stored at 4°C.[8] Under the same conditions, free PSA levels decreased by 4.8% within 24 hours and by 5.4% within 72 hours of blood being drawn.
5. One study (n=15) measured total PSA levels when blood samples were stored as serum on the clot at 4°C and found that levels decreased by 18.8% within 72 hours of blood being drawn.[9] The study authors suggest that this result showed blood samples left on the clot do not reflect PSA levels in the body.
6. A single study (6 samples from two patients) measured PSA levels in coagulated blood samples stored at 2–8°C and found that total PSA levels increased by more than 5% within 5 hours and free PSA levels increased by more than 5% within 2 hours.[10]
7. Storing blood samples for PSA testing at room temperature leads to more rapid changes in free PSA levels than samples stored in a refrigerator.

Contents

Definitions

Aliquot	an amount taken from a larger quantity for testing.[11]
Benign prostatic hyperplasia (BPH)	prostatic enlargement that can affect urination.[12]
People who have a prostate	men, transgender women and non-binary people assigned male at birth.
Plasma	the liquid that remains when cells have been removed from a blood sample and clotting has been prevented using an anticoagulant.[13]
Prostate	a small gland in the pelvis, located between the penis and the bladder and surrounding the urethra.[14]
Prostate specific antigen (PSA)	a protein that is produced by both normal and cancerous prostate cells.[1]
Serum	the liquid that remains when the cells have been removed from a blood sample after clotting.[13]

Abbreviations are listed in *Appendix 1*.

Introduction

PSA is a protein produced by both normal and cancerous cells in the prostate.[1] People who have a prostate have PSA in their bloodstream. Variations in PSA levels are normal. Elevated PSA levels can be caused by benign conditions such as prostatic hyperplasia or infections but can also indicate prostate cancer.

PSA is present in the blood in two forms, total and free PSA.[7, 15] Approximately 70–90% of total PSA is bound to other molecules in the blood. Free PSA is not bound to other substances and makes up the other 10–30% of circulating PSA.

A blood test is available that can measure PSA levels.[1] Blood samples can be drawn at a patient's general practitioner's (GP) surgery and sent to an NHS laboratory, usually in a hospital, for testing. Transportation of blood samples from GP surgeries to hospital laboratories requires temporary sample storage and the logistics can be affected by local geography in Scotland.[7, 16]

The stability of PSA, especially free PSA, is affected by its proteolytic properties which can cause changes in PSA levels in blood and serum samples over time.[2] Guidance in England and Belgium suggests that blood samples for PSA testing should arrive at a laboratory in time for the serum to be separated and the test run within 16–18 hours of the sample being taken.[2-5] Scottish cancer referral guidelines do not currently recommend a turnaround time for PSA test samples.[6]

Research question

How long do total and free PSA levels remain stable in blood and serum samples?

Literature search

A systematic search of the secondary literature was carried out between 14 October and 17 October 2024 to identify systematic reviews, health technology assessments and other evidence-based reports. Medline, Embase and Web of Science databases were also searched for systematic reviews and meta-analyses.

The primary literature was systematically searched between 14 October and 17 October 2024 using the Medline, Embase and Web of Science databases. Results were limited to English language publications. No date limits were applied.

Key websites were searched for guidelines, policy documents and clinical summaries.

Concepts used in all searches included prostate specific antigen, hours, storage, stability, temperature, timeframe, preanalytical conditions and handling. A full list of resources searched and terms used is available on request.

Health technology description

Several laboratory test kits are available to measure the amount of total and free PSA in blood samples.[2] Laboratories in NHSScotland generally only test for total PSA (Dr PH Hodkinson, Consultant Physician, NHS Ayrshire and Arran. Personal communication, 31 Oct 2024).

The normal value for total PSA levels varies with age.[6] *Table 1* shows normal PSA levels used in the Scottish suspected cancer referral guidelines, which were determined by clinical consensus from available evidence.[6]

Table 1: Age specific normal total PSA levels[6]

Age (years)	PSA level (ng/ml)
Under 60	<3
60 to 69	<4
70 to 79	<5

In blood or serum samples taken for testing, a change in PSA levels of more than 5% from baseline is considered a clinically important change that affects the test results.[8] For this assessment, we assumed that a change of more than 5% from baseline measurements of total or free PSA levels in

samples could affect the test result. This could change a test result from normal to elevated or vice versa.

Epidemiology

In Scotland, prostate cancer is the most common cancer among men, affecting approximately 1 in 10.[17] Between July 2020 and June 2021, 3,543 men were diagnosed with prostate cancer in Scotland.[18]

The incidence of prostate cancer increases with age.[17] While prostate cancer is very uncommon before the age of 40, 80% of men aged 80 or older will have cancerous cells in their prostate. Most of these older men will not need treatment and may not show any symptoms.

Men with a first degree relative who has or had prostate cancer are at increased risk of developing the condition.[17] Prostate Scotland has stated that men with African or Caribbean heritage are three times more likely to develop prostate cancer than men from other ethnic backgrounds.[17]

In Scotland, anyone aged 50 or older can ask their GP for a PSA test if they are concerned about prostate cancer.[19] Men aged 45 or older with a family history of prostate cancer, African or black Caribbean heritage, or symptoms suggestive of prostate cancer can also ask to be referred for testing.

In the United Kingdom (UK), an estimated 6% of men aged 45 or older have a PSA test each year.[20] In a large retrospective cohort study in men aged 45 to 69 in Scotland, 23.8% (7,212/45,717) had a PSA test over a 10 year period.[20] During the same time period, 2% of these men were diagnosed with prostate cancer. Men aged 65 to 69 were more likely to have a PSA test than younger men. Men in the least deprived areas were more likely to have a PSA test compared with men in the most deprived areas (46.3% versus 31.9%, p value for trend <0.001).

There is no prostate cancer screening programme in Scotland.

Safe storage of samples for PSA testing

Eight studies were selected for inclusion in this assessment.[7-10, 15, 16, 21, 22] The characteristics of these studies are outlined in *Table 2*. Patient numbers were small, ranging from eight to 45 men. Study designs consistently involved collecting blood samples, storing them as blood, serum or plasma for varying lengths of time, at differing temperatures and measuring PSA levels at prespecified timepoints.

The studies varied in whether they tested serum or whole blood, the timepoints at which they measured PSA levels, whether samples were centrifuged before or after storage, and the patients from whom samples were drawn.

Three studies reported on testing blood or serum samples stored at room temperature[7, 8, 16] and six reported on samples stored under refrigerated conditions.[8-10, 15, 21, 22] Most studies reported both total and free PSA measures. Two studies only reported 'PSA' levels and were assumed to be reporting total PSA. The included studies were low quality experimental studies with methodological limitations.

Two studies reported results only as line graphs, which prevented data extraction.[15, 22] Most studies failed to differentiate between statistically significant and clinically important changes in PSA levels.

Six of the eight included studies were published more than 10 years ago.[9, 10, 15, 16, 21, 22] Seven additional studies published in the 1990s were identified.[23-28] The results are not described in detail, but their findings were consistent with the results of the more recent studies.

Table 2: Overview of primary experimental studies included in this assessment

Study	PSA measures reported	Sample type (storage)	Time of centrifugation	Timepoints measured	Temperatures	n samples
Simanek (2024)[8]	Total, free and [-2]proPSA	Serum	Before storage (Within 1h of venipuncture)	1, 2, 4, 6, 8, 24 and 72h	Room temperature (22°C) and 4°C	45 volunteers: 36 with BPH and 9 healthy
Forde (2016)[7]	Total and free	Whole blood	After storage	4, 8, 24 and 48h	Room temperature (22°C)	20 urology outpatients
Henriksen (2014)[16]	Coefficient of variation and bias for total PSA	Whole blood	After storage – including transportation by car to laboratory (Within 30–90 minutes of venipuncture for baseline values)	10h	21°C ± 1°C	31 inpatients
Hsieh (2007)[21]	Total, free, free/total ratio	Unclear	Unclear (no mention of centrifugation)	0 min, 30 min, 7 days	Ambient temperature (unspecified) or 4°C	6 with prostate cancer, 24 with BPH
Kumari (2004)[10]	Total, free	Coagulated blood	Serum separated from clot 0–24 h after venipuncture	0–24h	2–8°C	6 samples: 1 with BPH, 1 with prostate cancer
		Serum	Allowed to clot for 30min then serum	1, 4, 9, 12, 14 and 25 days		1 healthy, 2 with BPH, 2

			separated after clot removed			with prostate cancer
Sokoll (2002)[22]	Total, free, complexed	Whole blood	After storage (Centrifuged within 2h of venipuncture)	0, 4, 8, 24 and 48h and 1 week	Room temperature (unspecified) and 4°C	3 with prostate cancer, 3 with BPH, 2 healthy
Liyanarachcy (2000)[9]	Assumed to be total	Serum left on the clot	Before storage (Allowed to clot for 2h at room temperature)	3, 5 and 7 days	4°C	15 healthy volunteers
Jung (2000)[15]	Total, free, alpha1-antichymotrypsin (ACT-PSA)	Whole blood	After storage	0, 4, 8, 12, 16, 20, 24h	Room temperature (unspecified)	13 with prostate cancer 2 with BPH
		Serum	Before storage (Allowed to clot for 1h)	At 37°C: 0, 4, 8, 12, 16, 20, 24h At room temperature: 0, 8, 16, 24, 32, 40, 48h At 4°C: 0–8 days	Room temperature (unspecified), 37°C or 4°C	13 with prostate cancer 2 with BPH

Total PSA

Storage at room temperature

Three studies experimented with storing blood or serum samples for total PSA testing at room temperature for different durations.[7, 8, 16] All three studies defined room temperature as 21–22°C. This may not reflect the typical indoor temperature in Scotland, particularly during winter.

The most recent study (Simanek, 2024) collected blood samples from 45 male volunteers aged 60 to 85 (mean age 68).[8] Thirty-six volunteers had benign prostatic hyperplasia (BPH), while nine were healthy. Men with a history of prostate cancer or a total PSA above 10ng/ml were excluded. The blood samples were centrifuged to obtain serum within 1 hour of venipuncture and divided into 17 aliquots. The aliquots were stored at 22°C and tested at baseline and after 1, 2, 4, 6, 8, 24 and 72 hours.

The study results, presented in *Table 3*, show that the decrease in total PSA levels was statistically significant at each time point when serum samples were stored at room temperature ($p<0.001$). These results were not considered clinically important because the change from baseline remained less than 5%.

The study by Forde (2016) collected blood samples from 20 men attending a urology outpatient clinic.[7] Blood samples were stored at 22°C for 4, 8, 24 and 48 hours before being centrifuged and tested. This allowed the blood to clot before the serum was separated. The reading taken after 4 hours was used as the baseline.

Mean total PSA levels in serum samples varied from a 1.26% decrease to a 2.53% increase compared with the baseline reading (*Table 3*). The variation in total PSA was neither statistically significant ($p=0.283$) nor clinically important at any time point.

The third study (Henriksen, 2014) assessed the feasibility of analysing total PSA levels in whole blood samples stored for 10 hours at 21°C before separation of serum.[16] Thirty-one samples were taken from hospitalised men with a baseline PSA level (assumed to be total PSA) greater than 4ng/ml. Each blood sample was halved; one half was centrifuged and the serum tested immediately to get the baseline 'true' PSA value, while the other half was stored as whole blood for 10 hours at 21°C before centrifuging and testing. During the last 90 minutes of the 10 hours storage, the blood samples were transported by car to the laboratory for centrifuging and testing.

The Henriksen (2014) study did not report the actual or percentage change in total PSA levels. The study measured bias and imprecision in test results using a coefficient of variation. The samples stored for 10 hours and then tested for total PSA showed no statistically significant bias or variance compared with the baseline samples ($p=0.083$).

Two older studies tested variations in total PSA levels in blood or serum samples stored at room temperature for up to 1 week.[25, 28] The conclusions from these studies are consistent with the more recent analyses described above, that total PSA is relatively stable in serum for up to 48-72 hours.

Refrigerated storage

Six studies investigated the effect of refrigerating blood or serum samples prior to total PSA testing.[8-10, 15, 21, 22] Only two studies reported results in a format that allowed for data extraction at multiple time points (*Table 3*).[8, 21]

Simanek (2024), described in the previous section, also reported total PSA results for serum samples stored at 4°C.[8] At this lower temperature, changes in total PSA levels remained low (0.8% to 1.5% decrease) over the 72 hours of testing (*Table 3*). These changes were statistically significant ($p<0.001$) but not clinically important.

The study by Hsieh (2007) analysed blood samples collected from 30 men participating in a prostate cancer screening programme.[21] The men were aged between 44 and 75. Six men had a recent diagnosis of prostate cancer and 24 had BPH. It is unclear when, or if, the blood samples were centrifuged to obtain serum for testing. The blood samples were divided into three groups with BPH and one group with prostate cancer. Baseline total PSA levels were measured at room temperature. The baseline results were then compared against testing of the same samples after they were refrigerated at 4°C for 30 minutes and 7 days. Total PSA levels decreased by 3.6% after 30 minutes at 4°C. After 7 days at 4°C, total PSA levels had decreased by an average of 7.5% which was clinically significant (*Table 3*).

A study by Liyanarachcy (2000) explored the stability of PSA levels in samples stored at 4°C for up to 7 days.[9] Blood samples were collected from 15 apparently healthy male volunteers aged 30 to 50 years. It is unclear how much time elapsed from blood samples being collected to them arriving in the laboratory for testing. Blood samples were allowed to clot at room temperature for 2 hours before being centrifuged. Serum remained on the clot. The serum was then assayed to obtain a baseline reference PSA value (assumed to be total PSA). Testing was repeated after 3, 5 and 7 days of storage at 4°C.

Mean percentage change for PSA levels exceeded the clinically important difference within 3 days (18.8% decrease). Liyanarachcy (2000) noted that within 24 hours of storage at 4°C, the percentage change in PSA levels exceeded both the individual biological variance (18.1%) and the predetermined assay variation limit (18.2%). This finding may not be reliable as the study did not report testing PSA levels within 24 hours. PSA levels in samples stored on the clot may not accurately reflect the true in vivo levels.

Kumari (2004) explored the stability of total PSA in coagulated blood and serum samples stored at 2–8°C.[10] Six blood samples were taken from two male patients; a 65 year old man with BPH and a 60

year old man with prostate cancer. Only the blood samples from the man with BPH were tested for total PSA. These samples were stored as coagulated blood and tested at baseline, and at 1, 2, 5, 10 and 24 hours. In the coagulated blood samples total PSA levels increased by 6.38% after 5 hours.

Kumari (2004) also collected blood samples from a healthy male, two men with BPH and two men with prostate cancer and stored them as serum at 2–8°C. No age is given for the patients in this part of the study. Six aliquots of each sample were made and tested after 1, 4, 9, 12, 14 and 25 days. The decrease in total PSA levels was large and clinically significant after 4 days compared to baseline (1 day) for the serum samples taken from men with BPH or prostate cancer. The small number of men tested in this study reduces the reliability of these results.

Two other studies exploring the effects of storing samples in refrigerated conditions presented their findings only as black and white line graphs.[15, 22] We were unable to extract data from these graphs, which, along with the small number of men included, limited the usefulness of these studies.

The first study (Sokoll, 2002) took blood samples from three men with histological diagnoses of prostate cancer, three men without prostate cancer (possibly men with BPH) and two healthy men.[22] No information is given about the men's age or other underlying conditions. Serum samples were stored at 4°C and tested at baseline (0 hours), 4 hours, 8 hours, 24 hours, 48 hours and 7 days. Total PSA levels decreased by an average of ≤10% between 48 hours and 1 week when stored at 4°C. Changes in total PSA in this study would be clinically important after 24–48 hours.

Jung (2000) tested blood samples from 13 men with prostate cancer and two with BPH.[15] No additional information is supplied about the men providing blood samples. The authors seem to have measured total PSA levels after:

- 0–24 hours at room temperature before serum separation
- 0–24 hours storage at room temperature after serum separation
- 0–7 days storage at 4°C after serum separation.

Testing at 0 hours formed the baseline values for total PSA.

When whole blood was stored at room temperature for up to 24 hours before separation of serum, total PSA levels remained stable. Total PSA levels also remained stable in serum stored for up to 24 hours and showed a statistically significant decrease after 48 hours at room temperature or 4°C.

Six older studies conducted similar experiments and reached the same conclusions about the stability of total PSA levels in samples stored in refrigerated conditions.[23-28] All six studies found total PSA to be stable at 4°C for at least 24 hours, with the exception of when samples are stored on the clot.

Table 3: Change in total PSA levels over time when stored at room temperature or refrigerated

Study	Blood or serum	n samples	Temperature (°C)	Total PSA level change compared with baseline (%)					p value
				0–4h	5–10h	24h	48h	3–7 days	
Room temperature									
Simanek (2024)[8]	Serum	45	22	-1.0%	-1.3%	-1.7%	–	-3.1%	<0.001
Forde (2016)[7]	Serum	20	22	Baseline	+2.5%	-1.3%	+1.3%	–	0.283
Refrigerated									
Simanek (2024)[8]	Serum	45	4	-1.4%	-1.1%	-0.8%	–	-1.5%	<0.001
Hsieh (2007)[21]	Whole blood?	24*	4	-3.6%	–	–	–	-7.6%	–
		6**		-3.6%	–	–	–	-7.4%	

**Men with confirmed BPH*

***Men with diagnosed prostate cancer*

****Healthy men*

Free PSA

Storage at room temperature

Two of the three studies that reported total PSA testing at room temperature also investigated free PSA testing.[7, 8]

Simanek (2024) found that the change from baseline in free PSA levels in serum samples exceeded the clinically important threshold after 24 hours at room temperature, showing a 6.2% decrease (*Table 4*).[8]

Forde (2016) found that mean free PSA levels in samples stored as whole blood before being centrifuged, decreased by 10.7% within 24 hours of blood collection (p=0.024).[7]

Two older studies also tested variations in free PSA levels in samples stored at room temperature for up to 1 week.[25, 28] The conclusions from these studies are consistent with the more recent analyses described above, that changes in free PSA are likely to exceed the clinically important difference within 24 hours at room temperature.

Refrigerated storage

The same six studies that reported total PSA testing of refrigerated blood or serum samples also described free PSA levels.[8-10, 15, 21, 22] Only two studies presented results in a format that allowed for data extraction at multiple time points (*Table 4*).[8, 21]

Simanek (2024) found that free PSA levels in serum samples approached the clinically important threshold after 24 hours (4.8% decrease) and had decreased by 5.4% after 72 hours (*Table 4*).[8] The variation in free PSA levels was consistently smaller in serum samples stored at 4°C compared with serum samples stored at room temperature and tested at the same time points.

Hsieh (2007) found that free PSA levels increased from baseline after both 30 minutes and 7 days (*Table 4*).[21] The increase in free PSA levels was clinically significant in samples from men with prostate cancer after 7 days of storage (14% increase). It is unclear why the free PSA results from this study showed an increase in free PSA over time instead of the overall decrease described in other studies.

Kumari (2004) tested samples from one patient with prostate cancer for free PSA levels.[10] The minimum clinically important change in free PSA levels occurred within 2 hours (5.38% increase). In the same study, free PSA levels only started to decline after 12 days in the samples from a healthy male. The small number of men tested in this study reduces the reliability of these results.

Two other studies exploring the effects of storing blood or serum samples in refrigerated conditions presented their findings only as black and white line graphs.[15, 22] We were unable to extract data from these graphs, which limited the usefulness of these studies.

The first study by Sokoll (2002) found that free PSA levels started to decrease after 24 hours at 4°C (15% decrease) and had decreased by approximately 70% after 1 week.[22] Changes in free PSA in this study would be clinically important after 24–48 hours.

The second study (Jung, 2000) found that free PSA levels decreased significantly within 4 hours of being drawn from the patient.[15] It is unclear if this change was clinically important. Free PSA levels were less stable, with a mean decrease of 3.5% to 5% after 4 to 24 hours of storage at room temperature. At 4°C free PSA levels showed statistically significant decreases after 1–7 days of testing.

Six older studies conducted similar experiments and reached the same conclusions about the stability of free PSA levels in samples stored in refrigerated conditions, that free PSA levels decreased beyond the clinically significant threshold within 1–3 days when stored at 4°C.[23-28]

Table 4: Change in free PSA levels over time when stored at room temperature or refrigerated

Study/ country	Blood or serum	n samples	Temperature (°C)	Free PSA level change compared with baseline (%)					p value
				0–4h	5–10h	24h	48h	3–7 days	
Room temperature									
Simanek (2024)[8]	Serum	45	22	-1.5%	-3.8%	-6.2%	–	-10.8%	<0.001
Forde (2016)[7]	Serum	20	22	Baseline	-0.5%	-10.7%	-11.2%	–	0.024
Refrigerated									
Simanek (2024)[8]	Serum	45	4	-1.2%	-1.7%	-4.8%	–	-5.4%	<0.01
Hsieh (2007)[21]	Whole blood?	24*	4	+2.8%	–	–	+3.8%	–	–
		6**		+3.9%	–	–	+14.0%	–	

**Men with confirmed BPH*

***Men with diagnosed prostate cancer*

****Healthy men*

Organisational issues/context

Storage and transportation times for PSA testing samples presents potential challenges for NHS Boards supporting people living in remote, rural or island communities. For example, approximately 320,000 people live in NHS Highland across an area of 32,500km^2.[29]

An estimated 47,000 people live on inhabited Scottish islands, many of which rely on hospital services on the mainland.[30] Some island health boards can offer local PSA testing but experience long transport times (S Willis, Laboratory and Quality Manager, NHS Shetland. Personal communication, 22 Nov 2024). For example, NHS Shetland processes all PSA samples at the hospital in Lerwick. On average it takes about 11 hours to get blood samples transported to Lerwick from the other Shetland isles.

Storage and processing time challenges may also affect people living in remote and rural parts of mainland Scotland.

Conclusion

The evidence on how long total and free PSA levels remain stable in blood or serum samples is of limited quality. Most studies conclude that PSA levels should be tested within 24 hours of a blood sample being drawn from a patient. This has potential implications for PSA testing among residents of remote, rural and island communities in Scotland.

Total PSA appears to be more stable over time compared with free PSA. A 5% change in PSA levels from baseline is viewed as a clinically important change that affects the accuracy of the test result. Changes in total PSA levels remained below 5% for approximately 3 days at room temperature, while free PSA levels changed by more than 5% within about 24 hours, even at refrigerated temperatures. This supports continuing the current practice in Scotland of measuring only total PSA levels.

There is evidence that storing blood or serum samples at lower temperatures (in refrigerated conditions) leads to smaller and slower changes in total and free PSA levels over time.

PSA levels appear to remain stable for longer when samples are centrifuged and stored as serum rather than whole blood (including serum on the clot or coagulated blood). In one study, when blood samples were allowed to coagulate before testing, the change in total and free PSA levels exceeded the minimum clinically important difference of 5% within 5 hours and 2 hours, respectively.

The stability of total and free PSA and the acceptable storage duration for blood or serum samples for PSA testing is further complicated by evidence that different PSA assays can yield varying results.[2, 31] This variability is higher with free PSA, which further supports the practice of measuring only total PSA in Scotland.

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Appendix 1: Abbreviations

BPH	benign prostatic hyperplasia
°C	degrees celsius
GP	general practitioner
h	hours
km²	square kilometres
mg	microgram
ml	millilitre
ng	nanogram
NHS	National Health Service
PSA	prostate specific antigen
SHTG	Scottish Health Technologies Group
UK	United Kingdom