BIOS

PRIMER ON BIOELECTRONIC REIMBURSEMENT MODELS

A CASE STUDY IN HEART FAILURE

BIOS in partnership with Legal & General

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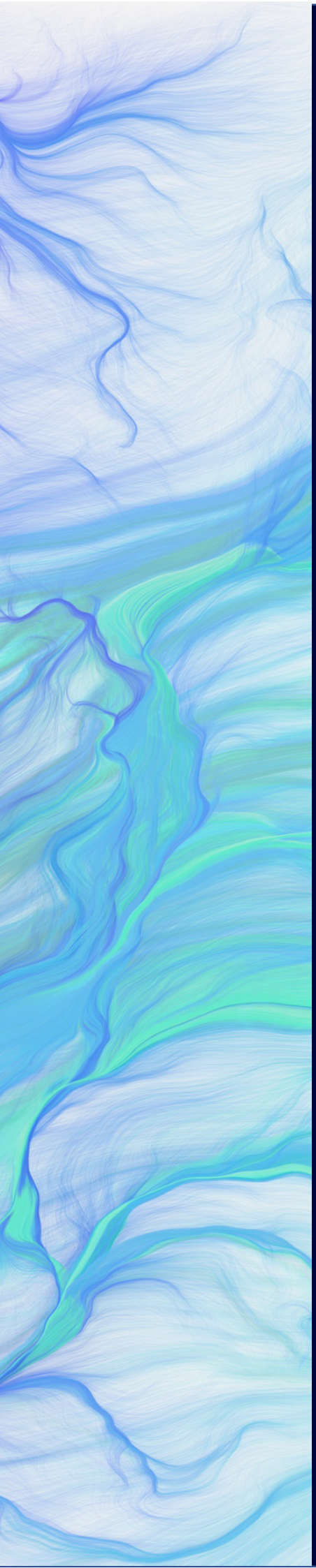


Overview

Neural data is the next frontier of precision medicine, powering a range of new bioelectronic, molecular, and digital therapies. New technologies in bioelectronics hold the promise of dramatically improving patients' quality of life while reducing healthcare costs. However, current reimbursement strategies fail to account for the significant benefits that they deliver.

This primer has been produced by BIOS in collaboration with Legal & General and aims to inform new audiences on a range of topics relevant to bioelectronic reimbursement models. We hope it encourages discussion between healthcare stakeholders (including innovators and payors), which will in turn support increased innovation in the industry.

BIOS is planning further research to validate potential reimbursement models to deliver the best outcomes possible to both patients and wider healthcare systems. If you are interested in working with us on this mission, reach out to partnerships@bios.health

Introduction

Over the past 50 years, novel therapeutic modalities ranging from biologics, to genomics, to mRNA therapies, have revolutionised medicine.[1,2] The next frontier in precision medicine is neural data. Just as unlocking DNA transformed genomics, reading and writing neural signals has the potential to transform the way we treat chronic diseases.[3,4,5]

"The next frontier in precision medicine is neural data"

Bioelectronics[a] are well established, and the pace of innovation is rapidly increasing with players in the space such as Galvani Bioelectronics entering clinical trials.[6] Other players in adjacent neural technologies, such as Neuralink,[7] are also preparing to launch clinical trials. While the regulatory pathway is developing and encouraging for bioelectronics, progress in updating reimbursement models has lagged as payors seek to better understand the range of potential benefits they can deliver, including interoperability and the value of data and algorithms. As a result, payors continue to rely upon existing reimbursement models to provide patients swift access to these cutting-edge treatments,[8,9] but these models generally fail to reflect the full range of potential benefits available to patients, clinicians, and healthcare systems. An AI-powered device capable of dynamically optimising treatment is reimbursed similarly to an artificial hip. As such, payment strategies must evolve to recognise the true value of current and future medical advances.

BIOS Health (BIOS) has developed a technology platform which leverages neural data recording to generate detailed insights about the nervous system in real time. These insights can be used to develop and deliver therapies for neurally-mediated diseases[b] such as diabetes, rheumatoid arthritis, chronic pain, and cardiovascular disease. BIOS calls this new class of therapies 'Neural Digital Therapies' (NDTs).

While NDTs can take many forms, the two main therapeutic categories are advanced bioelectronic NDTs and molecular NDTs. Advanced bioelectronic NDTs (effectively new technologies in bioelectronics) use neural interfaces to read and write (or modulate) neural signals in real time to generate a desired therapeutic effect. Molecular NDTs, meanwhile, use insights from neural recording to improve pharmacological treatments for chronic disease. These insights can enable more precise patient stratification, confirm mechanisms of action[c], or suggest novel uses for existing drugs.

Advanced bioelectronic NDTs hold the promise of dramatically improving patients' quality of life while reducing healthcare costs. BIOS has partnered with Legal & General[d] to demonstrate the

[a] Bioelectronic therapies use device technology to modulate the electrical signalling activity within the body's nervous system, opening new doors to real-time diagnostics and treatment options for patients.[1]

[b] The nervous system is the major controlling, regulatory, and communicating system in the body, and thus plays a major role in nearly every chronic disease. Specifically, the peripheral nervous system innervates the organs in our body and neural signalling is what allows the human body to efficiently manage organ function and maintain homeostasis. Neurally-mediated diseases are ones where messaging in the nervous system exacerbates existing disease or leads to organ malfunction through the electrical signals themselves or by affecting downstream mechanisms (e.g., molecular cascades).[7]

[c] Mechanism of action describes the process by which a molecule, such as a drug, functions to produce a pharmacological effect. A therapy's mechanism of action may refer to its effects on a biological readout such as cell growth, or its interaction and modulation of its direct biomolecular target, for example a protein or nucleic acid.[8]

[d] Following initial discussions on the challenges facing health technology companies and our aligned interest in helping this sector, BIOS Health and Legal & General's health and care team agreed to work together to develop this paper. For clarity and transparency, we declare that no funding was exchanged, with each party covering their own costs and contributing their expertise due to our aligned desire to support innovative health tech companies get their products to patients quicker.

need to modernise reimbursement models using early data from BIOS' first NDT to quantify the benefits to patients, clinicians, and healthcare systems.

In this primer, we take a detailed look at reimbursement models for bioelectronics. First, we survey existing reimbursement models and their limitations. Then, we examine what alternative models may be employed to more accurately reflect the value generated by advanced bioelectronic NDTs. Lastly, using early data from BIOS' first therapy as a case study, we catalogue and quantify the benefits of an advanced bioelectronic NDT for Heart Failure (HF). We hope this primer is the start of a discussion about how to optimally reimburse bioelectronics, including BIOS' own advanced bioelectronic NDTs. We believe new models can be a powerful force for innovation by more fairly rewarding innovators for the value they create. Therefore, providing potential frameworks for appropriate models to reimburse bioelectronic (and other novel neural) therapies is key to ensuring patients have access to, and benefit from, these cutting-edge treatments.

Analysis of current bioelectronic and Heart Failure therapy reimbursement models and their limitations

HOW ARE SIMILAR THERAPIES REIMBURSED TODAY?

BIOS and Legal & General conducted extensive secondary research to understand 1) how innovative bioelectronic and NDT analogue therapies are reimbursed today, and 2) whether a superior model of reimbursement exists. The research focused mainly on cardiovascular disease (specifically HF) in the US and UK markets, as BIOS' first NDT targets this therapy area.

We assessed ~50 devices, of which 32 were reimbursed commercial implantables.[e] Our analysis identified that all of these therapies were reimbursed using a transactional "Pay for Device" reimbursement strategy. This reimbursement model pays companies for their device (and for any components replaced thereafter), while the provider is paid for implantation surgery, programming, and associated hospitalisation costs, as well as any future revision, removal, and replacement procedures separately.[10-18]

[e]The stimulation targets covered in our research included: 24 spinal cord; 7 vagus nerve; 6 deep brain; 2 tibial nerve; 2 sacral neuromodulation; 2 hypoglossal nerve; and 2 cardiovascular systems (not including Implantable Cardioverter Defibrillators (ICDs) or Cardiac Resynchronisation Therapy (CRTs) devices, which were also assessed.) Conditions treated included: Heart Failure, hypertension, neurodegenerative diseases, epilepsy, OCD, depression migraines, chronic pain, paralysis, gastrointestinal and bladder/bowel control, sleep apnoea, undefined inflammatory diseases (such as Rheumatoid Arthritis, Crohn's Disease, etc.) and tinnitus. All implants with a defined reimbursement model were paid for as a device, however several products are pre-commercialisation and will be developing their reimbursement strategies.

- In the US, the commercially available implants all have reimbursement codes for implantation, replacement and removal. In addition, some have codes for calibration, analysis or reprogramming.
- In the UK, if cost effectiveness analysis from NICE is available then the cost of buying the device is provided. Note - there is the possibility that other commercial models may be agreed between the company and a provider.
- Two implants deploy a temporary device first, which is implanted for a trial period in a patient before moving to a permanent device if demonstrated to be efficacious.

Figure 1: Example neuromodulation and HF therapy reimbursement

Company	Product name	Indication	Reimbursement model	Approximate device reimbursement
CVRx[6,9,19]	Barostim Neo baroreflex activation therapy (BAT)	Heart Failure	Payment for device to company and any add-on procedures to service provider (e.g., implantation, programming, battery replacement, removal, etc.)	US: $22,750 EU: €15,000-€24,000
Boston Scientific[20]	Cardiac Resynchronisation Therapy (CRT)	Heart Failure		$18,000
Boston Scientific[20]	CRT with defibrillator (CRT-D)	Heart Failure		$36,000
Medtronic[20]	Implantable cardioverter-defibrillator (ICD)	Heart Failure		$23,000
Medtronic[10,11]	InterStim Micro Sacral Nerve Stimulator	Bladder and Bowel control		$25,000
SetPoint Medical[12]	SetPoint System	Rheumatoid Arthritis		$30,000 [targeted, not yet approved or reimbursed]

Figure 1: Current players in the bioelectronic medicine space, such as baroreflex activation therapy (BAT) using CVRx's Barostim Neo device for Heart Failure, are reimbursed using a device-based model. In the US, CVRx's device is reimbursed using a Medicare severity-diagnosis related group (MS-DRG) payment for the procedure and an add-on payment for Barostim Neo worth up to 65% of the device cost (up to a maximum amount of $22,750 USD). This is in line with European prices of €15,000-€24,000, and results in total reimbursement at a cost between $39,895 and $44,170 USD. Other invasive devices used in Heart Failure, such as Cardiac Resynchronisation Therapy (CRT), CRT with defibrillator (CRT-D) and implantable cardioverter-defibrillator (ICD) devices, are reimbursed in the same way, at a cost of $17,982, $36,153 and $23,317 USD, respectively (2020). Further, all invasive neuromodulation therapies we studied, such as Medtronic's InterStim Micro Sacral Nerve Stimulator for bladder and bowel control, are also reimbursed in this way. Even investigational treatments are targeting similar reimbursement models. For example, SetPoint Medical's is targeting a one-time reimbursement of $30,000 USD for their device to treat inflammatory conditions, whereas current drugs to treat these diseases (e.g., adalimumab, etanercept, infliximab) cost upwards of $70,000 USD per year. Note, this table and analyses are illustrative, not exhaustive.[10-18]

WHAT ARE THE LIMITATIONS OF CURRENT REIMBURSEMENT MODELS?

A "Pay for Device" reimbursement model limits collaborative engagement between innovators and providers, restricting stakeholders' ability to deliver 'state-of-the-art' healthcare for patients with chronic disease. Current models result in misaligned incentives and present several key limitations, all stemming from the fact that a pay for device reimbursement model does not focus on the value delivered to patients over time, and instead focuses on covering the cost of goods sold. This results in a transactional interaction between innovators and payors, which disincentivises innovation to develop ground-breaking therapies that improve patients' treatment experience and drive therapeutic benefits. The model therefore makes it challenging to deliver long term benefits to patients, especially when compared to procedures and drugs for similar indications.[5] The need for a new business model to capture this value has been well illustrated by Lux Capital.[21]

"Current reimbursement models limit collaborative engagement between innovators and providers"

Below we present examples of the types of benefits advanced bioelectronic therapies will bring, which are more likely to be developed if reimbursement models align to the true value delivered to patients:

1. Multiple indications treated with one implant: The pace of technological advancements in bioelectronics means treating multiple diseases via the same implant will be possible in the future (through different software-based therapies; electrical stimulation patterns with differing waveforms, amplitudes, frequencies, etc.). However, existing models do not recognise the value of treating additional indications with the same device, reducing the likelihood of their development. This is in line with challenges faced by oncology and immunology therapies that treat multiple indications, such as Herceptin (trastuzumab).[22]
2. Therapy personalisation: with the right neural reading technology, bioelectronic therapies can be titrated and programmed to maximise therapeutic efficacy and minimise side effects for each patient. Single payment for a device does not enable patients to benefit from personalised therapy programming or enable companies to cover the costs of developing these improvements.
3. Closed-loop therapy development: a closed-loop system can continuously monitor physiology (and, potentially, neural data) and make therapeutic adjustments in real time as a patients' bodies respond to external conditions, internal states, or to the device itself. Ultimately, this translates into improved therapies, which are more responsive and personalised, with better control of symptoms and fewer side effects. Similarly, current reimbursement models do not have the ability to reflect this value.
4. Remote monitoring to improve patient outcomes: remote monitoring technology can be used to identify patients who are likely to benefit from bioelectronic therapy to track outcomes and predict events. This information is very valuable to clinicians and patients, as showcased recently by Kennel et al., but current reimbursement models are unable to recognize this value.[23]

WHAT ALTERNATIVE REIMBURSEMENT MODELS EXIST?

BIOS and Legal & General believe that an optimal reimbursement model is one where patients, payors, and manufacturers are all better off compared to current models. Where patients have access to the best treatments possible, manufacturers are incentivised to innovate for their patients, and payors reimburse manufacturers at a fair value. Our aim was to identify a reimbursement model that would align stakeholders in this way.

Working together, BIOS and Legal & General identified several potential reimbursement strategies. Some are used to reimburse treatments outside of the bioelectronics space, while others are more novel to healthcare. We assessed how well these models fit our aim based on a set of five criteria: ease of implementation, commercial attractiveness, ability to capture NDT value, limitation of ethical hurdles, and mutual incentive alignment. After this assessment we arrived at three prioritised potential models: value-based reimbursement, device and services payments, and pay per activation period.

a. Value-based reimbursement: Reimbursement based on specific outcome metrics (adverse events avoided, operational productivity, costs saved, etc.) achieved for patients in real-world clinical practice. This model relies on data collection infrastructure being in place. Similar 'Managed Entry Agreements' or 'Innovative Agreements' have been used in other therapy areas such as oncology and hepatitis C.[24] For example, in 2015, a reimbursement scheme was agreed between NHS England and Janssen for the hepatitis C treatment Olysio (simeprevir). If the hepatitis virus was not cleared in 12 weeks, then Janssen would fund the cost of the treatment.[25]
b. Device and services payments: Reimbursement for implanted device upfront and recurring fees for additional services. A similar approach has been used by KardiaMobile from AliveCor, but we did not find evidence of this model being explored within the healthcare industry.[8]

c. Pay per activation period: A simple to implement model where payment is based on a (capped) amount of time a therapy is actively in use. This model has been successfully used by ElectroCore for their GammaCore device, an external vagus nerve stimulation (VNS) device. In the UK and US, payors reimburse ElectroCore for use over a fixed period – in the UK this is 93 days (after a free initial period), and in the US this is 31 days.[26,27]

We have outlined the three models which we believe demonstrate the most potential to address current reimbursement model limitations. However, they all have benefits and drawbacks which must be carefully considered (e.g., administrative burden for value-based reimbursement). Further discussion amongst the bioelectronics community, as well as engagement with payors, physicians, and both health technology assessment and regulatory agencies is needed to understand their attractiveness and feasibility.

Benefits of advanced bioelectronic NDTs, and their application to Heart Failure

BENEFITS OF ADVANCED BIOELECTRONIC NDTS

Advanced bioelectronic NDTs, or new technologies in bioelectronics, are being increasingly developed by many innovators. These technologies bring a multitude of benefits to patients and healthcare systems, and below we categorise these benefits as 'Therapy Discovery & Design' benefits (developing advanced bioelectronic therapies) or 'Therapy Delivery' benefits (improving value delivered to patients and providers and above existing therapies).

Figure 2: Value of advanced bioelectronic NDTs for patients, providers, and health systems

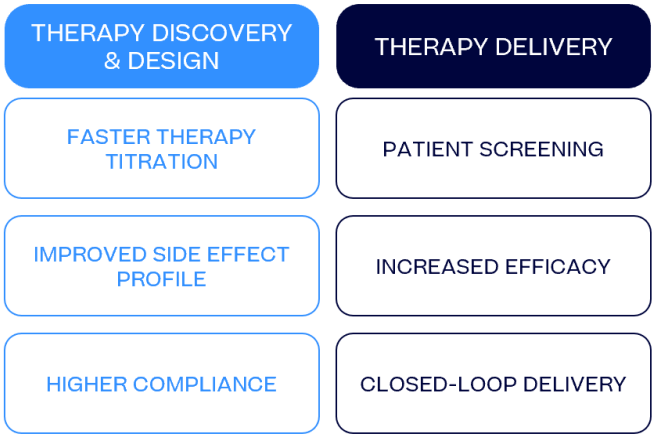


Figure 2: Framework classifying and listing potential benefit categories for bioelectronics and advanced bioelectronic NDTs.

Therapy discovery and design benefits

1. *Faster therapy titration*[f]*:* novel software can quantitatively predict personalised optimal stimulation parameters to maximise treatment efficacy, so patients experience treatment benefits sooner, with fewer clinical appointments.
2. *Improved side effect profile:* side effects are, unfortunately, an inherent part of both drug and bioelectronic treatments. However, unlike systemic therapies, biomarker driven advanced bioelectronic NDTs significantly reduce side effects through precision

[f] Titration is a method to determine the optimum dose, (or stimulation parameters for an NDT), needed to deliver therapeutic benefit to a patient, whilst limiting side effects.

therapy delivery, therefore improving patients' quality of life.

3. Higher compliance: all forms of bioelectronics are implanted, which removes patients' cognitive burden to take treatment – the patient experience becomes seamless.

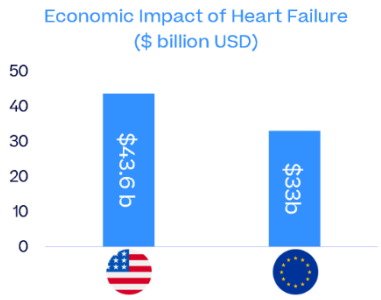
Therapy delivery benefits

1. *Identify suitable patients:* neural biomarkers[9] (gathered minimally invasively or non-invasively) can assist in patient profiling, enabling physicians to identify the candidates who are most likely to respond to bioelectronic therapy.
2. *Increased efficacy:* increased therapeutic efficacy can significantly improve patient outcomes. This can be further supported by remote monitoring tools for preventative care.
3. *Real-time therapy adjustments:* while acknowledging this benefit will require significant technological advancements, closed-loop systems could automate optimal 'dosing' for each patient as their body responds to environmental factors, internal states, or to bioelectronic treatment itself. This can maximise efficacy while also reducing side effects, with improvements accelerating exponentially over time.

BIOELECTRONIC THERAPIES FOR HEART FAILURE: A CASE STUDY

Existing landscape

Cardiovascular diseases (CVDs) are the leading cause of death globally, taking an estimated 17.9 million lives each year – accounting for approximately 32% of all deaths worldwide.[28] Heart Failure (HF) is a significant subset of CVD, with an estimated 64.3 million people living with HF worldwide[29]. An estimated 6.5 million people suffer from HF in the US alone,[30] and more than 10 million suffer from this condition in Europe. This translates to a global economic burden of approximately $108 billion per annum, with the total cost of care estimated at $43.6 billion and €29 billion (~$33 billion) in the US and EU, respectively.[30-32] Overall, HF represents an enormous global healthcare and economic burden, and innovative therapies to benefit patients while reducing costs are sorely needed.



Bioelectronics provide an avenue to address this unmet need. Existing bioelectronic therapies for HF include those offered by CVRx (Barostim Neo baroreflex activation therapy or BAT; currently commercialised)[33], and LivaNova (VITARIA Autonomic Regulation Therapy or ART; currently undergoing Phase 3 clinical trials)[34]. These therapies demonstrate significant promise for HF patients, including ~65% improvement in 6MWT, and 65% of patients improving by at least one NYHA class[33,35].

BIOS' advanced bioelectronic NDT for Heart Failure

To showcase the capabilities of some pioneering technologies, below we describe recent successes of BIOS' first NDT for HF. To date, BIOS has used its preclinical discovery system to identify targeted HF therapy candidates underpinned by data-driven insights from the nervous system. We aim to illustrate how next generation bioelectronics can deliver benefits to patients and healthcare providers, signalling the need for evolving reimbursement models. This case study focuses mainly on 'Therapy Discovery & Design' benefits as they are more applicable in the near term.

[9] Neural biomarkers are objective mappings of changes in the frequency, amplitude and firing rate of nerve signals as they relate to physiological changes of interest – they can be constructed using the plethora of signals in the nervous system and allow us to better understand the body's responses to diseases and drugs.

Faster therapy titration

Current methods for therapy titration habituate patients to side effects over time (both cognitively and biologically) by gradually increasing stimulation strength. This process can take up to eight clinical visits[35] or between 10 weeks[36,37] and six months[34] before a patient fully benefits from treatment. As a comparison, BIOS' HF advanced bioelectronics NDT uses software to quantitatively identify optimum stimulation parameters based on neural and physiological biomarkers[38]. Preclinical results have shown that this approach has the potential to deliver, at minimum, the same therapeutic benefit as existing bioelectronic HF therapies in as little as one clinical visit after device implantation.

Improved side effect profile

Side effects and therapy dosage are intrinsically linked in existing bioelectronic therapies for HF[39]. This means increasing the therapeutic index (or effectiveness of the therapy), often results in more severe side effects. In clinical trials for VNS, including VNS for HF, the following adverse events were reported directly related to the mechanism of therapy engagement: CV-related adverse events (e.g., sudden cardiac death), apnoea, cough, shortness of breath, voice alteration, dysphonia, gastrointestinal discomfort, and oropharyngeal pain at the implant site[36, 37,40, 41, 42]. This is consistent with major trials stimulating on the cervical vagus and similar targets. Livanova's ANTHEM-HF[36] trial reported 16 out of 46 patients had sustained adverse events, and CVRx's BEAT-HF[35] trial reported 9 serious adverse events from 125 patients (note grade 1-2 events were not reported in BEAT-HF).

BIOS' HF therapy uses AI-driven software to optimise stimulation while reducing adverse events. Preclinical results show promise in limiting off-target respiratory effects, including no observations of apnoea, a 25% reduction in coughing, and a 40% reduction in dysphonia. Compared to ANTHEM-HF, the most applicable comparator as Livanova's ART stimulates on the same site as BIOS' and defines adverse events in most detail (i.e., reporting minor as well as serious adverse events), this results in an expected c. 40% reduction in patients experiencing off-target effects. For some patients, side effects become the key barrier to therapy delivery[43], limiting stimulation thresholds significantly versus those that maximise therapeutic outcomes. Advancements in this space are therefore key to unlocking solutions for broader patient populations.

Figure 3: Visualisation of implied Therapy Discovery & Design benefits.

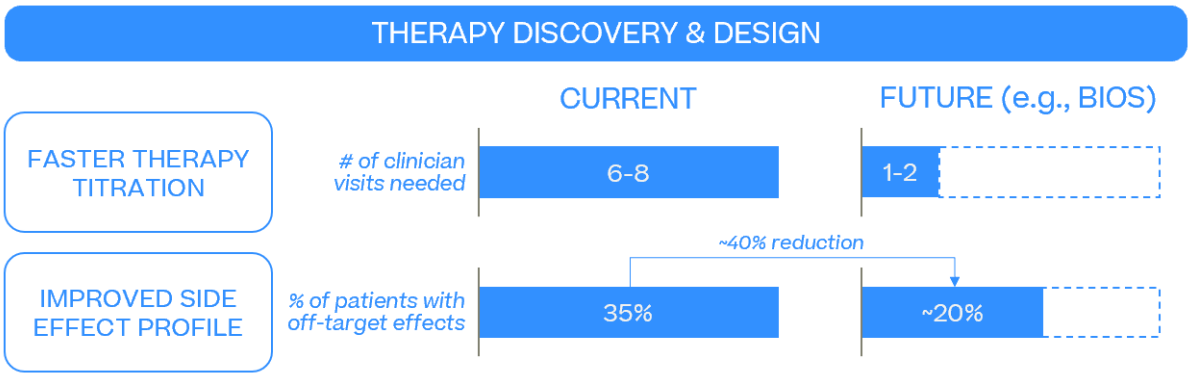


Figure 3: Quantification of NDT benefits vs. current bioelectronic therapies. Current visits are based on approved HF bioelectronics expected titration timelines. The reduction to 1 to 2 visits is expected based on early BIOS' HF advanced bioelectronic NDT data.
The side effect profile was calculated using all adverse events reported in the long-term follow up of the ANTHEM-HF study. Adverse event % was calculated as total number of adverse events, 16, divided by the number of patients, 46.[36,37]
The ANTHEM-HF study does not include a granular breakdown of non-serious adverse events. As a result, BIOS has mapped its side effect reduction data to an aggregate % vs existing therapies'. Side effect reduction of approximately 25% in cough, 40% in dysphonia, and no observable evidence of apnoea (i.e., 100% reduction) maps to ~40% expected reduction in aggregate (reducing the percentage of patients experiencing off-target effects from 35% to 20%). These reductions have been estimated based on BIOS' preclinical data.

While this case study presents the advantages of an advanced bioelectronic NDT for HF stimulating on the vagus nerve, we believe these improvements could apply equally across other diseases and nerve targets.

Advanced bioelectronic Neural Digital Therapy benefits to healthcare systems

Beyond the patient-specific benefits above, advanced bioelectronic NDTs also have a positive impact on stakeholders such as providers and payors. In this section, we aim to assess the broader set of benefits that make this class of therapies transformational, further illustrating the importance of reimbursement models that encourage innovators to develop new technologies.

THERAPY DISCOVERY & DESIGN BENEFITS: TITRATION AND SIDE EFFECT PROFILE

Faster therapy titration

A streamlined therapy programming and titration process reduces the number of visits needed to optimise treatment parameters. For example, by reducing postoperative visits from ~8 (in line with current bioelectronic therapies for HF[33,35]) to 1 (in line with early evidence from BIOS), Medicare could decrease costs by ~$975 per patient (at $139/visit)[10]. Similarly, the NHS could save ~£940 per patient (at NHS National Tariff Payments of £134/visit)[44]. Based on our market assessment[h], there are ~130,000 new US HF patients currently eligible for bioelectronic therapies pa and ~48,000 in the UK pa. This patient population is a subset with HFrEF (HF with reduced ejection fraction), the indication for which bioelectronics are approved at present. It is likely HFpEF (HF with preserved ejection fraction) also becomes applicable in the future, at which point an additional ~200,000 (US) and ~70,000 (UK) patients become eligible pa.

Of course, this does not consider any ancillary savings to other costs incurred by health systems because of these visits, or the significant resources that would be freed up to treat more patients. Further, a reduction in clinical visits helps drive equity of access (as patients don't need to travel to receive treatment as often) ensuring even those in rural or underserved areas can access these therapies. Finally, fewer visits will help health services reduce emissions from travel, aligning with ongoing efforts such as the UK's delivering 'Net Zero'.[51]

Improved side effect profile

These therapies' ability to mitigate side-effects means additional drug-based medications can often be decreased, and in fact, new technologies in bioelectronics could reduce or even replace medications with low patient tolerance or those that patients develop resistance to over time. For example, CVRx's BEAT-HF trial reported that after six months 17.5% of patients receiving Baroreflex Activation Therapy required a new class of HF drug compared with 28.8% of patients in the control group. [33,35] In 2000, the NHS projected the medication costs for HF patients to be ~£129 million.[52] In the last year, the cost of prescribing a single beta blocker (propranolol hydrochloride) was £27.5 million[53] and a single diuretic (Furosemide) was £12

[h]In the US there are an estimated 550,000 new HF patients per annum.[45] Of these 85% fall into NYHA Class II and III, 40% of which have HF with reduced ejection fraction (HFrEF) the indication and population current bioelectronics are approved for, and which BIOS HF therapy is targeting.[46,47] Roughly 70% are eligible for treatment with bioelectronics to improve HF symptoms and/or outcomes (as only 30% of CRT patients respond to treatment).[48,49] This leads to a total eligible treatment population of ~130,900 per annum.

In the UK there are 200,000 new HF patients per annum.[50] Applying the same subpopulation percentages as above[46-49], this leads to a total eligible population of ~47,600 per annum.

million.[54] Whilst not all these prescriptions would have been for HF, avoiding a percentage of these costs would have a material impact on healthcare systems.

THERAPY DELIVERY BENEFITS: PATIENT SCREENING, EFFICACY, AND CLOSED-LOOP DELIVERY

Patient screening

Incorporating remote monitoring to identify treatment-eligible candidates and track their outcomes, should ensure only likely responders are treated and reduce the strain to health systems.[23]

Increased efficacy

Bioelectronics treat diseases preventatively, and not when patients need emergency medical interventions. This means patients should not progress (and could potentially regress) through NYHA[i] classes and avoid cardiovascular events (e.g., myocardial infarction, strokes, etc). CVRx's BEAT-HF trial reported 65% of patients improved by at least one NYHA class and 97% were MANCE[j] free.[33,35] A study on UK patients in the Clinical Practice Research Datalink (CPRD)[55] found that patient mortality increased with frequent hospitalisations caused by HF, with those who were hospitalised three or more times due to HF having almost a six times greater risk of mortality.[56] Thus, avoiding hospitalisations can significantly improve patient outcomes while reducing health system costs to manage emergencies, patient rehabilitation, and co-morbidities.

As context, in the UK HF accounts for ~2% of the total NHS budget –~ £2 billion[31] - and one million patient bed days, each year. HF was the cause of over 63,000 emergency admissions in 2014/15. It is the most common cause of admission in people over 65. The number of admissions for HF is predicted to continue to rise with an ageing population[57]. In the USA, a recent study found that a single HF-specific hospitalisation costs almost $16,000 per patient[32], and NHS England will pay hospitals a best practice tariff of £7,000 for non-elective attendance for the most severe forms of HF, without considering diagnostic tests, follow up assessments, and other care.[58] Clearly, the economic impact of cardiovascular events is a strain to healthcare systems.

Closed-loop delivery and other benefits

As advanced bioelectronic NDTs progress and transition to using closed-loop devices that can perform daily titration and optimisation processes, the scope of value delivered by these therapies will significantly increase. This means an advanced bioelectronic NDT could adjust treatment based on a patient's changing environment, and keep up with their disease progression. Thus, the need for follow up appointments and prescription changes will become increasingly automated, further increasing savings. Other areas of potential savings yet to be quantified include the possibility for treating multiple conditions with one device to increase the value delivered to patients, providers, and payors.

Concluding Thoughts

Healthcare is progressing more rapidly than ever before. Technology advancements like those in bioelectronics are moving the needle for patients, and innovative reimbursement models can

[i] Heart Failure is usually classified according to the severity of an individual's symptoms. The New York Heart Association (NYHA) Functional Classification places patients in one of four categories (I-IV) based on how much they are limited during physical activity, with higher category numbers indicating increased limitations to physical activity.[55]

[j] MANCE: Major adverse neurological or cardiovascular system or procedure-related event rate. MANCE events include CV Death, Stroke, Cardiac Arrest, Acute MI, Acute Decompensated HF, Hypertensive Crisis, Severe Complication of HF Treatment, Systemic and Pulmonary Thromboembolism, Infection Requiring Explant, Cranial Nerve Damage, and Non-Elective Major Restorative Procedures.[35]

be a powerful force to ensure continuous innovation. This primer is intended to be accessible to a range of audiences, to motivate discussion and open the dialogue on a number of topics relevant to healthcare stakeholders – from existing reimbursement models to the wide-ranging benefits of advanced bioelectronics. There are still multiple challenges and solutions to explore, and BIOS and Legal & General look forward to engaging with payors, clinicians, and patients on further research on bioelectronic reimbursement models. If you're interested in working with us on this mission, reach out to partnerships@bios.health.

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