Pharmacist-led Thyroid Point-of-Care Testing

A thesis submitted in partial fulfilment of the requirements of the Degree of Doctorate in Pharmacy

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2025

I dedicate this work to my beloved ones, whose unwavering support and encouragement have been instrumental in making this dream a reality.

Acknowledgments

I would like to express my sincere gratitude to my research supervisors, Professor Lilian M Azzopardi and Dr Francesca Wirth, for their unwavering guidance, invaluable support, constructive feedback, and profound wisdom throughout the course of my research. I am also sincerely grateful to the Validation Panel for their discerning contributions to my dissertation and to Professor Liberato Camilleri for his expertise in statistical analysis.

My sincere thanks extend to the staff of the University of Malta's Pharmacy Department for the comprehensive knowledge and academic guidance they have provided me over the years. This support has been instrumental in shaping my academic journey and making this experience both enriching and memorable.

I am profoundly appreciative of all the staff at St. Andrews Clinics, whose assistance, motivation and encouragement were pivotal in the successful execution of my research.

I would also like to acknowledge Brown's Pharma Ltd for providing me with access to their facilities, all while fostering a balanced work-life balance that greatly supported my academic pursuits.

Finally, I extend my heartfelt appreciation to my friends and family for their constant love, reassurance, and belief in me.

The University of Malta Research Grant (PHRRP12) funded the point-of-care test devices, and the capillary pipettes were funded by Brown's Pharma Ltd.

Abstract

Early detection of thyroid dysfunction through point-of-care testing (POCT) is relevant for high-risk individuals and those previously diagnosed who may remain uncontrolled due to inadequate adherence or suboptimal dosing. Establishing pharmacist-led thyroid POCT enables timely screening and ongoing monitoring, enhancing long-term care.

The aim was to develop a framework for pharmacist-led thyroid POCT and assess feasibility of implementation in a community pharmacy setting.

Appraisal of thyroid POCT devices was conducted taking into consideration technical and analytical specifications, cost and accessibility. A POCT device was selected and validated by comparing POCT results to laboratory-based results for 20 participants attending a physician clinic for routine thyroid function testing, recruited by convenience sampling. A framework for pharmacist-led thyroid POCT was developed and validated by an expert panel. The developed framework consists of a Data Collection Tool to assess hypothyroidism risk factors, health status, knowledge on thyroid function testing and medication adherence; a standard operating procedure for performing POCT; an Action Plan for standardised and personalised patient actioning based on test results including physician referral as necessary; and a Patient Education Resource providing information related to hypothyroidism management. The framework was tested for feasibility in 75 participants recruited by convenience sampling from a community pharmacy according to inclusion and exclusion criteria: taking levothyroxine or medication/s which may affect thyroid function, no thyroid function testing in past 6 months, no acute illness, not pregnant or breastfeeding. Descriptive statistics were performed ($p<0.05$ statistically significant).

Fourteen thyroid POCT devices were compared, where two were found to be available locally. Following appraisal of devices, AcroBiotech Inc. Thyroid-stimulating hormone (TSH) rapid test cassette which screens for hypothyroidism was selected for use in this study (CE-marked, qualitative chromatographic immunoassay, sensitivity 5μIU/mL, specimen volume 50μL fingerstick blood, time for result 10 minutes). Validation of the selected POCT device revealed 95% concordance with laboratory-based results (κ=0.773), supporting device clinical reliability. The 75 participants for feasibility testing of the framework (female n=57; mode age range 45–54 years n=24), were taking levothyroxine (n=45) or medication/s that may affect thyroid function (n=30). Twenty-three participants had a positive result (TSH ≥5 μIU/mL) indicating hypothyroidism; of whom 15 were being treated for hypothyroidism, indicating inadequate adherence to levothyroxine (n=12) or dosage insufficiency (n=3), while 8 were taking medication/s which may affect thyroid function (newly identified). All participants with a positive TSH result were referred for physician assessment. Thirty-one participants reported two or more symptoms indicative of hypothyroidism and were referred for physician assessment. From the 45 participants taking levothyroxine, 44 were provided with the Patient Education Resource. A statistically significant association was observed between positive TSH result, symptoms of hypothyroidism, and incorrect levothyroxine use ($p<0.05$).

This study identified a clinically reliable POCT device which screens for hypothyroidism and presents a validated pharmacist-led framework which is feasible to be implemented in community pharmacy to support patient screening and monitoring within a collaborative care model.

Keywords: *collaborative care; community pharmacy; hypothyroidism; pharmacist-led service; point-of-care testing*

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List of Abbreviations

BMI	Body Mass Index
IVDR	In Vitro Diagnostic Regulation
POCT	Point-of-Care Testing
SOP	Standard Operating Procedure
TFT	Thyroid Function Testing
TSH	Thyroid-Stimulating Hormone

Chapter 1- Introduction

1.1 Pharmacists and Point-of-Care Testing

Community pharmacists play an increasingly significant role in providing patient-centred services, including point-of-care testing (POCT) (Kamusheva et al., 2020; Maduabuchi et al., 2023). POCT provides rapid results at the site of patient care facilitating real-time clinical decision-making and timely therapeutic interventions which can significantly improve patient outcomes (Dayan and Panicker, 2018; Albasri et al., 2020; Zammit, 2021; Chan et al., 2023).

Pharmacists possess the necessary expertise to perform POCT effectively, contributing to an improved healthcare system and empowering patients to actively manage their health (Zammit, 2021). Advancements in technology have further increased the accessibility of POCT devices, providing patients with immediate healthcare services. The 'ASSURED' criteria: Affordable, Sensitive, Specific, User-friendly, Rapid, Equipment-free, and Deliverable to end-users', are the standard criteria for all POCT (Howard, 2024). These characteristics enable pharmacists to deliver efficient and high-quality patient-centred care (Pezzuto et al., 2019; Albasri et al., 2020; Di Cerbo et al., 2021; Larsen et al., 2023; Maduabuchi et al., 2023).

Community pharmacists are among the most accessible healthcare providers, with patients visiting them twice as frequently as primary care clinics (Berenbrok et al., 2022). This accessibility positions pharmacists to play a critical role in managing minor ailments, screening and monitoring of chronic conditions, and promoting disease prevention (Kamusheva et al., 2020; Zammit 2021; Berenbrok et al., 2022). Research from the

International Pharmaceutical Federation highlights that pharmacist-led interventions and POCT enhances patient outcomes, improves service delivery, contributes to sustainable healthcare systems and the achievement of universal health coverage (Elrobaa et al., 2024).[1]

The European Union's In Vitro Diagnostic Regulation (EU) 2017/746 (IVDR), effective since May 2022, establishes a stringent, risk-based classification system for in vitro diagnostic medical devices, including POCT devices used by community pharmacists.[2] This regulation categorizes in vitro diagnostic devices into four classes (A to D) based on risk, with low-risk Class A devices allowing manufacturer self-certification, while higher-risk Classes B, C, and D require conformity assessments by Notified Bodies to ensure safety and performance.[3] POCT devices used in community pharmacy settings, typically fall under Class B to D, necessitating rigorous conformity assessment and CE marking to comply with IVDR standards (Spitzenberger et al., 2022). Healthcare professionals, including community pharmacists, must verify that POCT devices meet these regulatory requirements and hold a valid CE marking, ensuring proper device selection, operation, maintenance, and adherence to clinical governance and safety protocols. This regulatory framework enhances patient safety and care quality by mandating comprehensive oversight of POCT devices, supporting the delivery of reliable diagnostic and monitoring services closer to patients in community settings. Successfully implementing a new POCT service requires a thorough understanding of demand and supply factors, as well

[1] International Pharmaceutical Federation (FIP). Pharmacy-based point-of-care testing: a global intelligence report 2023 [Internet]. Netherlands: FIP; 2023 [cited 2025 Jan 10]. Available from: https://www.fip.org/file/5656

[2] European Commission. Regulation (EU) 2017/746 of the European Parliament and of the Council of 5 April 2017 on in vitro diagnostic medical devices and repealing Directive 98/79/EC and Commission Decision 2010/227/EU [Internet]. Official Journal of The European Union. 2017; L117:176-332 [cited 2025 Feb 8]. Available from: https://eur-lex.europa.eu/legalcontent/EN/TXT/PDF/?uri=CELEX:32017R0746

[3] Medical Device Coordination Group (MDCG). Guidance on Classification Rules for in vitro Diagnostic Medical Devices under Regulation (EU) 2017/746 [Internet]. MDCG. 2020 [cited 2025 Feb 9]. Available from: https://health.ec.europa.eu/system/files/2023-02/md_mdcg_2020_guidance_classification_ivd-md_en.pdf?utm

as their interaction in achieving the strategic objectives of the pharmacy (Maduabuchi et al., 2023). By integrating POCT into pharmacy services, community pharmacists have the potential to reshape healthcare delivery, enhance patient care, and contribute to a more sustainable healthcare system.[4]

1.2 Point-of-Care Testing in Malta and Internationally

POCT is gaining widespread adoption in community pharmacies in Malta, enhancing early detection and management of various health conditions. Recent studies and initiatives highlight this growing trend. A local study conducted by Zammit (2021) evaluated POCT for blood glucose, total cholesterol, triglycerides, blood pressure, and body composition. Results led to actionable health plans, including lifestyle advice and referrals to general practitioners. Notably, significant improvements ($p<0.05$) were observed in systolic blood pressure, total cholesterol, and glucose levels at follow-up intervals. Another study conducted by Busuttil et al., (2023) assessed the feasibility of Vitamin D POCT, where results detected high incidence (71%) of Vitamin D deficiency or insufficiency. Subsequently, participants who had insufficient levels of vitamin D were prescribed supplementation by the physician, to which they were adherent ($p < 0.001$), substantiating the positive outcome of vitamin D supplementation on quality of life.

[4] National Health Service (NHS). Point of care testing in community pharmacies [Internet]. UK: NHS; 2022 [cited 2025 Jan 14]. Available from: https://www.england.nhs.uk/wp-content/uploads/2022/01/B0722-Point-of-Care-Testing-in-Community-Pharmacies-Guide_January-2022.pdf

Internationally, the adoption of POCT in community pharmacies is also on the rise. A 2020 review found that POCT services, particularly for conditions like diabetes and lipid disorders, can lead to improved patient outcomes and more appropriate use of medications (Albasri et al., 2020). Organisations like the National Community Pharmacists Association and National Alliance of State Pharmacy Associations have published guidelines to assist pharmacies in implementing POCT services, emphasizing the benefits of rapid results and enhanced patient care.[5]

Thyroid dysfunction, particularly hypothyroidism is the second most prevalent endocrine disorder, yet a substantial proportion of affected individuals remain undiagnosed or inappropriately managed, leading to suboptimal therapeutic outcomes, increasing the risk of long-term health implications (Mendes et al., 2019; Larsen et al., 2023; Zamwar et al., 2023). Diverse health implications include cardiovascular disease, infertility, and impaired metabolic function (Atmis et al., 2021; Caruana et al., 2021; Liu et al., 2021; Biondi and Cappola., 2022; Das et al., 2022; Eom et al., 2022; Biondi, 2023; Holley et al., 2023; Lin et al., 2023; Mirahmad et al.,2023; Van Uytfanghe et al., 2023; Alomair et al., 2024). These gaps in diagnosis and treatment point towards a need for enhanced public health strategies, improved diagnostic protocols, screening, and optimized monitoring strategies, even in the primary care setting (Tudor et al., 2020; Wouters et al., 2020; Babić et al., 2021; Yadav et al., 2021; Larsen et al., 2023; Taylor et al., 2023; Zamwar et al., 2023).

[5] National Community Pharmacists Association (NCPA) and National Alliance of State Pharmacy Associations (NASPA). A Guide to Implementing Point-of-Care Testing Services in Community Pharmacy [Internet]. USA; 2023 [cited 2025 May 26]. Available from: https://ncpa.org/sites/default/files/2024-02/poct-implementation-guide.pdf

Thyroid-stimulating hormone (TSH) is a reliable early indicator of systemic thyroid status in various populations, often detecting dysfunction before hormone levels become clinically abnormal (Campbell et al., 2020; Yadav et al., 2021; Andersen et al., 2022; Hadgu et al., 2024). Due to TSH's "early warning system", it is used as the initial screening test for thyroid dysfunction, having high accuracy, sensitivity, stability and inverse relationship with thyroid hormone levels (Esfandiari and Papaleontiou, 2017). [6]

Several international studies have evaluated the effectiveness and reliability of TSH POCT for thyroid function. These studies highlight the potential of POCT devices to provide rapid and accurate assessments of thyroid function, facilitating timely diagnosis and management of thyroid disorders. These international studies found strong correlations between various TSH POCT devices and laboratory-based results (Di Cerbo et al., 2021; Dierks et al., 2022; Kahaly et al., 2022; Shurbaji et al., 2023).

1.3 Thyroid-Stimulating Hormone Point-of-Care Testing

POCT devices enable rapid and convenient measurement of TSH levels within minutes, facilitating timely diagnosis and monitoring without the need for advanced laboratory infrastructure (Di Cerbo et al., 2021; Yadav et al., 2021; Fairooz et al., 2024). The affordability and ease of use of TSH POCT make thyroid diagnostic testing feasible in low-resource environments, expanding access to thyroid care globally (Fairooz et al., 2024).[7] POCT TSH assays are particularly valuable for congenital hypothyroidism

[6] America Thyroid Association (ATA). Thyroid Function Tests [Internet]. Virginia: ATA; 2019 [cited 2025 Feb 2]. Available from: https://www.thyroid.org/thyroid-function-tests/

[7] America Thyroid Association (ATA). Point-of-Care Thyroid Diagnostics and Thyroid Disease Management [Internet]. Virginia: ATA; 2018 [cited 2025 Feb 5]. Available from: https://www.thyroid.org/wp-content/uploads/publications/lab-services/ata-poc-thyroid-management.pdf

screening in newborns due to rapid turnaround, minimal sample volume, and reduced haematocrit bias. Modern POCT devices often incorporate computational electronics, artificial intelligence for patient-specific interpretation, and connectivity with laboratory information systems, enhancing diagnostic precision and clinical decision support (Yazdaan et al., 2023). POCT may reduce unnecessary laboratory testing by quickly ruling out hypothyroidism in primary care, potentially streamlining patient management (Matthes et al., 2023). Studies have shown POCT methods to be accurate, sensitive, reproducible, and cost-effective in terms of materials and equipment required, thus made suitable for clinical use (Di Cerbo et al., 2021; Andersen et al., 2022; Chaker et al., 2022; Ezegbogu et al., 2022; Leirs et al., 2022; Arai et al., 2023; Hadgu et al., 2024).

Current thyroid POCT primarily measure only TSH, which is insufficient for comprehensive thyroid dysfunction diagnosis that requires free T3 and free T4 measurements, hence abnormal POCT results require confirmatory laboratory testing (Di Cerbo et al., 2021). Naked-eye interpretation of POCT results may be subjective and prone to error due to ambient light and user variability. Instrument-read tests improve precision but still face challenges such as haematocrit variability affecting accuracy. Interpreting thyroid test results requires consideration of individual patient factors (age, pregnancy, medications, comorbidities) and harmonization of reference ranges across laboratories remains a challenge (Chaker et al., 2022; Shamsadini et al., 2023; Yazdaan et al., 2023; Agahi et al., 2024 ; Cherim et al., 2024; Li et al., 2024 ; Lichtiger et al., 2024; Xu et al., 2024 ; Zúñiga et al., 2024; Mohamed et al., 2025). TSH POCT alone may not be sufficient for acute thyroid emergencies such as myxoedema coma or thyrotoxic crisis, limiting its utility in urgent care settings (Ylli et al., 2019). POCT immunoassays can be affected by interferences such as biotin supplementation, leading to inaccurate results and

requiring careful clinical correlation (De Carvalho and Drobrzenski, 2023). Thyroid diagnosis involves the integration of clinical symptoms, history, imaging, and multiple biomarkers thus, POCT is a tool used to support this complex decision-making process (Yazdaan et al., 2023).

1.4 Laboratory-Based Analysis of Thyroid-Stimulating Hormone

Laboratory-based TSH analysis offers highly sensitive and automated testing, critical for thyroid disease diagnosis and management, but faces challenges from assay interferences, biological variability, and standardization issues which require careful clinical and laboratory consideration (Cowper et al., 2024).

Third-generation immunometric assays particularly chemiluminescent and electrochemiluminescence immunoassays for TSH are widely used due to their high sensitivity (detection limits approximately 0.01 mIU/L) and specificity, enabling detection of thyroid dysfunction including subclinical hypothyroidism and hyperthyroidism (Favresse et al., 2018; Leirs et al., 2022; Arai et al., 2023; De Carvalho and Drobrzenski, 2023; Mallick et al., 2023). Advances over the past decades have transformed TSH testing from manual radio isotopic immunoassays to highly automated, non-isotopic immunometric assays, allowing for rapid, high throughput testing in clinical laboratories (Bikkarolla et al., 2022; Mirica et al., 2022; Arai et al., 2023; Spencer, 2023; Van Uytfanghe et al., 2023). Ongoing efforts to standardize and harmonize TSH assays aim to reduce inter-method variability and facilitate universal reference ranges, improving comparability of results across laboratories (Spencer, 2023; Van Uytfanghe et al., 2023;

Cowper et al., 2024). Central laboratories are equipped with rigorous quality assurance protocols, reducing variability and increasing reliability and regular calibration with international standards supporting consistent results. Laboratories use reference materials for calibration standards established by the World Health Organization and International Federation of Clinical Chemistry and Laboratory Medicine. For quality control measures, regular calibration of immunoassays is performed versus Isotope dilution liquid chromatography-tandem mass spectrometry to ensure diagnostic accuracy and inter-laboratory consistency (Favresse et al., 2018; Jongejan et al., 2020; Taibon et al., 2023); use of internal and external proficiency testing programs is adopted and batch-to-batch variation in assay performance is monitored (Arai et al., 2023). Laboratory- based analysis may combine TSH measurement with free T4 and free T3 assays, as well as thyroid autoantibodies, to provide a thorough assessment of thyroid health and disease monitoring with the ability to distinguishing between primary and secondary hypothyroidism (Soh and Aw, 2019; De Carvalho and Drobrzenski, 2023).

Laboratory tests typically require one to three days for results, potentially delaying clinical decisions in acute cases and are not ideal for bedside decision-making or emergency settings, unlike POCT. Laboratory tests require repeated visits, which may increase patient drop-out rates in follow-ups. Laboratory interferences including heterophile antibodies, human anti-animal antibodies, macro-thyrotropin, and biotin supplementation, can cause falsely high or low TSH levels, requiring careful timing of testing and awareness of patient medication history (Soh and Aw, 2019; Mirica et al., 2022; De Carvalho and Drobrzenski, 2023). TSH reference ranges vary by age, gender, ethnicity, and physiological states such as pregnancy, neonatal period, circadian rhythm, fasting status or illness, requiring population-specific reference values for accurate

interpretation (De Carvalho and Drobrzenski, 2023). In conditions like differentiated thyroid cancer, thyroglobulin antibody interference can affect related assays, complicating interpretation of results and requiring complementary imaging studies (Soh and Aw, 2023). While equilibrium dialysis coupled with mass spectrometry offers highly accurate TSH measurements, these methods are costly and technically demanding, limiting their routine clinical use (De Carvalho and Drobrzenski, 2023; Spencer, 2023). Despite improvements, different assay methods still produce varying numeric TSH values, complicating clinical decision-making and requiring clinicians to be aware of assay-specific reference intervals (Spencer, 2023; Van Uytfanghe et al., 2023).

Both laboratory-based and POCT methods for TSH analysis have proven to be reliable and accurate, with strong correlations observed between the two approaches (Fairooz et al., 2024). Laboratory-based assays offer high precision and are considered the gold standard, which are especially valuable in specialized settings requiring comprehensive thyroid function assessment (Cowper et al., 2024). POCT provides significant advantages in primary care and community pharmacy settings by delivering rapid results within minutes, reducing turnaround time, and improving patient compliance and convenience (Arai et al., 2023; Hadgu et al., 2024). This immediacy supports timely clinical decision-making, particularly important for screening and urgent cases (Yazdaan et al., 2023). Moreover, POCT devices are cost-effective, user-friendly, and suitable for decentralized healthcare environments where access to centralized laboratories may be limited (Matthes et al., 2023). POCT for TSH analysis is especially essential in primary care and community pharmacies to enhance accessibility and efficiency in thyroid disorder screening and management, complementing traditional laboratory testing (Di Cerbo et al., 2021; Yadav et al., 2021; Fairooz et al., 2024).

1.5 Thyroid-Stimulating Hormone Testing and Hypothyroidism Management

The TSH reference range remains debated among thyroid specialists. Determining appropriate TSH reference ranges is crucial for accurate diagnosis and treatment (Gunapalasingham et al., 2019; Oron et al., 2020; Taylor et al., 2023). Commonly cited ranges include: 0.5–4.5 μIU/mL (American Association of Clinical Endocrinology); 0.4-4 μIU/mL (American Thyroid Association, European Thyroid Association and NICE guidelines); and 0.45–2.5 μIU/mL (National Academy of Clinical Biochemistry) (Mele et al., 2022).[8- 10] Reference ranges may differ slightly depending on assay methods and local practices. For instance, a private laboratory in Malta uses a reference range of 0.4–4.0 μIU/mL, the reference range at the laboratory of Mater Dei Hospital is 0.3 - 3 μIU/mL and the University of Illinois Chicago Medical Centre laboratory uses a reference range of 0.35 – 5 μIU/mL. Age-adjusted ranges are not routinely reported, even though age, ethnicity, genetics and physiological conditions can affect TSH levels, and may require individualized reference ranges and management strategies (Oron et al., 2020).

Lowering the upper TSH limit to 2.5–3.0 μIU/mL would increase the number of people classified as hypothyroid by 20–26%, potentially leading to unnecessary treatment and associated healthcare costs (Feller et al., 2018; Xu et al., 2023). Elderly persons are at particular risk of subclinical hypothyroidism misclassification if age-related shifts are not considered. Interpretation of TSH levels should account for individual factors to

[8] American Thyroid Association (ATA). Thyroid Function Tests [Internet]. ATA. 2019 [cited 2025 Feb 11]. Available from: https://www.thyroid.org/wp-content/uploads/patients/brochures/FunctionTests_brochure.pdf

[9] European Thyroid Journal (ETJ). 2013 ETA Guideline: Management of Subclinical Hypothyroidism [Internet]. GER; 2013 [cited 2025 May 31]. Available from: https://www.eurothyroid.com/files/download/ETA-Guideline-Management-of-Subclinical-Hypothyroidism.pdf?utm

[10] National Institute for Health and Care Excellence (NICE). Thyroid disease: assessment and management [Internet]. UK; 2023 [cited 2025 Feb 10]. Available from: https://www.nice.org.uk/guidance/ng145/chapter/recommendations#:~:text=For%20adults%2C%20children%20and%20young%20people%20with%20TSH%20in%20the,2).

determine whether treatment is necessary (Chaker et al., 2022; Holley et al., 2023; Xu et al., 2023).[11]

TSH testing is recommended in cases of unexplained anxiety, depression, autoimmune disease, new-onset atrial fibrillation, abnormal growth or behavioural changes (Kamusheva et al., 2020; Mohammed et al., 2021; Kuś et al., 2022; Nuguru et al., 2022; Grigoriadis et al., 2023). The American Association of Clinical Endocrinologists and the American Thyroid Association recommends screening in all women starting at age 35 years and every five years thereafter, and routine TSH testing primarily in older patients, particularly women. Thyroid function should not be tested during acute non-thyroidal illness and in patients with only one non-specific symptom. According to the UK NICE guidelines, if primary thyroid dysfunction is suspected, then TSH should be measured depending on age, disease severity, and treatment response.[10]

Levothyroxine is the first-line treatment for primary hypothyroidism.[10] The UK NICE guidelines offer evidence-based guidelines for levothyroxine dosing, monitoring strategies, and considerations for special populations.[10] Dosing and titration depend on age, cardiovascular status, and severity of hypothyroidism. Lower doses of levothyroxine are often sufficient for older adults, while children require higher doses (Roberts et al., 2018; Thayakaran et al., 2019; Campbell et al., 2020; Wouters et al., 2023). The timing of levothyroxine administration is important and should be taken in the morning on an

[10] National Institute for Health and Care Excellence (NICE). Thyroid disease: assessment and management [Internet]. UK; 2023 [cited 2025 Feb 10]. Available from: https://www.nice.org.uk/guidance/ng145/chapter/recommendations#:~:text=For%20adults%2C%20children%20and%20young%20people%20with%20TSH%20in%20the,2).

[11] American Thyroid Association (ATA). Standardization and Harmonization [Internet]. ATA. 2019 [cited 2025 Jan 20]. Available from: https://www.thyroid.org/wp-content/uploads/publications/lab-services/ata-harmonization-standardization.pdf

empty stomach with a full glass of water, ideally 30–60 minutes before breakfast to maximize gastrointestinal absorption, maintaining a more stable serum TSH. Levothyroxine should not be co-administered with medications or supplements known to interfere with its absorption such as proton pump inhibitors, calcium or iron. It is recommended to maintain an administration interval of 4 hours (McAninch et al., 2018).

The goal of treatment is to maintain serum TSH within the reference range and alleviate symptoms while avoiding overtreatment (McAninch et al., 2018; Gunapalasingham et al., 2019). TSH normalization can take up to six months in severe or long-standing cases (Barhanovic et al., 2019). Regular monitoring and follow-up are essential, with dose adjustments as needed (Dayan and Panicker, 2018).

1.6 The Local Scenario

In Malta, hypothyroidism is on the rise. A study conducted by Caruana et al., (2021) investigated the frequency of thyroid dysfunction in patients presenting with acute coronary syndrome and assessed the impact of thyroid dysfunction on patient outcomes. The researchers found that in Malta, thyroid dysfunction particularly subclinical hypothyroidism, is common among patients presenting with acute coronary syndrome. A retrospective observational analysis of a Maltese cohort conducted by Vella et al, (2022) investigated the prevalence and impact of thyroid disorders on pregnancy over a ten-year period (2006-2016). An ecological study conducted by Cardona et al., (2024) analysed hypothyroidism in the Maltese Islands focusing on exposure to perchlorate, a by-product of fireworks. Perchlorate competitively inhibits iodine transport at the sodium-iodide symporter (NIS), suppressing thyroid hormone synthesis and prompting a compensatory

rise TSH secretion due to disrupted homeostatic feedback (Cardona et al., 2024). Cardona et al., (2024) analysed trends in TSH levels greater than 3.0 µIU/mL, which may be indicative of hypothyroidism, between 2009-2017 (Figure 1.1). The study highlighted that the incidence rate of hypothyroidism per year was greater in females than males with 2.33% and 1.34% per year respectively. As observed by Vella et al., (2022) and Cardona et al., (2024) the average incidence rate of hypothyroidism was observed to increase with age, and in patients having a higher body mass index (BMI).

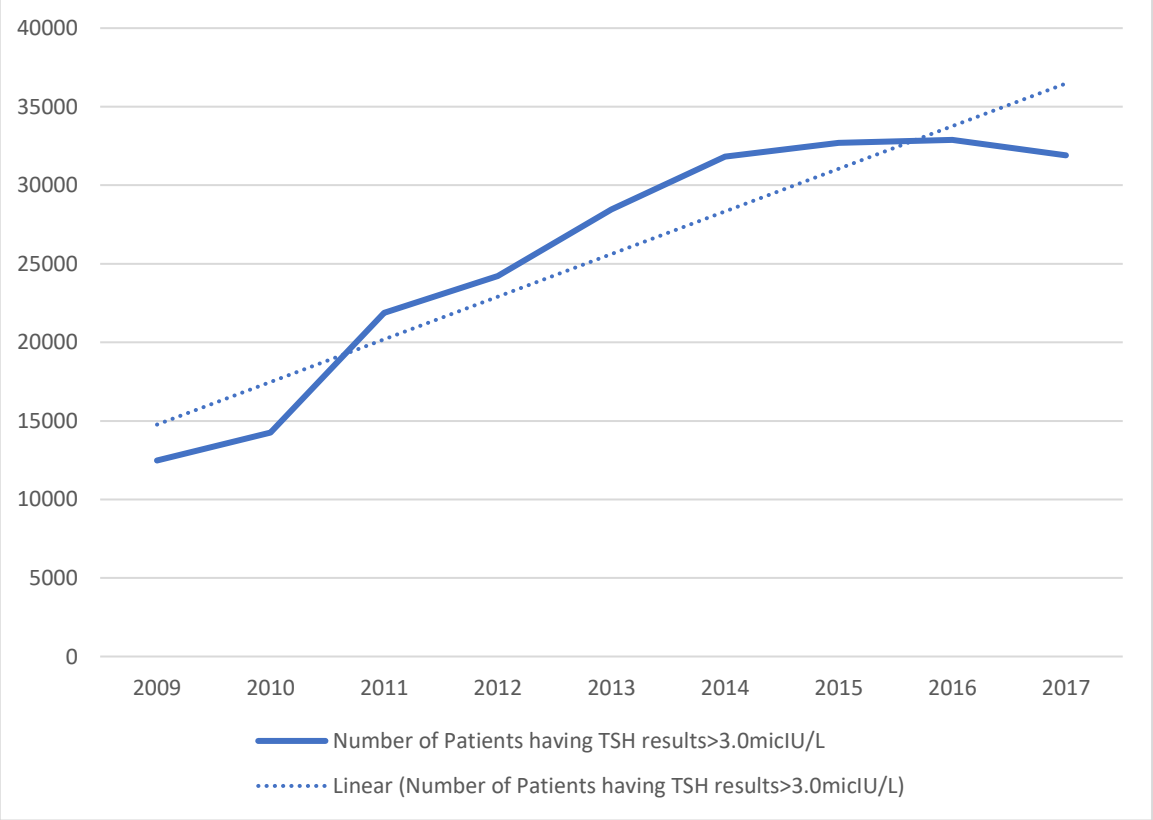


Figure 1.1: Number of patients having TSH results >3.0 µIU/mL

Adapted from: Cardona T, Brincat I, Calleja N, Debono R. Hypothyroidism and perchlorate: an ecological study of hypothyroidism in the Maltese Islands. Malta Medical Journal. 2024;36(1): 1-9.

1.7 Aims and Objectives

The research question was: What are the opportunities for pharmacist-led thyroid POCT in primary care?

The aim was to develop a framework for pharmacist-led thyroid POCT and assess feasibility of implementation in a community pharmacy setting.

The objectives were to:

(i) Appraise available thyroid POCT devices and select device for use in this study

(ii) Validate the identified thyroid POCT device versus laboratory-based results

(iii) Develop and validate a pharmacist-led thyroid POCT framework

(iv) Assess the feasibility of the developed framework in a community pharmacy

Chapter 2- Methodology

2.1 Study Design

The study followed a structured, multi-phase approach illustrated in Figure 2.1 including appraisal of thyroid POCT devices, device selection process, validation of the chosen POCT device versus laboratory-based results, development of a pharmacist-led thyroid POCT framework and validation by an expert panel, and feasibility assessment of the framework in a community pharmacy setting.

Ethics approval was granted from the University of Malta Faculty of Medicine and Surgery Research Ethics Committee (Ref No: MED-2024-00385) (Appendix 1).

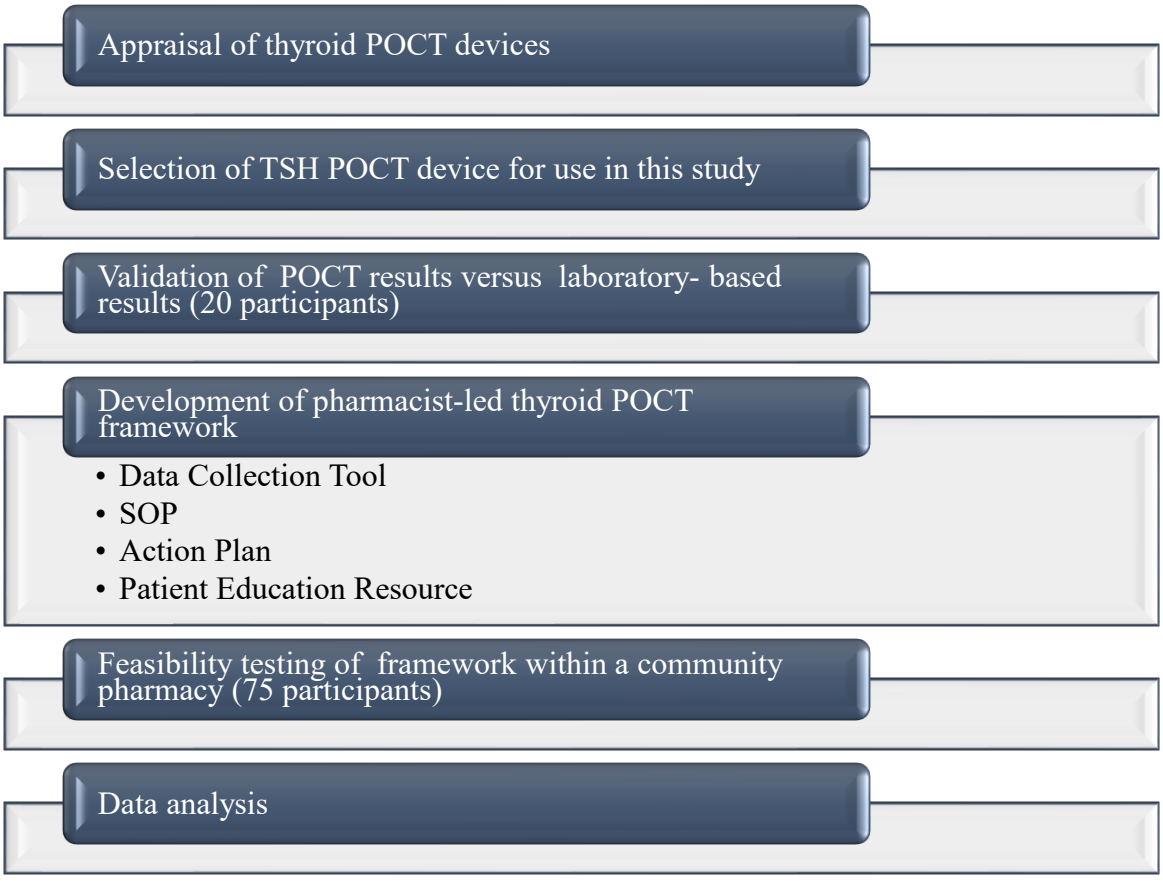
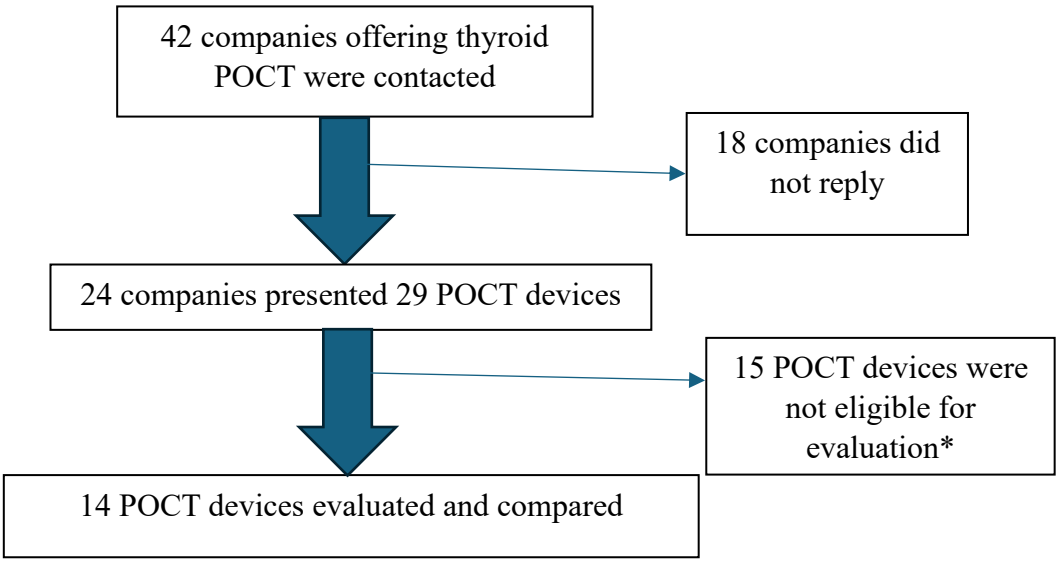


Figure 2.1: Flow diagram of study design

2.2 Appraisal and Selection of Point-of-Care Testing Devices

The initial phase of the study comprised a review of thyroid POCT devices conducted through an online search. Subsequently, all identified companies were contacted via email or direct messaging through their official websites (Figure 2.2).

The devices were appraised based on technique, result interpretation, TSH testing range, sensitivity, specimen, volume, testing time, cost and local availability. Based on these criteria, the Acro Biotech Inc TSH rapid test cassette (Whole Blood/Serum/Plasma) was selected for use in this study.



* No longer manufactured (n=6), required whole blood, serum, or plasma and not fingerstick capillary blood which is not practical in a community pharmacy setting (n=4), could not be shipped to Malta (n=2), only authorised for use by USA-based companies (n=2), not CE marked (n=1).

Figure 2.2: Appraisal process

2.3 Validation of Thyroid-Stimulating Hormone Point-of-Care Testing Device

The selected POCT device was validated versus laboratory-based results obtained from 20 participants recruited by convenience sampling. Patients 18 years or older attending St. Andrew's Clinics for routine follow-up testing of TSH levels were invited and recruited to the study by an intermediary. A Participant Information letter and Consent Form in English or Maltese were provided to the participants.

POCT was carried out in a private consultation room at St. Andrew's Clinics. The researcher carried out the POCT and interpreted the results based on the developed standard operating procedure (SOP). The testing procedure was completed in 10 minutes. Pseudoanonymised laboratory TSH values, obtained from the intermediary, were compared with POCT results to assess concordance between testing methods.

2.4 Development of Pharmacist-Led Thyroid Point-of-Care Testing Framework

A structured pharmacist-led TSH POCT framework was developed based on literature scoping and practice guidelines (Garber et al., 2012; Alsifri et al., 2022; Parakkal et al., 2023). The framework consisted of a Data Collection Tool, SOP, Action Plan and a Patient Education Resource (Appendix 2).

The Data Collection Tool was designed for use by the researcher during a structured interview conducted in English or Maltese with the participant. The tool includes 16 questions, three of which are sub-divided into two or more questions. The Data Collection Tool was structured into five domains relevant to thyroid health and the potential for

hypothyroidism. The Data Collection Tool allows for a non-invasive assessment of risk factors, health status, medication history, adherence and management, and knowledge on thyroid testing.

Modifiable and Non-Modifiable Risk Factors: This section comprised four questions examining risk factors of developing hypothyroidism. The first question assessed participant's age. Only participants aged 18 or older were eligible to participate in the study, in accordance with the manufacturer's specifications for the TSH POCT device, which is validated for use exclusively in adult populations. The second question focused on gender; this was included due to its established association with hypothyroidism risk (Khassawneh et al., 2020; Fu et al., 2021; Burlacu et al., 2022; Vella et al., 2022; Cardona et al., 2024). The remaining two questions in this section addressed modifiable lifestyle factors specifically smoking status and BMI. Both smoking and BMI have been implicated as potential contributors to altered thyroid function (De Sanctis et al., 2019; Gruppen et al., 22020; Habib et al., 2020; Kadkhodazadeh et al., 2020; Fu et al., 2021; Lossow et al., 2021; Zhang et al., 2022; Abiri et al., 2023; Duntas, 2023; Galanty et al., 2024; Shulhai et al., 2024).

Health Status: This section is comprised of 4 questions evaluating clinical signs and symptoms of hypothyroidism (Chaker et al., 2022; Jansen et al., 2023), comorbidities, history of head/neck procedures, and family history of thyroid disorders (Razvi et al., 2018; Aleksi et al., 2022; Ashok et al., 2022; Liu et al., 2022; Huang et al., 2022; Klubo-Gwiezdzinska and Wartofsky, 2022; Pooja and Varsha, 2022; Athanassiou et al., 2023;

Iqbal et al., 2023; Line et al., 2023; Vemula et al., 2023; Agahi at al., 2024; Xu et al., 2024).

Medication History, adherence and Management: This section captures use of levothyroxine or other medications known to affect TSH levels (Uyar et al., 2016; Zhang et al., 2016; Dineen et al., 2017; Benvenga et al., 2018; Biond et al., 2019; Medić at al., 2022). For individuals already prescribed levothyroxine, eight additional questions to assess treatment adherence and patient knowledge regarding their medication regimen were established (Kumar et al., 2019; Wiesner et al., 2021).[12]

Knowledge on Thyroid Testing: The fourth section consists of five questions assessing awareness of screening frequency and the perceived impact of thyroid health on general wellbeing. [13] - [15]

In the final section the researcher conducted the TSH POCT following the SOP and recorded the results in the Data Collection Tool.

The Action Plan was developed to standardise pharmacist's clinical action and provide personalised recommendations based on risk factors, clinical symptoms, comorbidities, and POCT results. It facilitates consistent, evidence-based patient education and care

[12] National Health Service (NHS). Levothyroxine [Internet]. UK: NHS; 2024 [cited 2025 Feb 12]. Available from: https://www.nhs.uk/medicines/levothyroxine/

[13] British Thyroid Foundation (BTF) Your Guide To Thyroid Function Tests [Internet]. UK: BTF; 2021 [cited 2025 Feb 12]. Available from: https://www.btf-thyroid.org/Handlers/Download.ashx?IDMF=c3ea2491-6ade-418a-9047-0ee5216d9ce4

[14] National Health Service (NHS) Thyroid Function Testing Strategy [Internet]. UK: NHS; 2016 [cited 2025 Feb 10]. Available from: https://www.nbt.nhs.uk/sites/default/files/TFT%20strategy%20-%20no%20appendix.pdf

[15] National Health Service (NHS). Thyroid Function Tests (TSH, FT4, FT3) [Internet]. UK: NHS; 2022[cited 2025 Feb 2]. Available from: https://www.gloshospitals.nhs.uk/our-services/services-we-offer/pathology/tests-and-investigations/thyroid-function-tests-tsh-ft4-ft3/

aligned with clinical guidelines. Advice and physician referrals were tailored to individual profiles, supporting a personalised medicine approach. This element of the framework supports the broader application of personalised medicine, wherein interventions are customised to the specific needs and characteristics of each patient.

The Action Plan was developed to support and educate participants that (i) are overweight (ii) are current smokers, (iii) have clinical symptoms suggestive of hypothyroidism, (iv) have specific co-morbidities, (v) have a history of procedures involving the head/neck region, (vi) have first-degree relatives diagnosed with thyroid dysfunction, (vii) are taking levothyroxine incorrectly, (viii) are non-compliant with thyroid testing, and (ix) obtain a positive result indicative of hypothyroidism with the TSH POCT device.

All participants received a result sheet indicating date and corresponding TSH result. Patients taking levothyroxine and who expressed a need for further guidance or were identified as requiring additional support on treatment were given the bilingual Patient Education Resource.

The SOP for TSH POCT was developed using the manufacturer's package insert for the AcroBiotech Inc. TSH rapid test cassette (Whole Blood/Serum/Plasma). To ensure proper regulatory and clinical alignment, the local distributor in Malta was consulted to verify the device's appropriate usage within the study context. The SOP was developed in accordance with the official template provided by the Department of Pharmacy, Faculty of Medicine and Surgery, University of Malta.

The SOP consisting of ten pages, was specifically developed for use in this study. It provides a detailed, step-by-step guide for conducting and standardising the TSH POCT encompassing procedures for sample collection, preparation, performing the test and interpretation of result. The SOP includes clearly defined responsibilities, health and safety guidelines, and protocols for quality control and maintenance. Flowcharts illustrating the procedures for sample handling and testing are incorporated. The SOP is tailored to the Acro Biotech Inc. TSH rapid test cassette (Whole Blood/Serum/Plasma). For applications in different healthcare environments or studies using alternative devices, a device-specific SOP would need to be developed accordingly.

2.5 Validation of Framework

The Data Collection Tool and the Patient Education Resource underwent validation by a multidisciplinary expert panel, which included a specialist in family medicine, an endocrinology consultant, an ENT and thyroid surgeon, a clinical pharmacist, a community pharmacist and two laypersons with no professional healthcare background. The same panel, excluding the two non-healthcare professionals, also validated the Action Plan. The panel was requested to evaluate the framework in terms of content relevance, comprehensibility, readability, and overall presentation. Additionally, the expert panel were encouraged to provide further comments or suggestions for improvement.

2.6 Feasibility of Implementing the Framework in Community Pharmacies

The feasibility of implementing the developed TSH POCT framework within community pharmacy was evaluated based on applicability to patient management and collaborative practice development. Feasibility testing was conducted in one community pharmacy following agreement with the managing pharmacist (Intermediary). The chosen community pharmacy was visited to ensure the availability of adequate facilities to perform the study. The selected pharmacy was found to be readily accessible to the general public, including individuals with mobility impairments, and housed a well-illuminated, private clinical space equipped with an appropriate workstation for conducting patient interviews and POCT procedures.

Seventy-five participants were invited and recruited using convenience sampling by the managing pharmacist in accordance with pre-established inclusion and exclusion criteria. Eligible participants included adults aged 18 years or older, any gender, were prescribed medications known to affect TSH levels (amiodarone, anti-diabetic medications, anti-epileptic drugs, isotretinoin, lithium, oestrogen and dopamine antagonists) or currently on treatment with levothyroxine. Individuals were excluded from participation if they had undergone thyroid function testing within the preceding six months, were experiencing an acute illness, or were pregnant or breastfeeding at the time of recruitment. Thirty-minute appointments were scheduled by the managing pharmacist based on availability identified by the researcher. The researcher used the Data Collection Tool to interview participants and conducted two interventions: (i) checking BMI and (ii) TSH POCT based on the SOP. Subsequently, the Action Plan was followed to provide a personalised

intervention. The pre-defined Action Plan provided all participants with a standardised result sheet outlining the POCT outcomes. If applicable, the Patient Education Resource was provided and explained to the participant and a referral note was used to relay positive test findings of 2 or more symptoms related to hypothyroidism, to the participant's physician. The referral note included a documented rationale for referral and clinical recommendations.

2.7 Data Analysis

All collected data were recorded in a Microsoft Excel® spreadsheet and subsequently analysed using IBM SPSS® software. Concordance between the POCT results and the reference laboratory findings was assessed using Cohen's Kappa coefficient. Associations between age, BMI, comorbidities, gender, smoking, medication intake, correct levothyroxine use, testing frequency, POCT results, and presentation of symptoms were evaluated through the Chi-square (χ^2) test. Associations with a p-value less than 0.05 were considered statistically significant.

Chapter 3 - Results

3.1 Comparative Analysis of Thyroid Point-of-Care Testing Devices

The 14 POCT devices appraised employ immunoassay-based technology. Tables 3.1 to 3.4 represent a comparative analysis of these devices. Table 3.1 details result interpretation, analytical technique and local availability. Only two of the devices identified are currently available locally.

Table 3.1: POCT devices- result interpretation, technique, and local availability

Device Name	Result Interpretation	Technique	Available Locally
Acro Biotech INC. TSH rapid test cassette	Qualitative	Chromatographic Immunoassay	Yes
PreventID® TSH		Sandwich Immunoassay	
SCREEN TSH		Chromatographic Immunoassay	No
TSH Fast test device			
Rapid™ Response TSH test cassette			
TSH rapid test cassette			
One Step® TSH rapid test cassette			
CLIAwaived™ INC rapid TSH cassette			
DCR1000	Quantitative	Fluorescence Immunoassay	
DCR2000			
Getein1160 analyser			
Palm F analyser			
TSH Test device			
SCREEN IFA TEST TSH			

As summarized in Table 3.2, the test devices exhibit diverse TSH testing ranges from 0.1 to 100 μIU/mL, with sensitivity ranging from 0.1 to 5μIU/mL.

Table 3.2: POCT devices- TSH test range and sensitivity

Device Name	TSH Test Range	Sensitivity
Acro Biotech INC. TSH rapid test cassette	≥ 5 μ IU/ml	5 μ IU/ml: Relative Sensitivity: 98.1%
PreventID® TSH		5 μ IU/ml: Relative Sensitivity: 97.3%
SCREEN TSH		5 μ IU/ml: Relative Sensitivity: 98.1%
TSH Fast test device		
Rapid™ Response TSH test cassette		5 μ IU/ml: Relative Sensitivity: 81.25%
TSH rapid test cassette		5 μ IU/ml: Relative Sensitivity: 98.2%
One Step® TSH rapid test cassette		5 μ IU/ml
CLIAwaived™ INC rapid TSH cassette		
DCR1000	0.1 - 50.00 μIU/mL	0.1 μIU/mL
DCR2000	0.1 - 100μIU/mL	
Getein1160 analyser	0.1 - 50.00 μIU/mL	0.27 μIU/mL – 4.20 μIU/mL
Palm F analyser	0.3- 100μIU/mL	0.3 μIU/mL
TSH Test device	0.1-100 μIU/mL.	0.1 μIU/mL
SCREEN IFA TEST TSH		

Table 3.3. specifies that sample requirements differ across devices, utilizing serum, plasma, or whole blood in volumes ranging from 40µL to 100µL. Time for result ranges from 10 to 15 minutes.

Table 3.3: POCT devices- specimen type, volume, and test time

Device Name	Specimen and Volume	Testing Time (minutes)
Acro Biotech INC. TSH rapid test cassette	50µL fingerstick whole blood or 2 hanging drops of whole blood	10
PreventID® TSH	2 drops of serum or plasma or 3 drops of whole blood	
SCREEN TSH	75 µL of capillary blood	10
TSH Fast test device	50 µL of serum, plasma or whole blood	10
Rapid™ Response TSH test cassette	2 drops of whole blood	
TSH rapid test cassette	50µL fingerstick whole blood	
One Step® TSH rapid test cassette	75µL fingerstick whole blood	10
CLIAwaived™ INC rapid TSH cassette	1 drop of whole blood	11.5
DCR1000	100 µL of serum or plasma	15
DCR2000	75 µL of serum or plasma	
Getein1160 analyser	100 µL of serum or plasma	
Palm F analyser	60 µL of serum, plasma or whole blood	
TSH Test device	40 µL of serum, plasma or whole blood	
SCREEN IFA TEST TSH	75 µL of serum or plasma	15

Devices requiring an immunoassay analyser are inherently more complex and costly to operate (Table 3.4). All POCT consumables can be stored at room temperature until their expiration date.

Table 3.4: POCT devices- type and pricing

Device Name	Type	Price/test
Acro Biotech INC. TSH rapid test cassette	Cassette	€2.42
PreventID® TSH	Cassette combined with blood collection tubes with heparin	€7.30
SCREEN TSH	Cassette	€1.11
TSH Fast test device		€1.45
Rapid™ Response TSH test cassette		-
TSH rapid test cassette		€8.50
One Step® TSH rapid test cassette		€7.18
CLIAwaived™ INC Rapid TSH cassette		€5.54
DCR1000	Test cards combined with DCR1000 Immunofluorescence Quantitative Analyzer	€1.75: DCR1000 Immunofluorescence Analyser - €1,019.13
DCR2000	Test cards combined with DCR2000 Immunofluorescence Quantitative Analyzer	€1: DCR2000 Immunofluorescence Analyser – N/A
Getein1160 analyser	Test Cards combined with Getein 1160 Immunofluorescence Quantitative Analyzer	€1.67: Getein1160 Analyzer- €926.35
Palm F analyser	Test Cards combined with Palm F analyser	€1.11: Palm F analyser- €111.20
TSH Test device	Cassette combined with Macro and Micro-Test Fluorescence Immunoassay Analyzer	-
SCREEN IFA TEST TSH	Cassette combined with SCREEN® Fluorescence Immunoassay Analyzer	€1.30: SCREEN IFA Analyzer- €700

The Acro Biotech Inc. TSH rapid chromatographic immunoassay test cassette was selected for use in the study based on the criteria outlined in Table 3.5.

Table 3.5: Advantages of Acro Biotech Inc. TSH rapid test cassette

Accessibility	Local Distributor
Cost	Least costly from devices available locally
Ease of Use	Test does not require use of additional consumables including blood collection tubes with heparin or immunoassay analysers and can be used in ambulatory care
Conformity	EC Declaration of Conformity attached in Appendix 3
Validity	Device has been compared to a commercially available TSH Enzyme-Linked Immunosorbent Assay devices showing a sensitivity of 98.1%, specificity 98.2% and accuracy 98.2% relative to Enzyme-Linked Immunosorbent Assay (N=220) [16]

3.2 Validation of Selected Point-of-Care Testing Device

The POCT device was validated with 20 participants versus laboratory-based results, demonstrating a 95% concordance rate between methods (Table 3.6).

Table 3.6: POCT versus laboratory-based results (N=20)

POCT Result	Laboratory-based result	Number of Patients
Negative	Negative	17
Positive	Positive	2
Positive	Negative	1

Cohen's Kappa: 0.773 ($p<0.001$)

[16] Acro Biotech Inc. TSH Rapid Test Cassette (Whole Blood/Serum/Plasma) Package Insert. Germany: Acro Biotech Inc; 2023.

3.3 Expert Panel Feedback on Framework

All documents presented to the validation panel were very well received and commented on the novelty of the pharmacist-led thyroid POCT service presented.

One of the recommendations from the expert panel regarding the development of the Data Collection Tool was the inclusion of a question prompting participants currently prescribed levothyroxine to indicate the dosage. This addition served to account for the direct relationship between levothyroxine dosage vs. TSH levels and medication adherence.

The expert panel noted that the Action Plan is content-rich and comprehensive, well-structured and follows a logical and coherent clinical pathway. The inclusion of a flowchart at the beginning of the document was particularly commended, as it enhanced clarity and provided a clear, stepwise approach to the decision-making process. One panel member suggested that the Action Plan could be further improved by including an explanatory section, detailing the clinical implications of TSH POCT results, an insight that would assist pharmacists in conducting clinical decision making.

The expert panel provided positive feedback on the Patient Education Resource, describing it as clearly articulated, well-structured, and highly informative. The resource was praised for effectively conveying essential information in a manner that is comprehensive for patients.

3.4 Feasibility of Framework

The pharmacist-led TSH POCT framework was implemented and evaluated for feasibility based on applicability to patient management and collaborative practice development. The devised Data Collection Tool and Action Plan were helpful in identifying and acting upon patient needs. The identified needs included achieving a normal BMI, smoking cessation, reducing symptoms suggestive of hypothyroidism, increasing knowledge on levothyroxine management and increasing awareness on thyroid testing. The Data Collection Tool and the performed TSH POCT identified participants requiring patient education and physician referral due to gaps in hypothyroidism patient care.

3.5 Participant Characteristics

A total of 75 participants were recruited for feasibility testing. Participant characteristics are described in Table 3.7.

Table 3.7: Participant characteristics (N=75)

Participant Characteristics		**Number of Participants**	
Gender	Female	57	
	Male	18	
Age (Years)	18-24	10	
	25-34	4	
	35-44	8	
	45-54	24	
	55-64	11	
	65-74	11	
	>75	7	
Risk Factors BMI Smoking	Overweight	25	
	Obese Class I	11	
	Obese Class II	6	
	Obese Class II	6	
	Current smokers	Occasional	2
		1-10	7
		11-20	2
Procedure affecting thyroid gland	Radioactive Iodine Therapy	3	All take levothyroxine
	Thyroidectomy	2	
	Laryngeal/ Pharyngeal surgery	1	
	Radiation (Head and neck)	1	
First-degree relatives with Thyroid Disease	No	45	23 take levothyroxine
	Yes	30	22 take levothyroxine

Presence of signs and symptoms suggestive of hypothyroidism and comorbid conditions relevant to hypothyroidism are described in Table 3.8. Thirty-one participants reported 2 or more signs or symptoms, and 51 reported at least one chronic condition.

Table 3.8: Participant symptoms and chronic conditions (N=75)

Participant Characteristics		**Number of Participants**
Symptoms	Fatigue	21
	Brain Fog	20
	Dry Skin	16
	Constipation	12
	Stiff muscles	12
	Unintentional weight gain	12
	Low mood	11
	Migraine	9
	Brittle hair	8
	Heavy menstruation	7
	Menstrual irregularities	3
Chronic conditions	Hypercholesterolemia	21
	Hypertension	19
	Osteoarthritis	16
	Polycystic Ovarian syndrome	13
	Type 1 Diabetes	8
	Gout	6
	Hashimoto Thyroiditis	5
	Atrial Fibrillation	4
	Fibromyalgia	4
	Type 2 diabetes	2
	Celiac Disease	1
	Rheumatoid Arthritis	1
	Thalassemia Major	1

Medication intake and thyroid testing are recorded in Table 3.9 and Table 3.10 respectively.

Table 3.9: Medication history (N=75)

Medication Intake		**Number of Participants**	**Medication which may alter thyroid function**	**Number of Participants**
Levothyroxine	Yes	45*	-	-
	No	30	Oral Contraceptive pill	14
			Insulin	4
			Olanzapine	3
			Quetiapine	3
			Sitagliptin	3
			Sodium Valproate	2
			Amiodarone	1
			Hormone Replacement Therapy	1
			Isotretinoin	1
			Lithium	1
			Phenytoin	1

*Recorded levothyroxine doses were between 25mcg and 225mcg

Table 3.10: Thyroid testing (N=75)

Medication Intake	**Thyroid function testing**	**Number of Participants**
Levothyroxine (n=45)	7-12 months ago	35
	2-4 years ago	7
	5years ago	2
	>5 years ago	1
	Never checked	-
Medications which may affect thyroid function (n=30)	7-12 months ago	16
	2-4 years ago	8
	5years ago	-
	>5 years ago	3
	Never checked	3

From the 72 participants who conducted thyroid testing, 67 participants underwent routine testing based on physician recommendation, with 41 of these individuals currently prescribed levothyroxine. Four participants pursued testing due to the presence of symptoms, of whom 3 are currently prescribed levothyroxine therapy. One participant was prompted by a friend to consult a physician regarding thyroid hormone levels and is on levothyroxine. A participant suggested that conducting thyroid tests in a pharmacy setting would enhance accessibility.

Participants' perceptions regarding the necessity of maintaining appropriate thyroid hormone levels for overall health was explored. Two participants disagreed with the assertion that thyroid function is essential for well-being. These individuals were aged between 18–24 years and 35–44 years, respectively.

Ten participants suspected that they might have hypothyroidism, comprising one male and nine females. These individuals were categorized as obese (n=6), overweight (n=3), or within a normal weight range (n=1). Symptoms varied widely, no symptoms (n=2), three symptoms (n=1), four symptoms (n=4), six symptoms (n=1), seven symptoms (n=1), or nine symptoms (n=1). These participants had either a single comorbidity (n=8), or none (n=2). None had undergone head/neck procedures, and six had a first-degree relative diagnosed with thyroid dysfunction. These participants had an established diagnosis of hypothyroidism and were already prescribed levothyroxine (n=8) or where on medication/s which may affect thyroid function (n=2). They had tested their thyroid function within the past 7–12 months (n=4) or two to four years ago (n=4).

The 45 participants taking levothyroxine were assessed on levothyroxine management and adherence and results are recorded in Table 3.11 and Table 3.12.

Table 3.11: Participant knowledge on levothyroxine adherence (n=45)

Participant Knowledge on Levothyroxine		**Reason**		**Number of Participants**
Daily Intake	Yes	-		33
	No	Forgetfulness	Daily	7
			Weekend	2
		Confusion in alternate dosing		1
		Medication shortages		1
		Lack of understanding of treatment importance		1
Consistency in intake timing	Yes	-		41
	No	Forgetfulness		4
Exceeding prescribed dose	Yes	Confusion in alternate dosing		3
		Compensatory double dosing		1
		Self-adjustment		1
		Medication unavailability		1
		No explanation		2
	No	-		37

Table 3.12: Knowledge on levothyroxine administration(n=45)

Participant Knowledge on Levothyroxine			**Number of Participants**
Administration practices by time of day	Morning		43
	Afternoon		3
	Evening		6
Food consumption practices	30 minutes after		35
	Immediately after		3
	10-20 minutes after		1
	Before		6
Intake methods	Whole with water		44
	Whole with tea/ coffee		11
	Chewed or crushed		2
Medication/s and supplement/s affecting levothyroxine absorption: intake practices	No intake *		19
	Intake	Separated by 4 hours or more	8
		Separated by 1-3 hours	9
		Take together	6
		Irregular intake	3

*A patient was prescribed calcium for osteoporosis but reported fear of interaction thus stopped taking calcium.

A total of 36 participants lacked adequate knowledge and they were given the Patient Education Resource. Nine participants were found to be taking levothyroxine correctly and were asked whether they would still like to receive more information on levothyroxine by the pharmacist. Eight participants expressed a desire for more information on hypothyroidism and medication management, prompting the provision of

the Patient Education Resource. They all provided reasons for seeking additional guidance and included concerns about online misinformation (n=3), dietary requirements and/or physical activity related to hypothyroidism (n=2), holistic thyroid disease management (n=1), brand interchangeability (n=1) and medication and dietary interactions (n=1). One participant stated that no further information is necessary as medication have been taken for a long time and personally conducted plenty of research. A total of 44 participants received the Patient Education Resource.

3.6 Point-of-Care Testing Results and Action Taken

A total of 23 participants had a positive TSH result ≥ 5 μIU/ml indicating hypothyroidism; of whom 15 were being treated for hypothyroidism with levothyroxine, indicating levothyroxine non-adherence (n=12), or dosage insufficiency (n=3). Eight participants were taking medication/s which may affect TSH levels and were never screened for hypothyroidism i.e. newly diagnosed cases.

Advice was provided regarding BMI and smoking, both recognised risk factors for hypothyroidism (n = 59), and the importance of annual thyroid function testing (TFTs) in individuals who had not undergone assessment within the preceding year (n = 24). A total of 36 participants were referred to their physician and 44 participants were provided with the Patient Education Resource (Figure 3.1).

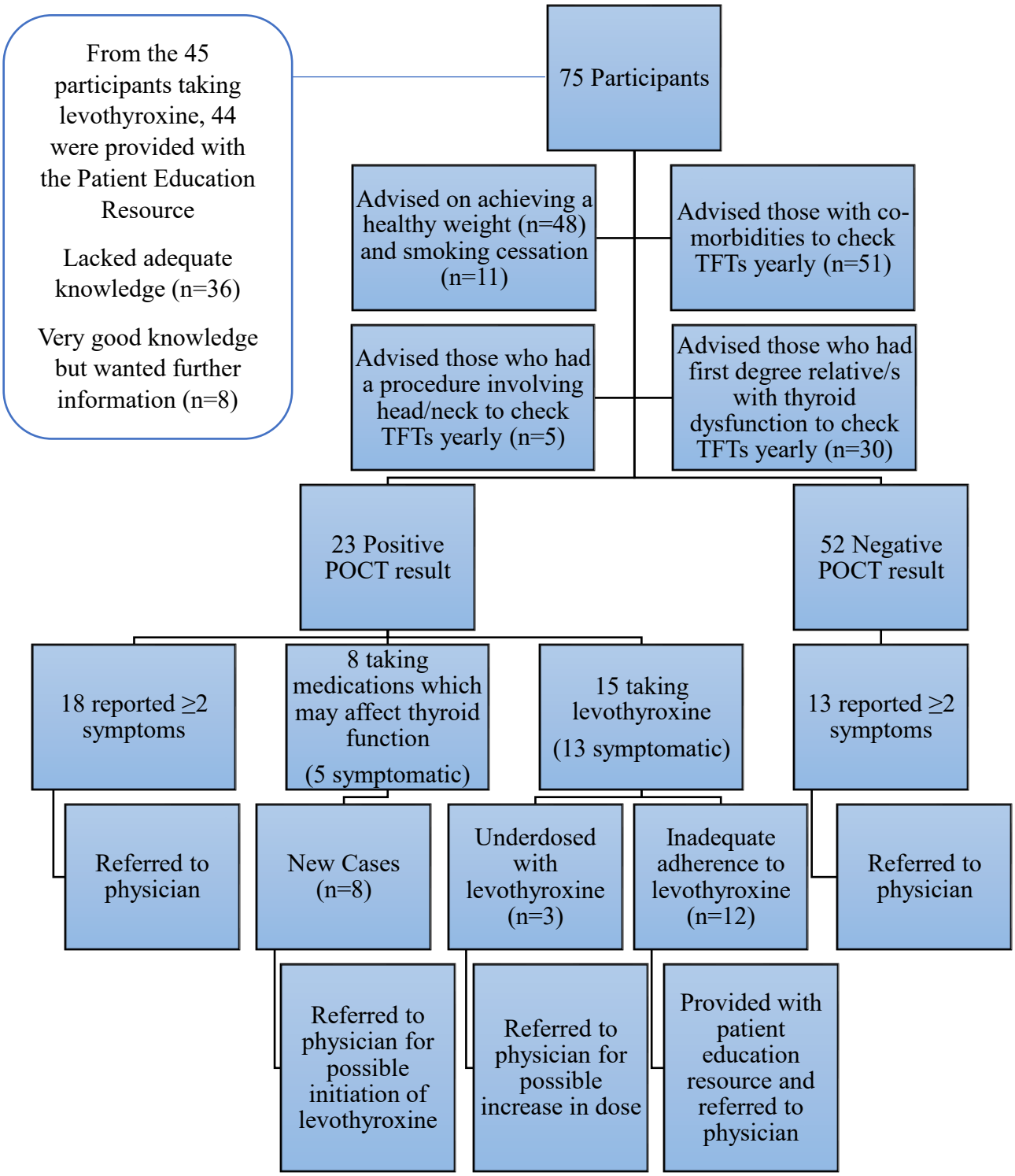


Figure 3.1: Action taken

3.7 Statistical Association of Results

The health status of participants relative to their POCT results is described in Table 3.13. Notably, most asymptomatic participants (n=39) tested negative, whereas most symptomatic individuals (n=18) tested positive. Table 3.13 show that a statistically significant association was observed between all participants experiencing signs and symptoms of hypothyroidism and TSH levels ≥ 5 μIU/mL ($p<0.05$).

Table 3.13: Participants' symptoms and test results (N=75)

			Test results	
			Positive	Negative
Symptoms	No	No. of participants	5	39
		Percentage	11.4%	88.6%
	Yes	No. of participants	18	13
		Percentage	56.7%	43.3%

$X^2(1) = 15.89$, $p<0.001$

Table 3.14 shows the significant statistical association between incorrect/correct levothyroxine use, symptoms and elevated TSH result (≥ 5 μIU/mL), indicative of hypothyroidism ($p<0.05$).

Table 3.14: Levothyroxine use, symptoms, and TSH result (n=45)

			TSH Results	
			Positive	Negative
Levothyroxine use and symptoms	Taking Levothyroxine correctly and no symptoms	No. of participants	1	4
		Percentage	20.0%	80.0%
	Taking Levothyroxine correctly and symptoms	No. of participants	2	2
		Percentage	50.0%	50.0%
	Not Taking Levothyroxine correctly and no symptoms	No. of participants	2	18
		Percentage	10.0%	90.0%
	Not Taking Levothyroxine correctly and symptoms	No. of participants	10	6
		Percentage	62.5%	37.5%

$X^2(3) = 11.93$, $p=0.008$

Table 3.15 shows the statistically significant association between participant perception of agreeing to the importance of appropriate thyroid ranges for good health with levothyroxine treatment ($p<0.05$).

Table 3.15: Participants' perception of thyroid health vs. levothyroxine use (N=75)

			Participants' perception of thyroid health			
			Strongly Agree	Agree	Neutral	Disagree
Levothyroxine treatment	Yes	No. of Participants	38	6	0	1
		Percentage	84.4%	13.3%	0.0%	2.2%
	No	No. of participants	15	11	3	1
		Percentage	50.0%	36.7%	10.0%	3.3%

$X^2(3) = 11.929$, $p=0.008$

The relationship between POCT results with age, BMI, comorbidities, gender, smoking, medication intake and testing frequency was not statistically significant ($p>0.05$).

Chapter 4 - Discussion

4.1 Thyroid-Stimulating Hormone Point-of-Care versus Laboratory Testing

TSH measurement remains central to the diagnosis and management of thyroid dysfunction (Hadgu et al., 2024). Traditional laboratory-based immunoassays provide quantitative data critical for discerning subtle deviations in thyroid status (Spencer, 2023; Van Uytfanghe et al., 2023). Methods such as chemiluminescent immunoassays and enzyme immunoassays are characterized by high sensitivity, specificity, and rigorous standardization using reference materials from international bodies such as the World Health Organization and International Federation of Clinical Chemistry and Laboratory Medicine (Gunapalasingham et al., 2019; Cowper et al., 2024). These laboratory assays remain indispensable for monitoring patients requiring precise levothyroxine adjustments. However, centralized analysis can introduce logistical delays, potentially prolonging diagnosis and treatment (Spencer, 2023).

The Acro Biotech Inc. TSH rapid test cassette, a membrane-based immunoassay employing monoclonal antibodies, qualitatively detects TSH levels above 5 μIU/mL a threshold indicative of hypothyroidism (Taylor et al., 2023). In this study, the Acro Biotech Inc. TSH rapid test cassette demonstrated a 95% concordance with laboratory values ($p < 0.001$), supporting its reliability as a screening tool. Results are available within 10 minutes, enabling pharmacists to initiate interventions, provide structured counselling, and refer patients for confirmatory testing when necessary.

In this study, POCT facilitated the identification of 23 participants (30%) with hypothyroidism. Among these, 8 (10%) individuals were newly diagnosed through screening, while 15 (20%) were previously known cases who were either nonadherent to treatment (n=12) or receiving an inadequate dose of levothyroxine (n=3). Without the implementation of POCT, these patients would have remained undetected, potentially resulting in the progression of various health complications. Despite advantages in speed and accessibility, POCT cannot replace laboratory testing in all clinical scenarios. The qualitative nature of POCT limits its ability to distinguish between subclinical and overt hypothyroidism or provide quantitative trends necessary for long-term management (Hadgu et al., 2024). In this study, any positive POCT result at or above the 5 μIU/mL threshold prompted patient referral for laboratory confirmation, ensuring diagnostic accuracy and minimizing the risk of inappropriate self-adjustment of medication. This complementary approach leverages the strengths of both POCT and laboratory testing, using the former for rapid identification of at-risk individuals and the latter for definitive diagnosis and treatment planning (Spencer, 2023).

A pharmacist-led POCT framework can bridge the gap between initial screening and comprehensive clinical care. In this study, participants were given clear pathways for further evaluation, when necessary, which may reduce delays commonly associated with traditional laboratory workflows. Immediate feedback from POCT also has the potential to enhance adherence to clinical guidance and support timely modifications in patient management.

4.2 Feasibility of the Thyroid Point-of-Care Testing Framework

The feasibility of implementing a pharmacist-led TSH POCT framework within a community pharmacy setting was assessed and confirmed in the study. Clinical feasibility is assessed on the ability of the POCT device to deliver results that are comparable to conventional laboratory methods (Spencer, 2023; Van Uytfanghe et al., 2023). The POCT framework supports adherence to clinical guidelines by enabling rapid assessment, prompt patient management, education, and timely referral for confirmatory testing.

The study was conducted in a community pharmacy equipped with a private clinic area that ensured privacy and accessibility, this is a feature common to most community pharmacies supporting feasible application in other pharmacies (Parnis, 2020).[17] Seventy-five participants were recruited based on defined inclusion and exclusion criteria, ensuring that the sample represented the target population for thyroid screening. The pharmacist-led framework involved scheduling appointments to minimize disruption in the community pharmacy, the thyroid POCT framework provides a structured protocol including an SOP, result interpretation, and patient counselling, which proves essential for the effective implementation and delivery of the service.

[17] World Health Organisation (WHO). The Legal and Regulatory Framework for community pharmacies in the WHO European Region [Internet]. CH: WHO; 2019 [cited 2025 May 25]. Available from: https://iris.who.int/bitstream/handle/10665/326394/9789289054249-eng.pdf

This study benefitted all participants, as TSH testing is recommended to be conducted every 6 months to 1 year in cohorts taking levothyroxine for their hypothyroidism management or taking medications that may alter thyroid function. The 75 participants were advised on achieving a healthy weight as they were overweight or obese (n=48), and on smoking cessation methods depending on the amount of cigarettes smoked by the participant (n=11), as described in the Action Plan, as both of these modifiable risk-factors may impact thyroid health. The participants were advised to check TFTs yearly if they have co-morbidities related to thyroid disorders (n=51), they had a procedure involving the head/neck region (n=5) or have first degree relatives with thyroid disorders (n=30).

In the feasibility testing involving 75 participants (18 males, 57 females; modal age range 45–54 years (n=24)), 23 (30%) exhibited TSH levels ≥ 5μIU/mL, indicative of hypothyroidism (Chaker et al., 2022). These patients were advised according to the Action Plan and referred to their physician accordingly. Among these 23 participants, 8 (10%) were taking medications which may affect thyroid function and had been previously undiagnosed, while 15 (20%) were already receiving levothyroxine therapy: 3 participants (4%) appeared to be undertreated due to inadequate dosing, and 12 (16%) were not taking levothyroxine correctly. Incorrect levothyroxine use was particularly apparent in participants aged 55 years or older, and in participants not taking a fixed dose of levothyroxine. Incorrect levothyroxine use was attributed to self-adjustment of doses, inconsistent administration times, and errors in how the medication is taken (e.g., taken with interfering medications and/or supplements). These findings resonate with international observational studies that have highlighted widespread challenges in both diagnosing and managing thyroid disorders, particularly the prevalence of undiagnosed and undertreated hypothyroidism (Chaker et al. 2022; Zamwar et al., 2023).

Regulatory and legal feasibility is a critical dimension. The EC declaration proves conformity for the device and POCT is conducted following a structured SOP.[2] This compliance not only ensures patient safety but also reinforces the credibility of the service. Economically, the rapid TSH POCT is cost-effective, as it reduces the need for expensive laboratory infrastructure and minimizes delays that can lead to further complications. Furthermore, patients reported high levels of acceptance due to the convenience and immediate results provided by the POCT. This accessibility is particularly valuable for individuals who might otherwise face barriers to traditional healthcare settings.

4.3 Community Pharmacist Intervention in Hypothyroidism

Community pharmacies offer a unique and accessible setting for the early detection and management of hypothyroidism (Dayan and Panicker, 2018). By leveraging POCT for TSH, pharmacists can provide rapid screening that not only identifies abnormal TSH levels but also uncovers critical gaps in patient adherence and education. This study, conducted within a community pharmacy, emphasises the potential of pharmacist-led interventions to enhance clinical care in hypothyroidism.

Following the assessment of the participant with the Data Collection Tool, knowledge gaps in hypothyroidism management were prevalent. From 45 participants taking levothyroxine, 36 (48%) lacked adequate knowledge concerning hypothyroidism management and levothyroxine adherence, and despite having very good knowledge 8

[2] European Commission. Regulation (EU) 2017/746 of the European Parliament and of the Council of 5 April 2017 on in vitro diagnostic medical devices and repealing Directive 98/79/EC and Commission Decision 2010/227/EU [Internet]. Official Journal of The European Union. 2017; L117:176-332 [cited 2025 Feb 8]. Available from: https://eur-lex.europa.eu/legalcontent/EN/TXT/PDF/?uri=CELEX:32017R0746

(10%) participants requested the pharmacist help to attain more knowledge on hypothyroidism and levothyroxine treatment. This allowed for a total of 44 (58%) Patient Education Resources to be explained and given to the participant for reference.

From the 36 participants that showed lack of knowledge on levothyroxine, 12 had TSH levels ≥ 5μIU/mL, suggesting the need for a pharmacist-led thyroid POCT service.

Hypothyroidism may also be attributed to signs and symptoms. A total of 31 (43%) participants reported 2 or more signs and symptoms indicative of hypothyroidism. These patients were advised according to the Action Plan and referred to their physician accordingly. Eighteen of these patients had a positive result with the POCT and 13 had a negative result.

Pharmacists, as trusted medication experts, are uniquely positioned to address these challenges, bridging gaps in thyroid care (Spencer, 2023; Zamwar et al., 2023). The integration of TSH POCT into community pharmacy practice enables accessible and immediate screening, timely patient counselling, and evidence-based targeted interventions, shifting pharmacists towards a more clinical and patient-centred role (Kamusheva et al., 2020). When abnormal results or any suggestive signs or symptoms are detected, pharmacists can provide immediate education, clarify proper medication usage, and, if necessary, collaborate with other healthcare professionals by issuing referral letters to physicians for confirmatory laboratory testing. This collaborative model not only enhances early detection of hypothyroidism. but also promotes better adherence to levothyroxine therapy, ultimately improving patient outcomes and reducing the burden of untreated and undiagnosed thyroid disease (McAninch et al., 2018).

4.4 Significance of the Study

This study addresses an opportunity for community pharmacists to support thyroid disorder management. Notably, a number of patients remain undiagnosed (n=8), underdosed (n=3), or non-adherent (n=36) to levothyroxine therapy, mirroring global trends (Tudor et al., 2020; Di Cerbo 2021; Chaker et al. 2022; Grigoriadis et al., 2023; Larsen et al., 2023; Taylor et al., 2023; Zamwar et al., 2023). In Malta, as in many other settings, access to laboratory-based TSH testing is limited by its reliance on invasive blood draws performed by physicians or nurses, as well as by the high cost of sophisticated analytical equipment (Spencer, 2023). Laboratory TSH assessments are typically ordered at the discretion of a physician and necessitate patient visits for blood sampling and result interpretation together with potential treatment modifications (Spencer, 2023). Patients often must attend these appointments within a 6-month to 1year period, if they exhibit symptoms, possess relevant co-morbidities, have undergone head/neck procedures, or are taking medications known to alter TSH levels, or even less frequently, such as every five years, if they are female, over 35 years of age, and do not have any thyroid related problems.[10] Such requirements can discourage routine thyroid monitoring and may inadvertently prompt self-dosing behaviours when patients gain access to their own blood test results without adequate professional guidance.

Data analysis revealed a strong association between positive POCT results (TSH ≥ 5 μIU/mL) and the presence of symptoms ($p<0.001$), suggesting that symptomatic

[10] National Institute for Health and Care Excellence (NICE). Thyroid disease: assessment and management [Internet]. UK; 2023 [cited 2025 Feb 10]. Available from: https://www.nice.org.uk/guidance/ng145/chapter/recommendations#:~:text=For%20adults%2C%20children%20and%20young%20people%20with%20TSH%20in%20the,2).

individuals benefit from POCT in community pharmacy settings. An association was identified between POCT results (TSH ≥ 5 μIU/mL), incorrect use of levothyroxine, and symptoms (p=0.008), highlighting the necessity for medication reviews to ensure proper levothyroxine use and to assess for clinical signs and symptoms indicative of hypothyroidism. The participants' perception of thyroid health was found to have an association with patients taking levothyroxine (p=0.008), indicating the importance of educating patients on thyroid health and the potential complications of untreated hypothyroidism in those receiving medications that may affect thyroid function.

This study demonstrates the need for a standardized, pharmacist-led TSH POCT service, incorporating a thorough medication review. By employing a rapid, non-invasive TSH testing device in community pharmacies, this innovative approach offers immediate, real-time screening that is both cost-effective and accessible. It enables early detection of hypothyroidism and supports prompt patient counselling, thereby reducing the burden on healthcare facilities. In addition, the Data Collection Tool, ensures that the structured assessment is conducted equally with all patients and the interpretation of results is harmonized with the personalized Action Plan addressing their specific risk factors. This model not only enhances patient outcomes by improving adherence to levothyroxine therapy but also positions pharmacists as key contributors in thyroid management, extending their traditional role into a more clinical, patient-centred practice (Kamusheva et al., 2020).

4.5 Strengths and Limitations

The proposed framework for TSH POCT demonstrates significant potential for early screening, particularly in primary healthcare settings. Recent literature supports the feasibility and accuracy of thyroid POCT versus conventional laboratory-based immunoassays, highlighting its potential to enhance screening (Ezegbogu et al., 2022; Leirs et al., 2022; Shurbaji et al., 2023; Ye et al., 2023). The integration of pharmacists into the management of thyroid disorders has been well-documented, with a focus on medication management, patient education, adherence support, and the identification of drug-related problems (Krishnananda et al., 2022; Parakkal et al., 2023; Ayhan et al., 2025). Notably, to the researcher's knowledge, this study is the first to implement a comprehensive framework that combines TSH POCT with the management of hypothyroidism in a community pharmacy setting, representing an innovative approach in patient-centred hypothyroidism management. This framework comprises a comprehensive Data Collection Tool, SOP, Action Plan and Patient Education Resource. The impact of this research lies in its capacity to pave the way toward a more economical and seamless healthcare system by facilitating easy access to TSH testing, early screening for hypothyroidism, and prompt patient referral when abnormal results or clinical symptoms are detected.

Limitations of the current POCT framework must be acknowledged. A primary limitation is that the TSH POCT device used in the study is qualitative in nature only testing for TSH and not for T3 and T4. It provides a binary result (positive or negative) based on a chromogenic colour indicator rather than an exact TSH concentration. This limitation

hinders its ability to distinguish between subclinical and overt hypothyroidism (Zamwar et al., 2023; Hadgu et al., 2024). Furthermore, the qualitative assessment, was only performed by one operator (the researcher) and relies on subjective interpretation by the professional performing the test, although efforts were made to ensure adequate lighting and standardized procedures.

Additional constraints include the validation of the POCT only for adult screening. Like laboratory-based assays, POCT results may also be influenced by factors such as recent illness, medication interactions, and patient-specific variables potentially leading to false-positive or false-negative outcomes (Van Uytfanghe et al., 2023). Consequently, any positive POCT result must be confirmed with a quantitative laboratory assay to ensure diagnostic accuracy and patients were referred (Spencer, 2023).

Data obtained via the Data Collection Tool depended largely on patient recall, which may be subject to bias; and participants may underestimate behaviours such as cigarette smoking practices. In addition, there exists a risk that participants might overstate their adherence to levothyroxine therapy or the frequency of their thyroid function tests. The current study was conducted with a small sample size and within a single community pharmacy setting, potentially limiting generalizability of the findings. A larger sample size and the evaluation in more than one community pharmacy could help mitigate these discrepancies.

Furthermore, variability in patient adherence, medication interactions, and environmental conditions could influence POCT device performance. For instance, inconsistent dosing schedules, improper administration practices, and fluctuations in patient behaviour can affect the reliability of the test outcomes. While POCT enhances accessibility and rapid decision-making, its successful integration into clinical practice necessitates rigorous pharmacist counselling and robust referral pathways to ensure that patients receive appropriate follow-up and management.

4.6 Recommendations for Future Research

The present research displays the necessity for a multifaceted exploration into the implementation and outcomes of pharmacist-led thyroid POCT services, combined with comprehensive medication use reviews within community pharmacy practice. Given the significant gaps identified in the diagnosis, dosing, and adherence of hypothyroid patients, further investigation is warranted.

Future studies should adopt longitudinal designs with larger sample sizes, more diverse populations and multiple practice sites to evaluate the immediate clinical outcomes of thyroid POCT and its sustainability over time while confirming broader applicability. Specifically, research should assess whether early detection via POCT, followed by structured pharmacist counselling and referral protocols, translates into long-term improvements in TSH control and overall patient health outcomes. In instances where patients have previously been non-compliant with levothyroxine therapy, a structured medication use review, supplemented by patient educational information, may enhance

adherence in levothyroxine use. It is essential to examine whether the initial gains observed post-intervention are maintained through regular follow-up assessments, including re-testing of TSH levels after any adjustments in medication adherence, weight management, or smoking cessation. Concurrently, studies should evaluate the long-term adherence to pharmacist recommendations and the efficiency of interprofessional referral pathways between community pharmacists and physicians. A robust, electronically accessible health system that facilitates the sharing of patient data among all healthcare professionals is also crucial to overcome current limitations in assessing patient history.

Further research should explore the validation of multi-parameter POCT devices. Unlike the current qualitative TSH POCT, which only indicates whether TSH levels are above or below a set threshold (5 μIU/mL), multi-parameter devices capable of simultaneously assessing TSH, free T3, and free T4 would enable a more nuanced differentiation between subclinical and overt hypothyroidism. Such devices would not only enhance diagnostic precision but also reduce the reliance on confirmatory laboratory tests.

It is imperative to examine the practical challenges encountered during the implementation of pharmacist-led thyroid POCT. Future research should investigate the perceptions of patients regarding POCT services and their willingness to engage in these initiatives when delivered by pharmacists. Equally, an assessment of pharmacists' own perspectives is necessary, examining if they feel adequately trained and supported in conducting POCT and performing medication use reviews, or if these responsibilities impose an undue burden that could potentially compromise the thoroughness of their clinical care. In parallel, research should seek to understand the views of physicians

regarding the pharmacist's role in this collaborative model, particularly in terms of trust, communication, and the overall efficiency of the referral system (Kamusheva et al., 2020).

An additional avenue for inquiry involves the potential reorganisation of pharmacy services. Research could explore whether establishing centralised clinics or dedicated hubs for medication use reviews and POCT, like models implemented in other healthcare systems such as University of Illinois Chicago medical centre, might improve patient outcomes (Assadi and Gulam, 2021).[18] These dedicated environments could foster a team-based approach where pharmacists are solely responsible for these clinical activities, thus enhancing patient education, medication adherence, and monitoring while reducing medicine wastage.[19] Furthermore, the facilitation of interprofessional collaboration in such a setting, where physicians routinely refer patients to pharmacists for comprehensive medication reviews, warrants further study to assess its impact on continuity and quality of care (Tasai et al., 2021).

The integration of technological innovations, such as artificial intelligence and tele-pharmacy, warrants investigation. Future studies should evaluate the feasibility and effectiveness of these technologies in streamlining communication between primary and secondary healthcare providers and in providing ongoing follow-up support to patients.

[18] University of Illinois Chicago (UIC). Medication Therapy Management Clinic (MTMC): UIC [Internet]. IL; 2025. [Cited: 2025 March 10]. Available from: https://hospital.uillinois.edu/primary-and-specialty-care/pharmacy/prescription-services/medication-therapy-management-clinic

[19] International Pharmaceutical Federation. Medicines reconciliation: a toolkit for pharmacists. The Hague (NL): International Pharmaceutical Federation [Internet]. 2021. [Cited: 2024 Oct 27]. Available at: https://www.fip.org/file/4949.

4.7 Conclusion

The developed framework for TSH POCT demonstrates feasibility to run a pharmacist-led service that provides patients with reliable and efficient thyroid function screening. Through a review, a POCT device was identified that meets the essential criteria for sensitivity and specificity, making it suitable for community pharmacist-led thyroid assessments within a collaborative care model. This framework enhances early detection of TSH levels ≥5 μIU/mL, thereby enabling timely intervention to prevent or delay the progression of hypothyroidism and its associated comorbidities and supports the standardisation of service provision.

The robustness of the TSH POCT results, confirmed through comparison with laboratory methods, reinforces the clinical utility of this approach. The ease of use and rapid turnaround of POCT decrease the load on centralized medical laboratories and enhance accessibility to thyroid testing for a wider population (Leirs et al., 2022; Arai et al., 2023; Maduabuchi et al., 2023).

The integration of this framework in community pharmacy services offers a holistic approach to thyroid screening and management. The standardised procedure, ensures consistency and promotes early detection, optimised therapeutic management, and improved patient outcomes.

The pharmacist-led TSH POCT framework paves the way for an efficient, patient-centred healthcare model. It addresses existing gaps in hypothyroidism management and positions community pharmacists as integral contributors to hypothyroidism screening and ongoing care, thereby benefiting both healthcare providers and patients alike.

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Appendices

Appendix 1: Ethics Approval

L-Università ta' Malta

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Ref No: MED-2024-00385

29 November 2024

Ms Mariah Vella
Qalb ta' Maria,
Triq il-Konti Manduca,
Naxxar, Malta

With reference to your application submitted to the Faculty Research Ethics Committee in connection with your research entitled:

Pharmacist-Led Thyroid Point-Of-Care Testing

The Faculty Research Ethics Committee is granting ethical approval for the above-mentioned application.

Professor Anthony Serracino Inglott
Chair
Faculty Research Ethics Committee

Appendix 2: Thyroid Point-Of-Care Testing Framework (English and Maltese)

Data Collection Tool

To be filled in by the researcher through an interview with the patient

Patient Study Number: _____ **Date: _____**

Section I: Modifiable and Non-modifiable Risk Factors

1. **Age (years)**

- ☐ 18 – 24
- ☐ 25 – 34
- ☐ 35 – 44
- ☐ 45 – 54
- ☐ 55 – 64
- ☐ 65 – 74
- ☐ >75

2. **Gender**

- ☐ Male
- ☐ Female
- ☐ Non-binary
- ☐ Prefer not to say

3. **Body Mass Index: To be measured**

Weight (Kg)	Height (m)	BMI = kg/m2

Classification	BMI Category (kg/m2)
Underweight	☐ < 18.5
Normal Weight	☐ 18.5 – 24.9
Overweight	☐ 25.0 – 29.9
Obese Class I	☐ 30.0 – 34.9
Obese Class II	☐ 35.0 – 39.9
Obese Class III	☐ ≥ 40

4. **Smoking**

   a) **What is your smoking status**

   ☐ Current smoker (go to Q 4b)

   ☐ Never smoked (go to Q 5)

   ☐ Previous smoker

   Kindly specify how long since you stopped smoking: _____ (go to Q 5)

   b) **If you are a current smoker, how many cigarettes do you smoke?**

   ☐ Occasional smoker

   ☐ 1-10 cigarettes daily

   ☐ 11-20 cigarettes daily

   ☐ > 20 cigarettes daily

Section II: Health Status

5. **Are you experiencing any of the following signs and symptoms suggestive of hypothyroidism?**

   ☐ Brain Fog

   ☐ Brittle hair

   ☐ Constipation

   ☐ Dry skin

   ☐ Fatigue

   ☐ Heavy menstruation

   ☐ Low mood

   ☐ Menstrual irregularities

   ☐ Migraine

   ☐ Stiff muscles

   ☐ Unintentional weight gain

   ☐ None of the above

6. **Do you suffer from any co-morbidities? (Interviewer refer to Appendix A)**

Comments:

_____

_____

7. **Have you ever had any of the following procedures?**

- ☐ Laryngeal/pharyngeal surgery
- ☐ Radiation (Head and neck)
- ☐ Radioactive iodine therapy
- ☐ Thyroidectomy
- ☐ None of the above

8. **Do you have first-degree relatives who have thyroid disease?**

- ☐ Yes
- ☐ No

Section III: Medication history and management

9. **Medication**

a) **Are you currently taking Levothyroxine?**

- ☐ Yes (Go to Q 10c) State dose: _____
- ☐ No (Go to Q 10b)

b) **Which of the following medications are you taking?** (Go to Q11)

- ☐ Amiodarone
- ☐ Anti-diabetic medicine (glimepiride, sitagliptin, vildagliptin, insulin)
- ☐ Anti-epileptics (carbamazepine, phenobarbital, phenytoin, valproic acid)
- ☐ Isotretinoin
- ☐ Lithium
- ☐ Oestrogen (oral contraceptive, Hormone Replacement Therapy)
- ☐ Dopamine Antagonists (aripiprazole, olanzapine, quetiapine)

c) Do you take levothyroxine every day?

☐ Yes

☐ No

Comments: _____

d) Do you take levothyroxine at the same time?

☐ Yes

☐ No

Comments: _____

e) Have you ever taken more levothyroxine than you should?

☐ Yes

☐ No

Comments: _____

f) What time of the day do you take levothyroxine?

☐ Morning

☐ Afternoon

☐ Evening

g) How long do you wait before consuming food?

☐ I eat before taking levothyroxine

☐ I eat immediately after taking levothyroxine

☐ 10-20 minutes after

☐ ≥ 30minutes after

h) Which statement do you agree with? Tick where applicable:

☐ I can chew or crush levothyroxine tablets

☐ I take levothyroxine tablets whole with water

☐ I take levothyroxine with tea or coffee

i) If you have adequate knowledge, do you still feel you need more information about your thyroxine medication?

☐ Yes

☐ No

Comments: _____

j) Are you currently taking any medication or supplement apart from Levothyroxine? (Interviewer refer to Appendix B)

Comments:

_____

_____

Section IV: Knowledge on Thyroid Testing

10. Have you ever had laboratory thyroid function tests performed?

☐ Yes (go to Q 12)

☐ No (go to Q 14)

11. Who referred you for thyroid testing?

☐ Physician

☐ Pharmacist

Other: _____

12. When have you last checked your thyroid levels?

☐ 7-12 months ago

☐ 2-4 years ago

☐ 5 years ago

☐ > 5years ago

13. Do you think having appropriate thyroid levels is essential for general health?

☐ Strongly agree

☐ Agree

☐ Neutral

☐ Disagree

☐ Strongly Disagree

14. To your knowledge, your current thyroid status is

☐ Normal

☐ Hypothyroidic

☐ Hyperthyroidic

☐ I Do not know

Section V: Documentation of TSH POCT Result

15. Thyroid-Stimulating Hormone Result obtained from point-of-care testing device

☐ Positive (suggestive of hypothyroidism)

☐ Negative

16. Tick accordingly:

ACTION	ASSESSMENT BY RESEARCHER	COMMENTS
ADVICE BY RESEARCHER	Section I: ☐ Overweight or Obese ☐ Current Smoker Section II: ☐ Symptoms reported ☐ Co-morbidities from Appendix A reported ☐ Procedure involving the head/ neck region ☐ First-degree relative with thyroid dysfunction Section III: ☐ Shows lack of knowledge on levothyroxine ☐ Feels the need for more information about levothyroxine	Refer to the 'Action Plan' if any of the boxes are ticked
REFERRED TO PHYSICIAN	☐ Yes ☐ No	Refer to the 'Action plan'

Appendix A

Classification of co-morbidities of relevance to thyroid Disease
Osteoarthritis (with falls)
Osteoarthritis (w/out falls)
Rheumatoid arthritis
Hypertension
Hypercholesterolemia
Atrial Fibrillation
Chronic Heart Failure
Chronic Kidney disease
Celiac disease
Diabetes (Type 1)
Diabetes (Type 2)
Fibromyalgia
Gout
Hashimoto thyroiditis
Pituitary disease
Polycystic ovarian syndrome
Systemic Lupus Erythematosus
thalassemia major

Appendix B

Classification of medication or supplements of relevance to thyroid disease
Amiodarone
Antacids (e.g. aluminum/magnesium hydroxide, sodium bicarbonate)
Anti-epileptics (Carbamazepine, phenobarbital, phenytoin, valproic acid)
Cholestyramine
Furosemide
Oestrogen (Oral Contraceptive, Hormone Replacement Therapy)
Orlistat
Proton Pump Inhibitors (Omeprazole, Pantoprazole, lansoprazole
Sucralfate
Calcium
Iron supplements
Iodine
Magnesium
Zinc

9ii. Formola tal-Ġbir tad-Data

Għandha timtela mir-riċerkatriċi permezz ta' intervista mal-pazjent/a

Numru ta' Studju tal-Pazjent: _____ **Data: _____**

Taqsima I: Fatturi ta' Riskju li jistgħu jiġu modifikati u li ma jistgħux jiġu modifikati

1. **Età (snin)**
   - ☐ 18 – 24
   - ☐ 25 – 34
   - ☐ 35 – 44
   - ☐ 45 – 54
   - ☐ 55 – 64
   - ☐ 65 – 74
   - ☐ >75
2. **Sess**
   - ☐ Raġel
   - ☐ Mara
   - ☐ Mhux Binarju
   - ☐ Nippreferi ma ngħidx
3. **Indiċi tal-Massa tal-Ġisem: Għandu jitkejjel**

Piż (Kg)	Tul (m)	BMI = kg/m2

Klassifikazzjoni	Kategorija tal-BMI (kg/m^2)
Piż baxx	☐ < 18.5
Piż normali	☐ 18.5 – 24.9
Piż żejjed	☐ 25.0 – 29.9
Obeżita Klassi I	☐ 30.0 – 34.9
Obeżita Klassi II	☐ 35.0 – 39.9
Obeżita Klassi III	☐ ≥ 40

4. It-tipjip

c) X'inhu l-istat tat-tipjip tiegħek?

☐ Tpejjep attwalment (mur M 4b)

☐ Qatt ma pejjipt (mur M 5)

☐ Kont tpejjep

Speċifika kemm ilu li waqaft tpejjep: _____ (mur M 5)

d) Jekk tpejjep bħalissa, kemm tpejjep sigaretti?

☐ Tpejjep soċjalment

☐ 1-10 sigaretti kuljum

☐ 11-20 sigaretti kuljum

☐ > 20 sigaretti kuljum

Taqsima II: Stat tas-Saħħa

5. Qed tesperjenza xi wieħed mis-sinjali u s-sintomi li ġejjin li jissuġġerixxu l-ipotirojdiżmu?

☐ Ċpar tal-moħħ

☐ Xagħar fraġli

☐ Stitikezza

☐ Ġilda xotta

☐ Għeja

☐ Mestrwazzjoni qawwija

☐ Burdata baxxa

☐ Irregolaritajiet menstruwali

☐ Emigranja

☐ Muskoli iebsin

☐ Żieda fil-piż mhux intenzjonata

☐ Xejn minn hawn fuq

6. **Tbati minn xi komorbiditajiet? (L-intervistatriċi tirreferi għall-Appendiċi A)**

kummenti**:**

_____

_____

7. **Qatt kellek xi waħda mill-proċeduri li ġejjin?**

☐ Kirurġija tal-larinġi/farinġi

☐ Radjazzjoni (ras u għonq)

☐ Terapija tal-jodju radjuattiv

☐ Tirojdektomija

☐ Xejn minn hawn fuq

8. **Għandek qraba tal-ewwel grad li għandhom mard tat-"Thyroid"?**

☐ Iva

☐ Le

Taqsima III: Stat u ġestjoni tal-medikazzjoni

9. **Medikazzjoni**

a. Bħalissa qed tieħu Levothyroxine?

☐ Iva (Mur M 10c) Iddikjara d-doża : _____

☐ Le (Mur M 10b)

b. Liema mill-mediċini li ġejjin qed tieħu? (Mur għal Q11)

☐ Amiodarone

☐ Mediċina kontra d-dijabete (glimepiride, sitagliptin, vildagliptin, insulina)

☐ Anti-epilettiċi (carbamazepine, phenobarbital, phenytoin, valproic acid)

☐ Isotretinoin

☐ Lithium

☐ Estroġenu (kontraċettiv orali, Terapija ta' Sostituzzjoni tal-Ormoni)

☐ Antagonisti tad-dopamina (aripiprazole, olanzapine, quetiapine)

c. Tieħu il-levothyroxine kuljum?

☐ Iva

☐ Le

kummenti: _____

d. Tieħu il-levothyroxine fl-istess ħin?

☐ Iva

☐ Le

Kummenti: _____

e. Qatt ħadt aktar levothyroxine milli suppost?

☐ Iva

☐ Le

Kummenti: _____

f. X'ħin tal-ġurnata tieħu levothyroxine?

☐ Filgħodu

☐ Wara nofsinhar

☐ Filgħaxija

g. Kemm tistenna qabel ma tikkonsma l-ikel?

☐ Jien niekol qabel nieħu il-levothyroxine

☐ Jien niekol immedjatament wara li nieħu il-levothyroxine

☐ 10-20 minuta wara

☐ ≥ 30 minuta wara

h. Ma' liema stqarrija taqbel? Immarka fejn applikabbli:

☐ Nista nomgħod jew infarrak il-pilloli tal- levothyroxine

☐ Nieħu il-pilloli tal-levothyroxine sħaħ bl-ilma

☐ Nieħu il-levothyroxine mat-tè jew il-kafè

i. Għalkemm qed tieħu il mediċina kif suppost, tħoss li xorta għandek bżonn aktar informazzjoni dwar il-medikazzjoni tiegħek tat-thyroxine?

☐ Iva

☐ Le

Kummenti: _____

j. Bħalissa qed tieħu xi medikazzjoni jew suppliment minbarra Levothyroxine? (L--intervistatriċi tirreferi għall-Appendiċi B)

Kummenti:

_____

_____

Taqsima IV: Għarfien dwar l-Ittestjar tat-"Thyroid"

10. Qatt għamilt testijiet tal-funzjoni tat-"thyroid" fil-laboratorju?

☐ Iva (go to Q 12)

☐ Le (go to Q 14)

11. Min irreferik għall-ittestjar tat-"thyroid"?

☐ Tabib

☐ Spiżjar

Oħrajn:_____

12. Meta ċċekkjajt l-aħħar il-livelli tat- "thyroid" tiegħek?

☐ 7-12-il xahar ilu

☐ 2-4 snin ilu

☐ 5 snin ilu

☐ > 5 snin ilu

13. Taħseb li jkollok livelli xierqa tat-"thyroid" huwa essenzjali għas-saħħa ġenerali?

☐ Naqbel ħafna

☐ Naqbel

☐ Newtrali

☐ Ma naqbilx

☐ Ma naqbilx ħafna

14. Sa fejn taf, l-istatus attwali tiegħek tat-“thyroid” huwa

☐ Normali

☐ Ipotirojde

☐ Ipertirojde

☐ Ma nafx

Taqsima V: Dokumentazzjoni tar-Riżultat TSH POCT

15. Riżultat miksub mit-“Thyroid-Stimulating Hormone -TSH point-of-care testing”

☐ Pożittiv (suġġerattiv ta' ipotirojdiżmu)

☐ Negattiv

16. Immarka kif xieraq:

Azzjoni	**VALUTAZZJONI MIR-RICERKATRICI**	**KUMMENTI**
PARIR MIR-RICERKATRICI	Taqsima I: ☐ Piż żejjed jew obeż ☐ Tpejjep attwalment Taqsima II: ☐ Sintomi tal-ipotirojdiżmu rrappurtati ☐ Ko-morbiditajiet mill-Appendiċi A rrappurtati ☐ Proċedura li tinvolvi r-reġjun tar-ras/għonq ☐ Qraba tal-ewwel grad li għandhom mard tat-“Thyroid Taqsima III: ☐ J/Turi nuqqas ta 'għarfien dwar il-levothyroxine ☐ I/Tħoss il-ħtieġa għal aktar informazzjoni dwar il-levothyroxine	Irreferi għall-‘Pjan ta’ Azzjoni’
RIFERUT LIT-TABIB	☐ Iva ☐ Le	Irreferi għall-‘Pjan ta’ azzjoni’

Appendiċi A

Klassifikazzjoni ta' ko-morbiditajiet ta' rilevanza għall-Mard tat- “Thyroid”
Osteoartrite (bil-waqgħat)
Osteoartrite (mingħajr waqgħat)
Artrite rewmatika
Pressjoni għolja
Iperkolesterolemija
Fibrillazzjoni Atrijali
Insuffiċjenza tal-Qalb Kronika
Mard kroniku tal-kliewi
Coeliac
Dijabete (Tip 1)
Dijabete (Tip 2)
Fibromyalgia
Gotta
Tirojdite Hashimoto
Mard pitwitarju
Sindromu tal-ovarji poliċistiċi
Lupus Eritematosus Sistemiku
Talassemija maġġuri

Appendiċi B

Klassifikazzjoni ta 'medikazzjoni jew supplimenti ta' rilevanza għall-mard tat- “Thyroid”
Amiodarone
Antiaċidi (e.g. “aluminum/magnesium hydroxide, sodium bicarbonate”)
Anti-epilettiċi (Carbamazepine, phenobarbital, phenytoin, valproic acid)
Kolestiramina
Furosemide
Estroġenu (Kontraċettiv Orali, Terapija ta' Sostituzzjoni tal-Ormoni)
Orlistat
“Proton Pump Inhibitors” (Omeprazole, Pantoprazole, lansoprazole
Sukralfat
Kalċju
Ħadid
Jodju
Manjeżju
Żingu

Standard Operating Procedure: Developed for this study

SOP Number	SOP TITLE
1	**ACRO BIOTECH INC. TSH RAPID TEST CASETTE (Whole Blood/Serum/Plasma)**

PART 1

Author	
Mariah Vella Doctorate in Pharmacy Student- Pharmacy Department	

PART 2

Approver	**Approver**
Dr. Francesca Wirth Lecturer- Pharmacy Department	**Prof. Lilian M Azzopardi** Head of Department- Pharmacy Department
Approver	

PART 3

Authoriser	**Date of Issue:** **Date of next revision:**

PART 4 (To be filled in by OOD, QSU or RSSD)

☐ This procedure has been revised and is no longer valid as from: (Write date)	☐ Date of NEXT REVISION is extended until: (Max. 4 years)	☐ SOP rendered obsolete on: (Write date)

Table of Contents

1. Definitions

1.1. Buffer: Used to obtain a valid result by washing the blood up the test strip. The buffer bottle should be held vertically to ensure correct drop size, and the number of drops added to the cassette need to be counted.

1.2. Capillary Dropper: Used to collect a sample of blood from the finger of the subject and to transfer the collected blood to the cassette.

1.3. Control Region: Area within the test cassette where a colour change may be observed confirming that the test has worked properly.

1.4. Fingerstick Whole Blood Specimen: A procedure in which a finger is pricked with a lancet to obtain a small quantity of capillary blood for testing purposes.

1.5. Lancet: Used for the collection of capillary blood from the fingertip in adult subjects.

1.6. Test Region: Area within the test cassette where a colour change giving a positive result may be observed.

1.7. TSH Rapid Test Cassette: A rapid chromatographic immunoassay for the qualitative detection of Thyroid Stimulating Hormone (TSH) in whole blood, serum, or plasma to aid in the screening the adult population for primary hypothyroidism by medical professionals. It is not indicated for use in screening neonates for hypothyroidism.

2. Procedure

2.1. Specimen Collection and Preparation

2.1.1. Wash the subject's hand with soap and warm water or clean with an alcohol swab. Allow to dry.

2.1.2. Massage the hand without touching the puncture site by rubbing down the hand towards the fingertip of the middle or ring finger.

2.1.3. Puncture the skin with a sterile lancet. Wipe away the first sign of blood.

2.1.4. Gently rub the hand from wrist to palm to finger to form a rounded drop of blood over the puncture site.

2.1.5. Add the fingerstick whole blood specimen to the test by using a capillary dropper.

2.1.6. Touch the end of the capillary dropper to the blood, do not push the bulb of the dropper inwards, the blood migrates into the dropper through the capillarity to fill all the capillary dropper. Avoid air bubbles.

2.1.7. Push the bulb of the capillary dropper inwards to dispense the whole blood to the specimen area of the test cassette.

2.1.8. Perform the test immediately after the fingerstick whole blood has been collected.

2.2. Performing a Test

2.2.1 Allow the test specimen, buffer and/or controls to reach room temperature (15°C – 30°C) prior to testing.

2.2.2 Remove the test cassette from the sealed pouch and use it as soon as possible.

2.2.3 Place the test cassette on a clean and level surface.

2.2.4 To use a capillary dropper, fill the capillary tube and transfer approximately 50µL of fingerstick whole blood specimen to the specimen area of test cassette, then add 1 drop of buffer (approximately 40µL) and start the timer. (Refer to Diagram 1)

2.2.5 Wait for the coloured line(s) to appear. Read results at 10 minutes Do not interpret the result after 20 minutes.

2.2.6 Interpret the result according to Table 1.

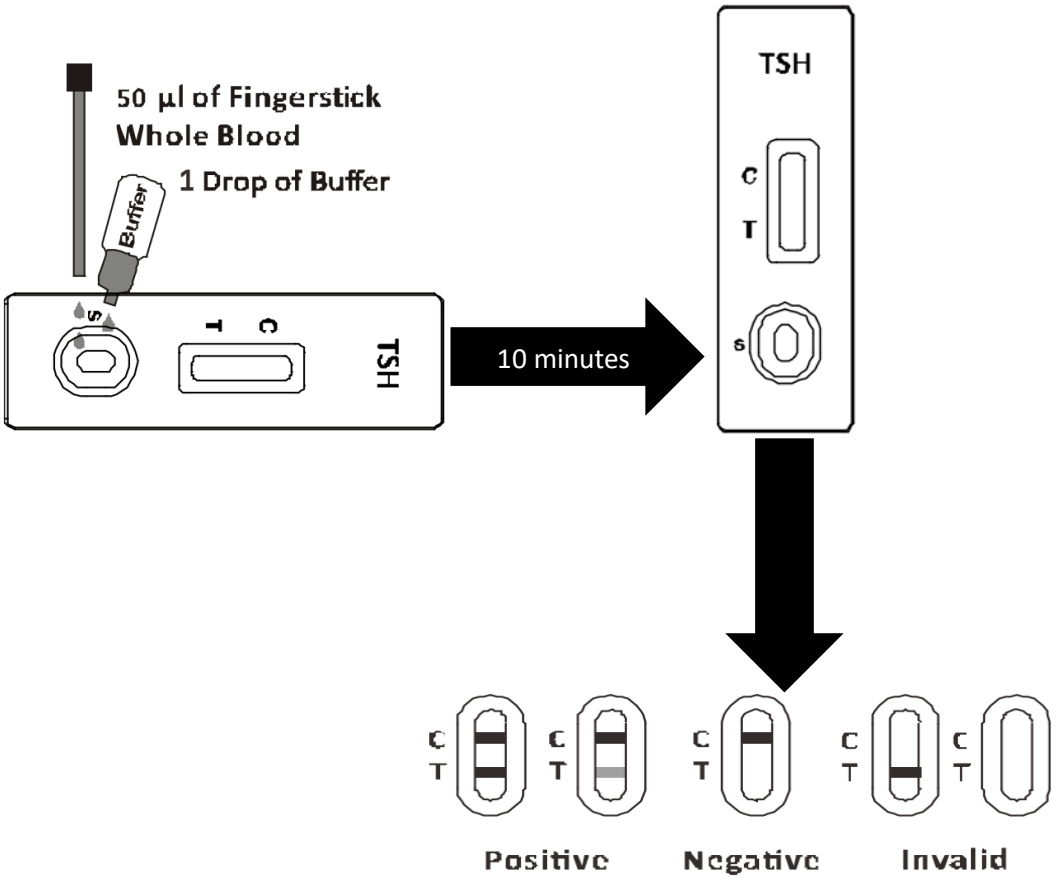


Diagram 1: Illustrative Diagram of Procedure

2.3. Interpretation of Results

Result	Interpretation	
Positive	Two coloured lines appear. One coloured line in the control region (C) and another coloured line in the test region (T). A positive result means that the TSH level is above the cut-off level of 5 µlU/mL. NOTE: The intensity of the colour in the test line region (T) will vary depending on the concentration of TSH present in the specimen. Therefore, any shade of colour in the test region (T) should be considered positive.	**Indicative of hypothyroidism**
Negative	One coloured line appears in the control region (C). No apparent coloured line appears in the test region (T). A negative result means that the TSH level is below the cut-off level of 5µlU/mL.	**Not indicative of hypothyroidism**
Invalid	Control line fails to appear. Insufficient specimen volume or incorrect procedural techniques are the most likely reasons for control line failure. Review the procedure and repeat the test with a new test cassette. If the problem persists, discontinue using the test kit immediately and contact your local distributor.	**Repeat Result**

Table 1: Interpretation of Results

2.4. Quality Control

An internal procedural control is included in the test. A coloured line appearing in the control region (C) is the internal procedural control. It confirms sufficient specimen volume and correct procedural technique. Control standards are not supplied with this kit; however, it is recommended that positive and negative controls be tested as a good laboratory practice to confirm the test procedure and to verify proper test performance.

2.5. Maintenance

Store as packaged in the sealed pouch at room temperature or refrigerated (2°C – 30°C) until use.

3. References

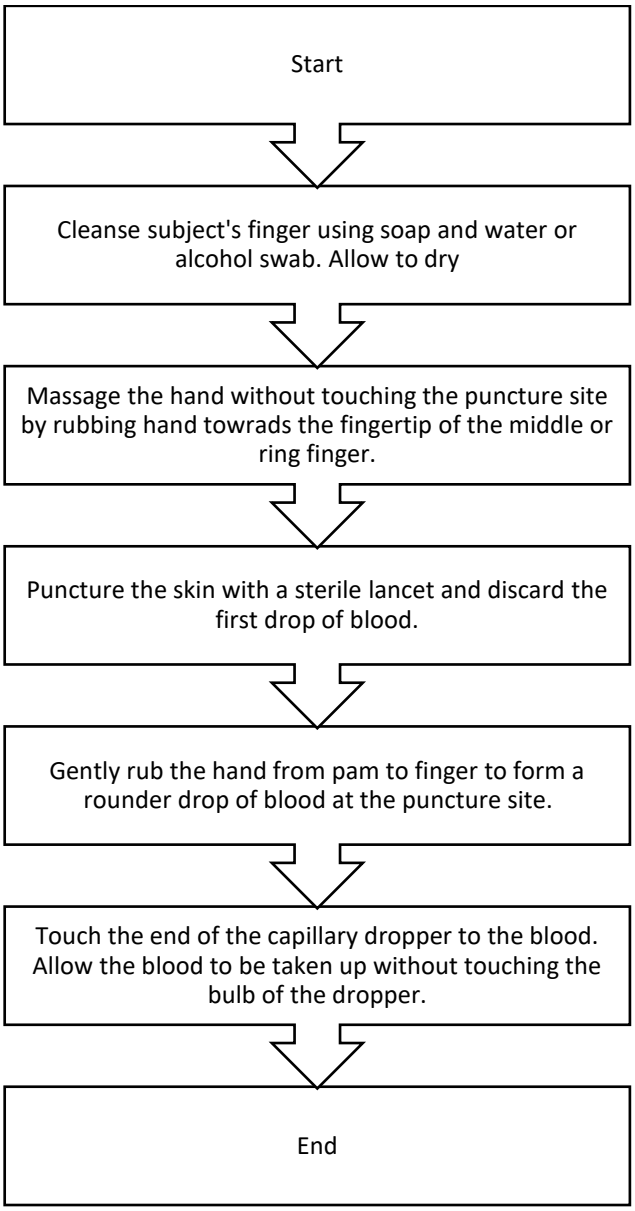
3.1. Merck Manual of Diagnosis and Therapy, Thyroid gland disorders.
3.2. The American Heritage Dictionary of the English Language, Fourth Edition. Houghton Mifflin Company. 2006. ISBN 0-395-82517-2.
3.3. Sacher R, Richard A. McPherson (2000). Widmann's Clinical Interpretation of Laboratory Tests, 11th ed. F.A. Davis Company. ISBN 0-8036-0270-7.
3.4. So, M; MacIsaac, RJ; Grossmann M (August 2012). "Hypothyroidism". Australian Family Physician 41 (8): 556–62.
3.5. Surkset. al., JAMA 291:228, 2004.
3.6. Daniel, GH, Martin, JB, Neuroendocrine Regulation and Diseases of the Anterior Pituitary and Hypothalamus in Wilson, JD, Braunwald, E., Isselbacher, KJ, et. al., Harrison's Principles of Internal Medicine, 12th Edition, McGraw-Hill, Inc., New York, NY, 1991, p. 1666)

4. List of Appendices/ Worksheets

4.1. Appendix 1: Flow Chart- Specimen Collection and Preparation
4.2. Appendix 2: Flow Chart- Performing a Test
4.3. Appendix 3: Limitations and Performance Characteristics

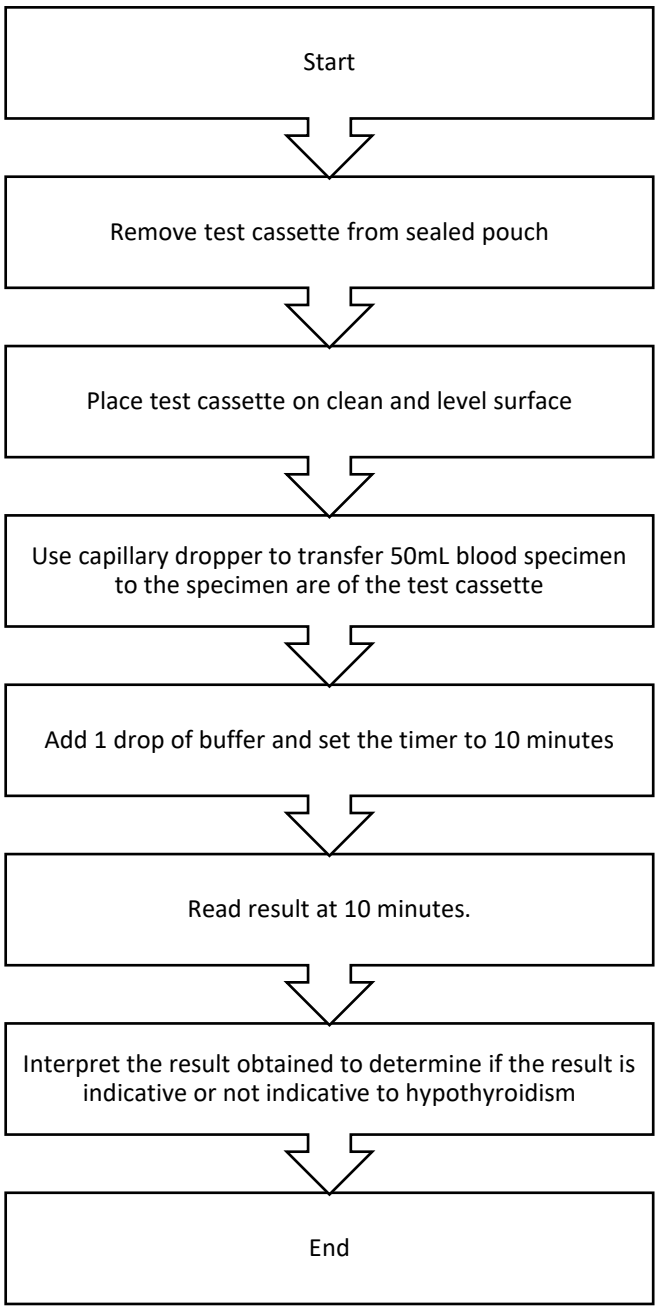
Appendix 1: Flow Chart- Specimen Collection and Preparation

FLOW CHART – SPECIMEN COLLECTION AND PREPERATION



Appendix 2: Flow Chart- Performing a Test

FLOW CHART – SPECIMEN COLLECTION AND PREPERATION



Appendix 3: Limitations and Performance Characteristics

LIMITATIONS

- The TSH Rapid Test Cassette (Whole Blood/Serum/Plasma) is for in vitro diagnostic use only. The test should be used for the detection of TSH in whole blood, serum or plasma specimens only. Neither the quantitative value nor the rate of increase in TSH concentration can be determined by this qualitative test.
- The TSH Rapid Test Cassette (Whole Blood/Serum/Plasma) is only for screening the primary hypothyroidism of adult population, not for neonates.
- As with all diagnostic tests, all results must be interpreted together with other clinical information available to the physician.
- A positive test must be confirmed using a quantitative laboratory TSH assay.
- False positive results can occur due to heterophilic (unusual) antibodies. In certain clinical conditions such as central hypothyroidism, TSH levels may be normal/ low, despite hypothyroidism.
- For Central/ Secondary Hypothyroidism, TSH is not a reliable biomarker, which occurs in 1 out of 1,000 Hypothyroidism cases

PERFORMACE CHARACTERISTICS

Accuracy

The TSH Rapid Test Cassette (Whole Blood/Serum/Plasma) has been evaluated with elevated TSH and normal TSH specimens. A commercially available TSH ELISA kit served as the reference method for the TSH Rapid Test Cassette (Whole Blood/Serum/Plasma). The specimen was considered positive if the result of ELISA was> 5 µlU/mL. The specimen was considered negative if the result of ELISA was <5 µlU/mL. The result shows that the sensitivity of the TSH Rapid Test Cassette (Whole Blood/Serum/Plasma) is 98.1% and the specificity is 98.2% relative to ELISA.

Method		**ELISA**		**Total Results**
TSH Rapid Test Cassette	**Results**	Positive	Negative	
	Positive	53	3	56
	Negative	1	163	164
Total Results		54	166	220

Sensitivity and Cross- reactivity

The TSH Rapid Test Cassette detects TSH at a concentration of 5 µlU/mL. The addition of LH (500 mIU/mL), FSH (2,000 mIU/mL), and 200,000 mIU/mL hCG to negative (0 µlU/mL TSH) and positive (5 µlU/mL TSH) specimens showed no cross-reactivity.

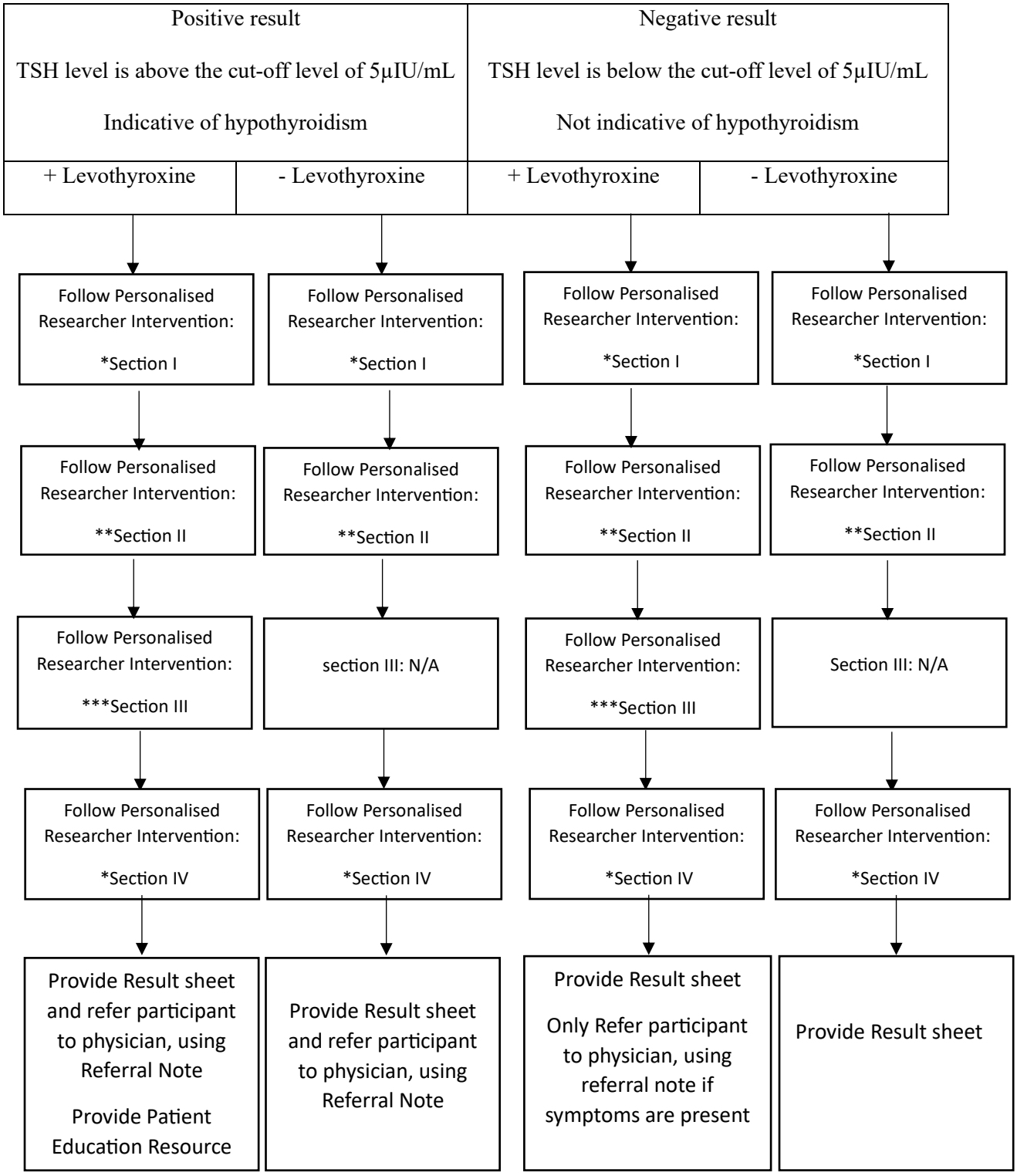
Intra-Assay Precision

Within-run precision has been determined by using 10 replicates of four specimens: 0 µlU/mL TSH, 5 µlU/mL TSH, 10 µlU/mL TSH, 50 µlU/mL TSH. The negative and positive values were correctly identified >99% of the time

Inter-Assay Precision

Between-run precision has been determined by 10 independent assays on the same four specimens: 0 µlU/mL TSH, 5 µlU/mL TSH, 10 µlU/mL TSH, 50 µlU/mL TSH. Three different lots of the TSH Rapid Test Cassette (Whole Blood/Serum/Plasma) have been tested. The specimens were correctly identified >99% of the time.

Action Plan


Positive result
TSH level is above the cut-off level of 5µIU/mL
Indicative of hypothyroidism
Negative result
TSH level is below the cut-off level of 5µIU/mL
Not indicative of hypothyroidism
+ Levothyroxine
- Levothyroxine
+ Levothyroxine
- Levothyroxine
Follow Personalised Researcher Intervention: *Section I
Follow Personalised Researcher Intervention: *Section I
Follow Personalised Researcher Intervention: *Section I
Follow Personalised Researcher Intervention: *Section I
Follow Personalised Researcher Intervention: **Section II
Follow Personalised Researcher Intervention: **Section II
Follow Personalised Researcher Intervention: **Section II
Follow Personalised Researcher Intervention: **Section II
Follow Personalised Researcher Intervention: ***Section III
section III: N/A
Follow Personalised Researcher Intervention: ***Section III
Section III: N/A
Follow Personalised Researcher Intervention: *Section IV
Follow Personalised Researcher Intervention: *Section IV
Follow Personalised Researcher Intervention: *Section IV
Follow Personalised Researcher Intervention: *Section IV
Provide Result sheet and refer participant to physician, using Referral Note
Provide Patient Education Resource
Provide Result sheet and refer participant to physician, using Referral Note
Provide Result sheet
Only Refer participant to physician, using referral note if symptoms are present
Provide Result sheet

Personalised Researcher Intervention:

***Section I of the Data Collection Tool captures data for modifiable and non-modifiable risk factors for hypothyroidism.**

1. Overweight or obese: Counsel participant on following a healthy balanced diet high in protein, eat small and frequent meals, conduct physical exercise and consult a dietician (Atif et al., 2020; Meier et al., 2021; Supsongserm et al., 2023; Schermerhorn et al., 2024)
2. Current Smoker: Promote smoking cessation and inform participant about nicotine replacement therapies such as patches (as per table 1), sprays (as per table 2) and gums (as per table 3) (Condinho et al., 2021; Lertsinudom et al., 2021; Thomas et al., 2023)

Table 1: Nicotine-replacement Patches

PATCHES	1-5 weeks	6-10 weeks	11-12 weeks
Heavy smokers: more than 20 cigarettes per day	STEP 1 25MG	STEP 2 15MG	STEP 3 10MG
Light smokers: 20 or less cigarettes per day	STEP 2 15MG	STEP 3 10MG	STEP 3 10MG

Adapted from: Electronic medicine Compendium (EMC). Nicorette Invisi 25mg Patch [Internet]. EMC; 2024 [cited 2024 Sept 12]. Available from: https://www.medicines.org.uk/emc/product/6435/smpc#about-medicine

Table 2: Nicotine-replacement Spray

SPRAY
1-2 sprays when you would normally want to smoke
Do not use more than 2 sprays at a time
Do not use more than 4 sprays per hour
The maximum is 64 sprays in any 24-hour period

Adapted from: Electronic medicine Compendium (EMC). Nicorette QuickMist 1mg/spray mouth spray [Internet]. EMC; 2024 [cited 2024 Sept 12]. Available from: https://www.medicines.org.uk/emc/product/5956/smpc#about-medicine

Table 3: Nicotine-replacement Gum

Number of cigarettes you smoke per day	Dose of Gums
Heavy smokers: more than 20 cigarettes per day	One 4mg gum as required to relieve cravings.
Light smokers: 20 or less cigarettes per day	One 2mg gum as required to relieve cravings
Chew one gum each time you want to smoke	

Adapted from: Electronic medicine Compendium (EMC). Nicorette 2mg Gum [Internet]. EMC; 2024 [cited 2024 Sept 12]. Available from: https://www.medicines.org.uk/emc/product/1089/smpc#about-medicine

****Section II of the Data Collection Tool captures data of participants' Health Status.**

(Negative Result Only)

1. Two or more Symptoms identified in Data Collection Tool:
    a. Negative result (not indicative of hypothyroidism):
        i. Taking Levothyroxine: Counsel participant that persistence of residual symptoms associated with hypothyroidism is reported in studies and may happen. (Freeman et al., 2019). Provide the Patient Education Resource to the participant to make sure they are taking the levothyroxine dose properly and optimize current treatment. Suggest referral to physician.
        ii. Not taking levothyroxine: Suggest referral to physician if symptoms persist for 1 week as symptoms might be due to other medical causes. Suggest referral to physician immediately if symptoms worsen.

(Conduct this section for all participants)

2. Co-morbidities identified in Data Collection Tool:
    a. Negative result (not indicative of hypothyroidism): Suggest participant that it is important to check thyroid function tests every year

3. Participant had a procedure involving the head and/or neck region:
    a. Negative result (not indicative of hypothyroidism): Suggest participant that it is important to check thyroid function tests every year
4. First-degree relatives who have hypothyroidism:
    a. Negative result (not indicative of hypothyroidism): Suggest participant that it is important to check thyroid function tests every year

*****Section III of the Data Collection Tool captures data of participants' medication history and medication management**

1. Lack of knowledge on levothyroxine: Provide participant with Patient Education Resource
2. Feels the need for more information on levothyroxine: Provide participant with Patient Education Resource

*****Section IV of the Data Collection Tool captures data of participants' knowledge on thyroid testing**

1. Suggest participant that it is important to check thyroid function tests every year due to levothyroxine or medication/s which may affect thyroid function

REFERENCES

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Condinho M, Ramalhinho I, Sinogas C. Smoking Cessation at the Community Pharmacy: Determinants of Success from a Real-Life Practice. Pharmacy. 2021;9(3):143. doi: 10.3390/pharmacy9030143

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Meier M, Singh RL, Thyagarajan B. Consumer's Opinion on a Pharmacist's Role in Nutritional Counseling. Innov;12(2): 1-9. doi: 10.24926/iip.v12i2.3634.

Lertsinudom S, Kaewketthong P, Chankaew T, Chinwong D, Chinwong S. Smoking Cessation Services by Community Pharmacists: Real-World Practice in Thailand. Int J Environ Res Public Health. 2021;12;18(22):1-12. doi: 10.3390/ijerph182211890.

Schermerhorn S, Aurora J Jr, McElligott M, Siegel RD. Implementation of a pharmacist-led weight loss service to improve medication access and weight loss. J Am Pharm Assoc. 2024:102085. doi: 10.1016/j.japh.2024.102085.

Supsongserm P, Thin SM, Nerapusee O, Sorofman BA, Watcharadamrongkun S, Kittisopee T. Factors contributing to pharmacists' intention to provide weight management service in community pharmacy settings: A systematic review. *Pharmacy Practice : Official Journal of the GRIPP (Global Research Institute of Pharmacy Practice)*. 2023; *21*(2): 1–19. https://doi.org/10.18549/PharmPract.2023.2.2790

Thomas T, Sykes B, Shah S, Corlett S. Pharmacist prescriber smoking cessation intervention during the COVID-19 pandemic. Tobacco Induced Diseases. 2023; 21:142. doi:10.18332/tid/170580.

Patient Education Resource (English)

Hypothyroidism

Hypothyroidism can be controlled by taking levothyroxine. Levothyroxine replaces thyroxine hormone if your thyroid gland cannot produce it. Levothyroxine dose is specifically calculated for you, by your physician. It is very important to take the medicine in the correct way, to be absorbed well in the body and produce a beneficial effect.

How to Take levothyroxine

- Take once a day in the morning, Swallow the tablets whole with water.
- Take 30 minutes before having breakfast or a drink containing caffeine, like tea or coffee.
- Take at least 4 hours apart from calcium, iron multivitamins and other medication.*

*Check with your pharmacist

If you forget to take Levothyroxine

- Take it as soon as you remember, unless it's almost time for your next dose.
- Do not take 2 doses together to make up for a missed dose.
- If you often forget doses, it may help to set an alarm to remind you.

If you take too much Levothyroxine

Taking more than your prescribed dose of levothyroxine can give you symptoms such as a racing heartbeat (palpitations).

Speak to your physician or pharmacist before stopping or adjusting dose of levothyroxine

Speak to your physician or pharmacist if

- You experience side effects such as palpitations, tremor, insomnia,diarrhoea
- You gain or lose a lot of weight
- You have switched to a different brand of levothyroxine and start to get symptoms
- You start new medications or supplements
- You are planning a pregnancy, are pregnant or breastfeeding

Check Thyroid Function Blood tests

- Every 3 months after initiation or change in dose
- Every 6 months to 1 year or as advised by your physician

Pharmacist-Led Thyroid Point-of-Care Testing

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Mariah Vella
B.Sc Pharm Sci (Hons), M.Pharm
Doctorate in Pharmacy Dissertation

References

1. National Health Service (NHS. Levothyroxine [Internet].NHS; 2024 [Cited 2024 Sept 14]. Available from: https://www.nhs.uk/medicines/levothyroxine/
2. Chaker L, Razvi S, Bensenor IM, Azizi F, Pearce EN, Peeters RP. Hypothyroidism. Nat Rev Dis Primers. 2022; 8(30): 1-17. https://doi.org/10.1038/s41572-022-00357-7

Patient Education Resource (Maltese)

Ipotirojdiżmu

L-ipotirojdiżmu jista' jiġi kkontrollat billi jittieħed il-levothyroxine. Il-Levothyroxine jissostitwixxi l-ormon tat-thyroxine jekk il-glandola tat-tirojde tiegħek ma tistax tipproduċih. Id-doża ta' Levothyroxine hija kkalkulata speċifikament għalik, mit-tabib/a tiegħek. Huwa importanti ħafna li tieħu l-mediċina bil-mod korrett, biex tiġi assorbita sew fil-ġisem u tipproduċi effett ta 'beneficċju.

Kif tieħu il-levothyroxine

- Ħu darba kuljum filgħodu, Ibla' l-pillola sħieħa bl-ilma.
- Ħu 30 minuta qabel ma tieħu l-kolazzjon jew xarba li fiha l-kaffeina, bħal tè jew kafè.
- Ħu mill-inqas 4 sigħat apparti mill-kalċju, multivitamini tal-ħadid u medikazzjoni oħra.*

*iċċekkja mal-ispiżjar/a tiegħek

Jekk tinsa tieħu il-Levothyroxine

- Ħudha malli tiftakar, sakemm ma jkunx kważi l-ħin għad-doża li jmiss.
- Tiħux 2 doži flimkien biex tpatti għal doża li tkun insejt tieħu.
- Jekk ta' spiss tinsa d-doži, jista' jgħin li tissettja allarm biex ifakrek.

Jekk tieħu wisq Levothyroxine

Jekk tieħu aktar mid-doża preskritta tiegħek ta' levothyroxine jista' jagħtik sintomi bħal taħbit tal-qalb qawwi (palpitazzjonijiet).

Kellem lit-tabib/a jew lill-ispiżjar/a tiegħek qabel ma twaqqaf jew taġġusta d-doża ta' levothyroxine

Kellem lit-tabib/a jew lill-ispiżjar/a tiegħek jekk

- Tesperjenza effetti sekondarji bħal palpitazzjonijiet, roghda, nuqqas ta' rqad, dijarea
- Iżżid jew titlef ħafna piż
- Qlibt għal marka differenti ta' levothyroxine u beda ikollok sintomi
- Tibda mediċini jew supplimenti ġodda
- Qed tippjana tqala, inti tqila jew qed tredda'

Iċċekkja l-Funzjoni tat-Tirojde b'testijiet tad-demm

- Kull 3 xhur wara l-bidu jew il-bidla fid-doża
- Kull 6 xhur sa sena jew skond il-parir tat-tabib/a tiegħek

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Referenzi

1. National Health Service (NHS. Levothyroxine [Internet].NHS; 2024 [Cited 2024 Sept 14]. Available from: https://www.nhs.uk/medicines/levothyroxine/
2. Chaker L, Razvi S, Bensenor IM, Azizi F, Pearce EN, Peeters RP. Hypothyroidism. Nat Rev Dis Primers. 2022; 8(30): 1-17. https://doi.org/10.1038/s41572-022-00357-7

Physician Referral Note

Point of Care Test: TSH rapid test cassette (Acro Biotech, Inc.)- Qualitative Lot No: _____

Date of Point of Care Test: _____

Test Result: **Positive**

TSH Level	
Serum TSH	µlU/mL
Positive	> 5 µlU/mL
Negative	< 5 µlU/mL

Reason for Referral:

Dear Doctor,

During a recent visit to the community pharmacy, the patient underwent a point-of-care TSH test, which returned a positive result suggestive of hypothyroidism. Recognising the limitations of this single parameter in fully assessing the patient's thyroid function, we would greatly value your expert assessment.

Patient information:

- ☐ Older than 35 years and/or is overweight and/or smokes.
- ☐ Has symptoms suggestive of hypothyroidism.
- ☐ Has co-morbidities which may be linked to hypothyroidism.
- ☐ Had procedures or received radiation in the head neck region.
- ☐ Has first-degree relatives who have hypothyroidism.
- ☐ Takes medication which may alter thyroid function tests.

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Physician Referral Note

Point of Care Test: TSH rapid test cassette (Acro Biotech, Inc.)- Qualitative Lot No: _____

Date of Point of Care Test: _____

Test Result:
NEGATIVE

TSH Level	
Serum TSH	µlU/mL
Positive	> 5 µlU/mL
Negative	< 5 µlU/mL

Reason for Referral:

Dear Doctor,

During a recent visit to the community pharmacy, the patient underwent a point-of-care TSH test, which returned a negative result. However, the patient has symptoms suggestive of hypothyroidism. Recognising the limitations of this single parameter in fully assessing the patient's thyroid function, we would greatly value your expert assessment.

Patient information:

- ☐ Older than 35 years and/or is overweight and/or smokes.
- ☐ Has symptoms suggestive of hypothyroidism.
- ☐ Has co-morbidities which may be linked to hypothyroidism.
- ☐ Had procedures or received radiation in the head neck region.
- ☐ Has first-degree relatives who have hypothyroidism.
- ☐ Takes medication which may alter thyroid function tests.

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Patient Result Sheet

Point of Care Test: TSH rapid test cassette (Acro Biotech, Inc.)- Qualitative Lot No: _____

Date of Point of Care Test: _____

Test Result

Positive ☐

Negative ☐

TSH Level	
Serum TSH	µlU/mL.
Positive	> 5 µlU/mL
Negative	< 5 µlU/mL

Comments:

☐ Positive: Indicative of hypothyroidism

☐ Negative: Not indicative of hypothyroidism

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Appendix 3: Acro Biotech, Inc. TSH rapid test cassette (Serum/Plasma/Whole Blood) EC Declaration of Conformity

ACRO BIOTECH, INC

EC Declaration of Conformity

Manufacturer:
Name: Acro Biotech, Inc.
Address: 9500, 7th str., Unit M, Rancho Cucamonga, CA 91730, USA

European Representative:
Name: MedNet GmbH
Address: Borkstrasse 10, 48163 Muenster, Germany

Product Name: See attachment 1
Model: See attachment 1
Classification: Other Device of IVDD 98/79/EC
Conformity Assessment Route: IVDD 98/79/EC Annex III (excluding point 6)
EDMA Code: See attachment 1

We herewith declare that the above mentioned products meet the transposition into national law, the provisions of the following EC Council Directives and Standards. All supporting documentations are retained under the premises of the manufacturer.

DIRECTIVES

General applicable directives:

DIRECTIVE 98/79/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 27 October 1998 on in vitro diagnostic medical devices

Standard Applied: EN ISO 13485:2016, EN ISO 14971:2012, EN 13975:2003, EN ISO 18113-1:2011, EN ISO 18113-2:2011, EN 13612:2002/AC:2002, EN ISO 17511:2003, EN ISO 23640:2015, EN 13641:2002, EN ISO 15223-1:2016

Place, Date of Issue: in Rancho Cucamonga on 24/05/2019

Signature: _____ ACRO BIOTECH, INC
Name: Joseph Fan
Position: President

ACRO BIOTECH, Inc.
9500 Seventh Street,
Unit M, Rancho Cucamonga, CA 91730, U.S.A.
Tel: +1 (909) 466-6892 info@acrobiotech.com
www.acrobiotech.com

OTS-402	TSH Rapid Test Cassette	12 70 01 90 00	WB/S/P	Cassette

Appendix 4: Dissemination of Results

UMRE Poster Presentation

L-Università ta' Malta | Research Expo 2025

Mariah Vella
Department of Pharmacy

Pharmacist-led thyroid point-of-care testing

Project brief

Pharmacist-led point-of-care testing (POCT) enhances clinical services in primary care by facilitating timely patient management and referrals. Hypothyroidism, a prevalent yet frequently underdiagnosed or undertreated condition, necessitates regular monitoring to achieve optimal care. Integrating thyroid POCT into pharmacy practice presents an opportunity to enhance early detection and long-term disease management, underscoring the value of developing a novel pharmacist-led service.
The aim of the study was to develop and evaluate a pharmacist-led thyroid POCT framework within a community pharmacy setting.

Methodology

The study comprised three phases (Figure 1):

i) Validating a thyroid POCT device by comparing it to a laboratory-based method.

ii) Developing a framework for pharmacist-led thyroid POCT.

iii) Feasibility testing of the framework in a community pharmacy. *Inclusion criteria:* Taking levothyroxine or medication which may alter Thyroid Stimulating Hormone (TSH) levels. *Exclusion criteria:* Had thyroid function testing within the preceding six months, experiencing an acute illness, pregnant or breastfeeding at time of recruitment.

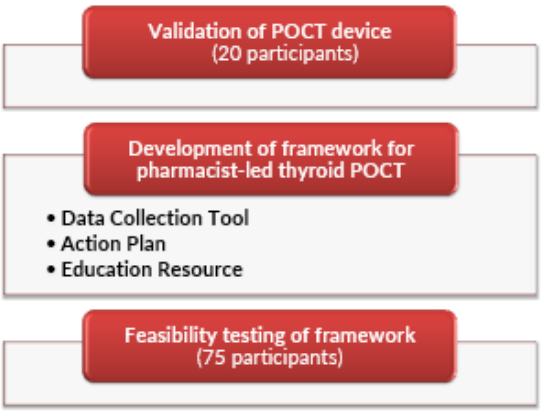

Figure 1: Flowchart of study design

Table 1: POCT vs. laboratory results (N=20)

POCT result	Laboratory result	Number of participants
Negative	Negative	17
Positive	Positive	2
Positive	Negative	1

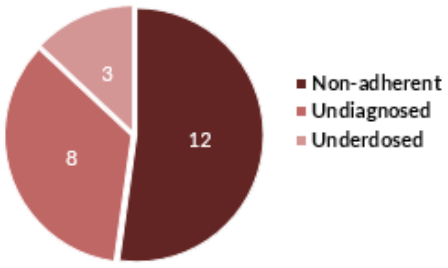

Figure 2: Participants with positive TSH result (≥5 µIU/mL) (n=23)

Results & Conclusions

The qualitative AcroBiotech Inc. TSH Rapid Test Cassette, with a sensitivity of 5µlU/ml and a testing time of 10 minutes, was selected following appraisal of available POCT devices.
Concordance between the POCT device and laboratory-based method was 95% (κ=0.773) (Table 1).
The developed framework consists of a data collection tool which examines risk factors associated with hypothyroidism and medication management, action plan to provide personalised patient advice, and a patient information leaflet on hypothyroidism.
From the 75 participants assessed, 57 required pharmacist intervention and 23 were identified to have hypothyroidism (Figure 2).

This study identifies a clinically reliable POCT device and presents a validated pharmacist-led thyroid POCT framework, facilitating early detection of hypothyroidism, addressing education gaps and offering appropriate referral within a collaborative care model.

Financial support: University of Malta Research Grant (PHRRP12); Brown's Pharma Ltd

Abstract submission accepted for oral communication at the 53rd ESCP Symposium on Clinical Pharmacy "From Interprofessional education to interprofessional practice" Grenoble, France, 26 – 28 November 2025

Pharmacist-led Thyroid Point-of-Care Testing in Community Pharmacy

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Department of Pharmacy, University of Malta, Msida, Malta

Background

Early detection of hypothyroidism through point-of-care testing (POCT) is relevant for high-risk individuals and those previously diagnosed who may remain uncontrolled due to inadequate adherence or sub-optimal dosing. Establishing pharmacist-led thyroid POCT enables timely screening and ongoing monitoring of hypothyroidism.

Aim

To develop a framework for pharmacist-led thyroid POCT and assess feasibility of implementation in a community pharmacy setting.

Method

The qualitative Thyroid Stimulating Hormone (TSH) Rapid Test Cassette (AcroBiotech) (sensitivity 5µlU/ml, time for result 10 minutes) was selected. For validation of the POCT kit, POCT results were compared to laboratory-based results for 20 participants recruited by convenience sampling. A framework for pharmacist-led thyroid POCT was developed, validated by an expert panel, and tested for feasibility in 75 participants, recruited from a community pharmacy, taking levothyroxine or medication/s which may affect thyroid function. Descriptive statistics were performed ($p<0.05$).

Results

Validation of the POCT revealed 95% concordance with laboratory-based results (Cohen's kappa=0.773). The framework includes a data collection tool (hypothyroidism risk factors, health status, medication intake, levothyroxine use, knowledge on thyroid testing), an action plan (standardises patient advice according to test result), and a patient education resource (information about hypothyroidism). In the feasibility testing (N=75, female n=57, mode age range 45-54 years n=24), participants were taking levothyroxine (n=45) or medication/s that may affect thyroid function (n=30). Twenty-three participants (31%) who had a positive result (TSH ≥5 μIU/mL) indicative of hypothyroidism were referred to a physician: 15 were being treated for hypothyroidism, indicating either incorrect use of levothyroxine (n=12) or sub-optimal dosing (n=3), and 8 were taking medication which may affect thyroid function. For participants identified as using levothyroxine incorrectly during application of the data collection tool (n=36), there was an association with TSH ≥5μIU/mL and symptoms of hypothyroidism ($p<0.05$).

Conclusion

This study proposes a community pharmacy clinical service to support patient screening and monitoring of individuals at risk of hypothyroidism. A limitation of the POCT identified is that only TSH level is measured. Strengths include the use of a validated POCT device which can be applied within a primary care setting and the framework developed. The framework ensures standardised pharmacist service and supports pharmacist training in the deployment of the service in other community pharmacies.