Cancer

Digital Health Solutions*

**Extracted from Echino's upcoming 'Innovation Briefings on Biological and Physical Diagnostics, Digital Health and Patient Management Solutions'. These reports contain complete epidemiology, demographics, staging, population health dynamics, regulations and standards, Research and Development costs, market sizes and values. These briefings are designed to complement the innovation briefings for Therapeutics.*

Dr. Jonathan Dando

We interrogated over 8000 published Clinical Trial Protocols that indicated a digital health component, corresponding to studies commencing from January 2010 to May 2021 to determine

- Focuses
- Solution creation as a function of the patient journey
- Solution classification related to regulatory definition
- Characteristics of evidence-based generation

They were screened to confirm a digital health focus, sorted and analysed:
370 studies were focused on Digital Health Solutions for Cancer

Study focus	Number of studies
Breast Cancer	151
Prostate Cancer	51
Colorectal Cancer	30
Cervical Cancer	19
Lung Cancer	19
Melanoma and skin cancer	16
Leukaemia, lymphoma & HSCT (5 are also paediatric)	16
Kidney Cancer	9
Head and Neck (all types)	9
Brain and CNS Cancer	8
Pancreatic Cancer	7
Endometrial Cancer	6
Paediatric cancers (children and adolescents <19 years of age)	6
Ovarian Cancer	5
Multiple Myeloma	5
Bladder Cancer	4
Gastrointestinal Cancers	3
Liver Cancer	3
Musculoskeletal Cancers	2
Thyroid Cancer	1

*Methodology: The NIH clinical trial database was interrogated 3 independent times. Under the advanced search option, the first two search criteria were i) digital in other terms only for generic digital solutions that incorporated all diseases and ii) pathology in condition + digital in other terms. Recruitment terms were not yet recruiting, recruiting, enrolling by invitation, active not recruiting and completed. For each pathology this generated two data files, that after mining indicated keywords, that along with those obtained from our innovation briefings, were used in the third search to extend the data set beyond the major applications. This was performed identically to search ii) except the keyword was inserted in place of the pathology, thereby extending the data set extensively beyond the study focus, and also into other diseases. Dates of screening were for all clinical studies submitted up to May 24, 2021. For each search no geographic, lingual or digital solution constraint was used prior to generation of the data files. The three different data files were screened to confirm the health issue, a clear digital innovation (based upon peer reviewed literature sources such as Lancet Digital, Health Informatics Journal, Nature digital medicine, UK NICE, FDA, ICER, WHO). Each data file was then sorted to remove any duplicates and all remaining study files evaluated for key metrics including pathology, type of **Digital Health Solution**, primary purpose within **the Patient Journey** and suballocation.*

The Patient Journey* & Digital Health Solutions

Lifestyle management and
prevention

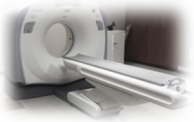
Health Services

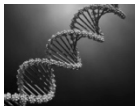
Symptoms awareness and monitoring

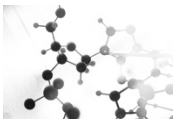
Family Healthcare Practitioners (FHP)
First evaluation

Population Health Dynamics:
Screening of at-risk
populations

Secondary and Tertiary care specialists
Diagnosis: confirmation and definition







Outpatient or Tertiary care
Treatment and supportive care

Successful
treatment

Relapse monitoring

Outpatient or FHP
Supportive Care, Follow up +/- specialised clinics
(Mol. Diag. Labs/Imaging clinics)

*(*low granularity)*

Digital Health Solution Classifications

Digital Health Solutions have been focused around 8 Primary Purposes (**PP**) with up to 5 different suballocations depending on what it is, where it will have an impact and outcome measures to confirm it.

PP: Device feasibility
Sub allocation(s):
Device.

PP: Supportive care
Sub allocation(s):
Behavioural
Device
Other

PP: Diagnostic
Sub allocation(s):
Device
Diagnostic test
Other
Procedure

PP: Prevention
Sub allocation(s):
Behavioural
Device
Other

Digital Health Clinical Trials Focus

Cancer

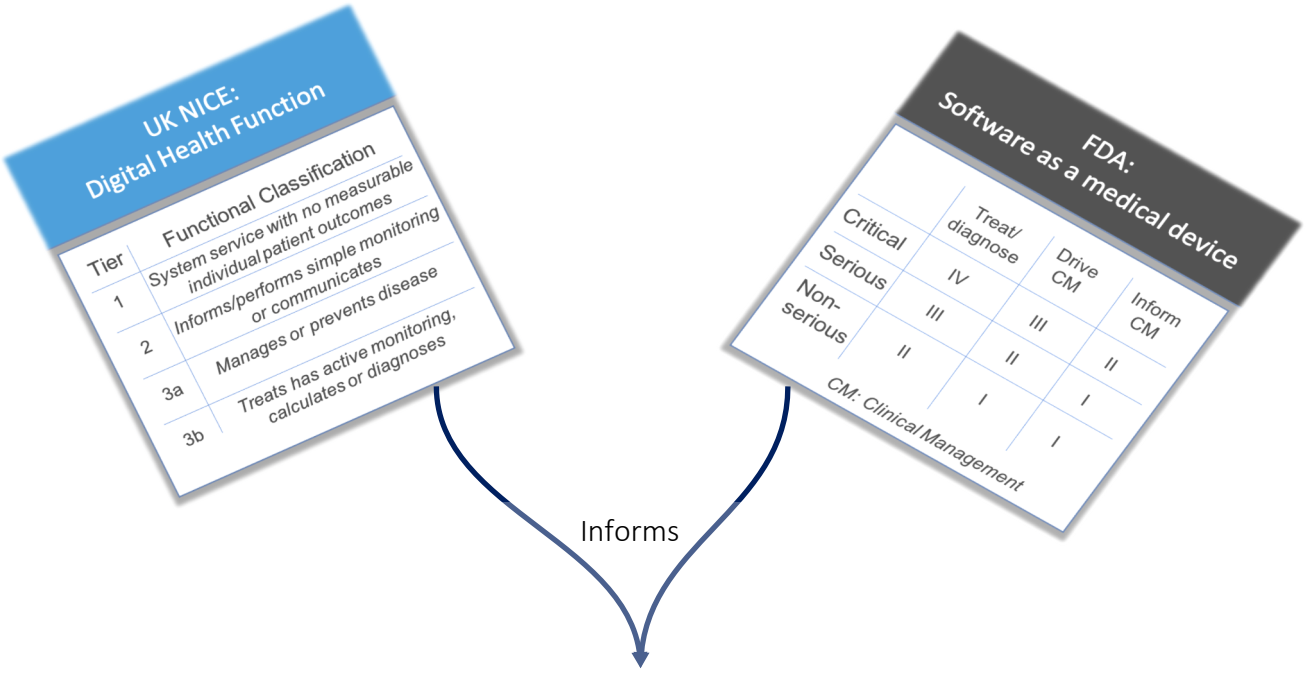
PP: Treatment
Sub allocation(s):
Behavioural
Device
Procedure

PP: Screening
Sub allocation(s):
Behavioural
Device
Diagnostic test
Other
Procedure

PP: Basic Science
Sub allocation(s):
Diagnostic test

PP: Health Services Research
Sub allocation(s):
Behavioural
Other

Each country has its own digital health framework and strategy, and classification and evidence requirements. Global Healthcare payment typically falls in the spectrum from Majority publicly to Majority privately funded. But there is also the system where no structured healthcare exists at all, whose people need healthcare the most; using this spectrum while integrating the stakeholders needs in each location, we can assess clinical and economic evidence needs, and how to generate data that best demonstrates the solutions beneficial impact.



- Clinical Trial Design
- Clinical Efficacy requirements
- Health Economic Evidence needed

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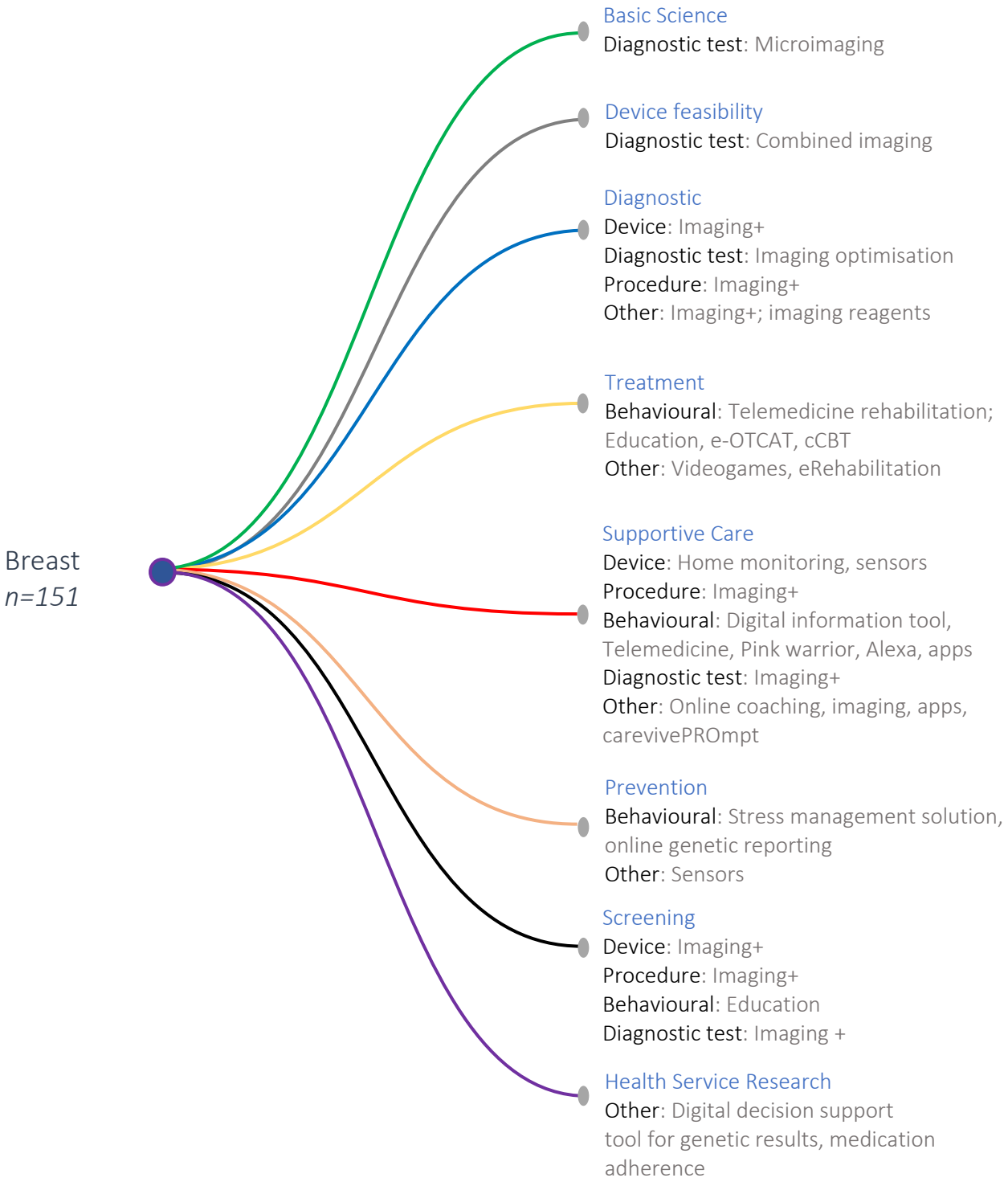
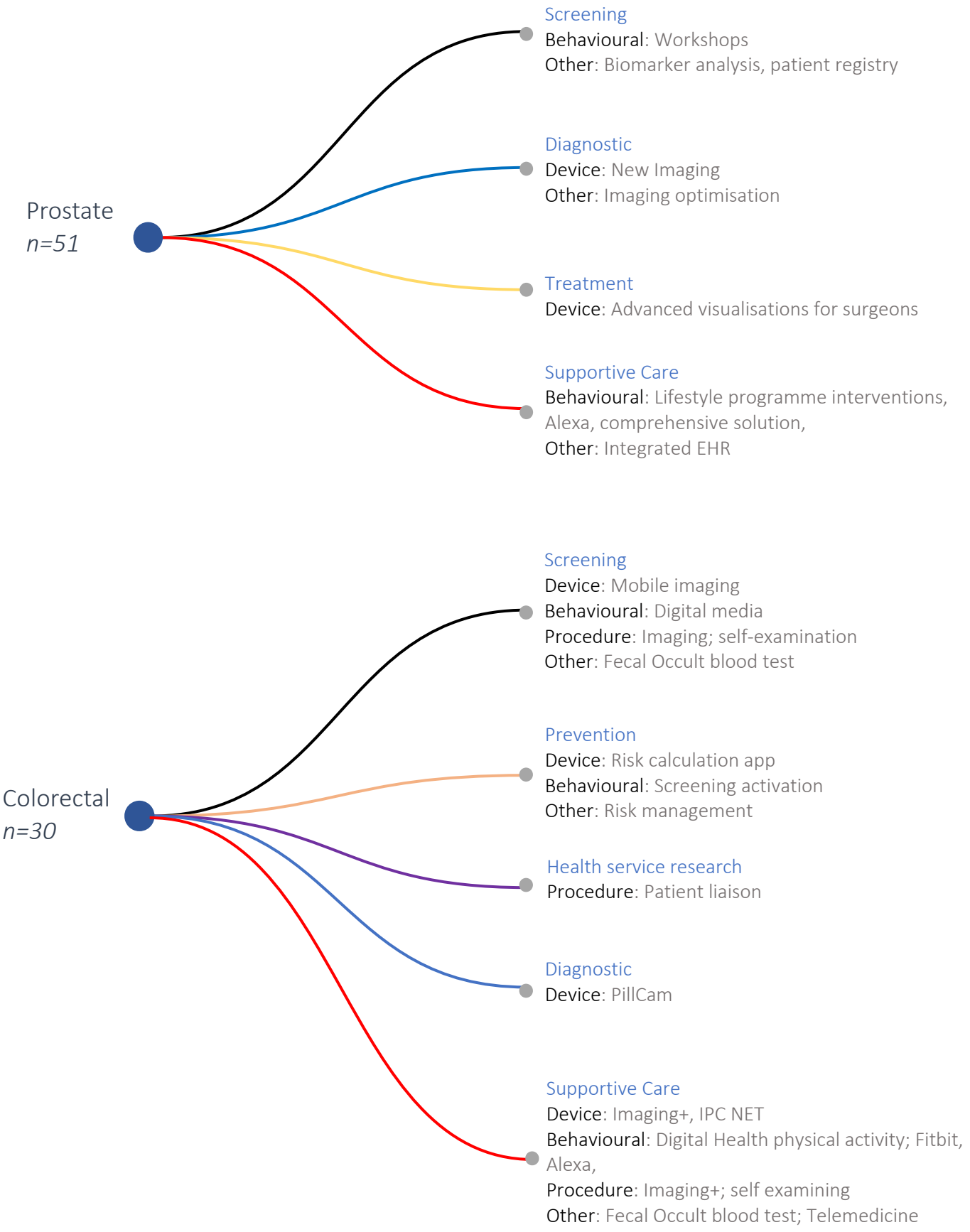
Clinical trial details by primary purpose and sub allocation for Cancer focused digital health solutions

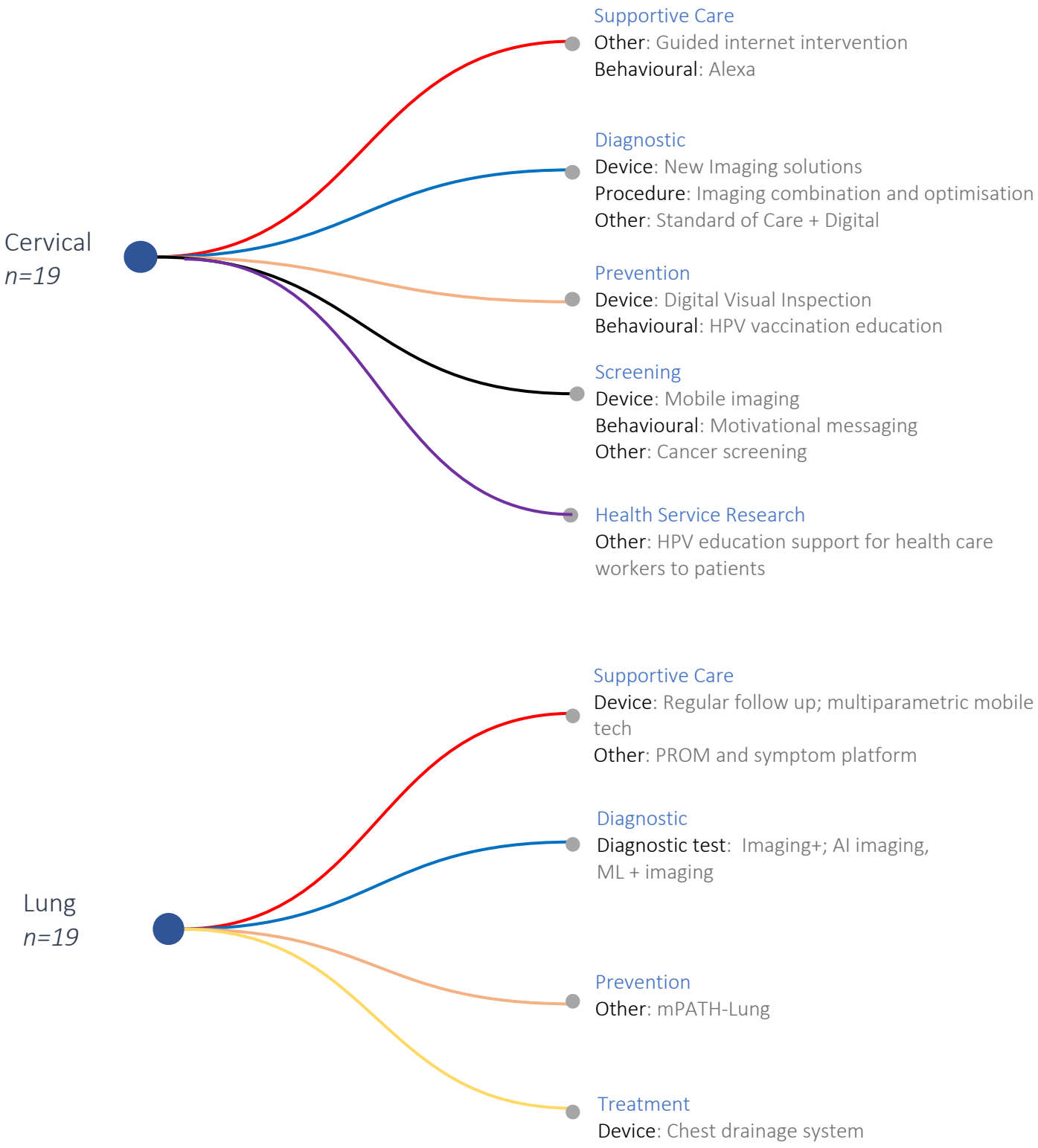
Primary Purpose	Sub Allocation	Clinical Trial structure(s) followed	Median number of patients per trial	Median duration of each trial (months)*
Physical Device	Device	Single Group Assignment	90	2
Screening	Behavioural	Randomised Parallel	775	8
	Device	• Single Group Assignment • Cohort • Case only	442	12
	Diagnostic test	Randomised Parallel	28764	30
	Other	• Randomised Parallel • Single Group Assignment	793	9
	Procedure	Randomised Parallel	1494	3
Health service Research	Behavioural	Randomised Parallel	130	6
	Other	• Single Group Assignment • Non-Randomised Parallel • Randomised Parallel	134	1
Basic Science	Diagnostic test	Sequential Assignment	10	0.2
Diagnostic	Device	• Single Group Assignment • Non-Randomised Parallel • Randomised Parallel • Case-Control • Case-Crossover	129	3
	Diagnostic test	• Single Group Assignment • Randomised Parallel • Case-Control • Case-Only • Cohort	157	4
	Other	• Single Group Assignment • Randomised Parallel	107	2
	Procedure	• Single Group Assignment • Randomised Parallel	183	1
Supportive Care	Behavioural	• Single Group Assignment • Randomised Parallel	78	4
	Device	• Single Group Assignment • Randomised Parallel	100	1
	Other	• Single Group Assignment • Randomised Parallel • Case-Only	161	3
Prevention	Behavioural	Randomised Parallel	128	3
	Device	Single Group Assignment	620	7
	Other	Randomised Parallel	205	6
Treatment	Behavioural	Randomised Parallel	66	3
	Device	Randomised Parallel	20	1
	Procedure	Randomised Parallel	60	12

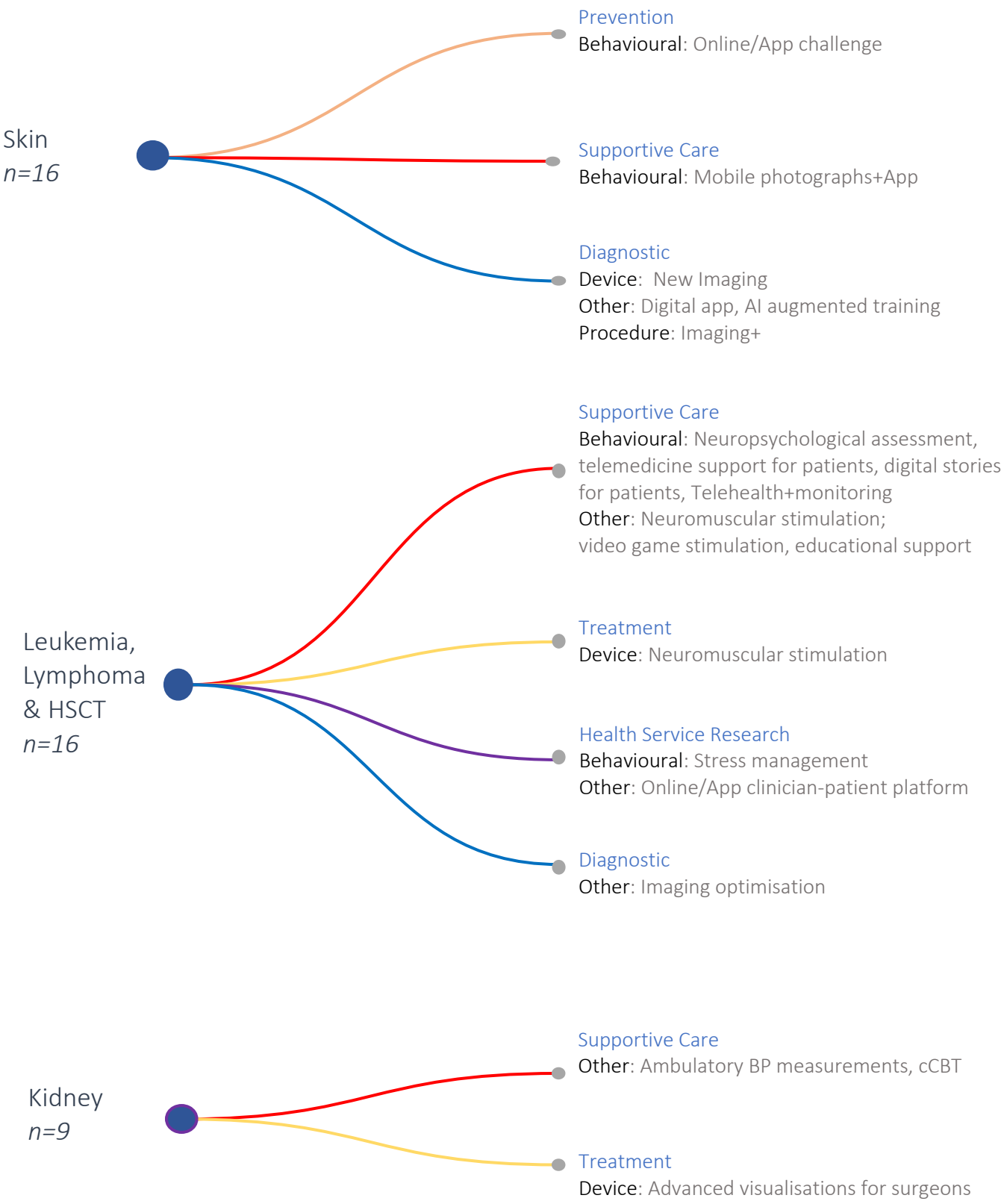
**It is worthwhile reading the increasing number of reports and guidance documentation being produced by global reimbursement bodies regarding expert opinion on clinical trial duration and structure. The increasing trend of expert critique corresponds to the absence of long-term modelling of the impact of the solution vs the standard of care within a non-biased clinical design, that prevents accurate effectiveness analysis being performed.*

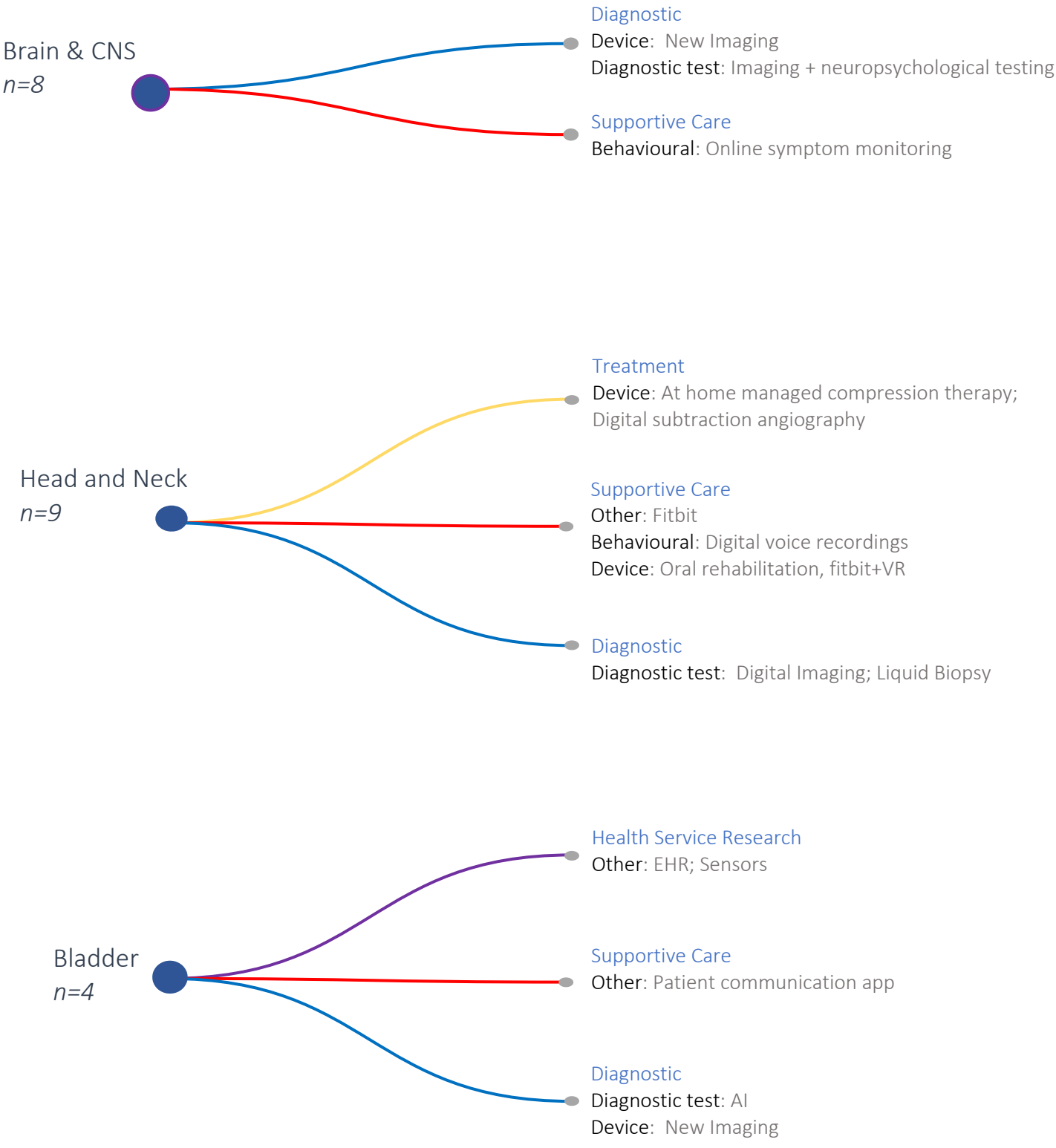
Solutions developed for each cancer type

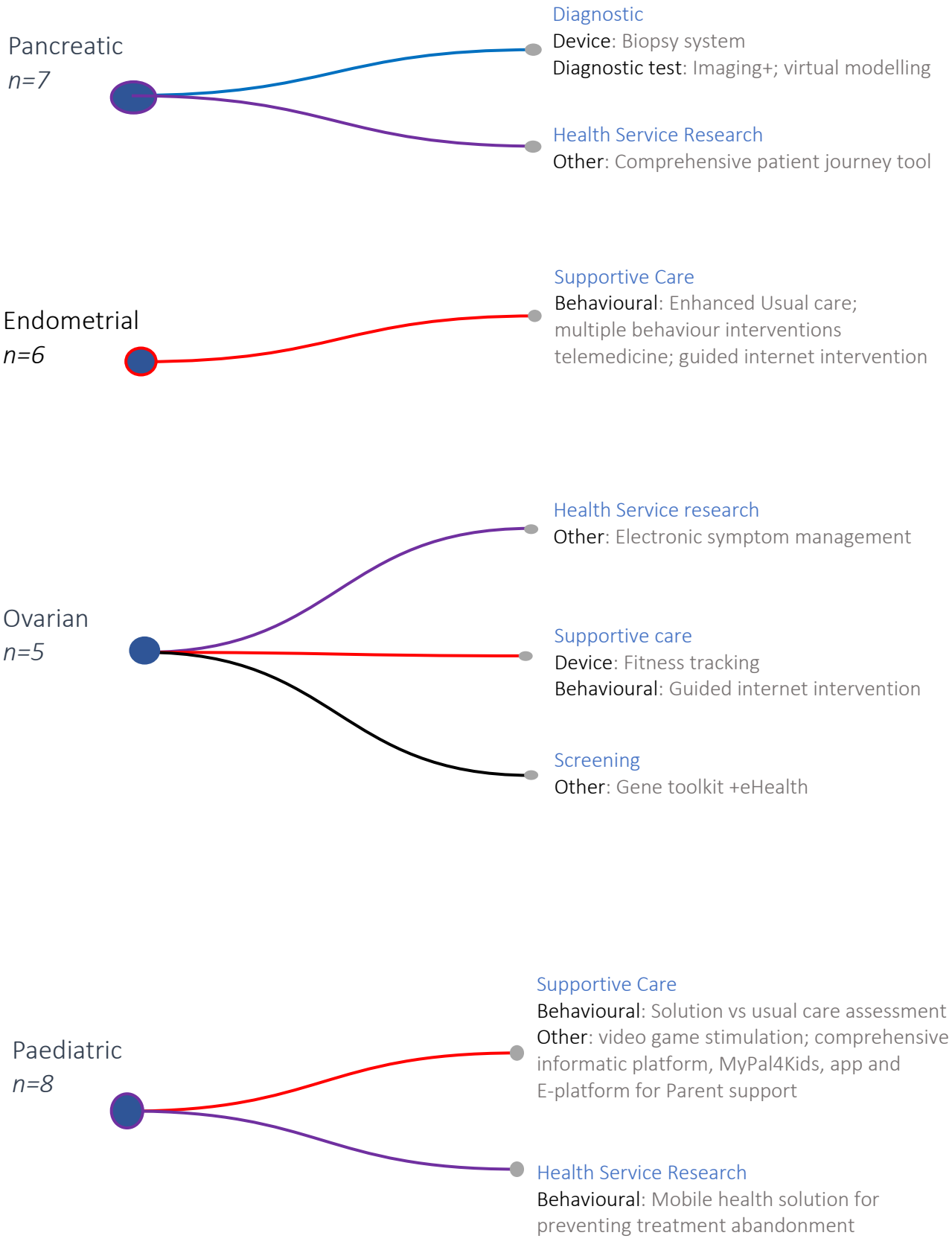


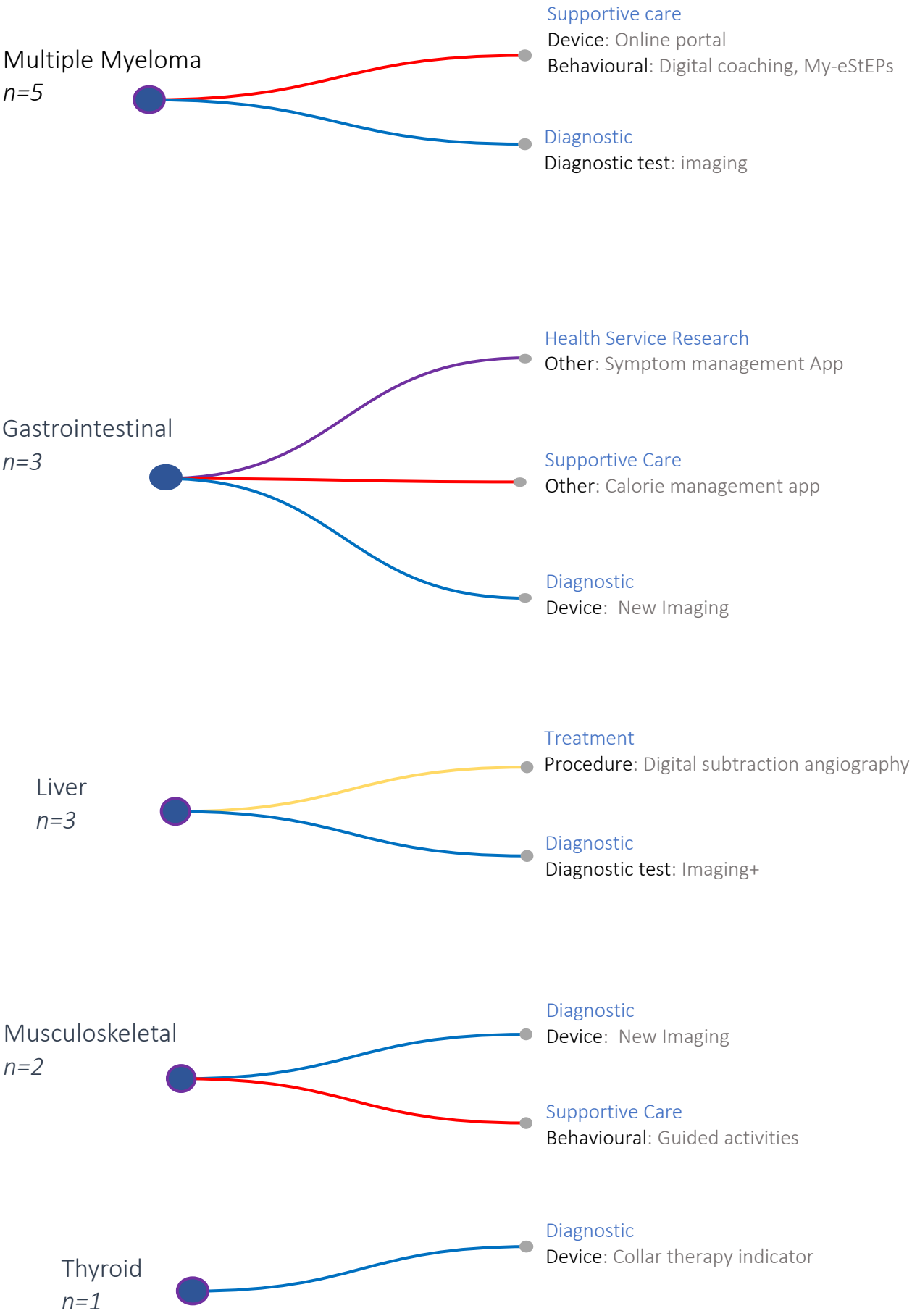












Valuations and solution vs stakeholder integration.

We have not included estimated market values or potential forecasts: the market is so fragmented that for every assumption why a value calculation variable should be fixed to permit value outcome modelling, there were (and are) a dozen confounders that rendered the calculation unreliable.

Ideally, value calculations are based upon an as precise as possible defined population, using that solution. This is then stratified by population health dynamics, where in the healthcare work flow it has relevance and what it is doing: study focus vs patient journey location vs patient population it is designed for vs classification vs primary purpose (see: https://www.echino.eu/aib).

For example, a private health insurer that provides services to a wide socioeconomic base may increase or decrease deductibles if a patient or healthcare worker uses a certain digital health solution, the value of which changes as a function of the risk profile and present health status of the patient. This can hinge on age, gender, ethnicity, salary, education, environment, family history, comorbidities, access to solution and healthcare infrastructure. These same profiles will also influence whether, with or without reimbursement entity advice, a person will a) buy and then b) use the digital solution.

Evidence bases for economic or health impact of the majority of digital health solutions are unestablished, and from our analysis there are significant and positive motivations, and amounts of effort being engaged to generate them; but there are still some critical aspects not being considered, that includes full stakeholder involvement. Best illustrated by the increasing numbers of peer reviewed publications authored by healthcare workers for mHealth apps that follow a work flow of:

> *'Based on pathology A, we searched the google and apple stores for solutions linked to it. 249 applications were identified, that after a sorting algorithm corresponding to actual patient healthcare measurement metrics, 9 merited in depth analysis to assess if they had been generated on an evidence base, of which 2 actually did what it said on the box'.*

Design and functionality considerations

Clinical trial design

Make sure it is of the highest quality including the necessary patient numbers for a valid power calculation. A typical solution requires over 1000 patients to demonstrate an effect if the difference between positive and negative is significant with a 90% power: if the difference is small, over 6000 patients are normally needed.

Clinical trials performed in different settings, with different healthcare practitioners, on different populations and in different scenarios result in non-comparable data obfuscating the value.

Total inclusion of evidence and regulatory requirements

So far, many solutions are revealing that clinical trial data vs real world setting outcomes and data are not correlating during post marketing assessments: in most cases the real world data is indicating that the clinical trial data was optimistic.

The solution needs to be positioned with the most relevant healthcare worker in the most pertinent location to identify, clarify and emphasise the value. There also may be the need for routine and continued education of the patient and healthcare workers to maintain impact of the solution.

With regards to Artificial Intelligence and Machine Learning Algorithms the integrity and completeness of training and validation data sets can influence and, in some cases, have been shown to increase healthcare provision disparity.

Healthcare practice location usage and available infrastructure

A family doctor, specialist nurse or hospital physician using the same solution on the same patient can generate data variations: this creates confusion, which most healthcare workers do their utmost to avoid.

This can create stakeholder misalignment: conflicting stakeholder opinions creates subjective norm barriers. Stakeholder requirements need to be integrated into your solution design: remember that the healthcare worker has to approve, prescribe or recommend the solution.

Interoperability with various EHRs or other IT solutions typically used in that specific geography, are still an issue, resulting in poor conceptual integration of solution into healthcare delivery workflow that is still occurring.

Integrate total system, pathway or workflow impacts and Total Costs of Ownership when costing your solution: no customer likes a surprising bill.

The solution is difficult to roll out: needs specific infrastructure and trained personnel.

IT connectivity: The GSMA 2020 report on mobile internet connectivity indicates that only 600 million people live in areas with no connectivity; but nearly half the world's population, despite living in areas with a mobile broadband network do not use mobile internet. Lack of digital skills, computer literacy and device/data plan affordability represent barriers to usage.

There is also a significant gender gap on mobile internet usage, biased against women, that is geography dependent, with a higher relevance in LMIC geographies. We need to reprioritise.

Accuracy, sensitivity and specificity is everything

Contradictory diagnosis is a problem: if the output data does not correlate with existing standards of care or gold standard approaches health care workers will have justifiable doubts: the buck stops with them. Remember that this has geographic relevance: different thresholds in different countries influence application and accuracy assessments, that can hinge on healthcare worker education.

In every country evidence of misdiagnosis is fatal: false positives and false negatives, true positives and true negatives define every intervention: Diseases getting missed, or incorrectly diagnosed can result in no treatment or unnecessary surgery and treatment. No stakeholder wants that.

Understand the patient

This needs to be long-term and educational. Poor understanding of enduser(s) needs and level of involvement can sink your solution at the post market level. Some patients do not want to be constantly reminded they are ill.

Lack of consideration for impacts of income level, age, ethnicity or gender will result in bias or health disparity: Lack of integration of normal human behaviour or disease characteristics such as comorbidities will reveal inherent design weaknesses that will only occur when a practicing specialist committee reviews the data.

Understand the healthcare worker

There are insufficient numbers of healthcare staff in every location: Low number of healthcare workers vs high patient load routinely creates message over saturation, 'alert or alarm' fatigue, mental overload, decreased situation awareness, resulting in incorrect decisions. Make sure your solution is not just creating a different problem.

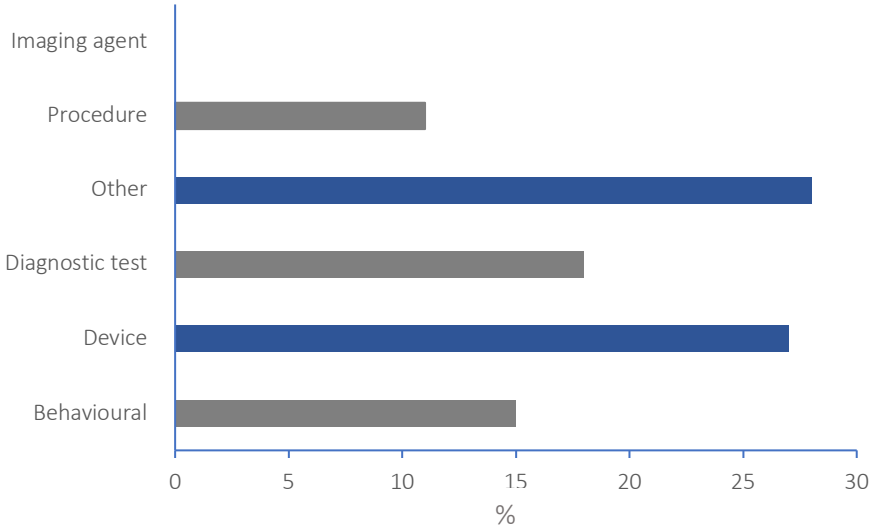
Do you understand the enduser(s) time constraints and decision making as a function of where they work in the healthcare ecosystem?

Healthcare workers are not IT specialists: they have IT management, IT security and privacy issues. Many healthcare workers have to buy their own IT solutions without knowing IT issues related to security, software and operating systems. If your solution fails and there is patient harm via health damage or data breach, they are likely liable. A nice GUI is always reassuring, but the problem is not there. Healthcare workers need tailored IT training that corresponds to real world needs and their availability.

Annex: Trend analysis

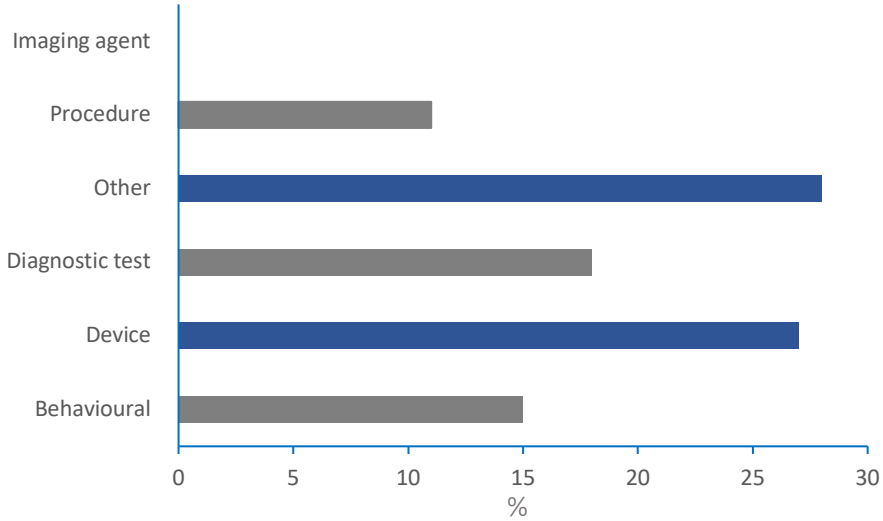
Screening over 8000 files provided a unique opportunity to also look at trends: digital health solutions do not go through the same trial phases as therapeutics and by being performed in accredited healthcare settings trend analysis gives a view of what solutions healthcare specialists and Key Opinion Leaders think are the best to try and the most necessary for each work flow focus and the patient.

Screening: major solutions groups and types



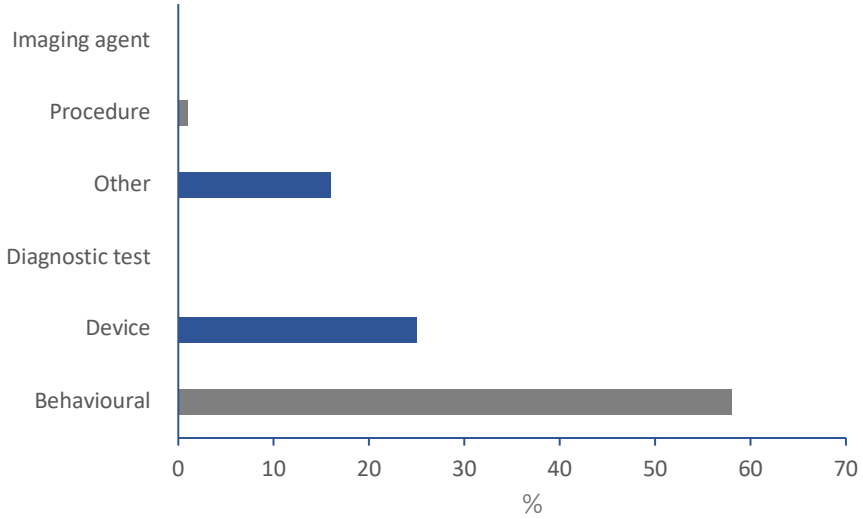
- Behavioural: raising awareness of the potential for the disease
- Device: almost 100% new imaging approaches within existing work flows
- Diagnostic test: almost 100% application of existing imaging platform and imaging optimisation within existing work flows or mobile imaging +/- telemedicine
- Other: genetics, online questionnaires, family gene toolkit, fecal occult blood test
- Procedure: introduction of imaging into existing workflows

Treatment: major solutions groups and types



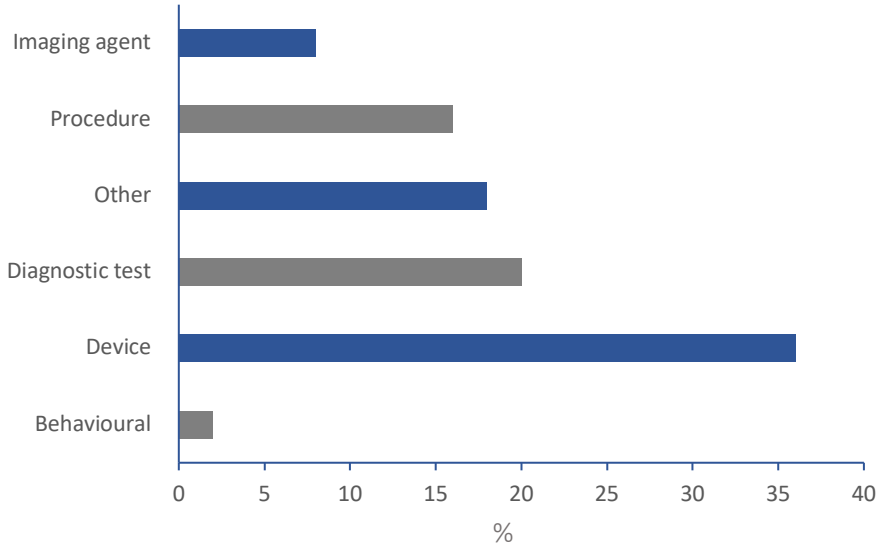
- Behavioural: guides, counselling, education, telemedicine, sensor+app, communication solutions, ePillbox, gaming, cognitive support through all informatic platforms
- Device: virtual reality, gaming solutions, hand held stimulation devices, mental rehabilitation through mHealth, every type of informatic platform rehabilitation
- Other: virtual reality solutions, app/mobile/tablet cognitive therapy, musical solutions
- Procedure: drug monitoring/adherence, digital subtraction angiography, deep brain stimulation, telemedicine

Prevention: major solutions groups and types



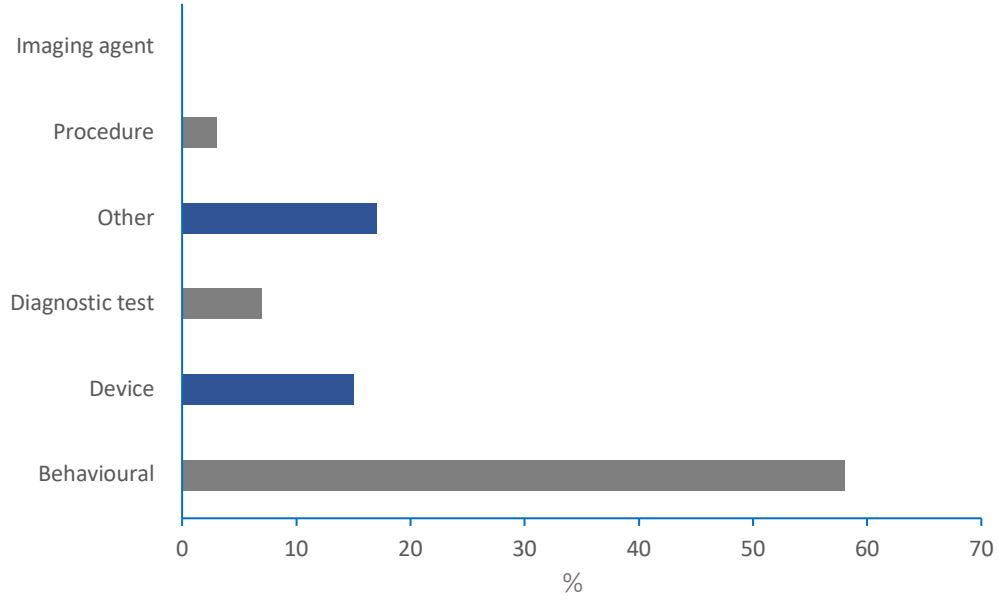
- Behavioural: tele-education, tele-counselling, virtual reality, augmented reality, apps and mHealth +/- activity training/augmentation, online cognitive training,
- Device: sensors, sensor+app, home based comprehensive solutions, mobile imaging
- Other: smartHealth solutions, gaming, apps, messaging, cognitive training
- Procedure: connected informatic solutions

Diagnostic: major solutions groups and types



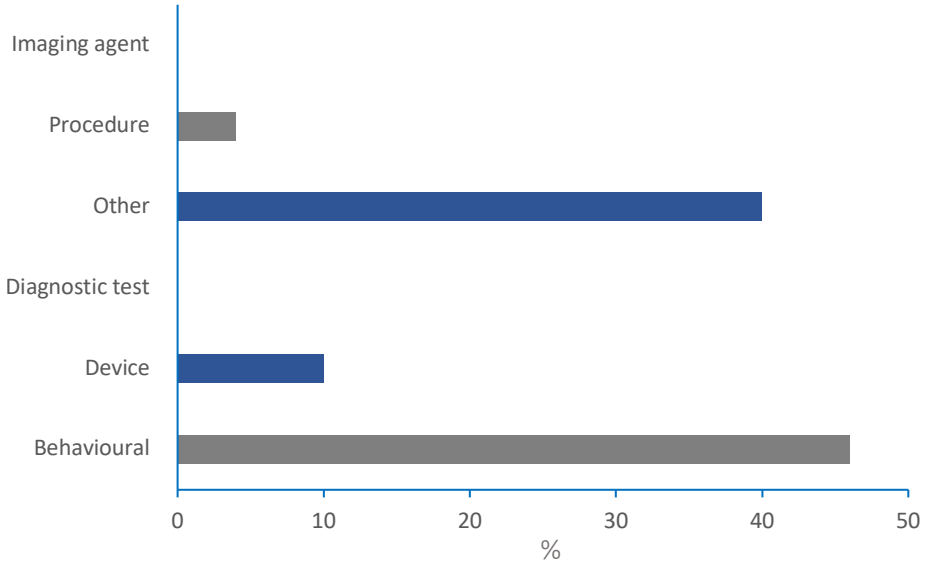
- Behavioural: cognitive questionnaires
- Device: imaging, sensors, monitoring systems, gaming, cognitive evaluation
- Diagnostic test: imaging, sensors, sensor+app, cognitive assessment, virtual biopsy/digital biomarker
- Drug: imaging agents
- Other: apps, augmented reality, AI, mental health questionnaires
- Procedure: mostly imaging related

Basic science: major solutions groups and types



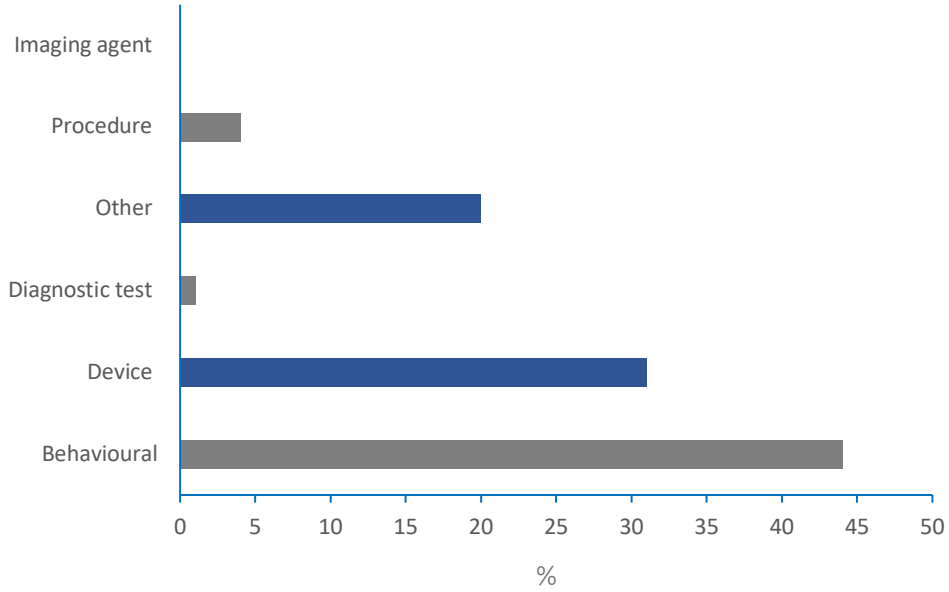
- Behavioural: music, apps, gaming, exergaming, physical/diet changes
- Device: sensors, monitors, ehealth, electrical stimulation, wearables
- Diagnostic test: imaging
- Other: imaging, sensors, music
- Procedure: electrical stimulation

Health service research: major solutions groups and types



- Behavioural: self-management solutions, education, counselling, sensors, PROM/symptom reporting, physical activity encouragement, virtual reality, mental health support
- Device: gaming, cognitive aids, sensor/phone+app
- Other: integrated mHealth, virtual reality, telemedicine, home based monitoring and sensors
- Procedure: home monitoring, telemedicine

Supportive care: major solutions groups and types



- Behavioural: counselling, education, apps, mHealth, sensors, gaming, activity support, self management, cognitive support, mental health support
- Device: sensor/smart device+app, smart device+new sensor, physical activity support and tracking, virtual reality, self care, telemedicine, telemonitoring,
- Diagnostic test: imaging
- Other: imaging, eHealth platforms, at home sensors/monitoring+/- apps,
- Procedure: gaming, home monitoring

About Echino Limited: an internationally focused programme management and medical communications company that specialises in global programme management and convergent technology project implementation, with a particular focus on optimising operations.

About the author: Dr. Jonathan Dando has approaching 30 years global insight in life science and health, with work experience in Austria, the United States, Italy, France, Switzerland, the UK and Spain. He started his career in the early 90's working in Gene Therapy for Novartis and SyStemix (USA), has held academic positions in Foundation and National research institutes, including TIGET and Inserm, as well as Executive Directorships and Board positions in commercial enterprises, some of which he started. Since 2002 he has specialised in aiding, designing and managing international research, development and clinical trial partnerships and alliances between all stakeholders and actors, in which he has also raised over €150 Millions, and in helping private foundations with their international projects. He has an Honours Degree in Biophysics and a PhD in the Genetic Engineering of Viruses; he also holds a micro masters in Cloud computing, has been trained as a Facilitator for the UK NICE's Medtech Early Technical Assessment system, and also acquired several continuing professional education certificates in clinical trial design, health technology assessment, eHealth, population health and data management.

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