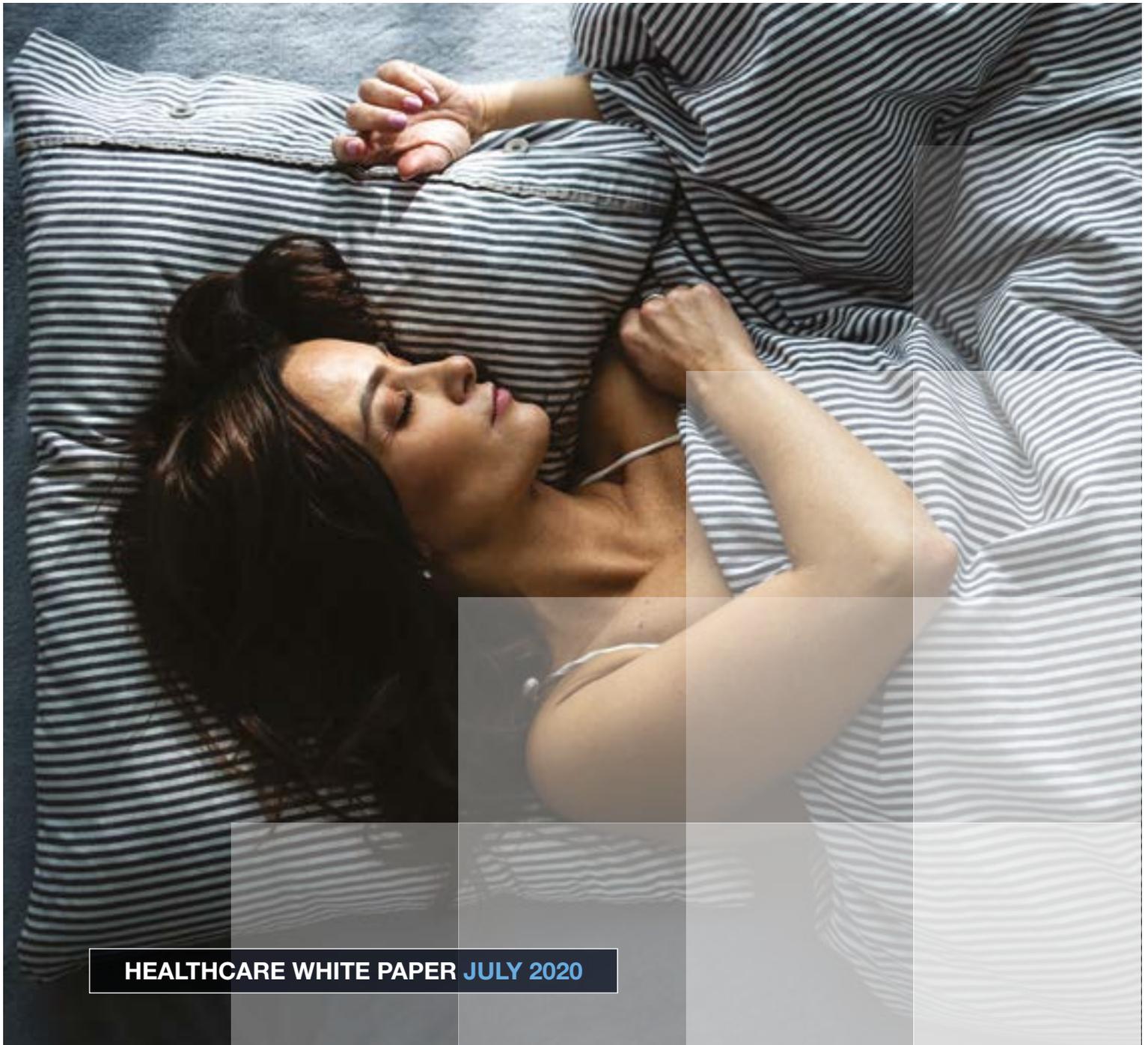




BRYAN, GARNIER & CO

Digital health

**COULD DIGITAL SOLUTIONS HELP UNLOCK SLEEP,
ONE OF BIOLOGY'S BLACK BOXES?**



HEALTHCARE WHITE PAPER JULY 2020

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In the past decade, digital solutions have emerged to help patients manage chronic diseases such as diabetes, hypertension and asthma, which affect 147 million adults in the United States alone.

Using cognitive, behavioural and psychological methods, these solutions have gained momentum in recent years, buoyed by technological advances and compelling medico-economic evidence that has driven payers to extend coverage. This trend has led to the emergence of successful companies such as Livongo, Omada Health and Big Health.

Digital adoption has now spread to mental health care, especially in relation to sleep. Poor sleep is one of the most common health problems, leading to increased healthcare costs and lost productivity across the world. Evidence of behavioural solutions for sleep problems indicates that annual savings of up to USD1,000 in healthcare costs per patient are possible, which should lead to strong adoption by payers who are early adopters of innovative solutions for driving healthcare costs down.

Finally, we believe that digital solutions will improve our understanding of sleep, which remains one of the “black boxes” of biology. The new generation of accurate and reliable sleep-monitoring wearables will contribute to a better understanding of sleep by enabling big data analysis, and will have potential applications in the early diagnosis of cognitive disorders, treatments and remote monitoring at large scale.

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Sleep: a public health priority costing billions

Poor sleep is one of the world's most common health problems

Sleep is a crucial biological process which plays an essential role in regulating our emotions, behaviour and physiology. While not all of its functions are fully understood, sleep restores energy, promotes healing,

bolsters the immune system and impacts on both brain function and behaviour.

Getting enough quality sleep at the right times contributes to mental and physical health, as well as quality of life. Sleep experts agree that most adults need at least seven hours of sleep for optimal health and

wellbeing¹. Yet, in many countries, people get one to two hours less of sleep each night than their forebears did 50-100 years ago.

Poor sleep is very common across the United States, affecting four out of 10 adults and leading the Centers for Disease Control and Prevention (CDC) to classify it as a serious public health concern. But it is not exclusively a US problem. Poor sleep affects people across OECD countries including the United Kingdom, Japan, Germany and Canada.



FIG. 1: PREVALENCE OF SLEEP PROBLEMS IN THE ADULT POPULATION

COUNTRIES	POOR SLEEP SYMPTOMS	CHRONIC INSOMNIA	SLEEP APNEA
USA	56%	10%	11%
China	40%	15%	4%
Japan	23%	13%	3%
Germany	33%	6%	7%
UK	36%	7%	3%
France	34%	13%	7%
India	30%	19%	4%
Italy	30%	7%	4%
Canada	40%	13%	6%

Source: Company Data; Bryan, Garnier & Co

CASE STUDY



A disruptive solution for sleep apnoea

As shown in Fig.1, obstructive sleep apnoea (OSA) is increasingly prevalent, and is associated with a significant social, health and economic impact. The gold-standard OSA treatment is continuous positive airway pressure (CPAP), however compliance rates can be low, resulting in a high unmet medical need for patients not suitable for this treatment. Nyxoah's solution uses a device implanted under the chin and a disposable patch worn on the chin every night. The patch wirelessly stimulates the nerves of the tongue to make it contract and prevent obstruction of the airway. Thanks to its discreet form factor and easy implantation, Nyxoah's Genio has the potential to disrupt the way we treat sleep apnoea.

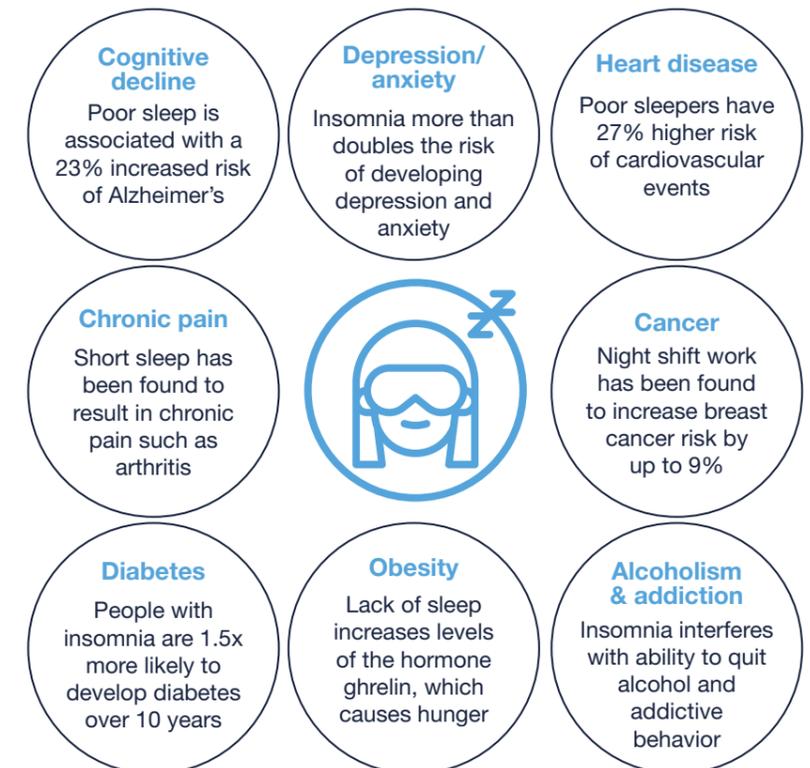
The proportion of people getting less than the recommended hours of sleep is rising. This trend is associated with lifestyle factors relating to the 24/7 society, including psychosocial stress, an unbalanced diet, physical inactivity and the excessive use of electronic media².

Poor sleep costs up to USD700 billion across five OECD countries

Insufficient sleep is associated with a range of negative health and social outcomes. It has been linked with seven of the fifteen leading causes of death in the United States, including heart disease, cancer, stroke, accidents, diabetes, septicaemia and hypertension, contributing to increase healthcare costs³.

1: National Sleep Foundation's updated sleep duration recommendations: final report. *Sleep Health*, 1(4), 233-243 | Hirshkowitz, M. et al. (2015)
 2: The Human Sleep Project | Roenneberg, 2013
 3: Mortality in the United States | Kochanek, K.D. et al. 2013

FIG. 2: POOR SLEEP IS THE CORNERSTONE OF SEVERAL CHRONIC DISORDERS



Source: Digitally Diagnosing and Treating Sleep: No Longer a Dream | 7 Wire Ventures | February 2020

Sleep problems have been associated with both higher healthcare utilization and costs. These can include costs related to direct care, such as outpatient visits and prescription medications; and indirect costs, for example increased use of healthcare for related problems that are exacerbated by poor sleep. Research shows that poor sleep is linked with increased inpatient care, including the number of days hospitalized and increased emergency visits. Inpatient care is the healthcare category most impacted by poor sleep.

Effective management of poor sleep has potential to help decrease the severity of related health problems

and in turn, reduce healthcare costs and improve quality of life.

Alongside sleep's impact on health and wellbeing, evidence suggests that it plays an important part in determining cognitive and workplace performance. Poor sleep leads to traffic and industrial accidents, medical errors and lower productivity.

Taken as a whole, the social burden of poor sleep is substantial, with direct and indirect costs exceeding 1% of GDP in some of the largest industrialized countries. In the US, costs are thought to exceed USD400 billion per year, with employer-based health plans shouldering much of the cost burden.

Treating sleep problems could therefore substantially reduce the associated costs and negative health impacts.

Treatments exist, but come with limitations

The two most widely accepted treatments for sleep problems are pharmacotherapy and cognitive behavioural therapy for insomnia (CBTi), a psychological treatment. Due to its long-term effects and safety, CBTi is considered the “gold standard” treatment for sleep problems. However, its widespread use has been limited due to a shortage of specialists and associated high costs.

Digital solutions have the potential to make CBTi widely available, while driving the costs down.

Hypnotics: purely symptomatic and the de facto first-line treatment

Drug treatment, with a class of drugs known as “hypnotics”, is only indicated as a short-term solution for poor sleep and is inappropriate for the long-term management of chronic sleep problems. As a “symptomatic” treatment, it addresses only the symptoms of the problem rather than the underlying cause. However, with access to CBTi limited, hypnotics are the most commonly used treatment

for sleep problems. Even though they are associated with a challenging safety profile, hypnotics were used by 6-10% of US adults in 2010⁴.

In 2019, the US FDA added a Boxed Warning to some of the most widespread hypnotics for risk of serious injuries caused by “complex sleep behaviours” (e.g. sleepwalking). This followed decades of safety warnings related to sleep medications, such as the risk of abuse or dependence.

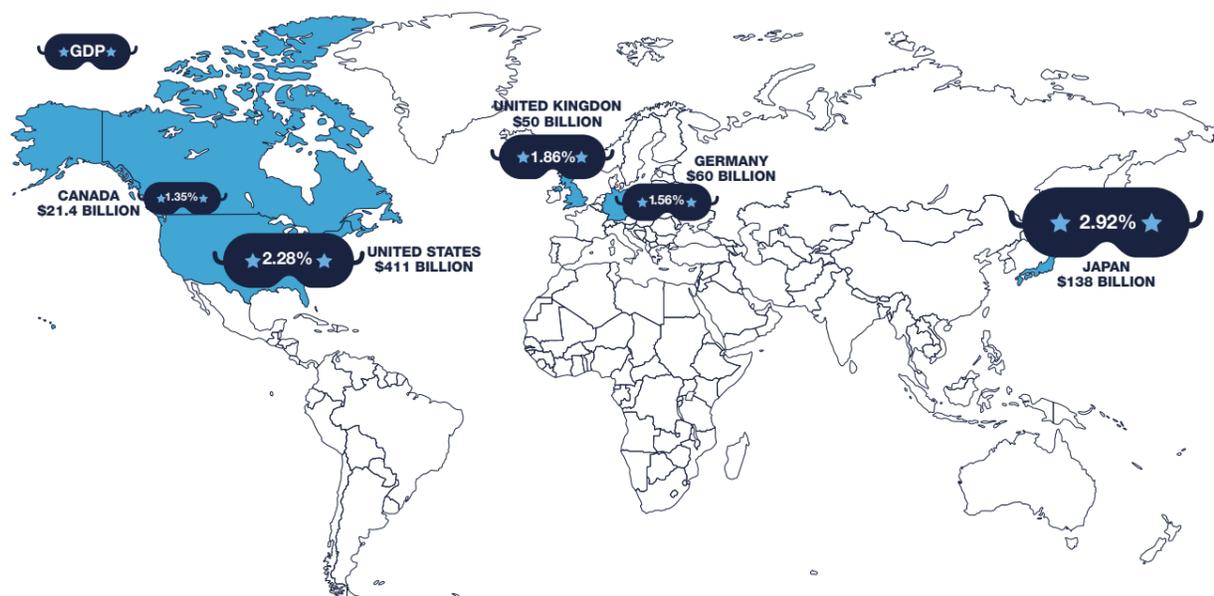
New additions to the therapeutic arsenal, such as orexin receptor antagonists, have recently been introduced. However, while they address some of the limitations of current hypnotics, they

are still only symptomatic treatments. The American College of Physicians guidelines state that they should be used alongside the “gold-standard” non-pharmacological approach.

CBTi: a gold standard, but not yet a first-line treatment

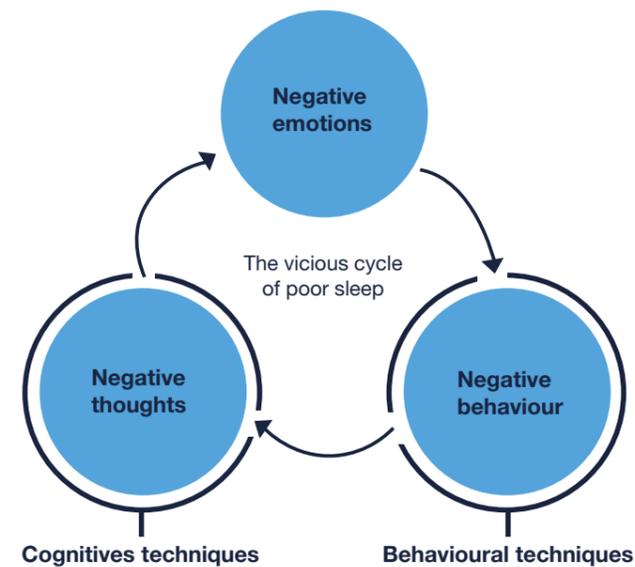
CBTi is a psychological treatment designed to break patterns of maladaptive thinking and behaviour. It helps identify and thoughts and behaviours that cause or worsen sleep problems and replace them with habits that promote sound sleep. Unlike hypnotics, CBTi helps overcome the underlying causes of sleep problems.

FIG. 3: ECONOMIC COSTS OF INSUFFICIENT SLEEP ACROSS FIVE OECD COUNTRIES



Source: Why Sleep Matters—The Economic Costs of Insufficient Sleep | Rand Health | January 2017

FIG. 4: THE VICIOUS CYCLE OF POOR SLEEP AND HOW CBTI FOR SLEEP CAN HELP OVERCOME IT



Source: CBT for insomnia – the science behind Sleepio | Big Health

⁴: Kripke DF, Langer RD, Kline LE. Hypnotics' association with mortality or cancer: a matched cohort study. *BMJ Open* | 2012



FIG. 5: COMPONENTS OF CBTi FOR SLEEP PROBLEMS

COMPONENT	DESCRIPTION
Cognitive therapy	This aims to identify, challenge, and replace dysfunctional beliefs and attitudes about sleep and insomnia. Such misconceptions may include unrealistic expectations of sleep, fear of missing out on sleep, and overestimation of the consequences of poor sleep.
Stimulus control	Behavioral instructions aimed at strengthening the association between bed and sleep and preventing conditioning of the patient to associate bed with other stimulating activities. Such instructions include avoiding nonsleep activities in the bedroom; going to bed only when sleepy; and leaving the bedroom when unable to sleep for 15–20 min, returning to bed only when sleepy.
Sleep restriction	Behavioral instructions to limit time in bed to match perceived sleep duration in order to increase sleep drive and further reduce time awake in bed. Time allowed in bed is initially restricted to the average time perceived as sleep per night and then adjusted to ensure sleep efficiency remains >85%.
Sleep hygiene	General recommendations relating to environmental factors, physiologic factors, behavior, and habits that promote sound sleep. Specific instructions include advice on control of the bedroom environment, including avoiding visual access to a clock; regular sleep scheduling and avoiding long daytime naps; and limiting alcohol, caffeine, and nicotine intake, especially before bed.
Relaxation	Any relaxation technique that the patient finds effective can be used to limit cognitive arousal and reduce muscular tension to facilitate sleep. Specific techniques that may be used include meditation, mindfulness, progressive muscle relaxation, guided imagery, and breathing techniques.

Source: Cognitive Behavioural Therapy for Chronic Insomnia | Trauer et al. | August 2015

CBTi trains people to use techniques that address the mental factors associated with insomnia, such as a “racing mind”, and to overcome the negative emotions that accompany the experience of being unable to sleep. It comprises five components, which are outlined in Fig. 5.

CBTi has achieved gold-standard status as an insomnia treatment. And because of the limited likelihood of side effects, it has been recommended by American College of Physicians as the first line-treatment for adults with sleep problems.

However, **CBTi’s biggest challenge is its inherent lack of scalability.** Traditionally delivered face-to-face by a specialist psychological therapist, it is dependent on a rare and expensive resource. It seems inconceivable that any face-to-face therapy could replace, for example, the 80 million prescriptions for hypnotics that are written each year in the US⁵.

This is why digital solutions represent an unprecedented opportunity to widen access to CBT for sleep to as many people as possible. They have the potential to make this gold standard a first-line treatment.

⁵: *Brain-Disabling Treatments in Psychiatry: Drugs, Electroshock and the Psychopharmaceutical Complex, Edition 2* | Peter R. Breggin, MD | 2007

Digital is disrupting care and treatment

Digital therapeutics: a 10-year journey finally bearing fruit

Advances in digital technology have converged with medical science, allowing digital health to become a critical part of routine clinical care. This has led to the launch of a new category of therapeutics that integrate digital technology: digital therapeutics (DTx).

DTx deliver evidence-based interventions to prevent, manage or treat medical disorders and diseases. They are driven by high-quality software programs and operate as a standalone therapy or to optimize current medication and treatments.

The emergence of this new class of therapeutics has been driven by the need to care for an ageing global population using fewer resources. DTx could extend physicians' reach by overcoming the constraints of time, place and personnel to build a "one-to-many" model of care.

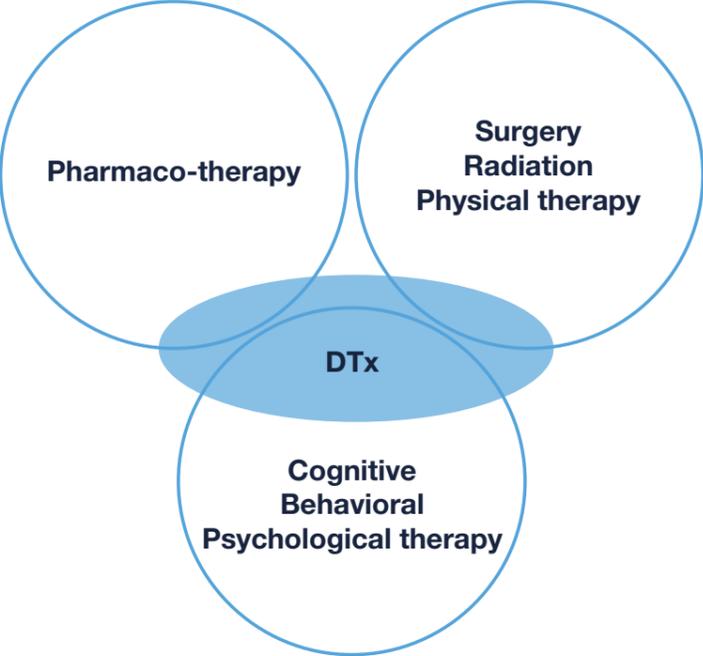
As shown in Fig.6, DTx make particular use of cognitive, behavioural and psychological therapies, reflecting their intent to effect behaviour change at scale.

In 2002, a study⁶ showed the potential of intensive behavioural intervention to reduce people's risk of developing type 2 diabetes by targeting diet and exercise in a face-to-face setting. This led companies including Omada Health to attempt to deliver the intervention digitally, and in doing

so, to make it infinitely scalable and accessible to millions of people.

Omada Health's success paved the way for digital delivery of behavioural therapy for conditions beyond diabetes. Since then, multiple digital therapeutics companies have emerged in various therapeutic areas, supported by a clearer business model that relies on US private payers. For example, Hinge Health followed Omada's path, but focusing on musculoskeletal issues.

FIG. 6: CONCEPTUAL POSITION OF DTx IN RELATION TO EXISTING THERAPEUTIC OPTIONS



6: Diabetes Prevention Program Research Group | New England Journal of Medicine | 2002

Source: Digital therapeutics and clinical pharmacology | Chung | March 2019

CASE STUDY

Omada Health, one of the first companies to demonstrate clear ROI from a digital solution

Omada's programme consists of a year-long educational curriculum and personalized health coaching, using devices to track people's nutrition, activity and weight. A peer-reviewed study has reported strong clinical outcomes in more than 200 participants, confirming the effectiveness of digital-based behavioural therapy. Omada proved that its solution led to a significant reduction in risk for Type 2 diabetes, stroke and heart disease, resulting in a ROI of over USD1,300 per person per year for the payer.

CASE STUDY

Hinge Health extended the reach of digital solutions to musculoskeletal conditions

With nearly 40,000 cumulative participants since inception, more than 100 employer customers and up to USD4,000 of savings in healthcare costs at one year per patient from its digital programme, Hinge Health proved that the Omada business model was scalable beyond metabolic conditions. Hinge's massive USD90 million raise of the beginning of 2020 is further confirmation of strong investor appetite for the digital health space.



FIG. 7: EXAMPLES OF DIGITAL THERAPEUTICS UNDER DEVELOPMENT OR ON THE MARKET

COMPANY NAME	PRODUCT NAME	DESCRIPTION	THERAPEUTIC AREA
Pear Therapeutics	reSET® reSET-OTM	An adjunct therapy to standard, outpatient treatment for Substance Use Disorder (SUD)	CNS
Propeller Health & Boehringer Ingelheim	RESPIMAT®	Combined software and hardware program to improve asthma and COPD control and optimize healthcare utilization	Respiratory
Akili Interactive	AKL-T01	Utilizing adaptive sensory stimulus software for the treatment of ADHD delivered through an engaging video game experience	CNS
Dthera Sciences	DTHR-ALZ	Delivering reminiscence therapy to Alzheimer's sufferers in a scalable and personalized manner.	CNS
Big Health	Spleepio™	Sleep improvement program featuring Cognitive Behavioral Therapy (CBT) techniques.	CNS
Cognoa	Various	AI-based digital diagnostics and personalized therapeutics for pediatric behavioral healthcare.	CNS Pediatrics
KAIA	Motion coach	Delivery of physical exercises, behavioral therapy, and education for chronic back pain patients.	Musculo-skeletal
Glooko	MIDS	Insulin mobile dose calculator for adults with Type 2 diabetes.	Metabolism
WellDoc	BlueStar®	Engaging individuals with Type 2 diabetes, hypertension, and obesity, and their providers, to improve self-management and outcomes.	Metabolism
Omada Health, Noom, Etc		Personalized digital program to help people prevent the onset of diabetes and other chronic diseases.	Metabolism
MedRhythms		Neurologic music therapy to address motor, speech, and cognitive dysfunction caused by neurologic disease or injury.	CNS

Source: Digital therapeutics and clinical pharmacology | Chung | March 2019

More recently, the US FDA gave the green light to Akili Therapeutics' game-based therapy for children with attention deficit hyperactivity disorder (ADHD). This move is a landmark decision in several respects: it is the first game to be marketed as a therapy for any type of condition; and it is the first digital therapeutic intended to improve symptoms associated with ADHD.

As a prescription-based therapy, and in contrast with Omada and Hinge's employer-based business model, Akili has followed the approach of Pear Therapeutics, which specializes in prescription digital therapeutics, by

aligning its solutions with traditional pharmacotherapies that are usually only available on prescription. However, the recent ending of collaboration between Sandoz and Pear has been a major blow for the prescription-based approach.

A business opportunity mostly driven by US employers for now

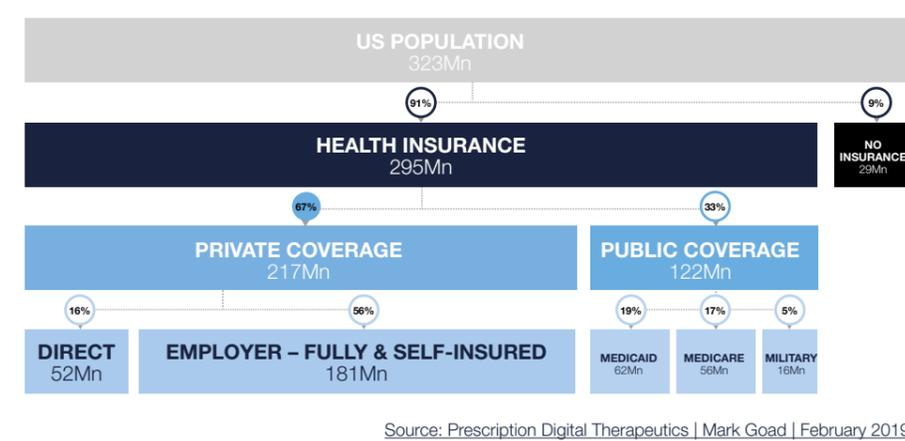
Commercialized digital therapeutics are new, so there is no well-established framework for the pricing and reimbursement of new products. It is unlikely that there will be a singular approach to securing reimbursement,

as there is with traditional pharmacological interventions.

Juniper Research expects that in the medium term, most revenue will come from direct payments from employers, with public health interest confined to a handful of markets⁷. This makes sense, given that most Americans are insured by their employers, who are early adopters of innovative solutions for driving healthcare costs down.

⁷ Digital Therapeutics & Wellness: Disruption, Innovation Opportunities & Forecasts 2019-2024 | Juniper Research | May 2019

FIG. 8: MOST AMERICANS ARE INSURED BY THEIR EMPLOYERS



Source: Prescription Digital Therapeutics | Mark Goad | February 2019

Employers are doubly concerned with maintaining employee health, both to improve productivity and retention and to avoid high healthcare costs, especially in the US. They have a strong motivation to support improvements in healthcare that push the boundaries of innovation.

The outstanding success of digital health group Livongo, a US-listed company with a market cap of USD6bn, suggests that a go-to-market strategy focusing on big US employers can deliver fast, strong growth if the technology is backed by a solid medico-economic case.

EQ CASE STUDY



Livongo's success confirms the appeal of an employer-based business model

Livongo is best known for its diabetes management application, which helps patients manage their blood sugar levels using a Bluetooth-enabled blood glucose meter and associated app that provides personalized recommendations for diet, exercise, and related behavioural changes.

In July 2019, Livongo delivered one of the most high-profile digital health IPOs ever. Following successive price raises, the company raised USD355m, claiming a market value

around USD2.5bn. Since then, flawless operational execution contributed to drive the stock price to an all-time high, making Livongo currently worth USD6.0bn.

Livongo has pioneered a new business model, convincing multinationals, government bodies and pharmacy benefit managers to pay for its technology, which enables users to manage chronic conditions while contributing to drive down healthcare costs.

This stands out from companies such as Pear Therapeutics or Click Therapeutics, which focus on prescription-based business models. We believe Livongo's outstanding success compared to others makes a strong case for the employer-based business model.

Sleep care is digital health's next big opportunity

Recent studies have confirmed the medico-economic case for digital sleep solutions

On top of the economic costs of sleep problems, recent research has also looked at the individual cost impact. Those studies are all the more important as they raise awareness of the financial burden for payers and help them to make informed decisions about the allocation of resources.

Big Health, a digital health company focused on sleep, has conducted a study evaluating the impact of poor sleep and mental health on medical and pharmacy claims for employee populations across multiple industries. While it confirmed bad sleep's impact on productivity (poor sleepers were found 3.5x less productive at work) and mental health (3.7x more likely to be stressed), the most important takeaway relates to the total annual healthcare claims spending for employees with sleep problems. On average, these employees cost over 2.4 times as much as those without insomnia, representing a difference of **USD 7,600 per employee.** (Fig. 9).

More specifically, Big Health showed that its digital sleep improvement programme based on cognitive and behavioural techniques (Sleepio) led to an average USD1,068 adjusted savings in health costs per person per year, corresponding to 18% adjusted savings in total healthcare costs at the 18-month follow-up. While this result did not reach statistical significance, it contributes to the argument that digital administration of behavioural therapy for sleep disorders can help reduce healthcare costs, while paving the way for more innovative solutions in this area.

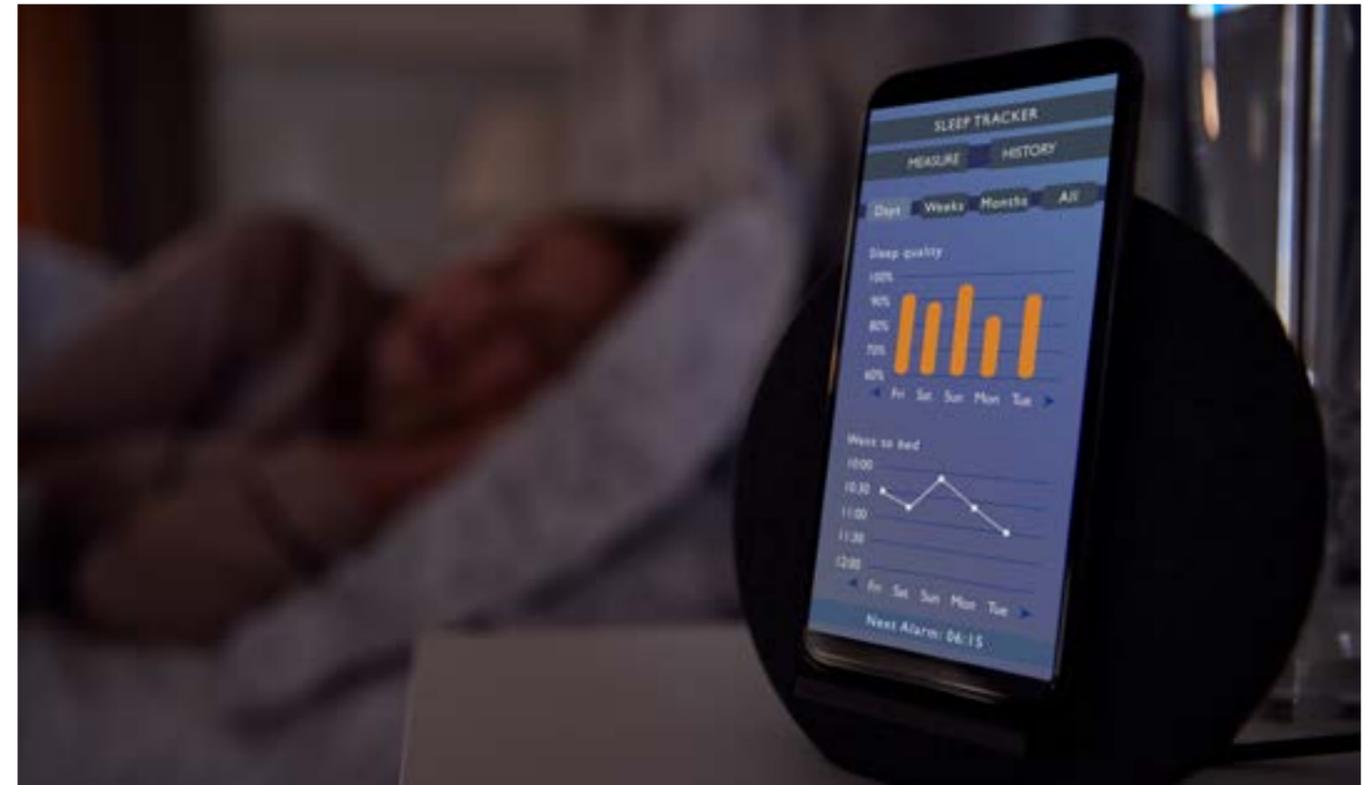
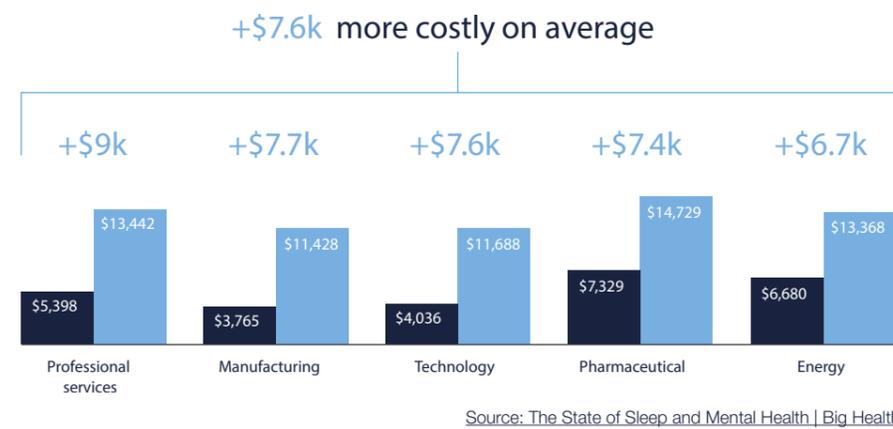
EQ CASE STUDY

Big Health

Big Health: one of the very first DTx solution dedicated to poor sleep

Big Health has developed Sleepio, a digital sleep improvement program comprising cognitive and behavioural techniques. Available via web and mobile applications, it has the potential to scale to large populations. Several studies have shown that it was able to help people make significant improvements in their sleep, confirming that poor sleep should be the next condition to benefit from advances in digital solutions.

FIG. 9: INDIVIDUALS WITH INSOMNIA COST 2.4X MORE



US employers are now embracing digital solutions for sleep

Historically, sleep has been at the top of employees' considerations but employers have been reluctant to cover it as the economics are not clear. Castlight's 2018 The State of Digital Health report highlighted that good sleep is one of the top three health goals for employees and that 70% of employees are likely to use a sleep solution if it is offered by their employer.

With a clearer view of clinical outcomes and achievable savings, employers are taking a closer look at digital solutions for sleep. According to the 24th Willis Towers Watson report Best Practices in Health Care Employer Survey, 56% of US employers are now planning to implement a sleep plan by 2021. McKinsey's 2018 Consumer Health Insights Survey found that the innovative feature of insurance plans most appreciated by consumers was an incentive to change behaviour.

The majority said they would be willing to change their behaviours — exercise more, for example — to reduce their insurance premiums.

Overall, we are witnessing an alignment between different stakeholders — employers, vendors, employees — contributing to the adoption of digital solutions to reduce sleep problems. We expect multiple players to emerge to replicate Livongo's success in metabolic diseases.

The future of sleep health: a big-data revolution in the making

Outdated technology has limited our understanding of sleep

Great advances have been made in understanding sleep. We now know which brain regions are involved in sleep and how the internal circadian clock works. However, there remain many unknowns, for example around the role of genetic and environmental factors in sleeping patterns and the quantity of sleep needed.

One reason for this lack of understanding is that most of what we know comes from laboratory studies, with people instructed to sleep in controlled conditions with electrodes fastened to their heads. Since the 1960s, polysomnography (PSG) has been the standard technique for sleep measurement in clinical and laboratory settings, as well as to diagnose sleep disorders. However, its use is limited as it remains impractical for long-term

sleep monitoring or for measuring sleep outside laboratory conditions.

A PSG sleep study is typically a single overnight assessment that usually takes place in a sleep centre. It records physiological signals including electroencephalographic (EEG), electromyographic (EMG), and electrooculographic (EOG) activity, as well as breathing effort, airflow, pulse, and blood oxygen saturation.

Overall, PSG is expensive, costing 1,500-\$2,000 per night in the US. It is also time and resource-intensive, with an expert needing **one to two hours** to score a night of clinical PSG recordings. Yet the cumbersome nature of the PSG process means it does not reliably capture a patient's typical sleep.

In response, industry and academia have invested heavily in the development of smaller, less obstructive and more portable devices for the continuous monitoring of sleep.

This is motivated by a desire to enable data acquisition in larger participant groups, over more extended periods and in a more natural setting, by reducing both the cost of monitoring and the burden to participants.

Recent advancements in data acquisition opened the door to a big data revolution in sleep

To understand the role of sleep in health and disease, sleep must be monitored in a natural environment and in a non-obstructive way to ensure that data is as representative of typical sleep as possible. This needs low-cost, wearable sleep detection systems that give reliable sleep architectures in real-life settings.

While options such as actigraphy and heart rate sensing are available to monitor sleep outside of a laboratory, none have demonstrated comparable results to PSG, because a single metric such as heart rate alone is not enough to provide sophisticated sleep stage classification.

More recently, a new group of devices has emerged for home sleep monitoring that uses EEG electrodes to measure brain activity. These include headbands and devices placed around the ear. Unlike traditional PSG, these more compact devices are usually cheaper,

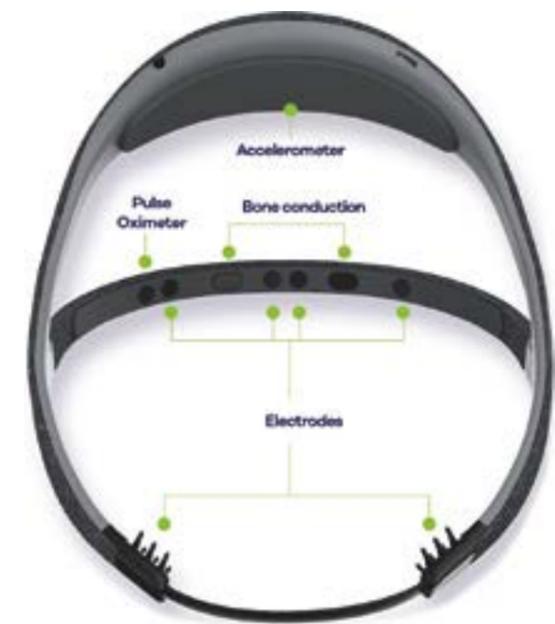
less burdensome, designed to be worn for multiple nights at home to enable longitudinal data collection, and require minimal or no expert supervision. However, most have reported mediocre accuracy and reliability compared to PSG.

The Dreem Headband is establishing itself as an affordable, comfortable, and user-friendly alternative to PSG. Illustrated in Fig.11, it features physiological signal acquisition and automatic sleep analysis using a deep learning algorithm along with five dry EEG electrodes, a 3-D accelerometer and a pulse oximeter.

FIG. 10: POLYSOMNOGRAPHY (PSG)



FIG. 11: ILLUSTRATION OF THE DREEM HEADBAND



Dreem Headband | Image courtesy of Dreem

Through a direct comparison to PSG in 25 subjects over one night, the Dreem Headband showed reliable recording of high-quality sleep EEG, heart rate, and breathing data while being considerably more comfortable and easier to install than PSG. It was able to acquire EEG during sleep with sufficient signal quality; reliably measure breathing and heart rate during sleep; and perform automatic sleep staging classification with performance similar to that of a consensus of five scorers using medical-grade PSG data.

These results make the Dreem Headband an ideal candidate for high-quality large-scale longitudinal sleep studies in the home or laboratory environment. Along with other new technologies, it should contribute to leveraging the big data potential for sleep.

Big data in sleep has unlimited potential

Recent advances in sensing technology, big data analytics, and artificial intelligence will allow continuous sleep monitoring, which is going to impact a wide and growing range of key areas. We expect technologies that digitalize sleep will disrupt the way we understand, monitor, diagnose and treat a vast list of medical conditions far beyond sleep itself.

FIG. 12: OVERVIEW OF THE ROLE OF BIG DATA IN SLEEP RESEARCH

Potential role of big data	Definition	Examples
Understanding	Explaining the mechanisms of sleep	Emergence of new digital biomarkers
Monitoring	Using new technologies for non-intrusive sleep monitoring	Remote monitoring for clinical trials
Diagnosis	Predicting an individual's risk of developing conditions	Alzheimer's disease Parkinson's disease Obstructive Sleep Apnoea, Narcolepsy
Treatment	Personalizing treatment and clinical decision-making	Moderate Sleep Apnoea, Adherence CPAP therapy Depression

Source: Bryan, Garnier & Co

Monitoring: from clinical to post-market studies

Advancements in sleep measurement wearables make it possible to deploy remote sleep monitoring at scale, in the large populations that are required for late-phase clinical trials. Monitoring can be also be used to provide better and earlier evidence of treatment efficacy, facilitating drug development. On top of that, we expect low-burden monitoring to facilitate sleep data collections in trials, and to potentially increase trial participation and reduce attrition. Finally, it could be particularly interesting for big pharmaceutical companies looking to gather data for post-market surveillance studies.

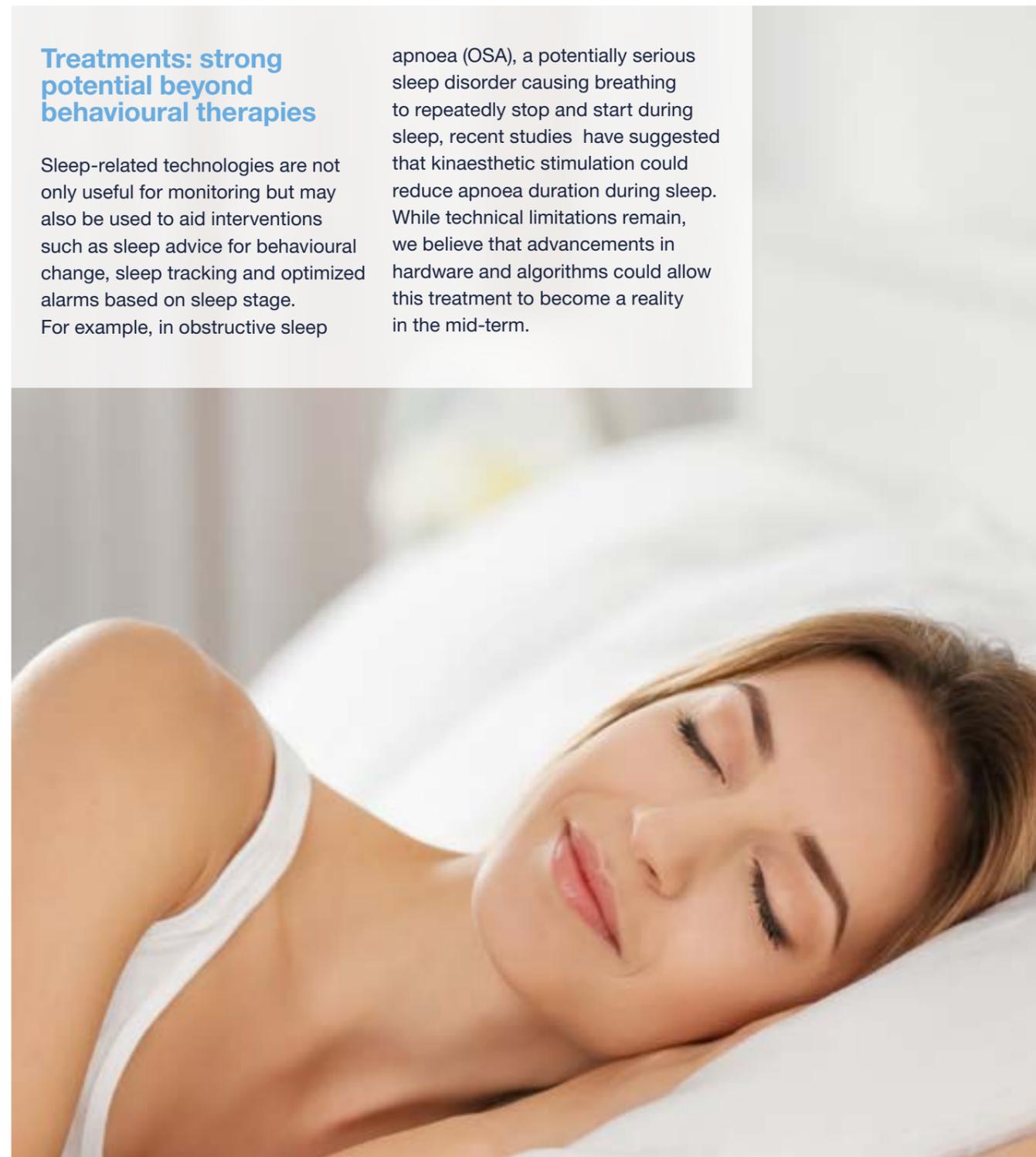
Diagnosis: a tool to diagnose degenerative diseases

Several studies have linked sleep with conditions including Alzheimer's Disease (AD) and Parkinson's Disease (PD). Research has shown that the primary pathological features of AD were associated with both objective and subjective changes in sleep, suggesting that sleep monitoring could help diagnose AD, while treatment for sleep deficiencies could delay the progression of AD. Recent work on PD identified REM sleep behaviour disorder as an early biomarker for PD, suggesting that better sleep screening could result in earlier treatment.

Treatments: strong potential beyond behavioural therapies

Sleep-related technologies are not only useful for monitoring but may also be used to aid interventions such as sleep advice for behavioural change, sleep tracking and optimized alarms based on sleep stage. For example, in obstructive sleep

apnoea (OSA), a potentially serious sleep disorder causing breathing to repeatedly stop and start during sleep, recent studies have suggested that kinaesthetic stimulation could reduce apnoea duration during sleep. While technical limitations remain, we believe that advancements in hardware and algorithms could allow this treatment to become a reality in the mid-term.





Conclusion

We believe that digitalization of sleep and ubiquitous sleep monitoring will have important implications for the characterization of sleep, diagnostics and therapeutics. Large epidemiological studies exploring the impact of sleep will be possible thanks to large-scale collection of longitudinal sleep data with “lab-level” wearables.

We expect digital solutions for sleep to thrive, supported by additional medico-economic evidence that drives adoption from private and then public payers. Beyond sleep, those solutions should expand their footprint into brain health. In the medium-term, sleep-based diagnosis of medical conditions should become a reality and facilitate better and earlier diagnosis and decision-making for patients.

Finally, Big Health’s recent USD39m Series B funding round highlighted the strong appetite from investors for digital solutions dedicated to poor sleep. We believe that several other companies will emerge in the near future with innovative digital solutions for sleep, driven in particular by employers, who are more willing than ever to tackle this costly public health priority.

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Bryan, Garnier & Co is a European, full-service growth-focused independent investment banking partnership founded in 1996. The firm provides equity research, sales and trading, private and public capital raising as well as M&A services to growth companies and their investors. It focuses on key growth sectors of the economy including Technology, Healthcare, Consumer and Smart Industries & Services. Bryan, Garnier & Co is a fully registered broker dealer authorized and regulated by the FCA in Europe and the FINRA in the U.S. Bryan, Garnier & Co is headquartered in London, with additional offices in Paris, Munich, Stockholm, Oslo, Reykjavik as well as New York and Palo Alto. The firm is a member of the London Stock Exchange.

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