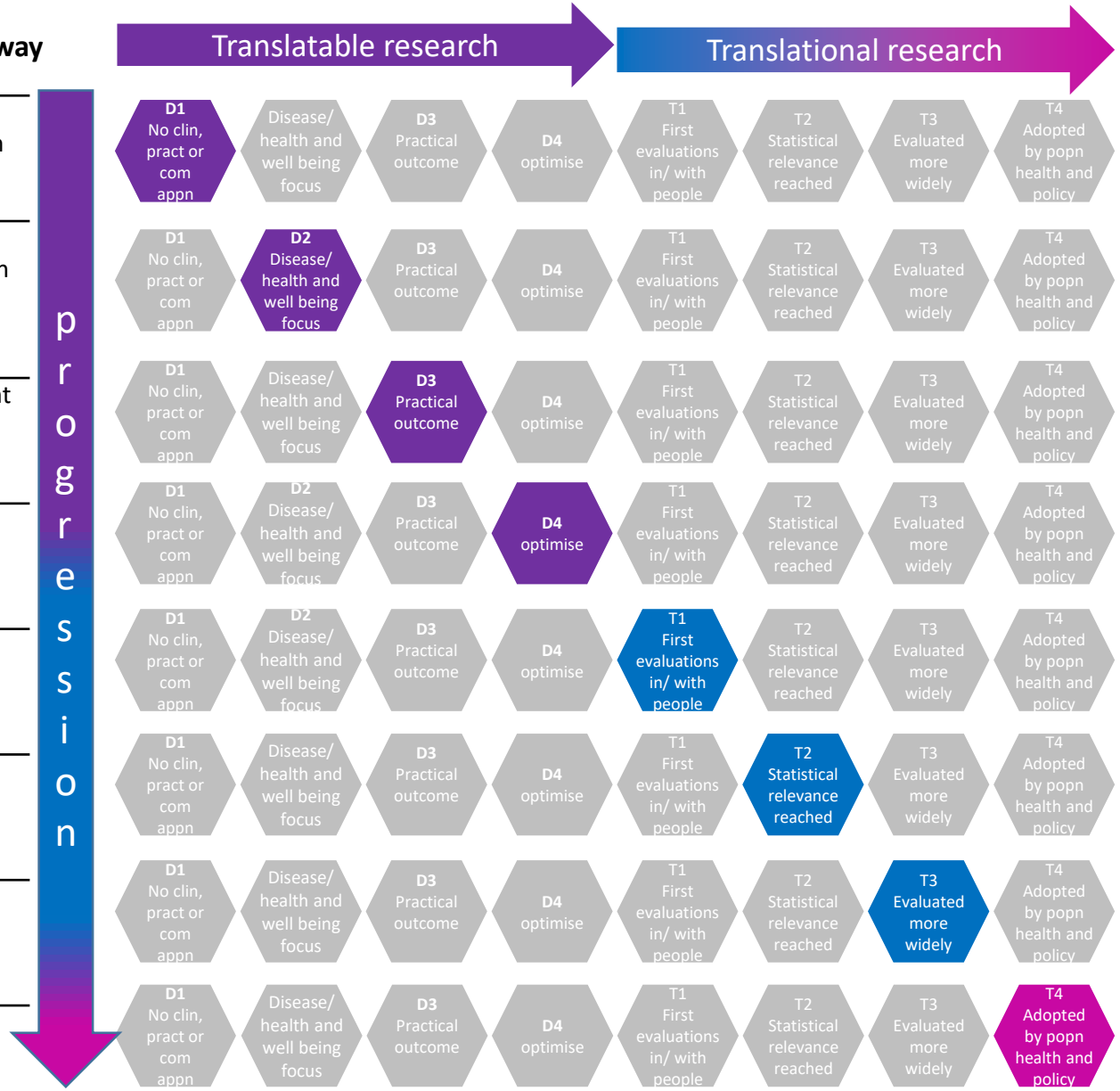
Pre-conceived perception of journey along the Translational Research Pathway

Assumed translational pathway

1. Interesting research question developed to gain knowledge
2. Research progresses to having a disease or a health and well-being focus
3. A disease or health relevant outcome is identified
4. The outcome is optimised before being used in healthy people
5. An early clinical trial is conducted
6. Larger clinical trials are conducted
7. The research outcome is being used routinely
8. Policy adopts the research outcome



There is an assumption that translational research occurs in a linear and sequential way, progressing stage by stage from D1 to T4.

Often this is not the case and research can skip stages and/or go backwards (from clinic to discovery).

Translational research does not always start at D1 and does not always end at T4.

The starting point can be at any stage of the translational pathway, depending on the research question.

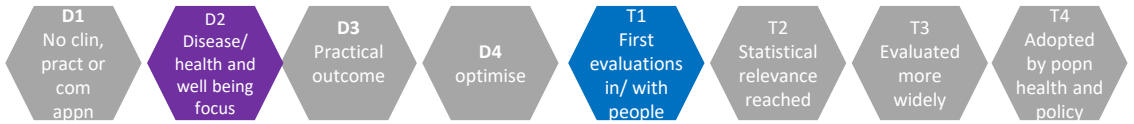
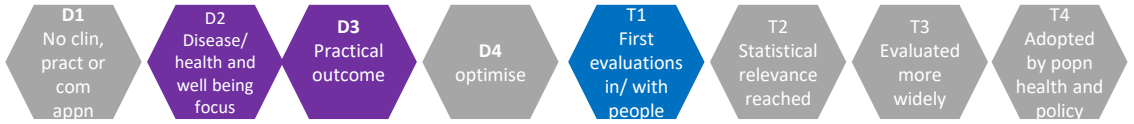
The ‘end point’ is reached when the maximum benefit to patients and clinical practice has been established.

Case Study 1:
Jacky Smith, Cough monitor (**Medical Device** Development)

- This case study uses all of the stages of translation (D1-D4, T1-T4) but not in sequential order and often with overlap between the stages.

Considerations prior to the research

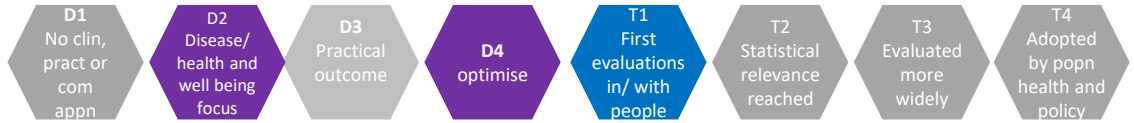
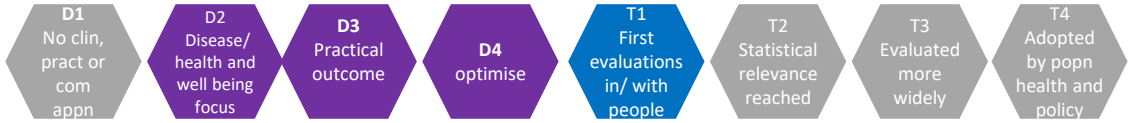
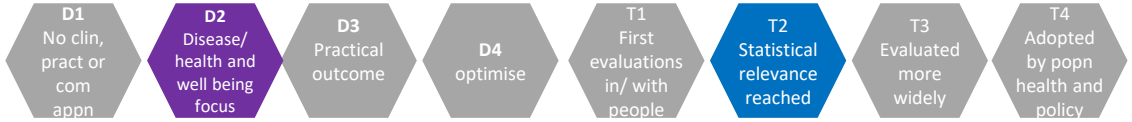
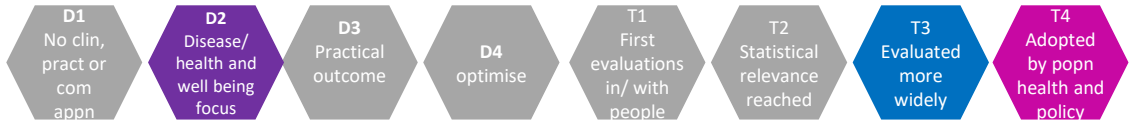
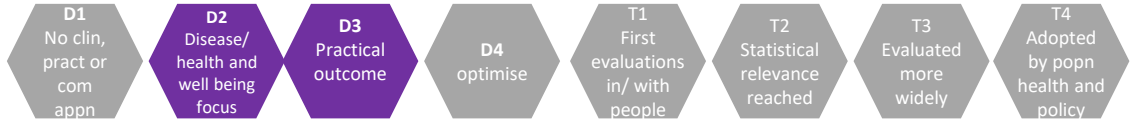
- Animals don't cough in the same way that humans do so there are no animal models to monitor cough BUT humans can be used as long as there is no invasive or 'unsafe' practice. This would simply record patient's cough
- BARRIER: study started before the availability of any digital equipment or technology so needed a novel approach
- SOLUTION: tape recorder/ MP3 player and microphone
- BARRIER: speech recognition software could not accurately identify cough
- SOLUTION: develop new software that is fit for purpose

1	Question: Can cough patterns be captured, classified and used to diagnose patient disease and disease progression?		D2 as it is investigating a condition related to disease T1 as it must be performed in people
2	'home-made' devices (MP3 player, microphones) to determine whether cough sound/ pattern could be detected		D2 as there is a condition focus (cough) D3 as looking at a practical outcome – the identification of cough patterns T1 as conducted in patients with cough
3	Engaged mathematicians and engineers to encompass signal processing and speech recognition for a voice detection device		D1 as no disease interest – only human voice recognition D3 as a practical outcome – can voice be detected? T1 as conducted in patients with a cough
	Barrier 1: Speech recognition software didn't work	*The lack of functionality of the speech recognition software meant that there was no readily available technology that was suitable to capture cough in patients. This required a new, innovative approach to progress the research*	

progression

Case Study 1 continued

progression

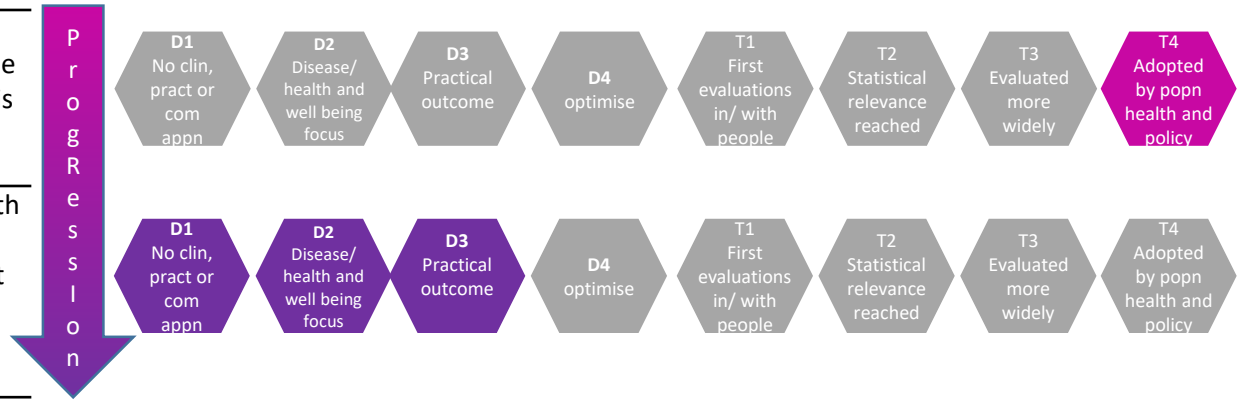
4	Developed new software that would recognise cough		D2 as there is a condition focus (cough) D3 as looking at a practical outcome – the identification of cough patterns T1 as conducted in patients with a cough
	Barrier 2: Funding	*Funding was not available to develop a commercial medical device but the identification of a relevant company with interest in the area (respiratory medicine) provided the funding and support to take the software and device development forward*	
5	Identified commercial partner (Vitalograph) to develop the device		D2 as there is a condition focus (cough) D4 as the device is being validated for clinical use T1 as conducted in patients with a cough
	Barrier 3: Medical application for patents	*There were difficulties with patenting an NHS focussed device through the University system. The patents were filed by Trustech as the device had a medical application, rather than scientific*	
6	Development of a diagnostic tool		D2 as there is a condition focus (cough) D3 as a practical outcome – the diagnosis of cough patterns D4 as the device is being validated as a diagnostic test T1 as conducted in patients with a cough
7	Evaluation of a diagnostic tool		D2 as there is a condition focus (cough) T2 as being used in cough patients on a wider scale than previous
8	Cough monitor available for sale, *eventually being adopted into policy*		D2 as there is a condition focus (cough) T3 as safety has been shown in in a small population of humans and the product is available for purchase
9	Question: can the developed cough monitor be used to identify cough patterns in Guinea pigs with Idiopathic pulmonary fibrosis (IPF)?		D2 as it is investigating a condition related to disease D3 as this is a practical outcome in an animal model
10	Patterns identified but do they show disease progression?		D2 as there is a condition focus (cough) D3 as looking at a practical outcome – the identification of cough patterns in disease progression D4 as optimising parameters of cough pattern in disease progression
11	Are Guinea pig cough patterns comparable to human cough patters during the progression of IPF?		D2 as there is a condition focus (cough) D3 as a practical outcome – comparing animal and human cough patterns in disease progression T1 as including IPF patients with a cough

Case Study 2:
Jacky Smith, **drug repurposing**

- This pathway starts in T4 as repurposed drugs are often recognised treatments for other condition(s) and are widely used
- The purpose of the research is to understand the drug mechanism in the 'repurposed' clinical condition as opposed to understanding the mechanism in its original clinical condition.
- The research counts as D1 as there is unlikely to be any new application, practical or commercial use – the purpose of the research is to understand the drug mechanism and mode of action for scientific and clinical information only

  Caveat: if an interesting mechanism is identified, it could facilitate new research

1	A repurposed drug is being successfully used in the clinic but the mode of action for the 'repurpose' is not fully understood	T4 as it is a drug that is being successfully used in the clinic
2	The drug mechanism is revisited with respect to its revised (repurposed) use in the alternative condition (not what the drug was originally developed for)	D1 as this knowledge is unlikely to have a new clinical, practical or commercial outcomes – it is research to understand a drug mechanism for pure information and knowledge D2 as there is a [different] disease focus D3 as there will be a practical outcome – the mode of action in the 'repurposed' condition



Case Study 3: Cath O'Neill,
Skin Bio (**Medical Device** and **Cosmetic Product** Translational Pathways)

- For a medical device, the principal intended action is typically fulfilled by physical means (including mechanical action, **physical barrier**, replacement of, or support to, organs or body functions) [1].
  - A cream represents a physical barrier
- A 'cosmetic product' is any substance or mixture intended to be **placed in contact with the external parts of the human body** (epidermis, hair system, nails, lips and external genital organs) or with the teeth and the mucous membranes of the oral cavity with a view exclusively or mainly to cleaning them, perfuming them, changing their appearance, **protecting them**, keeping them in good condition or correcting body odours[2].
  - In this example , the cream is also a cosmetic product
- The pathway starts in D1 and T1 simultaneously as it is pure research BUT using a human tissue model rather than an animal model
- The pathway does not require optimisation or phase 3/4 clinical trials and will not be adopted into policy so in this example, **steps D4, T2, T3, T4 do not apply to the translation pathway.**

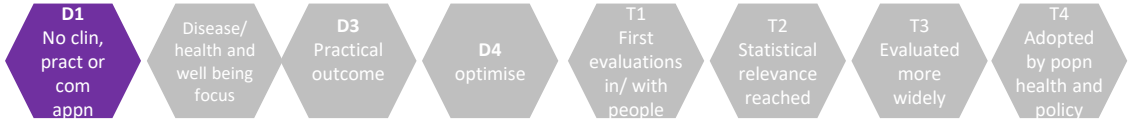
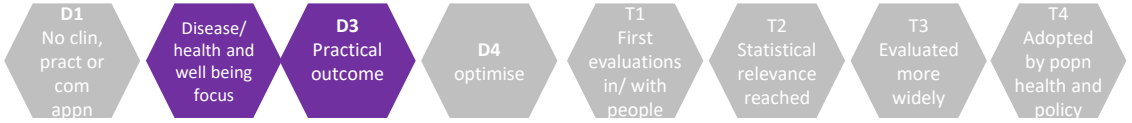
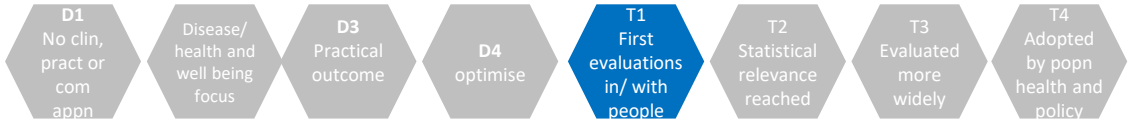
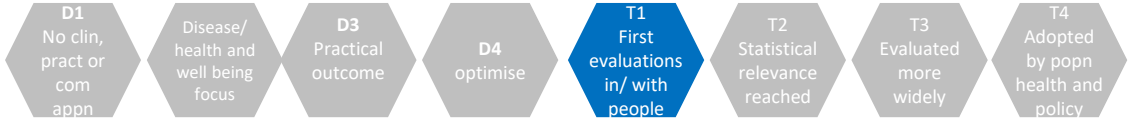
Considerations prior to the research

- The impact/ validity of a commercial path in academia - has proven to be highly lucrative for both academic and non-academic progression

1. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/284493/Borderlines_between_medical_devices_and_medicinal_products.pdf
2. https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:02009R1223-20160812&from=EN

Case Study 3 : Cath O'Neill,
Skin Bio (Medical Device and Cosmetic Product Pathways)

progression

1	Question: Do bacteria do anything to change skin physiology?		D1 as pure discovery research T1 as it requires human tissue, (plastic surgery excess).
2	Model 1: effects on healthy skin barrier		D1 as no disease interest – only healthy human skin D3 as looking at a practical outcome – the effect on the skin T1 as using human skin, no animal models or model systems
3	Model 2: effects on breached skin (Eczema, wound healing)		D2 as there is a disease focus D3 as looking at a practical outcome – the effect on the skin T1 as using human skin, no animal models or model systems
	Barrier 1: funding	*Research provided an evidence base which was published and IP established to protect future developments. BUT funding was not available to research the science behind formulation (cream/ lotion) or scaling up (lab vs. commercial production). Small scale, in house methods were not successful and had no commercial viability*	
4	What formulation would be most appropriate? How can it scale up?		D1 as pure discovery research to identify a formulation and scale up method – (not to make a scaled up product, which would be D3, practical outcome)
	Barrier 2: research vs. commercial application	*Change of approach from 'What happens if…..' to 'This can be applied to….' BUT this introduced a series of regulatory hurdles for medical devices and cosmetic products*	
5	Tried in a number of 'available' formulations in *in vitro* models through commercial collaboration		D2 as there is a disease focus D3 as looking at a practical outcome – the effect of the formulations in in vitro models of human skin cells
	Barrier 3: commercial safety and regulatory pathway	*Company collaborations provided access to formulations and in vitro models (independent laboratory testing) to provide proof of concept for safety through the use of human derived cell lines to check for toxicity (skin and ocular with and without photosensitivity checks), they also provided a source of funding for the safety testing, formulation development and provided invaluable expertise in the provision of regulatory advice and support, (not available in academic environments)*	
6	Clinical study in humans		T1 as safety has been shown in vitro and is being tested in a small population of humans
7	Product scaled up and available for sale		T1 as safety has been shown in in a small population of humans and the product is available for purchase