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MONASH HEALTHCARE INNOVATION SUMMER SCHOLARSHIPS

Project Pluto

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Research, Monash Health**

Executive Summary

Klinefelter's Syndrome is a group of chromosomal disorders characterized by the presence of at least one additional X chromosome [1], with a prevalence of 150 patients per 100,000 males on average [2,3,4]. The symptoms of the disorder, such as reduced testicular size, hypogonadism, fertility issues, gynaecomastia, and learning difficulties [3,4], are often unidentifiable, leading to undiagnosis rates of around 50% [2].

Therefore, this project's mission is to formulate a method that will increase the rates of diagnosis for Klinefelter's Syndrome. The lack of public awareness of Klinefelter's Syndrome is a prominent issue that contributes to the high undiagnosis rates. In order to raise awareness effectively, the solution needs to be informative and should provide patients with preliminary first-steps on how to be proactive. Additionally, it should be easily accessible and utilisable for patients. These requirements provide a framework for new alternative solutions to consider.

These new solutions will increase the number of patients diagnosed, so that they can receive the appropriate treatment to live a better quality of life. These treatments include testosterone replacement therapy, which can improve energy levels, sexual function, lean body mass and further benefits related to bone density and cardiovascular risk factors [5,6]. Additionally, diagnosis can also prompt fertility treatment such as a semen analysis [7] or surgical procedures such as microTESE (microdissection testicular sperm extraction [8]). These procedures provide patients with greater chances of fatherhood.

Acceptance Criteria

Top 3 Acceptance Criteria:

1. The solution will effectively initiate the diagnosis process.
2. The solution is less confrontational and can be used by patients alone.
3. The solution can be easily accessed by the user.

Patients exhibit Klinefelter's Syndrome symptoms such as reduced testicular size, infertility, gynecomastia, etc, [3,4] and will decide to visit a clinic to obtain a diagnosis. The initial step for diagnoses is a genital examination in a clinic, which involves a clinician examining a patient's testicles for indication of size and shape, by comparing to an orchidometer. Furthermore, clinicians may additionally prescribe a scrotal ultrasound for further testicular size measurement. From this examination, clinicians may be prompted to obtain blood for a karyotype analysis to confirm the diagnosis.

The pain points with the gold standard aren't directly associated with the current clinic procedures, but rather the lack of patients that visit clinics for check-ups due to:

1. A combination of avoidance and intimidation, associated with genital examinations, as well as the realisation of being diagnosed with a genetic condition.
2. Complete lack of awareness of Klinefelter's Syndrome symptoms.

Existing Solutions

As mentioned above, there are two main methods for testicular volume measurement:

1. Genital examination in the clinic using an orchidometer

Clinicians examine the testicles by making comparisons to an orchidometer - an instrument containing large beads of different volumes (mL).

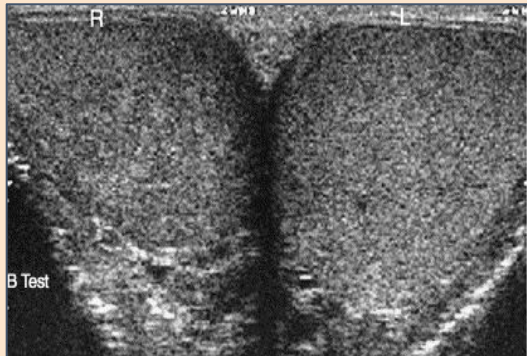
Through this examination, practitioners can identify whether a patient's testicular size is small. Since testicular size is a prominent anatomical indication of Klinefelter's Syndrome, this method can prompt further investigation, such as ultrasounds or karyotypes.

2. Scrotal ultrasound for testicular volume

A testicular ultrasound will scan the extreme at different angles, emitting high-frequency waves directed towards the target anatomy, these waves are reflected, creating an image [9].

If results from genital examinations are insufficient for a conclusion to be made, practitioners may advise a testicular ultrasound to be completed. Ultrasound is less common, however it was used more prominently during COVID when genital examinations were less accessible.

Gaps analysis

Existing solution	1. Genital examination in the clinic using an orchidometer  Figure 1. Genital examination instrument known as an orchidometer [14]	2. Ultrasound for testicular volume  Figure 2. Scrotal ultrasound, image of the testes [15]
Economic profile	According to MBS Item 23, professional attendance by general practitioners cost \$39.75, with 100% benefit from Medicare [10].	According to MBS Item 55048, the fee for scrotal ultrasound is \$113.95. This can be bulk-billed (covered by Medicare) depending on the GP, as well as if the individual meets certain criteria [11,12]
Solution alignment	❖ Solution initiates the diagnosis, which will prompt a karyotype analysis or not. ❖ Practitioners will maintain confidentiality	❖ Solution initiates the diagnosis process, by providing an accurate estimation of testicular volume, which may prompt further review. ❖ Practitioners will maintain confidentiality
Solution gaps	❖ Primary concern is the confrontational aspect of an in-person genital examination. ❖ Many general practitioners don't actually own an orchidometer, and aren't fully equipped to treat KS patients. ❖ Heavy reliance on patients coming into clinics.	❖ Ultrasound cannot be done by individuals on their own, and must be advised by a practitioner ❖ Heavy reliance on patients coming into clinics.

Systems Map

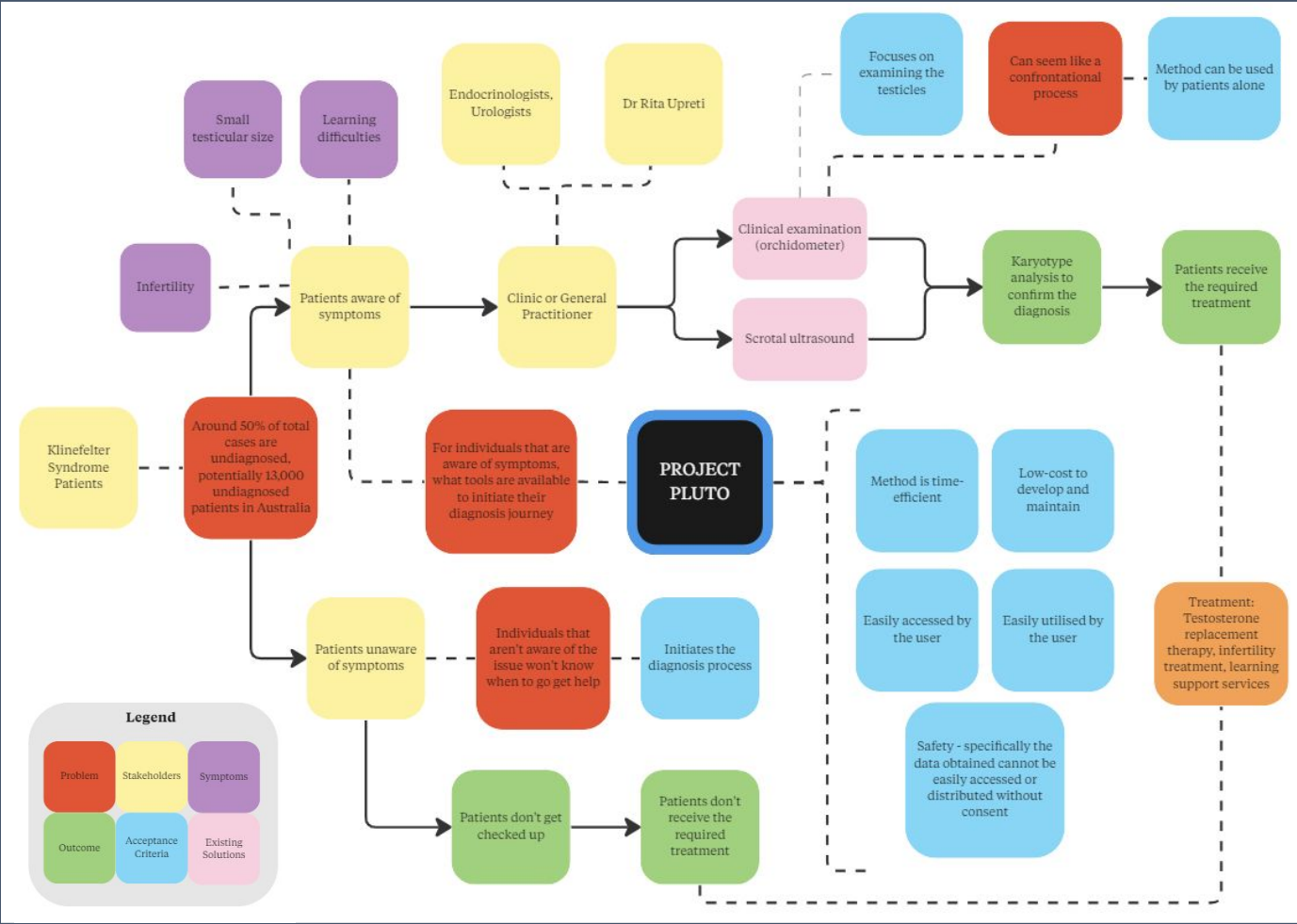


Figure 3. Systems Map

This diagram maps the stakeholders involved and their relation to problems associated with existing solutions. The map also presents an acceptance criteria which provides a framework for potential alternative solutions, targeting the primary problem: that around 50% of total Klinefelter’s Syndrome cases are undiagnosed.

Stakeholder Map

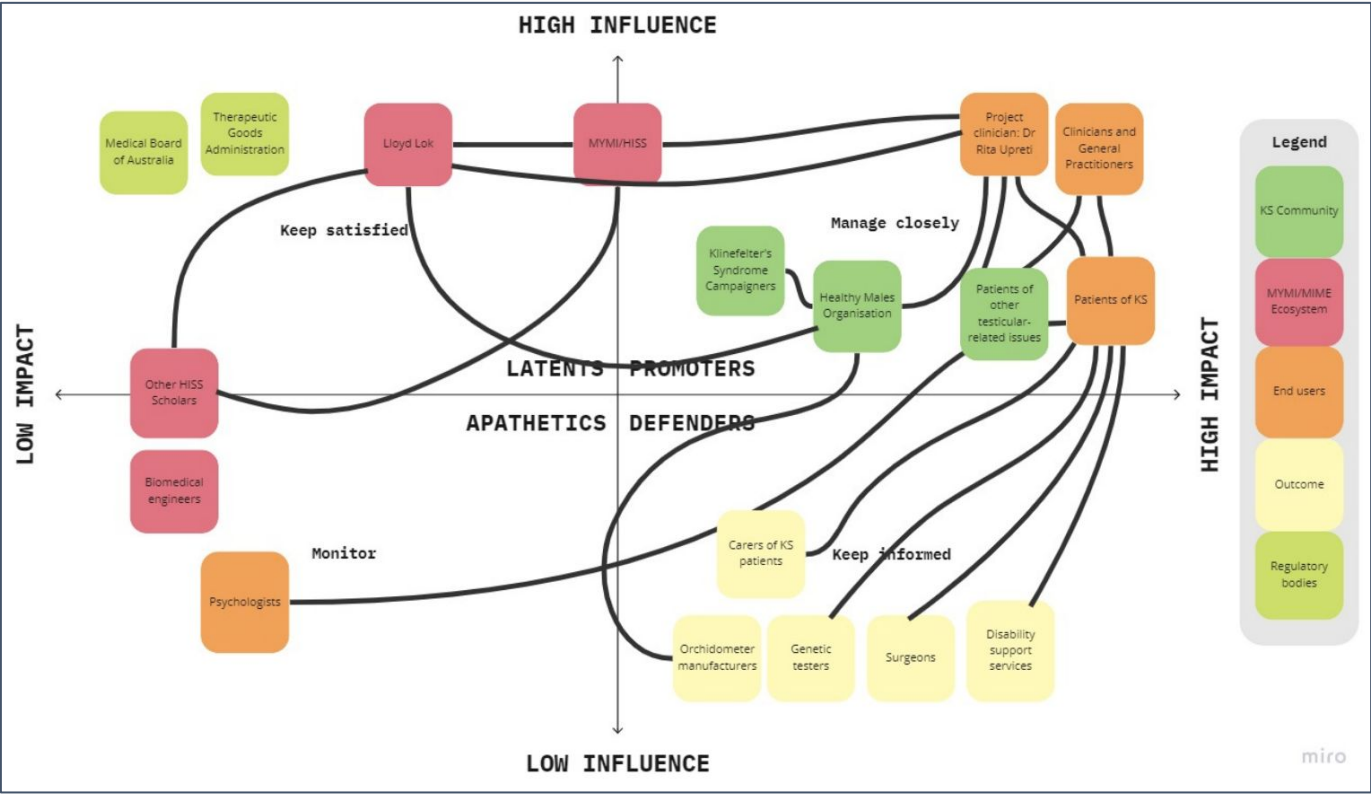


Figure 4. Stakeholder Map

There are many stakeholders involved in the project, which have been grouped into 5 branches: end-users, regulatory bodies, MYMI/MIME ecosystem, Klinefelter’s Syndrome community, and others affected by the outcome. This map summarises the stakeholders involved in this project and their position on a set of axes based on the influence they have on the project and the impact the project has on them. In summary, the largest stakeholders in the project are Klinefelter’s patients, practitioners and clinicians, myself, and existing men’s health awareness organisations.

Outcomes of Qualitative and Quantitative Research

Klinefelter's Syndrome is a group of chromosomal disorders that is characterised by the presence of at least one supernumerary X chromosome [1], with a prevalence of 150 patients per 100,000 males on average [2,3,4], which predicts a potential 25,000 patients in Australia [2]. Around 80-90% of patients have a 47XXY karyotype whilst remaining patients will have more than one supernumerary X chromosome. Although most patients only have one additional chromosome, the severity of phenotypes such as small testicular size, hypogonadism, fertility issues, gynaecomastia, learning difficulties [3,4], correlates with the number of additional X chromosomes [1]. These symptoms are often quite unidentifiable, which has led to underdiagnosis by around 50% [2].

According to andrology clinicians, general practitioners and leaders at Klinefelter's Syndrome awareness organisations, the prominent issue that contributes to the condition's undiagnosis rates is that very few patients visit the clinic. Common themes from interviews suggest that there is a lack of public awareness of Klinefelter's Syndrome.

Awareness has been noted as one of the driving forces of this project. After speaking to the CEO at an awareness organisation, it was recognised that despite repeated campaigns over the past 20 years, the major issue has been the lack of effectiveness due to the constant flow of media which makes it hard for messages to be relayed. Additionally, there were inadequate methods to measure effectiveness of campaigns on increasing Klinefelter's Syndrome diagnosis rates.

In order to effectively raise awareness, the solution can't just be informative but should also provide preliminary first-steps on how to be proactive. According to clinicians and practitioners, some of their current patients admit they were tentative to be examined even when they were aware of potential symptoms. Therefore, the solution should also be very easily utilised and accessible to patients inside and outside of the clinic. These suggested requirements provide a framework that new alternative solutions should consider, also known as the acceptance criteria.

Top Solutions	Pros	Cons
A clinical decision support system that'll ask about some common first symptoms of KS patients, providing a next step response	❖ Could provide definitive response as to whether patients should seek further help. ❖ The support system would be accessible as it would likely be a website.	❖ The inputs required to be entered would likely be information that individuals need from clinicians, which would defeat the purpose of patient independency. ❖ There are potential issues with the storing of patient data on online support systems.
Promotional devices or objects that are oval/egg shape that can be given out so individuals can have an idea whether their testicles are abnormal size.	❖ Could potentially be paired with awareness promotion campaigns. ❖ Great representation of testicular size. ❖ Physical objects would be easily comparable.	❖ Potential cost-effectiveness issues, related to whether the potential effectiveness of promoting these objects is of value.

Final Concept

The final solution is an interactive infographic focusing on self-examination which can be promoted through awareness tools. The infographic will provide essential information on Klinefelter's Syndrome and its symptoms, and provide a method of self-examination that will help prompt further investigation. The solution will be presented in a poster form which can be displayed digitally or on paper. The infographic will provide testicular size indications (that can be cut out), the step-by-step self-examination process, links to videos that provide additional help, QR codes for digital copies or for printing.

To reach men that are unaware, a partnership can be established with existing men's health awareness organisations to promote the solution. Additionally, when this solution is further developed, it can be offered by clinicians in the clinical setting to patients as an alternative method if they are hesitant to do a genital examination. In order to adopt this into clinical workflow, awareness must also be promoted among clinicians and practitioners.

This solution can present risks if individuals treat this as a method of diagnosis, when rather it is a preliminary self-examination tool that can potentially prompt a further examination or diagnosis in the clinic by a practitioner or clinician. Furthermore, this may induce feelings of anxiousness or fear if patients self-examine incorrectly. The derisking strategy to deal with these risks is to provide a clear disclaimer that the information on the infographic will not diagnose patients.

Promoting an interactive infographic is competitively advantageous over existing awareness tools because it offers a proactive solution that doesn't involve individuals immediately visiting the clinic.

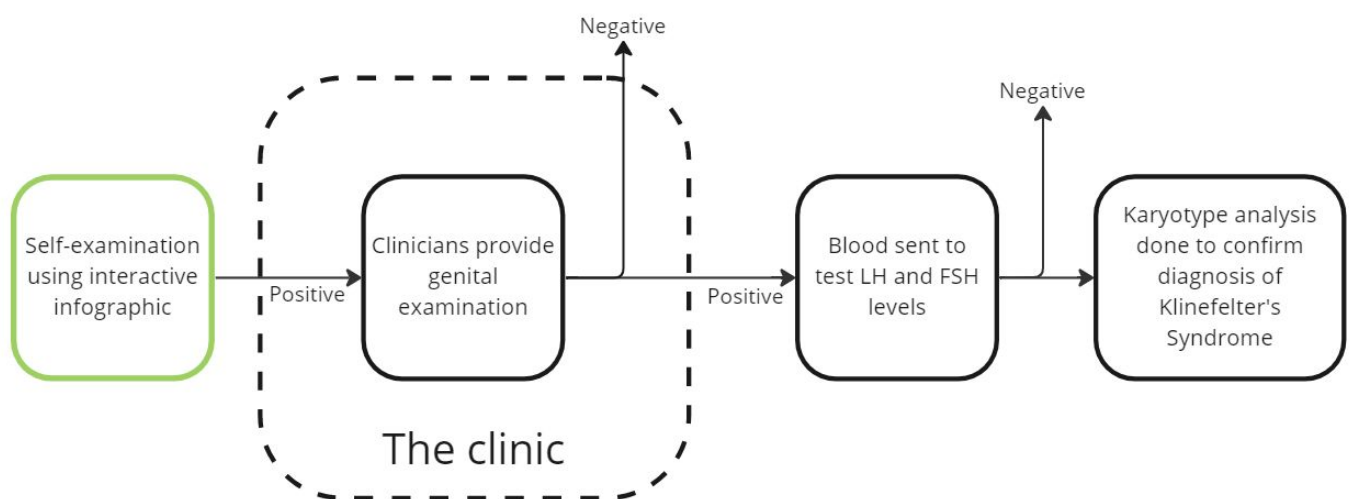


Figure 5. Flowchart of a patient journey, and where the solution is ideally situated.

Since this is an awareness-driven solution, the focus of this project is not revenue-generation as the solution is not a product or service that will be paid for by any entities. If this solution was a paid service, this would only keep awareness at very minimal effectiveness.

The focus is rather on spreading awareness so that there can be early intervention for patients, which will lower costs that patients may have been required to finance, if their condition was to have lead to other complications. Furthermore, early intervention will mean that patients will receive treatment and live better quality lives, becoming more active in increasing the economy

Proposed KPIs

In relation to the Monash Health Key Performance Priorities 2021-2022, the proposed solution will provide:

- ❖ Positive patient experiences, as more individuals will be able to access consultation/physical examinations
- ❖ Timely access to care, as the solution may prompt early intervention so that potential patients can obtain a diagnosis and thus receive the treatment they require.

Furthermore, this project solution can be measured across other performance indicators such as cost effectiveness and accessibility. There will be minimal expenses in producing the infographic as this will be sourced from the team and industry professionals. The only potential expenses could be contributed to through marketing and exposure. Additionally, this awareness tool should be very accessible to the public as it will be in digital form, potential displayed on partnering awareness organisations, as well as being displayed in physical print-out form.

The mission of this project is to increase the rate of diagnosis for Klinefelter's Syndrome patients. To achieve this, the advised solution is to use an infographic to support awareness campaigns, which can increase the number of patient visits at clinics for examinations. Therefore, this solution is neither a product or service and doesn't involve any monetary costs to end-users or clinical entities.

The market reach of this solution has been focused more on the potential target population. The target population of awareness campaigns should ideally target all the men in the world, as this relies on spreading awareness. The reach of this solution can be instead be focused on the population of potential Klinefelter's Syndrome patient as shown in Figure 6.

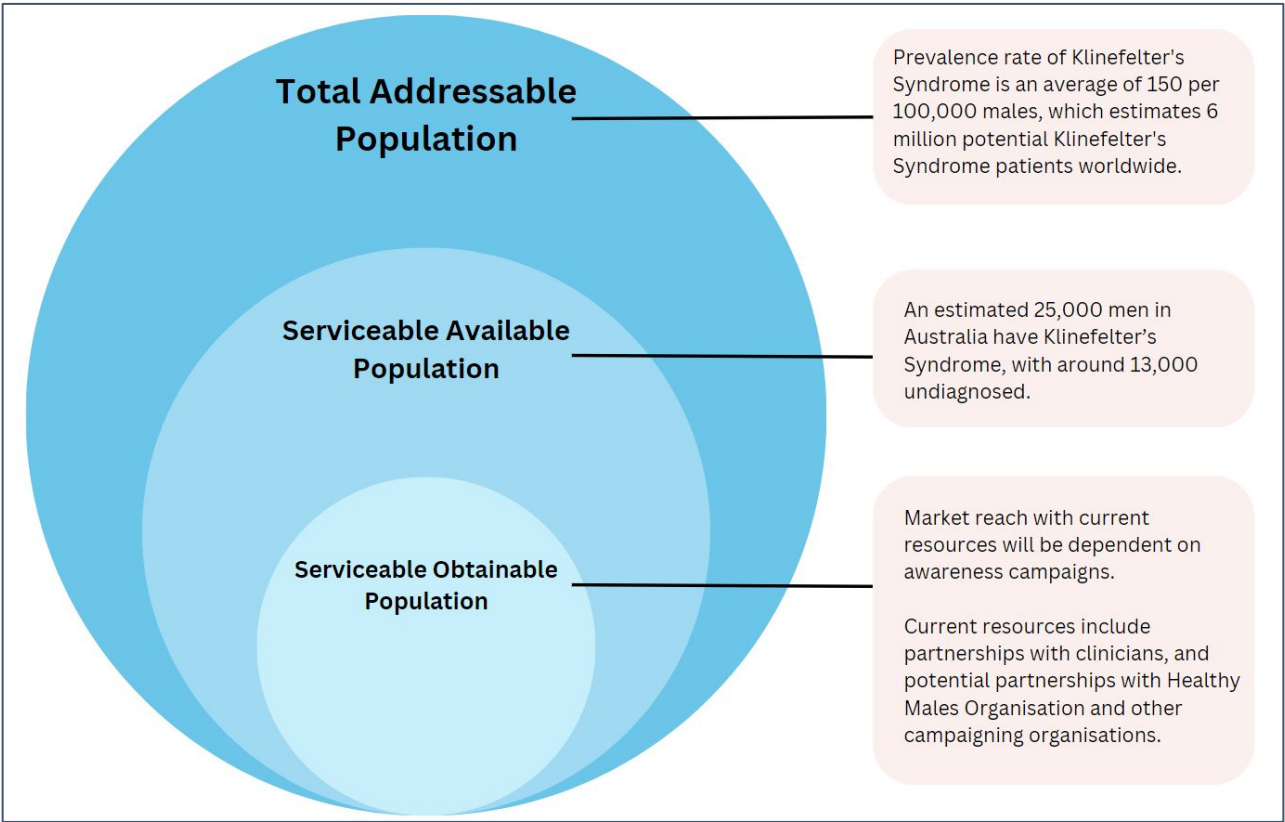


Figure 6. Representation of the Total Addressable Population (TAP), Serviceable Available Population (SAP) and Serviceable Obtainable Population (SOP).

Healthy Males Organisation, and Australian X and Y Spectrum Support, are existing organisations who promote similar solutions. However these organisations are not considered competitors, since we share a mission to raise awareness, and the demise of one organisation would not benefit that mission. Additionally, our campaigning isn't revenue oriented. Therefore these organisations can potentially be used as partners in raising awareness for Klinefelter's Syndrome.

The Team

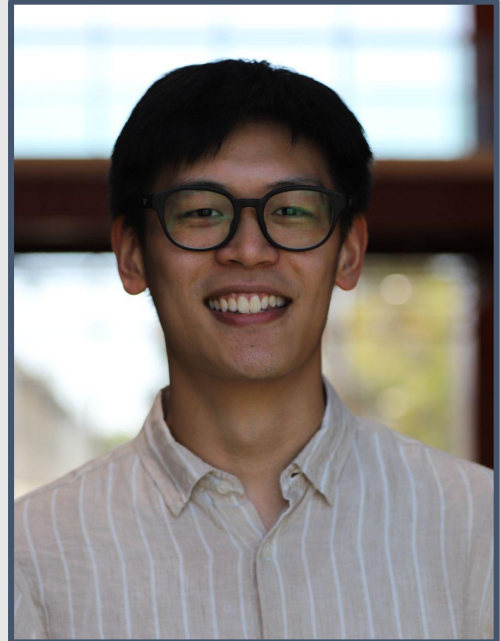


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Clinical Champion

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Our Ask

The team currently consists of Dr Rita Upreti, Project Pluto's Clinical Champion and Lloyd Lok, the Project Lead. Dr Rita Upreti brings first hand experience of the clinical workflow involved in examining patients with Klinefelter's Syndrome, and understands patient journeys to diagnosis, which is valuable for identifying the optimal method to target the population. Lloyd Lok brings a background in Biomedical Engineering, as well as skills in critical thinking and problem evaluation.

The solution will potentially require a UX/UI or graphics designer to focus on the presentation of the awareness tool. Additionally, to assess the effectiveness of the awareness tool, a data analyst is required for interpreting quantitative data to form conclusions on effectiveness of awareness promotion.

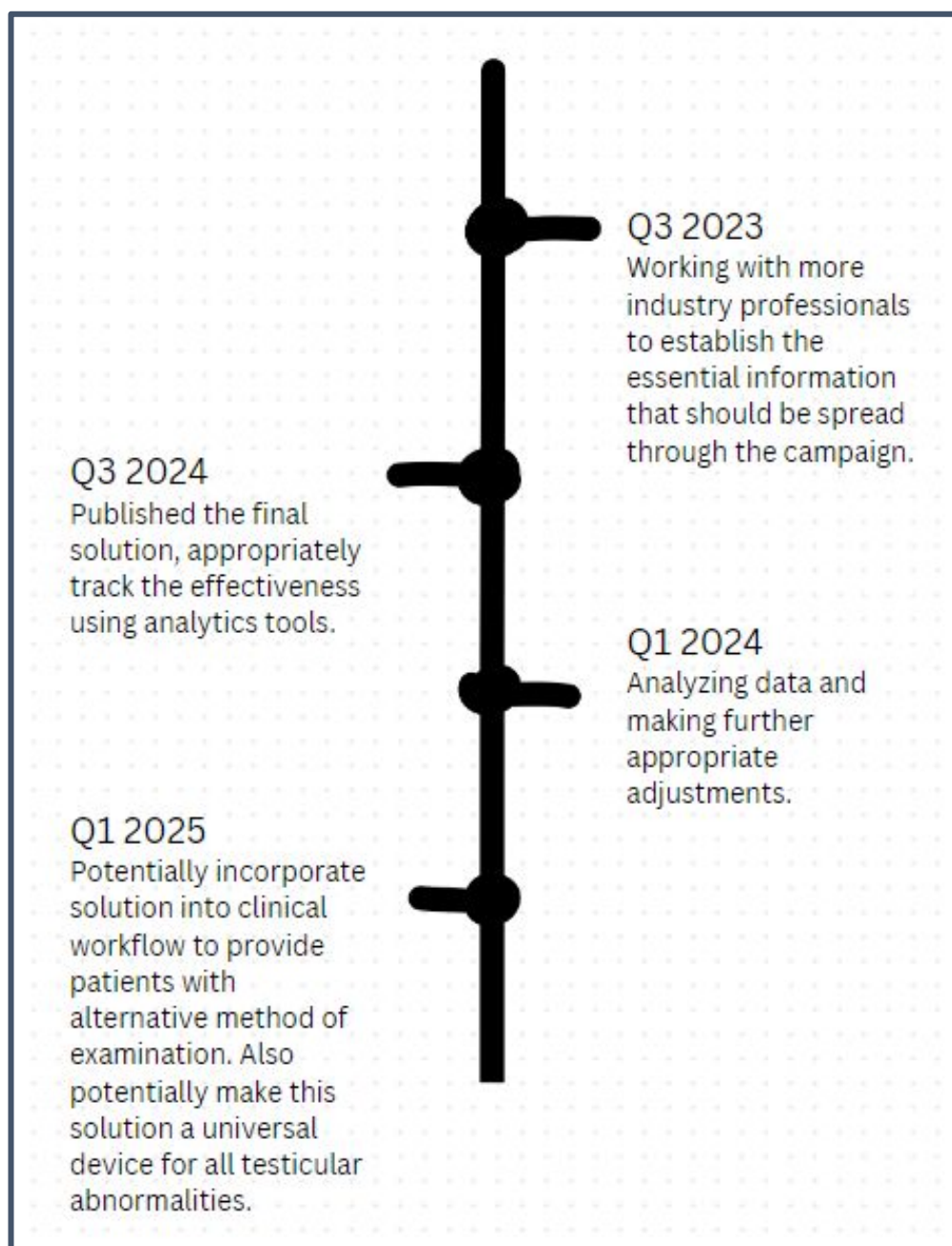


Figure 7. The potential timeline of this project extends to 2025.

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