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The New Collection

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The New Collection 2017

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Editorial Welcome

Welcome to the 12th edition of *The New Collection*, an interdisciplinary student-led academic journal that publishes research done by postgraduates at New College.

Authors submitting to *The New Collection* take upon themselves a challenging but rewarding task; since all articles are required to be accessible to a general academic audience, the authors must address a readership with backgrounds and practices quite divorced from their own. Whilst there is much focus nowadays on the importance of outreach, and on developing the ability to communicate ideas and research in simple terms to the layman, equally important is the ability to learn to communicate one's research to academics working in other disciplines. Such a skill can be best learned by talking to peers and exchanging ideas, which is precisely what occurs during the review process at *The New Collection*: thanks to a common effort between the Middle Common Room (MCR) and Senior Common Room (SCR), articles are edited several times and many comments from experts and non-experts are submitted, in an effort to make the articles truly accessible to a general academic audience. Thus not only is *The New Collection* a way for MCR members to experience the peer review process first hand, often for the first time; it also offers a unique opportunity to be exposed to research practices in fields very far from one's own. One small but significant aspect of this – which you may notice reading through the pages of this volume – is that all articles have different reference styles, according to the field to which they belong.

I would like to thank the authors, the editors from the MCR, and the reviewers from the SCR for the enormous effort they put into making the volume you are holding in your hands possible.

On behalf of the editorial team,

Nina Otter, Editor-in-Chief

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The Warden's Foreword

'Research Excellence' is one of the Higher Education buzz phrases of our time. In the obsession with measurement which has overtaken the sector, the highest level of quality is defined – and measured – as comprising 'originality, significance and rigour'.

At the beginning of their own journeys in research, our New College graduates are already pushing hard and confidently in all these directions.

As they do so, *The New Collection*, published annually at the MCR's initiative, gives them the opportunity to have their work tested and reviewed by both their peers and our Senior Common Room, and then exposed to a wider audience. As such, *The New Collection* not only is a catalyst for encouraging good academic writing but it also plays a part in building a vibrant community within the college as a whole. Research becomes accessible and shared, not hidden in private silos.

This is the first volume of *The New Collection* I have read. Collections tend not to be as interdisciplinary as this, so the sheer range of subjects covered here – from transcranial magnetic stimulation to sex education, from the interests of social entrepreneurship in the 20th century to the medicalization of the workhouse in the 18th century, from a new perspective on Romanian children in care to a re-definition of the placebo – cannot fail to impress. But all express an interesting point of view, soundly evidenced. Though early days for the authors, what they are producing is indeed original, significant and rigorous.

Miles Young, Warden of New College, Oxford

MCR President's Foreword

What matters to children in care? What is Transcranial Magnetic Stimulation? Are we doing enough in relation to sex and relationship education in secondary schools? The great genius of the collegiate University is that it brings together a community of scholars of varied interests, creating a group of people who ask the most diverse and fascinating questions, and then fosters an immersive learning environment to give those scholars a chance to answer what they have asked. This year's edition of *The New Collection*, one of the only student-led academic journals published by an Oxbridge Common Room, is a showcase for the incredible intellectual talent present in this place.

That being said, talent without direction is nothing. This twelfth edition of *The New Collection* owes its existence to the dedicated labors of Nina Otter, this year's editor-in-chief, and her editorial team, who have put in many weeks of work to curate the collection of articles you're holding now. They have earned our thanks. I'd also like to thank the members of the Senior Common Room who donated their valuable time to review all of this year's pieces, as well as our new Warden, Miles Young, who has seamlessly continued the College's tradition of support for *The New Collection*.

On behalf of the entire postgraduate community at New College, it is my sincere hope that you will find enlightenment and enjoyment within these pages.

Daniel Hatem, MCR President 2016-2017

Papers published by MCR members

This is the second year in which The New Collection does not only publish its own articles, but also a list of articles by New College MCR members that are accepted by other peer-reviewed journals between June 1st 2016 and June 1st 2017. We are happy to present and congratulate the following entries:

- Yanyan Liu et al, 'Particles for Simultaneous 3D Imaging and Optical Tweezing in Dense Colloidal Materials', *Advanced Materials* (2016), 28(36), 8001-8006. Available at <http://doi.org/10.1002/adma.201602137>.
- Xiaoyu Lu et al, 'Relativistic Monte Carlo', *Proceedings of the 20th International Conference on Artificial Intelligence and Statistics* (2017), 40, 1236-1245. Available at <http://proceedings.mlr.press/v54/lu17b.html>.
- Kinan Muhammed et al, 'Reward sensitivity deficits modulated by dopamine are associated with apathy in Parkinson's disease', *Brain* (2016), 139(10), 2706-272. Available at <http://doi.org/10.1093/brain/aww188>.
- Kinan Muhammed et al, 'Clinical significance of apathy in Parkinson's disease', *European Medical Journal* (2016), 4(1), 56-63. Available at <http://ora.ox.ac.uk/objects/uuid:132cc807-95d9-4d37-8a46-dd02e103b934>.
- Kevin Noles, 'Renegades in Malaya: Indian volunteers of the Japanese, F. Kikan', *British Journal for Military History* (2017), 3(2), 100-118. Available at <http://www.bjmh.org.uk/index.php/bjmh/article/view/154/123>.
- Bhavin Siritanaratkul et al, 'Transfer of photosynthetic NADP+/NADPH recycling activity to a porous metal oxide for highly specific, electrochemically-driven organic synthesis', *Royal Society of Chemistry* (2017), 8(6), 4579-4586. Available at <http://doi.org/10.1039/C7SC00850C>.

The historical development of social entrepreneurship in England

Tanja Collavo*

Saïd Business School

Social entrepreneurship has been on the rise in the world in the past twenty years. Several organizations have been created to support the rise of the sector or have decided to enter in it with programs, awards and provision of support. This article aims to clarify the trajectory of the sector's establishment and growth in England, highlighting the struggles deriving from the presence and interest in the sector of both the government and several private players coming from the business and social traditions. The story of the English social entrepreneurship sector, as one of the most developed in the world, provides insights for supporters of this concept as well as warnings about its potential drawbacks.

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Introduction

Social entrepreneurship – any action that has a focus on a mission centred around the creation of social value, a certain degree of innovation, and that uses entrepreneurial techniques and models¹ – as a sector and concept has gained increasing recognition and support since the early 2000s and, in particular, in the last decade. In a very broad sense, social entrepreneurs and enterprises are seen as mechanisms compensating for market and business failures, i.e. as providers of social services and social products that neither businesses nor public authorities are willing or able to guarantee to disadvantaged populations. The expansion of this sector has been particularly fast and evident in England, where both public and private players have engaged significant resources in the development of social entrepreneurial projects. Their presence and interest in social entrepreneurship has led to the development of a growing social investment sector, of several umbrella bodies and intermediaries and of specific business-led projects aimed at nurturing and growing social ventures.

As a result, many observers and experts consider the social entrepreneurship sector in England as the most advanced in the world at present². Nonetheless, despite its success, the sector is less cohesive and strong than it might seem and several factors might menace its survival and growth in the future. This paper aims to examine the forces that made this quick development possible, together with those that have created past and existing issues, by adopting an historical approach. It traces the evolution of social entrepreneurship as a concept and as an economic and social sector from its origins in the late 1990s to 2016, highlighting the role that different players have had at different stages of its development and the political struggles involved in the creation of a new sector. The lessons learned from England show the way for other countries interested in supporting the development of social entrepreneurship and highlight the difficulties and traps that might be involved in the establishment of this sector.

Portraying the history of social entrepreneurship in England can be relevant for both practitioners and academics. On the one hand, knowing what worked well (and less so) in England can be helpful for policy makers and organizations

¹Austin J.E., Stevenson H., Wei-Skillern J. 'Social and Commercial Entrepreneurship: Same, Different, or Both?' *Entrepreneurship Theory and Practice* 2006;30(1):1-22; Bacq S., Janssen F. 'The multiple faces of social entrepreneurship: A review of definitional issues based on geographical and thematic criteria.' *Entrepreneurship & Regional Development* 2011;23(5-6):373-403.; Corner P.D., Ho M. 'How Opportunities Develop in Social Entrepreneurship.' *Entrepreneurship Theory and Practice*. 2010;34(4):635-659.

²Villeneuve-Smith F., Temple N., Brown B., Gregory D., BMG Research. 'State of Social Enterprise Survey 2015: Leading the World in Social Enterprise?'. Research Paper. Social Enterprise UK. 2015.

interested in growing social entrepreneurship in other countries. Furthermore, it could enhance the sector's understanding of players based in England, who might not have the chance to see the 'broader picture' due to the daily efforts of operating in a constantly changing environment. On the other hand, this topic is of interest for scholars working on social entrepreneurship. Most of the existing literature focuses on the different definitions of this concept and on the consequences that the definitional debate has on the advancement of social entrepreneurship as a research field³. Other common themes in the social entrepreneurship literature are the institutions and institutional logics surrounding social entrepreneurship, cross-sector partnerships⁴, the hybrid nature of the sector and of its players⁵ and the role and characteristics of social entrepreneurs and enterprises⁶. Only recently, attention has moved towards the systems and environmental characteristics supporting the growth of social innovation and social entrepreneurship. More research is thus required in this sense in order to understand how players can create the right conditions to sustain the growth of these new sectors⁷. This study contributes to this recent stream of literature, presenting examples of what stakeholders from the private, public and private sectors can do to contribute to the support of social entrepreneurs and enterprises. The paper will proceed as follows: it will describe the three phases of evolution of social entrepreneurship in England (Phase 1: 1995-2005, Phase 2: 2006-2010 and Phase 3: 2011-2016) and then it will briefly summarize current strengths and challenges present in the sector.

³Bacq, Janssen 2011; Alter K. 'Social Enterprise Typology', 2007.; Choi N., Majumdar S. 'Social entrepreneurship as an essentially contested concept: Opening a new avenue for systematic future research.' *Journal of Business Venturing*. 2013:1-14.; Dacin P.A., Dacin M.T., Matear M. 'Social entrepreneurship: why we don't need a new theory and how we move forward from here.' *Academy of Management Perspectives*. 2010;24(3):37-58.; Defourny J., Nyssens M. 'Conceptions of social enterprise and social entrepreneurship in europe and the united states: convergences and divergences.' *Journal of Social Entrepreneurship*. 2010;1(1):32-53.; Hoogendoorn B., Pennings E., Thurik R. 'What do we know about social entrepreneurship: an analysis of empirical research.' Report SRI: June. Erasmus Research Institute of Management (ERIM). Rotterdam; 2010.; Perrini F. 'Social entrepreneurship domain: setting boundaries.' In: Perrini F., ed. 'The New Social Entrepreneurship: What Awaits Social Entrepreneurial Ventures?' Edward Elgar Publishing Limited. 2006:1-25.

⁴Phillips W., Lee H., James P., Ghobadian A. 'Social innovation and social entrepreneurship: a systematic review.' *Group & Organization Management*. 2015;40(3):428-461.

⁵Santos F.M., Pache A.-C., Birkholz C. 'Making hybrids work: aligning business models and organizational design for social enterprises.' *Calif. Manage. Rev.* 2015;57(3):36-59.; Doherty B., Haugh H., Lyon F. 'Social enterprises as hybrid organizations: A review and research agenda.' *Int. J. Manag. Rev.* 2014;16(4):417-436.

⁶Hoogendoorn, Pennings, Thurik 2010

⁷Phillips, Lee, James, Ghobadian 2015

The government-led decade: 1995-2005

Social entrepreneurial practices have existed since the dawn of society, in England as elsewhere. In the late 19th century, it was impossible for a company in the UK to obtain limited liability unless its main goal was to produce a public benefit. Almost a century later, in the UK as well as in Italy, there was the rise of cooperatives, organizations increasing workers' participation by granting them part of the ownership of the venture and thus participation to the strategic decisions and to the financial value created. However, despite these long-existing practices, the concept of social entrepreneurship appeared in England only in the mid-nineties, thanks to left wing think-tanks that saw in social entrepreneurs an opportunity to regenerate local communities and to re-integrate them in the economic and social tissue of Britain after the Thatcher government⁸.

The reports of think-tanks such as Demos and Joseph Rowntree Foundation inspired Tony Blair and his Labour government⁹. In 1999, the latter published *The Compact*, in which it explained how social enterprises could be an ideal vehicle to tackle social exclusion and to complement the government's delivery of social services to local communities¹⁰. In 2002, a Social Enterprise Unit was created within the Department of Trade and Industry¹¹ and in 2003, a new legal form, the Community Interest Company (CIC), was developed to enable the incorporation (and thus recognition) of social enterprises¹². In the same years, the government provided funds to third sector organizations willing to lobby for the sector and it created a trade association – the Social Enterprise Coalition (SEC) – to ensure social enterprises representation with the government. Furthermore, between 2001 and 2004, the government supported specific funds destined to social enterprises or to third sector organizations that could take over public services and/or sustain community renewal such as Bridges Community Ventures, Adventure Capital Funds or Futurebuilders¹³.

Seeing the government's keenness for social enterprises, many constituents

⁸Huckfield L. 'The Rise and Influence of Social Enterprise, Social Investment and Public Service Mutuals.' Working Paper 3. National Coalition for Independent Action. 2014.; Grenier P. 'The Role and Significance of Social Entrepreneurship in UK Social Policy.' Doctoral Work. Department of Social Policy and Administration, London School of Economics. 2008.

⁹Grenier 2008

¹⁰Zimmeck M. 'The Compact 10 years on: government's approach to partnership with the voluntary and community sector in England.' Voluntary Sector Review. 2010;1(1):125-133.

¹¹The British Council. 'Social enterprise in the UK: developing a thriving social enterprise sector.' 2015.

¹²Little M. 'Enterprise plan gives profit "lock".' Third Sector. March 26, 2003:9.

¹³Nicholls A., Teasdale S. 'Neoliberalism by stealth: exploring continuity and change within the UK social enterprise policy paradigm.' Policy & Politics 2016:1-19.

such as businesses, media and academic institutions started to pay attention to this emerging sector and to get involved in it. The ‘best’ social entrepreneurs and enterprises soon began to be awarded by many different institutions in exclusive and sometimes public ceremonies¹⁴. Seven organizations interested in sustaining the establishment of social entrepreneurship in the UK created a foundation – UnLtd – to be able to manage and distribute to social entrepreneurs-to-be the interests coming from the Millennium Awards Fund established by the British government with a £100 million endowment. In 2003, the American entrepreneur Jeff Skoll announced his desire to establish an academic centre dedicated to social entrepreneurship at Said Business School, Oxford University. His ambition was to generate knowledge on social entrepreneurship at an academic level and to provide training to social entrepreneurs and members of social enterprises so to accelerate the growth of their projects¹⁵.

The work and partially diverging views of multiple private organizations pushing for the sector’s growth together with the government made the definition of social entrepreneurship increasingly vague. In an article published in 2002 in *The Economist*, social entrepreneurship was said to encompass cooperatives, charities and non-profits getting multiple revenue streams, businesses with social conscience and businesses reinvesting profits¹⁶. This broad definition was a consequence of the multiple schools of thought originating in various parts of the world such as the UK, the European Union or the United States, all finding fertile terrain in England¹⁷.

For example, the Department of Trade and Industry described social enterprises as businesses with a social purpose generating revenues through trade and reinvesting the majority of their profits into the generation of social impact or into their community. This definition was close to the U.S. school of thought calling social enterprises the trading arms of charities and NGOs. Private organizations such as Ashoka UK were instead promoting social entrepreneurs as people innovating the third sector by introducing entrepreneurial solutions to the causes of social problems, a concept resonating with the ‘Social Entrepreneurs Schools’ developed in the U.S. by academics such as Gregory Dees¹⁸. Finally, the inclusion within the social entrepreneurship space of cooperatives operating in sectors such as banking or food, reflected as well the influence of the European

¹⁴Grenier 2008; Finn W. ‘Soul Traders.’ *Director* 2004:58-62.

¹⁵Cater N. ‘Skollarship, or how to forget your scruples.’ *Third Sector*. November 15, 2006.

¹⁶The Economist ‘The third way in action; social enterprise.’ August 10, 2002:30.

¹⁷Teasdale S. ‘The potential for the social economy to combat social exclusion.’ Doctoral Work. University of Manchester. 2006.

¹⁸Defourny, Nyssens 2010

Union, which promoted the concept of co-operatives and social enterprises as a means for economic development and community support¹⁹. At this point in time, social enterprises included charities, businesses, co-operatives, charities with commercial branch, socially focused corporates and public sector projects²⁰. Thanks to this multiplicity of organizational models present in the sector, in 2005 the Department of Trade and Industry estimated the existence of around 15,000 social enterprises in the UK, accounting for more than 1 percent of business activity in the country²¹.

The growth of private players: 2006-2010

The last term of Labour government (2006-2010) saw a steady rise in social enterprises as well as in the number and visibility of private organizations supporting and lobbying for the sector. In 2006, only one year after estimating the presence of 15,000 social enterprises in the UK, the Department of Trade and Industry released a new figure affirming the existence of around 55,000 social enterprises, contributing more than £8 billion a year to the economy²². A couple of years later, a survey of the Office of the Third Sector identified 79 different organizations supporting social enterprises at national, regional, sub-regional and local level²³. This led to a widespread replication of efforts as well as to an increasingly vibrant definitional debate. For example, in 2008, the support organization CAN announced its first directory of social enterprises²⁴, thus duplicating existing directories of other entities such as Social Enterprise London, UnLtd and the government, which had launched one in the previous year. Furthermore, contrasts emerged between the most influential and vocal organizations about the meaning of the sector and its location in the wider economic system.

Some representatives of the charity sector were anxious about the entrepreneurial side becoming increasingly relevant. They believed this would have implied excessive risk-taking and thus a low consideration for funders' money²⁵. On the other side, business-minded people reflected on how many charities such

¹⁹Grenier 2008

²⁰McCurry P. 'Enterprise Culture – Where social benefit meets business.' Third Sector. January 19, 2005:26.; Plummer J. 'The next decade: don't stop now.' Third Sector. January 12, 2005:26.

²¹Little M. 'Social enterprise could be three times bigger than first thought.' Third Sector. July 20, 2005:9.

²²Little M. 'Social enterprise worth pounds 8.4bn.' Third Sector. May 31, 2006:7.

²³Warrell H. 'Money matters.' Third Sector. April 16, 2008:9.

²⁴Warrell H. 'Online directory for social enterprises.' Third Sector. March 12, 2008:9.

²⁵Cater 2006

as Oxfam had already in place revenue-generating activities as a means of survival and were worried that the inclusion of a social component might have provoked a wave of refusal for capitalism and for sound profit-making business practices²⁶. Their non-acceptance of the social side of the sector became clear in 2007, when a social enterprise was quickly dismissed from the BBC's *Dragon's Den* TV program due to its attempt to generate at the same time financial and social value²⁷. Even in the public and third sectors signs of resistance against social enterprises intensified, especially against the employment of social enterprises for healthcare, where NHS spin-offs incorporated as CICs were progressively taking over most of the public service²⁸. While charities protested because they felt excluded from this opportunity or because they were scared of losing independence and becoming a 'government arm', trade unions and other members of the public sector expressed concerns about this trend showing a hidden privatization and the pursuit of efficiency at the expense of good service and accountability²⁹.

The confusion created by the presence of multiple definitions and debates around the role and essence of social entrepreneurs and enterprises began to cause practical problems³⁰, which were initially discarded given the constant growth of the sector and the multiplicity of contrasting interests at stake³¹. Firstly, public awareness of the social entrepreneurship sector remained quite low in England. A survey conducted by the Office for the Third Sector in 2008 estimated that 72 percent of people did not know what a social enterprise was and could not distinguish it from other third sector organizations. Secondly, the inclusion of multiple models and definitions within the brand social enterprise made it difficult for entrepreneurs to understand what exactly they wanted to set up³². Thirdly, the lack of clarity complicated relationships with funders for many third sector organizations³³. According to some CEOs of prominent social enterprises based

²⁶The Economist 'Survey: The rise of the social entrepreneur.' February 25, 2006:12.

²⁷Jump P. 'BBC dragons burn Fruity Faces chief.' Third Sector. March 21, 2007.

²⁸Plummer J. 'Service delivery: The public sector by another name?' Third Sector. August 8, 2007.

²⁹Currie R, Allen M, Clitheroe P. "'Foul play" – but no action.' Third Sector. August 8, 2007.; Darden-Phillips C. Public eye: Stated aims. The Guardian. May 28, 2008:10.

³⁰Dey P., Teasdale S. 'The tactical mimicry of social enterprise strategies: Acting "as if" in the everyday life of third sector organizations.' *Organization* 2016;23(4):485-504.; Little M., Warrell H. 'Is it time to be more enterprising?' Third Sector. February 7, 2007.; Palmer P. 'Social enterprise: new spin, old story.' Third Sector. May 10, 2006:21.; Nicholls A. 'Introduction.' In: Nicholls A., ed. 'Social Entrepreneurship: New Models of Sustainable Social Change.' Oxford University Press; 2006:1-35.

³¹Grenier 2008; Little 2006; Lyon F., Ramsden M. 'Developing fledgling social enterprises? A study of the support required and means of delivering it.' *Social Enterprise Journal* 2006;2(1):27-41.

³²Warrell H. 'Social enterprises categorised.' Third Sector. July 30, 2008:3.

³³Nicholls A. 'Endnote.' In: Nicholls A., ed. 'Social Entrepreneurship: New Models of Sustainable

in England, the impossibility for customers and funders to distinguish social enterprises from more grant-supported organizations mined their possibility to generate trust and to obtain investments³⁴. The proposed solutions to these problems were several: from the creation of campaigns and exclusive awards ceremonies that would generate media and general public awareness³⁵, to the development of a brand like Fairtrade that could make social enterprises easily recognizable by individual customers³⁶. Additionally, in order to improve the funding problem, the umbrella body Social Enterprise London published a guide explaining social enterprises how to manage their finances and marketing³⁷.

Between 2008 and 2009 the sector was also hit by the economic crisis, which reduced funds and revenues for social enterprises³⁸. This prompted a critique of the financial support given by the government to intermediaries such as Bridges, UnLtd, Futurebuilders, or the Adventure Capital Fund in order for them to support the sector. This money was indeed not translating into funds given to social enterprises when they most needed it or in a significant growth in the operations or number of existing social enterprises³⁹. It was mainly used to grow these intermediaries or stored in bank accounts for lack of proposals that the investors were willing to support. The financial crisis also led to the closure of several social enterprises or to their acquisition by traditional businesses. Following this news, the sector divided between those that saw this as the signal that social enterprises were increasingly becoming mainstream businesses, thus proving the overall success of the sector, and those worried that this shift would imply a reduction in the quality and in the certainty of the social impact delivered by social enterprises⁴⁰. At the same time, however, the ongoing economic crisis generated a renewed interest for social enterprises as organizations providing valuable services at local level and reducing unemployment and inactivity rates in communities especially hit by the recession⁴¹.

Social Change.' Oxford University Press; 2006:407-412.

³⁴Simms J. 'Moral behaviour.' *Director* 2008:52-55.

³⁵Egawhary E. 'Social enterprise's crowing glory.' *New Statesman* 2007:28-29.

³⁶'Sector to discuss whether social enterprise needs "a brand".' *Third Sector*. March 8, 2006:9.

³⁷Warrell H. 'Revised guide to climbing social enterprise ladder.' *Third Sector*. January 10, 2007.

³⁸Warrell H. 'Crunch time for social enterprises.' *Third Sector*. April 30, 2008:3

³⁹Schwartz R. 'What is the best way to develop a social economy?' *Third Sector*. July 14, 2009:22.

⁴⁰Warrell H. 'What's the price of social enterprise?' *Third Sector*. July 2, 2008:10.

⁴¹Brookes M.M. 'The importance of Social Enterprise.' *The Western Mail*. April 8, 2009:7.;
McCurry P. 'Focus on enterprise' *The Guardian*. June 3, 2009:3.

The private-public ecosystem of support: 2010-2015

In 2010, the general election meant a transition in government from Labour to a coalition of the Conservative Party and the Liberal Democrats. The Conservatives had already started while in opposition to focus on social enterprises and on how to best grow the sector with the help of the think-tank Centre for Social Justice⁴². Their idea was that government intervention in the sector should be progressively reduced, especially in terms of grants-giving, in order to make a more efficient use of scarce public resources and to let individual citizens free to develop their potential of delivering social innovations⁴³. Additionally, not only in the new government but also in some umbrella bodies, there was an increasing belief that if social enterprises were defined as businesses, they had to become more independent from public funds and more proactive in engaging with the business sector rather than with the public one⁴⁴. Consequently, the new government policy focused on strengthening the social investment sector as main provider of financial resources for social enterprises and on setting initiatives to improve the financial and leadership skills of social entrepreneurs and managers of third sector organizations.

Firstly, the coalition government piloted the Social Impact Bonds⁴⁵ and completed the creation, initiated without too much drive by the Labour government, of Big Society Capital, a ‘wholesaler’ bank meant to provide money for investing in third sector organizations delivering public services⁴⁶. Secondly, it proposed to the parliament the Public Services Bill, meant to favour third sector organizations in public sector contracts. The argument was that by awarding public services to social enterprises, the money spent by local authorities and public bodies would have a stronger and wider social impact⁴⁷. Thirdly, the government decided to rationalize the support infrastructure for social entrepreneurs and enterprises by cutting from £12.2 to £2 million in three years the funds given to umbrella bodies

⁴²Duncan Smith, MP RHI ‘The CSJ Story.’ Available at: <http://www.centreforsocialjustice.org.uk/about/story> [Accessed 23/02/2017].; Third Sector Working Group ‘Denying the Vulnerable a Second Chance: Undervaluing Britain’s Third Sector in the Fight against Poverty’, 2006.

⁴³Nicholls, Teasdale 2006; Dey, Teasdale 2006; Thompson J. ‘Reflections on social enterprise and the Big Society.’ *Social Enterprise Journal* 2011;7(3):219-223.

⁴⁴Ainsworth D. ‘Interview – Sam Conniff: “I think social enterprise is too timid.”’ *Third Sector*. February 23, 2010:7.; Marsh M. ‘Comment: In my view – The social sector should be defined and recognised in charity law.’ *Third Sector*. September 28, 2010:10.

⁴⁵Ainsworth D. ‘Analysis: Social impact bonds – An investment in a better society.’ *Third Sector*. November 1, 2011:8.

⁴⁶Ainsworth D. ‘Big society bank gets pounds 200m.’ *Third Sector*. February 15, 2011:4.

⁴⁷Nieri R. ‘Law & governance - Keep it legal - This enterprising bill would make a difference to society.’ *Third Sector*. February 22, 2011:17.; Youde K. ‘Can this bill give the state more bang for its buck?’ *Third Sector*. November 30, 2010:2.

for lobbying activities in representation of third sector organizations.

In 2013, three years after the coalition took over and changed the government approach towards the social entrepreneurship sector, 12 percent of the turnover of social enterprises was generated by NHS spin-offs being awarded healthcare contracts and 52 percent of social enterprises traded with the public sector⁴⁸. Consequently, it was possible to observe that the government had indeed transformed grants into payments but it had not transformed social enterprises into actual businesses competing in the private sector. Additionally, the policy of stressing the business side of social enterprises and of favouring those able to grow widened the gap between social enterprises and charities and created a vision of the third sector as stuck between big but inefficient charities and innovative but incapable of growing social enterprises⁴⁹.

Debates and issues kept arising even within the sector. Given the low number of organizations incorporating as CICs compared to the total number of social enterprises, there was the realization of the need to create a general brand making social enterprises easily recognizable for investors and customers⁵⁰. The Social Enterprise Mark was created for this purpose but its success did not last long. In fact, even if the government and SEC (whose name had become Social Enterprise UK after a re-branding in 2001) had officially supported it, they soon started to diverge from the definition and criteria that the Mark had set for social enterprises to be labelled as such⁵¹. Furthermore, as soon as the Mark was launched, several prominent organizations began to complain about it. For example, the Social Enterprise Network campaigned to clarify the meaning of social enterprise against ‘the mist that shrouds the debate’⁵². ClearlySo, an influential social investor, expressed its concerns for reducing the variety of social entrepreneurial projects within a single model or definition⁵³.

To solve these controversies, in 2013 SEUK decided to set up its own mark for social enterprises. To obtain it, it was sufficient for an organization to certify

⁴⁸The British Council. ‘Social enterprise in the UK: developing a thriving social enterprise sector.’ 2015.

⁴⁹Dearden-Phillips C. ‘Charities should reach out to social entrepreneurs - not grow their own.’ Third Sector. November 20, 2012:13.; Pharoah C. ‘In my view – Consolidation or growth? The sector struggles to resolve the contradiction.’ Third Sector. October 9, 2012:13.

⁵⁰Burne James S. ‘Points of law - CIC or charity? Discuss.’ Third Sector. May 13, 2014:17.

⁵¹Ashton A. ‘Social enterprise marks come in many flavours.’ Regeneration & Renewal. June 14, 2010:17.

Ainsworth D. ‘Interview – John Mulkerrin wants more back-up for the CIC model.’ Third Sector. April 20, 2010:6.

⁵²Jolly R. ‘Social Enterprise.’ Liverpool Post. June 7, 2012:36.

⁵³Schwartz R. ‘We must get investors onto the ladder of social finance.’ Third Sector. June 4, 2013:19.

that it considered itself a social enterprise and that it met the core criteria present in the government's definition (generation of part of the revenues through trade and re-investment of the majority of profits into the business or the community)⁵⁴. Their initiative obtained the consensus of several intermediaries lobbying for the sector, such as ACEVO, NCVO, Locality, NAVCA, Coops UK and UnLtd, whose survival depended on keeping the sector as inclusive as possible⁵⁵. However, it also raised more criticism. Several organizations commented that keeping the definition of social enterprises broad and vague was making this brand a convenient choice for small and medium enterprises in search for undeserved funds and that, in turn, this was bringing ineffectiveness to the social investment sector, since it refused most of the funds applications it received⁵⁶.

With all this focus going onto social enterprises and their growth and public recognition, other sector intermediaries, such as the School for Social Entrepreneurs (SSE), UnLtd, Ashoka UK and the Thompson Reuters Foundation, kept trying to keep alive the concept of social entrepreneurs. These were defined either as disruptive individuals transforming society for the better or as developers of projects supporting and improving their communities⁵⁷. They were therefore contrasted to social enterprises by organizations such as SSE, which stressed how the former were generating a community benefit, while the latter often compromised their social impact in favour of financial gains⁵⁸. Even the social entrepreneur definition, however, was not exempted from criticism, especially from those who remembered that the origins of the sector lay in the cooperative movement of the 1970s, and thus in organizations with the intent of guaranteeing more democratic structures and widespread participation in the economic sphere rather than focused on the efforts of a single individual⁵⁹. Additionally, the encouragement to take risks and innovate intrinsic in the definition of social entrepreneurship appeared as potentially in contrast with the leadership needs of organizations, such as social enterprises, delivering public services. They required, indeed, sustainability, accountability and implementation skills more than imagination and risks⁶⁰.

⁵⁴Third Sector 'Seven Days in the Sector: SEUK unveils identity badges.' January 15, 2013:6.

⁵⁵Huckfield 2014

⁵⁶Huckfield 2014; Panel on the independence of the Voluntary Sector. 'Independence under threat: the voluntary sector In 2013.' The Panel's Second Annual Assessment. London, 2013.

⁵⁷Richardson C. 'Good Practice: Social Enterprise – Update.' Third Sector. November 1, 2014:62.; Brodie D. 'Talks over role of social enterprise. East Anglian Daily Times.' December 15, 2010:BIZZ.

⁵⁸Prosser D. 'Small talk: entrepreneurship as a force for social good.' Independent.co.uk. March 4, 2013:SME, <http://www.independent.co.uk/news/business/sme/small-talk-entrepreneurship-as-a-force-for-social-good-8518613.html> [Accessed 20/02/2017]

⁵⁹Huckfield 2014

⁶⁰Pharoah C. 'In my view – The diversity of the sector means we need a range of leadership styles.'

Ultimately, the lack of agreement among the sector's supporters complicated the life of social entrepreneurs and enterprises, which lamented the persistence of low awareness among the general public⁶¹ and of funding and contract issues due to the inability of their counterparts – investors, businesses or local authorities – to distinguish them from other organizations⁶². Nonetheless, the sector kept growing at rapid pace even during this period of turbulence. In 2012, the government estimated the presence of around 70,000 social enterprises in the UK and three years later the newspaper *The Guardian* announced that one every five small and medium enterprises in the UK was a social enterprise and that the sector sustained the national economy with around £55 billion every year⁶³. In 2015, the sector was considered such a success that the British Council partnered with SEUK to export it internationally, leveraging the experience of UK-based organizations to reproduce in other countries the English ecosystem to make social enterprises thrive⁶⁴. A report on the sector published by the British Council in the same year discussed how in the presence of a government policy aiming at reducing government's intervention in and support for the social entrepreneurship sector in England, in the last few years the sector ecosystem had been driven by the efforts of private players. Indeed, umbrella bodies such as Social Enterprise UK had driven several policies such as the Social Value Act and had supported important campaigns to improve public awareness of the sector. Furthermore, financial institutions, consulting companies and multinational corporations had entered the sector with tailored programs, while national and regional networks offering training opportunities as well as information and advice had proliferated⁶⁵.

Third Sector. 2014:14.

⁶¹Sarah Morrison. 'Special report: social entrepreneurship – it's boom time for businesses with heart; they are diverse, dynamic – and doing well in the market. And now social enterprises are to get their own "champion"' *Independent.co.uk*. July 14, 2013:NEWS. Available at <http://www.independent.co.uk/news/business/news/special-report-social-entrepreneurship-its-boom-time-for-businesses-with-heart-8707525.html> [Accessed 21/02/17].

⁶²Ainsworth D. 'Define social investment.' *Third Sector*. October 1, 2013:8.

⁶³Patton A. 'Making it mainstream: six ways government can drive the social economy; Europeans seek inspiration from the UK's support for social enterprise.' *The Guardian*. April 23, 2015:Partner zone.

⁶⁴The British Council. 'Our Global Social Enterprise programme; The British Council creates international opportunities for the people of the UK and other countries and builds trust between them.' *The Guardian*. October 22, 2014:Partner zone.; Pillsbury A. 'A little shared knowledge goes a long way in helping to scale social enterprise; UK experience is helping to scale social enterprise and build an enabling environment worldwide, the British Council has found.' *The Guardian*. November 4, 2015:Partner zone.

⁶⁵The British Council 2015

Conclusion

The social entrepreneurship sector in England has had a steady despite controversial growth in the last twenty years. Its establishment was initially driven by the government's interventions such as favourable legislation or the establishment of funds and grants for social enterprises and sector intermediaries. However, as the government progressively lost either interest (Labour 2006-2010) or willingness to directly provide grants to the sector (the coalition government and subsequently the Conservative government, 2010-2016), several private organizations took over and kept pushing the growth of the sector in England. These organizations were as diverse as umbrella bodies created by the government to lobby for the sector, foundations and networks privately set up to support social entrepreneurs and enterprises, charities and NGOs interested in becoming more financially sustainable, and members of the business sectors such as banks, consulting companies, law firms and multinational corporations. This wide array of organizations meant that the stakeholders involved never reached an agreement around a definition of social entrepreneurship, around its boundaries with other sectors and around its role in the wider economic and social environment.

The multiplicity of definitions, on the one hand, has caused several issues. Examples of these would be the difficulty of generating public awareness and understanding of the sector, the struggles for social entrepreneurs and enterprises to obtain funds and the debates around whether the sector should help reduce the inefficiencies and stagnation of the public and third sectors or transform the mainstream business sector by making it more sustainable. On the other hand, however, it has developed the sector by allowing different players to find their niche and to sustain it in whatever way they wanted. Overall, the sector has been increasingly shifting towards the business one and has been especially supportive of organizations that were financially self-sustainable and adopting a scalable business model generating social change while also obtaining profits. However, if all businesses do become socially-minded and socially sustainable, what is the point of the social entrepreneurship sector? On the other hand, if the sector remains principally a way to privatize public services and to increase community participation in the economic environment, what are the risks associated with social enterprises being considered and treated as businesses? The definitional debate among multiple competing sector intermediaries often seems trivial given the growth and success of the sector. However, it might suggest future challenges as well as delaying potential responses and solutions to these questions.

The medicalisation of the workhouse in eighteenth century England

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Introduction

The original late seventeenth century conception of the workhouse as a poorhouse to contain, set to work and morally rectify able-bodied paupers – did include the provision of a safety net for the infirm and lame, but took no account of the need for medical relief¹. The first workhouses were established under individual Acts of Parliament (such as the Bristol workhouse in 1696), but hundreds of others were built in England after Knatchbull's Workhouse Test Act of 1722-23². Many advocates of the workhouse system saw them primarily as panaceas for idleness, immorality, unemployment and high taxes. It soon became clear, however, that many of the poor that were admitted were sick and required – and were entitled to – medical assistance³. Parish officers quickly realised they needed to adapt their workhouses to accommodate the sick poor, and this essay will examine this process of 'medicalisation'⁴. Voluntary hospitals also were established in the eighteenth century often with the intention to treat the poor though, as will be shown, their impact was limited. Medicalisation was a universal feature of eighteenth century workhouses and indeed of poor law provision generally, but the degree to which this occurred was often different in the capital from the rest of the country. In addition, medicalisation was bound to occur. The original conceivers of the workhouse movement were ideologically blinkered concerning their expectations of the workhouse system and failed to acknowledge the connection between poverty and ill health.

¹T. Hitchcock, 'Paupers and preachers: the SPCK and the parochial workhouse movement', in *Stilling the grumbling hive: the response to social and economic problems in England, 1689-1750*, eds. L. Davison, T. Hitchcock, T. Keirn, R.B. Shoemaker (Stroud: Alan Sutton, 1992), pp. 145-66 at p. 145; K. Siena, 'Contagion, exclusion and the unique medical world of the eighteenth-century workhouse', in *Medicine and the workhouse*, eds. J. Reinarz, L. Schwarz (Rochester: University of Rochester Press, 2013), pp. 19-39 at p. 20-1; S. Ottaway, 'The elderly in the eighteenth century workhouse', in *Medicine and the workhouse*, eds. J. Reinarz, L. Schwarz (Rochester: University of Rochester Press, 2013), pp. 40-57 at p. 45.

²Ottaway, 'The elderly in the eighteenth century workhouse', p. 41; J. Boulton, J. Black, 'Paupers and their experience of a London workhouse: St Martin in the fields, 1725-1824', in *Residential institutions in Britain, 1725-1970: inmates and environments*, eds. J. Hamlett, L. Hoskins, R. Preston (London: Pickering and Chatto, 2013), pp. 79-91 at p. 79.

³Siena, 'Contagion, exclusion and the eighteenth-century workhouse', p. 20; Ottaway, 'The elderly in the eighteenth century workhouse', p. 41.

⁴K. Siena, *Venereal disease, hospitals and the urban poor* (Rochester: University of Rochester Press, 2004), p. 138; Merriam-Webster Dictionary, online edn <http://www.merriam-webster.com/medical/medicalise> accessed 15 June 2015] (medicalize is defined as 'to view or treat as a medical concern, problem or disorder').

Ideologies underpinning the workhouse movement

The seventeenth- and early eighteenth-century philosophies that underpinned the foundation of the workhouse movement and the origins of the Workhouse Test Act proved to be flawed in practice. The Elizabethan Poor Law Act of 1601 specified that the old, the impotent (disabled), poor children and the able-bodied unemployed were to be provided with ‘care’ (medical assistance), and sought remedies for poverty including setting the poor to work by providing them with raw materials and giving cash payments⁵. By the late-seventeenth and early-eighteenth centuries, England’s population boomed, became more urbanised and experienced a rise in living standards. As a result, more of the labouring class was seen as ‘poor’, and these early measures came to be seen as unfit for purpose⁶. Reformers in the late-seventeenth century, influenced by humanitarianism, religious reformation ideology (especially the German Lutheran Church’s ‘pietist’ movement) and religious societies (including the Quakers) came to believe that poverty was something that could be ‘cured’, and that the poor, once their labour was properly directed, would develop wealth and no longer burden the parish⁷. Instrumental thinkers such as John Bellers promoted the concept of ‘a college of industry’ to provide ‘a plentiful living for the poor’. Through these and other ideas, driven by the Society for the Promotion of Christian Knowledge (SPCK, founded 1698), the workhouse stood out as the instrument to inculcate the poor with a disciplined work ethic, provide opportunities for them to become productive labourers profitable to themselves and provide a platform for preaching a religious agenda to the poor as a captive audience⁸. The Workhouse Test Act, largely written by the SPCK, emphasised work ethic and moral correction and reconciled a duty to the poor with an attempt to distinguish the deserving from the undeserving. Essentially, it deterred anyone but the truly destitute from applying⁹. This represented a deliberate hardening of comparison with the 1601 Poor Law and empowered overseers of the poor to refuse to provide relief to any applicant who declined to enter a workhouse. Hence the Workhouse Test Act was an enabling test, not a requirement, and was not

⁵J. Lane, *A social history of medicine: health, healing and disease in England, 1750-1950* (London: Routledge, 2001), p. 44; K. Siena, ‘Hospitals for the excluded or convalescent homes? Medicalization and the poor law in long eighteenth century London and pre-confederation Toronto’. *Canadian Bulletin of Medical History*, 27 (2010), 5-25 at p. 7; A. Brundage, *The English poor laws, 1700-1930* (Basingstoke: Palgrave Macmillan, 2002), p. 17.

⁶Hitchcock, ‘Paupers and preachers’, pp. 146-7.

⁷Hitchcock, ‘Paupers and preachers’, p. 148 (refers to: the ideas of Samuel Hartlib, 1600-1662).

⁸Hitchcock, ‘Paupers and preachers’, pp. 145, 148-52, 156; Ottaway, ‘The elderly in the eighteenth century workhouse’, pp. 41, 46; Siena, *Venereal disease*, pp. 137-8.

⁹Hitchcock, ‘Paupers and preachers’, p. 145.

universally adopted¹⁰. The reformers' premise of curing the poor by instilling a work ethic proved optimistic. Workhouses never made a profit and the reformers' supposition ignored the connection of poverty with ill health¹¹. A medical need was belatedly given some recognition in Gilbert's Act of 1782, which specifically provided for 'reception of the sick and distempered poor and an apothecary or surgeon to be sent for to attend them when there shall appear necessity for it'¹².

The influence of the ideologues of the late eighteenth and early nineteenth centuries on poor law provision and the functioning of workhouses, constrained reformers in their consideration of medical provision. Instead, poor law emphasised what amounted to punishment of the able-bodied poor and seemingly ignored the obvious need for medical provision revealed over the preceding decades. The recognition of the requirements for paupers who were infirm or old was partial and incidental. Jeremy Bentham felt that poor relief should be harsh but agreed with it to prevent the peasantry from becoming a revolutionary mob¹³. Adam Smith had no quarrel with mandatory public support, but several contemporaries did. Joseph Townsend believed that relief encouraged idleness and that the poor should come face-to-face with their situation to develop the character to survive. In his 1798 *Essay on Population*, Thomas Malthus asserted that poor laws simply aggravated the pressure on a limited food supply¹⁴. William Young's 1796 *Relief of the Poor Act* forbade the use of workhouses for the able-bodied and effectively recognised the workhouse as a place for the aged, infirm and poor children by default¹⁵. The *New Poor Law Amendment Act* of 1834 required indoor relief for able-bodied paupers¹⁶. The only concession to medical provision was to permit justices of the peace to order medical relief in the case of sudden illness¹⁷. However, the inclusion of infirmary wards on contemporary plans drawn up for workhouses did demonstrate tacit acknowledgement that such arrangements were required.

¹⁰S. King, *Poverty and welfare in England, 1700-1850. A regional perspective* (Manchester: University of Manchester Press, 2000), pp. 24, 39; Hitchcock, 'Paupers and preachers', p. 145.

¹¹Siena, 'Hospitals for the excluded', p. 7.

¹²Ottaway, 'The elderly in the eighteenth century workhouse', p. 47 (refers to: The statutes at large, from the twentieth year of the reign of King George the Third to the twenty-fifth year of the reign of King George the Third (London: Charles Eyre and the executors of William Strahan, 1786), 14, p. 282).

¹³M. Quinn, 'Jeremy Bentham on the relief of indigence: an exercise in applied philosophy', *Utilitas*, 6 (1994), 81-96 at pp. 86-8.

¹⁴Brundage, *The English poor laws*, pp. 29-32 (refers to: Adam Smith, *Wealth of Nations*, 1776, Joseph Townsend, *Dissertation on the Poor Laws*, 1786, Thomas Malthus, *Essay on Population*, 1798).

¹⁵Brundage, *The English poor laws*, pp. 26-7.

¹⁶Brundage, *The English poor laws*, pp. 76-7, 96.

¹⁷Brundage, *The English poor laws*, pp. 76-7, 96.

Treatment options for the sick poor in the eighteenth century

In theory, sick paupers in eighteenth-century England had several options to gain access to medical care, but, in some places, many found themselves excluded and the ill poor clustered in the workhouse. Paupers could not afford private medical practitioners but may have sought assistance from hospitals¹⁸. The London hospitals such as St Thomas' and St Bartholomew's (both founded by Royal charter) were already well established, but by the beginning of the eighteenth century both had started to charge fees, which paupers could not afford¹⁹. Newly founded voluntary hospitals operated admission policies that frequently excluded the sick poor. Overseers of the poor were thus obliged to take sick paupers (and pregnant unwed women) denied or unable to obtain medical relief elsewhere. Overall, these rising costs and restrictions contributed to the medicalisation of the workhouse – the 'sickness provider of last resort'.

The nonexistence of medical facilities in the early workhouses followed from the initial reformers' lack of understanding of (or perhaps, disregard for) the nature of poverty. The high proportion of sick paupers that presented themselves to the workhouse door forced initially reluctant overseers of the poor to modify their premises for medical purposes to cope with the problem. Practices in provincial towns and rural areas were often different from those in the capital. London was a special case as it had experienced the greatest in-migration, had the biggest population by far with the largest workhouses, and already had well-established 'royal' hospitals and a medical establishment that could lead on developments²⁰. Workhouses became feared because of the likelihood of dying once entered, hence The Lancet's 1841 editorial 'The diseases which prove so fatal therefore assail the poor after their entrance into these ante-chambers of the grave'²¹. For example, St Martin accounted for at least 15 percent of all parish burials when only 2-3 percent of the parish resided in the workhouse²². Since the probability of death receded with length of stay, those who died did so because they were admitted in a very sick state rather than through acquisition

¹⁸Siena, 'Contagion, exclusion and the eighteenth-century workhouse', pp. 22-3.

¹⁹Siena, Venereal disease, pp. 75-7, 102-5.

²⁰J. Boulton, L. Schwarz, 'The medicalization of a parish workhouse in Georgian Westminster: St Martin in the Fields, 1725-1824', *Family and Community History* 17 (2014), 122-40 at pp. 122-5; J. Boulton, R. Davenport, L. Schwarz, "These ante-chambers of the grave": Mortality, medicine, and the workhouse in Georgian London, 1725-1824', in *Medicine and the workhouse*, eds. J. Reinartz, L. Schwarz (Rochester: University of Rochester Press, 2013), p. 59.

²¹T. Wakley, Editorial, *The Lancet*, May 1 (1841), pp. 193-6 at p. 194.

²²Boulton, Davenport, Schwarz, 'Ante-chambers of the grave', pp. 69-71 (refer to: City of Westminster Archive Centre, St Martin in the Fields sextons' burial books, 1747-1824, 419/123, 233-44; Accession, 419/265-9, F2465, F2467, F2469).

of a disease in the institution²³. However, there were some outbreaks of typhus, and the mortality of inmates resident over six months was still greater than that in the wider population²⁴. St Martin accounted for 84 percent of all foul (venereal) disease deaths in the parish, indicating the role it played in treating persons with this infection²⁵. The obvious medical requirements at St Martin were recognized during the 1772 rebuild, when sick wards were designated, though no separate infirmary was constructed²⁶.

Adaptions for sickness in the London workhouses

Paupers at other London workhouses had similar levels of ill health to those at St Martin in the Fields. At St Margaret's Westminster, the original 1725 design took no account of medical requirements but within two years, after requests from the workhouse surgeon, rooms were converted to house the sick, the venereal and mentally ill ('lunatics') and contagious. Fifteen of the 33 rooms were given over to a medical purpose²⁷. Similar figures pertain for St Luke's Chelsea where, over the years 1743-50, 55 percent of inmates were sick, infirm, lame, injured or 'foul', and for St Sepulchre's, at which, during the year of 1735, 27 percent of applicants were in the non-abled bodied categories²⁸. Clearly, for London workhouses, a sizeable proportion of paupers were already ill when admitted.

To a large extent, poor law medical relief in London seems to have been delivered on an indoor basis, that is through workhouses, but this was not the case in the rest of England²⁹. It has been estimated that by 1782 only one third of the 13,000 English poor law administration units had access to a

²³Boulton, Davenport, Schwarz, 'Ante-chambers of the grave', p. 63, 72-3, 79.

²⁴Siena, 'Contagion, exclusion and the eighteenth-century workhouse', p. 27.

²⁵Boulton, Davenport, Schwarz, 'Ante-chambers of the grave', p. 78 (records outside the workhouse probably understate foul disease as a cause of death).

²⁶Boulton, Davenport, Schwarz, 'Ante-chambers of the grave', p. 65.

²⁷Siena, 'Contagion, exclusion and the eighteenth-century workhouse', pp. 20-1, 24 (refers to: Westminster City Archives 1735; Margaret's Workhouse Committee Minutes 1730-6, E2634; Westminster City Archive Margaret's Workhouse Committee Minutes, 1730-6, E2634, pp. 383-6) (38 percent of applicants having cited illness or injury as the reason for admission; three quarters of these had the pox, the itch or fever).

²⁸Siena, 'Hospitals for the excluded', p. 7 (refers to: London Metropolitan Archives, St Luke's Chelsea Workhouse Admissions and Discharges, 1743-69, 1782-99; microfilm x/15/37; Guildhall Library, St Sepulchre (London Division), Workhouse Committee minutes, manuscript 3137/4).

²⁹S. King, 'Poverty, medicine and the workhouse in the eighteenth and nineteenth centuries', in *Medicine and the workhouse*, eds. J. Reinarz, L. Schwarz (Rochester: University of Rochester Press, 2013), pp. 228-51 at p. 241: Siena, 'Contagion, exclusion and the eighteenth-century workhouse', p. 21.

workhouse³⁰. Uptake of the workhouse system varied widely. Kent and East Anglia embraced the concept but the North Riding and Lancashire rejected it³¹. Uptake in Berkshire and Oxfordshire was limited – only 10-20 percent of parishes had access in 1815. By 1803, for Lancashire, the West Riding, Cornwall, Northumberland, Nottinghamshire, Herefordshire and Westmorland, only 11.5 percent of permanent paupers were in institutional care³². The costs of medical relief in northern England were lower than in the south during the nineteenth century (and probably in the eighteenth century as well). Of course, there was also regional variation in the medical relief offered in the workhouse³³. In the early nineteenth century, prior to the New Poor Law, expenditure on medical relief in the north was said to be one sixth of that in southern and midland counties³⁴. There were several reasons for this difference. Overall, people in the north were wealthier than those in the south so there were fewer permanent paupers. Additionally, poverty from unemployment was often temporary, and there was a strong network of supportive medical and friendly societies³⁵.

Medicalisation in provincial workhouses

Outside of London, workhouses were often located in cities or county towns. Parishes grouped together into ‘unions’ to build an institution to which they then had access³⁶. Most of the two thousand or so workhouses built in response to the 1723 act were smaller, sometimes by quite a bit, than the ones in London³⁷. Additionally, rules for workhouses and overseers often varied. In 1803 an average English workhouse contained between 20 and 50, compared to 257 in London³⁸.

³⁰King, *Poverty and welfare in England*, pp. 38-9.

³¹King, *Poverty and welfare in England*, pp. 38-9, 160.

³²King, *Poverty and welfare in England*, pp. 204-5; P. Anderson, ‘The Leeds workhouse under the old poor law: 1726-1834’, *Publications of the Thoresby Society* 56 (1980), 75-113 at p. 90 (the figure for Leeds in 1800 was 19 percent).

³³H. Marland, *Medicine and society in Wakefield and Huddersfield, 1780-1870* (Cambridge: Cambridge University Press, 1987), pp. 57-8.

³⁴Marland, *Medicine and society in Wakefield and Huddersfield*, pp. 58-9 (refer to: the Select Committee on Medical Poor Relief, Third Report, PP, 1844, IX (531), Evidence of G.C. Lewis (Poor Law Commissioner), p. 8, Q.13).

³⁵Marland, *Medicine and society in Wakefield and Huddersfield*, pp. 54, 56-8; King, *Poverty and welfare in England*, pp. 216-17.

³⁶King, *Poverty and welfare in England*, pp. 24, 274.

³⁷Boulton, Black, ‘Paupers and their experience of a London workhouse’ p. 79; King, *Poverty and welfare in England*, p. 39.

³⁸Boulton, Schwarz, ‘The medicalisation of a parish workhouse’, p. 123 (refers to: ‘Abstract of answers and returns, made pursuant to Act 43 Geo. 3, relative to the expense and maintenance of the poor in England’, P.P. 1803-4 XIII).

Yet most workhouses were small. In 1776, less than 200 workhouses could hold more than 100 inmates³⁹. Even if there was the demand to convert space for medical purposes, only larger institutions could make this change. Consequently, in many places, sick paupers were housed with the able-bodied. In these instances, medicalisation by function – a visiting surgeon or expenditure on medicines – could still occur. Medical relief included the costs of burial, nursing, extra food and fuel, as well as payments to doctors and medical institutions. Over the period 1730 to 1820, these costs absorbed about 25 percent of the irregular payments made by some parishes in south and east England⁴⁰. Comparable figures for parishes in the north and west were lower in the first half of the eighteenth century but increased to similar levels after 1770⁴¹.

Workhouses in towns outside of London, such as Wakefield and Huddersfield, only admitted the old, infirm and helpless under the old poor law. Of course, these limitations represented a small portion of demands on medical relief provision⁴². Since many of these workhouses were so small, they could only care for small numbers of paupers. In 1780s Mirfield, for example, only 25-35 paupers could be admitted at a time⁴³. Mr Alfred Power, Assistant Poor Law Commissioner for the West Riding and Lancashire, commented on medical provision under the Old Poor Law in his region: ‘with scarcely any exception, through the whole district, the medical relief, of which any distinct account could be found in the township books, bore an extremely small proportion to the population, and to the general expenditure on the poor’⁴⁴. Overall, the provision of medical relief in the northern small town workhouses can be accepted as being ‘small scale’ in contrast to the situation in the large workhouses of London⁴⁵.

³⁹King, *Poverty and welfare in England*, pp. 38-9; Ottaway, ‘The elderly in the eighteenth century workhouse’, p. 49.

⁴⁰King, *Poverty and welfare in England*, pp. 156-7.

⁴¹King, *Poverty and welfare in England*, pp. 200-1.

⁴²Marland, *Medicine and society in Wakefield and Huddersfield*, pp. 64-6.

⁴³Marland, *Medicine and society in Wakefield and Huddersfield*, pp. 65-6 (refers to: Township of Mirfield, Overseers accounts, 1772-1803; Township of Mirfield, Workhouse expenses book, 1804-1830, manuscript Huddersfield Public Library; Township of Mirfield, Workhouse diary and accounts book, 177-9, manuscript Huddersfield Public Library) (money was spent predominantly on midwifery cases, bleeding, treatment of injuries, leeches, pills and potions. Expenditure on medical relief there at the beginning of the nineteenth century was only £300-400 per annum compared to the £1500-2000 cost of outdoor relief.).

⁴⁴Marland, *Medicine and society in Wakefield and Huddersfield*, p. 57 (refers to: ‘Report of the Poor Law Commissioners on the further amendment of the poor laws’, PP, 1840, XVII (253), App. B, ‘Reports of arrangements for medical relief, No. 6, III, Mr. Power’s report, Lancashire and the West Riding of York’, pp. 164-5).

⁴⁵Marland, *Medicine and society in Wakefield and Huddersfield*, p. 57 (refers to: ‘Report of the Poor Law Commissioners on the further amendment of the poor laws’, PP, 1840, XVII (253), App. B,

Perhaps the reasons were more related to scale and pragmatism than lack of intent?

Voluntary hospitals and the sick poor

It might be thought that the voluntary hospitals would relieve the workhouses of some clinical load, but, in practice, their effect was minimal. Outside of London, infirmaries were established by subscription in cities and towns including Birmingham, Chester, Hull, Leeds, Liverpool, Manchester, Northampton, Oxford, Shrewsbury and York⁴⁶. The poor were entitled to apply to these charitable hospitals, but the process required nomination by a hospital governor, who might administer a test of the applicant's moral character⁴⁷. Many of the destitute were incapable of negotiating the niceties of the application even if they were able to pass the morality test.⁴⁸ Some parishes subscribed to gain admission rights for their poor, but certain infirmaries such as the London Lock Hospital, Norfolk and Norwich Hospital and the Radcliffe Infirmary in Oxford either did not permit overseers subscriptions, assumed that poor law relief already provided for workhouse paupers or excluded them since they were potentially infectious⁴⁹. Royal and voluntary hospitals admitted more men than women; 55-65 per cent of patients were male (mostly of working age)⁵⁰. Of course, men were more likely than women to have sufficient funds to pay expenses, yet there was also gender and mercantile bias. Returning the breadwinner to work prevented a family from falling on the parish. Furthermore, occupational injuries, a common reason for admission, primarily happened to men⁵¹. Between 1747-55 in the Shrewsbury Infirmary, for example, paupers made up only 10-11 percent of admissions⁵². Although limited, evidence suggests that newly founded voluntary infirmaries barely had an impact on the workload of workhouses.

⁴⁶Reports of arrangements for medical relief, No. 6, III, Mr. Power's report, Lancashire and the West Riding of York', pp. 164-5).

⁴⁶Tomkins, *The experience of urban poverty*, pp. 136-7.

⁴⁷Siena, 'Contagion, exclusion and the eighteenth-century workhouse', p. 22.

⁴⁸Tomkins, *The experience of urban poverty*, p. 139; Siena, 'Contagion, exclusion and the eighteenth-century workhouse', pp. 22-3.

⁴⁹Thomas, 'The old poor law and medicine', p. 5; Tomkins, *The experience of urban poverty*, pp. 143-4; Siena, 'Contagion, exclusion and the eighteenth-century workhouse', p. 26.

⁵⁰Tomkins, *The experience of urban poverty*, pp. 137-8; Siena, 'Hospitals for the excluded', pp. 10, 142 (refers to: A. Berry, 'Patronage, funding and the hospital patient, c. 1750-1815: three English regional case studies', unpublished DPhil thesis, University of Oxford (1985), p. 182) (royal and voluntary hospitals were described by Amanda Berry as catering for the 'non-pauperised poor').

⁵¹Tomkins, *The experience of urban poverty*, pp. 137-8; Boulton, Davenport, Schwarz, 'These ante-chambers of the grave', p. 65; Siena, *Venereal disease*, p. 166.

⁵²Tomkins, *The experience of urban poverty*, pp. 145-7.

In London, however, voluntary hospitals impacted on the exclusion policies of the workhouses. Though there was variation, most hospitals in London and many in the provinces, routinely excluded applicants with venereal ('foul') disease – men might get a sympathetic hearing but women would be turned away – contagious diseases such as smallpox, leprosy and other skin diseases, and sometimes those with fever⁵³. Several would not admit children under the age of six, the mentally ill, the dying or pregnant women. Many of the sick poor fell into one of these categories. Hence they were excluded from the main hospitals, directed to the overseers and were sent to the workhouse. Since expectation of help elsewhere was low, some applied to the workhouse directly⁵⁴. Large London workhouses, and to a lesser extent in the larger provincial ones, responded with specialised medicalisation. Fever wards were established in many workhouses in the capital and in some of the provinces, and venereal wards became common in London⁵⁵. Voluntary hospitals' exclusion of pregnant women further pressurised workhouses to medicalise. Although frequently lacking specialised wards, midwifery services developed in London, larger provincial establishments such as that in Leeds, and even in smaller institutions⁵⁶. Frequently unwed pauper mothers-to-be used these facilities⁵⁷. In St Luke's, London, Shrewsbury, and Oxford, a third to three-quarters of prospective mothers were married. Charities that provided lying-in beds (or home support) were founded in London and the provinces during the eighteenth century and had the potential to take the pressure off the workhouse provision of midwifery in the capital and larger urban areas⁵⁸.

⁵³Siena, 'Contagion, exclusion and the eighteenth century workhouse', p. 23 (refers to: The laws of the London Infirmary (London: Henry Woodfall, 1743), p. 8); Tomkins, The experience of urban poverty, pp. 137-8 ('The itch', the primary dermatological presentation, was probably scabies but other pruritic skin diseases would have been included. Patients with venereal disease were admitted to hospitals at times during the eighteenth century, though by the nineteenth they tended to be excluded).

⁵⁴Siena, 'Contagion, exclusion and the eighteenth-century workhouse', p. 23.

⁵⁵Boulton, Black, 'Paupers and their experience of a London workhouse', pp. 81-2; Boulton, Schwarz, 'The medicalization of a parish workhouse', p. 133; Siena, 'Contagion, exclusion and the eighteenth-century workhouse', p. 28; J.V. Pickstone, *Medicine and industrial society: a history of hospital development in Manchester and its region, 1852-1946* (Manchester: Manchester University Press, 1985), p. 24; Tomkins, The experience of urban poverty, pp. 126-7; R. Davenport, *Medicine and the workhouse*, oral paper, Madingley Hall, Cambridge, 16 May 2015, slide 7.

⁵⁶Tomkins, The experience of urban poverty, pp. 126-7; T. Hitchcock, 'Unlawfully begotten on her body: illegitimacy and the parish poor in St Luke's Chelsea', in *Chronicling poverty: the voices and strategies of the English poor, 1640-1840*, eds. T. Hitchcock, P. King, P. Sharpe (Basingstoke: Macmillan, 1997), pp. 70-87 at p. 75; Anderson, 'The Leeds workhouse under the old poor law', p. 90.

⁵⁷Tomkins, The experience of urban poverty, pp. 126-7; Hitchcock, 'Unlawfully begotten on her body', p. 75; Anderson, 'The Leeds workhouse under the old poor law', p. 90.

⁵⁸Tomkins, The experience of urban poverty, pp. 126-7 (charities this might not have had a major effect since they often specified that the woman had to be married).

The association of poverty with ill health was not well recognised

Much of the need for medicalisation of workhouses resulted from the association of poverty with ill health. Although this correlation is well recognised in the present day, this does not seem to have been apparent or perhaps was disregarded in the eighteenth century, when common belief considered workhouses as the cause of ill health⁵⁹. The changes in the societal structure of England during the eighteenth century included: increased agricultural unemployment, rapid urban in-migration and population increase. The resulting urban poverty increased the mortality rate and decreased life expectancy in larger cities⁶⁰. Of course, overcrowding in substandard lodgings with insanitary conditions and a poor diet contributed to epidemics of infectious diseases such as smallpox, typhus and measles⁶¹. In terms of scale and intensity, poverty increased during the years 1750-1850. Aside from expanding urban areas, poverty also expanded in rural communities because fewer agricultural labourers were needed⁶². A better recognition of the associations of poverty with disease by eighteenth century opinion leaders and lawmakers may have reduced the need for workhouses to medicalise. Instead of addressing poverty as a cause of ill health, these individuals merely responded to its consequences.

Conclusion

Medical relief was not built into the late seventeenth century concept of the workhouse but developed as a pressurised response to poverty-related diseases that accompanied eighteenth and nineteenth-century urbanisation. Workhouses primarily were seen as a means to correct the idleness and immorality of the destitute poor. The founding reformers were influenced by the hard rhetoric of the SPCK into believing that firm instruction would convert the poor to abundant self-sufficiency, but reality proved to be different. Workhouses, often founded after the 1723 Workhouse Test Act, were taken up with varying degrees of

⁵⁹Boulton, Davenport, Schwarz, 'Ante-chambers of the grave', p. 63.

⁶⁰Siena, 'Hospitals for the excluded', p. 7; Lane, *A social history of medicine*, p. 45; R. Davenport, J. Boulton, 'New insights into urban mortality, 1750-1820', Working paper, Department of Geography, University of Cambridge, URL <http://www.geog.cam.ac.uk/people/davenport/davenport16.pdf> accessed 18 June 2015], pp. 1-20 at pp. 1, 15-16, 18.

⁶¹Boulton, Davenport, Schwarz, 'Ante-chambers of the grave', pp. 74-7; C.E.A. Winslow, 'Poverty and disease', *American Journal of Public Health Nations Health* 38 (1948), 173-84.

⁶²King, *Poverty and welfare in England*, p. 105; I. Gazerley, N. Verdon, 'The first poverty line? Davies' and Eden's investigation of rural poverty in late 18th century England', *Explorations in Economic History* 51 (2014), 94-108 (the surveys of David Davies and Frederick Eden demonstrated that rural communities needed fewer agricultural labourers in the 1790s).

enthusiasm. The system was widely adopted in London, but other parts of England such as the north, reluctantly approached indoor relief. On admission to London's large workhouses, 27-50 percent or more of paupers had an illness or infirmity of some sort, which, under the terms of the 1601 Poor Law Act, they expected to have treated. The degree of medical relief needed when the London workhouses opened surprised the overseers, who had to modify the physical usage and functioning of their establishments accordingly – to medicalise them. Although obliged to offer medical services, the smaller workhouses in other parts of England showed less in the way of adaption of premises. The opening of the voluntary hospitals, from the first half of the eighteenth century onwards, had little impact on the medical workload of workhouses. Persons with infections, venereal disease and pregnancy were often excluded from admission, and paupers were particularly susceptible to these problems. The effect for workhouses, notably those in the capital, was to medicalise them specifically to cope with infections, midwifery and, in London, venereal disease. The association of ill health with poverty, which the founders of the workhouse system either failed to recognise or chose to ignore, proved to be tenacious and not amenable to 'cure' by the application of a work ethic. In conclusion, medicalisation of the workhouse in the eighteenth century was universal but the degree to which it occurred varied. Large institutions in London had rooms given over to specific medical purposes. Although these resources were less common in smaller provincial workhouses, they still provided functional medical relief.

Sex and relationships education in secondary schools: are we doing enough?

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Introduction

While one of the main functions of schooling is to provide high quality education to students, it is important to also recognise the pastoral support and education that schools deliver. Within the latter falls the aspect of sex education, a topic that needs to be handled sensitively, maturely and in a manner that makes it accessible and relevant to all students. Sex and relationships education (SRE) forms part of the personal, social, health and economic (PSHE) education that pupils receive from their school. PSHE itself is not compulsory in secondary schools, however, ‘all schools should teach PSHE, drawing on good practice’ (Department for Education, 2013). As there is no defined curriculum for PSHE, schools are able to tailor their teaching to the individual pupils’ needs. SRE is, however, a statutory requirement in maintained schools, but this is not the case in academies and free schools. As of January 2016, 66 percent of secondary school pupils attended an academy. Given that this number is set to increase in light of government plans for all schools to convert to academy status by 2022, (House of Commons library, 2016) there is a worrying proportion of students who will have varying levels of sex and relationships education. To assess the situation of sex and relationships education within secondary schools I aim to investigate several key areas. Firstly, I will discuss the current legislation and policies for school led SRE, as well as consider proposed changes. Secondly, I will debate the issue of how SRE should be best taught in secondary schools, including which content should be included such as consent or LGBTQ+ relationships. Finally I will review the barriers to effective teaching and whether delivery of SRE should be compulsory in all schools.

Literature review

Current legislation, policy and guidance

At this point it is important to make clear the difference between schools’ obligations in providing SRE and how this differs from the teachings within the science national curriculum. Science lessons focus on the biological terms associated with puberty, human reproduction and pregnancy, and this is a topic studied in detail throughout secondary science (Department for Education, 2015). This aspect of education is compulsory; students and their parents are not able to forego this topic and as such the biological aspect of SRE will not be discussed in the context of this work. However, in the context of PSHE, parents do have the right to remove their child from SRE lessons for moral, social, cultural, religious or personal reasons (Great Britain, Education Act, 1996).

The government previously produced the ‘Sex and Relationships Guidance’ booklet, a 34 page document outlining a framework to support the teaching of SRE. This document was produced in 2000 following the introduction of a new curriculum in the previous September. However, there appears to be no further revisions since this date. The guidance stresses that SRE ‘does not encourage early sexual experimentation’ and instead promotes ‘spiritual, moral, cultural, mental and physical development of pupils’ (Department for Education and Employment, 2000).

In 2013, Ofsted (2013) found 40 percent of PSHE teaching ‘required improvement or was inadequate’. Nicky Morgan, the Secretary of State for Education between 2014-16, was asked by the Chair of the Education Select Committee, as well as the Health and Home Affairs Committees, to review the status of PSHE and SRE within the national curriculum (Nicky Morgan, 2016). However, despite the Ofsted finding, Ms Morgan failed to implement any changes. The current Secretary of State for Education, Justine Greening, has recently outlined a series of changes to be implemented in a move to make SRE compulsory (BBC News, 2017) something many teachers, parents and external organisations have indicated their support for (Change.org, 2016; Schools Week, 2016).

What are students being taught?

In a study by Strange et al (2007), which utilised 12 sample schools from the RIPPLE study team and investigated peer led sex education, it was discovered that the content of sex education varied significantly between schools. While between 75 percent and 83 percent of schools reported teaching pupils about the use of contraception, and 58 percent of schools taught students about STI’s, over the course of 3 years, only 1 school of the sampled 12 discussed LGBTQ+ relationships. In addition, only 17 percent of schools educated pupils about sexual harassment. The same percentage of schools also introduced the legal responsibilities regarding sex and relationships. It would appear that a large majority of schools are failing to educate their pupils adequately with regards to consent.

Consent education has, in recent years, developed as something of a hot topic and area for debate. A particularly high profile example of this came when the University of Oxford took the decision to make ‘consent workshops’ compulsory for all new undergraduates from 2016 (BBC News, 2016). Cambridge University has been running similar sessions for the past 2 years (The Guardian, 2014). It vital to appreciate that universities are needed in many cases to fill the gap in

some student's knowledge over an aspect of SRE not always delivered during secondary education. Consistent with the findings of Strange et al (2007), it can be suggested that rape, consent and sexual assault are not discussed adequately in school, which can lead to universities filling the gap.

While the average age that people lose their virginity in the UK is 16, the same as the legal age of consent, it is still the case that up to 30 percent of teenagers are experiencing sex before this age (Family Planning Association, 2009). I believe it is critical that all individuals are adequately educated in all aspects of SRE, of which consent, rape and sexual assault are just one part. Statistically, 31 percent of 18-24 year old women report having experienced sexual abuse during childhood, and it has been estimated that 11 rapes occur every hour (Rape Crisis, 2016). For these reasons alone, it is of extreme importance that our schools fully educate pupils about what does and does not constitute consent. Of course, simply providing information will not prevent all rapes, but education could reduce the incidence. Hence, there is a great movement to make SRE, and consent particularly, a compulsory part of all students' secondary education (Campaign4Consent, 2016).

Other debated areas of sex education that have gained much media attention are those of LGBTQ+ relationships, sex for pleasure and the role of religion in SRE. Looking at LGBTQ+ issues specifically, 'Schools are often deeply heterosexist institutions and gay and lesbian identities are marginalised within the classroom' (Buston and Hart, 2001). On this basis alone, schools are not fulfilling their moral and social duty to educate students and to tailor education to their individual needs.

Vincent (2007) raises many valid and considered points in her discussion of teenage pregnancy rates in the UK with regards to SRE. A key point is that SRE often fails to address the emotional implications of sex to pupils. They may be taught how to use a condom, although Strange et al (2007) found only 25 percent received condom demonstrations at school. However, students are often not taught how to communicate and discuss their thoughts and opinions with a partner. It has been suggested that even if a teenager feels ready to have a sexual relationship, they may not be able to effectively communicate their want to use a condom. As Olser and Vincent (2003) have concluded, in many cases 'their communication skills were not at a level where they could keep themselves safe'. This is a sentiment reiterated by Hoggart (2003) and by Halstead and Waite (2003), who comment that SRE 'should include the education of emotions'. There are numerous implications for pupils should they be unable to effectively communicate their emotional and physical needs with a partner. The most obvious are the risk of pregnancy and STI's, as well as the potential emotional harm

and damage to self-esteem and mental health from a poor sexual relationship (Keirnan, 1995).

Barriers to teaching Sex and Relationships Education (SRE)

As highlighted by Strange et al (2007) there are several barriers to teaching SRE, which can be largely divided into four categories:

- The confidence, enthusiasm and personal characteristics of the teacher
- Senior management support
- Timetable constraints
- Adequate training and preparation of teaching staff.

Examining each of these further reveals some of the shortcomings of SRE within secondary education. With regards to the personal characteristics, confidence and enthusiasm of the teachers, sometimes students feel their teacher is ‘embarrassed’ to teach SRE. This is a remark backed up by Alldred, David and Smith (2003), who comment that many teachers ‘did not feel confident to use discursive pedagogic approaches’.

Secondly, the support of senior management is a significant limitation on the delivery of appropriate, supportive and structured SRE. Without the backing of the senior management team (SMT) SRE fails to be addressed adequately, and becomes a ‘low priority’ (Vincent et al 2007). This attitude can then trickle down to the remainder of school staff, and ultimately to the pupils, who are then more likely to receive inadequate sex education. Strange et al (2007) echo the beliefs of Vincent et al, citing a ‘lack of clarity regarding who was responsible for the coordination of the programme’ as to why there was such a variation in the teaching standards and content of SRE across a sample of 12 schools.

Following on from this are timetable constraints. These are beyond the control of classroom teachers and are the responsibility of senior management to coordinate. As noted by Buston et al (2002), SRE is often ‘hindered by competition for curriculum time’. Strange et al (2007) recognised in their sample data that 13-16 year olds received an average of 7 lessons in SRE over the course of three school years (years 9-11). Within this sample of 12 schools, it was found that five provided no SRE for at least one school year between years 9 and 11, and one school did not teach SRE at all.

The final barrier to delivering SRE is the training and support provided to teachers (Strange et al 2007; Wight and Buston, 2003). Strange’s report (2007)

recommended that SRE should be delivered where possible by specialist teachers. This recommendation was made after discovering that from the 12 sample schools there was a lack of consistency in how teachers are trained to deliver SRE. Two had been given information during their initial teacher training (which may have been many years ago), five had been given information at an INSET day, and the remaining five schools had teachers trained by an external agency. Most of the SRE at the sample schools was delivered by form tutors, although it was recognised that on some occasions a school nurse or external agencies (such as family planning and church youth groups) took individual sessions to address specific needs. Strange et al (2007) also identified two cross curricula links to SRE: science, which (in this context) teaches the biological nature of human reproduction, and religious education. One school in the study was observed to debate abortion ethics and discuss how different religious groups view this practice and their beliefs around contraception.

Should sex and relationships education be compulsory?

This is a long-standing debate with heated arguments on both sides. On the one hand there is the view that sex education should be the responsibility of the parents as opposed to the schools. A poll from the Association of Teachers and Lecturers (ATL) found that only 6 percent of adults believe sex education to be a teacher's job (Daily Mail, 2016). However, there is also a group of individuals who believe that sex education promotes sexual promiscuity. Tabloid newspapers often reflect these views through the use of shocking headlines with titles such as 'Teen pregnancies increase after sex education classes' (Telegraph, 2004), 'Handing out condoms will encourage teenage sex' (Telegraph, 2002) and 'Lessons in Porn' (Daily Mail, 2016). With headlines such as these it is little surprise that there is some resistance to sex education and that it is met with great apprehension by many. There is data to support parental led sex education, with Crosby, Hanson and Rager, (2009) finding that females who did not have parental discussions about sex and relationships were almost five times more likely to have had multiple sexual partners in recent months. They were also 70 percent less likely to have talked about HIV prevention with a partner, compared to those who received a parental education. Of course, it would be naïve to assume that all students have the parental support available to them to have these open discussions. There are close to two million lone parents with dependent children in the UK (Office for National Statistics, 2015) and more than 43,500 children aged over 10 are in care (Department for Education, 2016b). While these two factors alone do not indicate a lack of sex education, they can be

indicative of other factors such as parental working hours, relationships and caring responsibilities, which may lead to constraints on parent-led SRE. Factoring in some parents discomfort in discussing sex and relationships with their children, as well as those who believe the school is giving a full and in-depth education, there may be an alarming number of children who won't receive a parental sex education. On this basis alone, it can be seen as important that all students receive competent sex education from their schools, so that every student is given the information they need to make safe and informed decisions about their sexual lives.

If SRE were to be made compulsory, would it have an impact on the teenage pregnancy rates in young women, or lower the number of STI's contracted in the under 25s? Whilst we cannot definitively answer this question, we can examine other European case studies as examples. The Netherlands presents a surprising paradox; the country is typically famed for its Red-Light District and perceived promiscuity with sex and drugs. However, it has one of the lowest conception and birth rates in teenagers across the whole world (The Telegraph, 2007). One potential explanation for this is the sex education delivered in Dutch schools where SRE is compulsory from the age of five. This openness about sex and relationships seems to have created an environment where teenagers are able to make more informed decisions and where they are able to communicate decisions more effectively. This may in turn underlie the phenomenon of Dutch teenagers typically losing their virginity one year later than their British counterparts, and being significantly more likely to use contraception (The Telegraph, 2007). Given these findings contradict the argument that SRE education promotes early sexual activity, it puts forward a strong case for having compulsory sex and relationships education in all secondary schools, including academies.

Another solution that has been proposed for the lowering of teenage pregnancy is an increase in compulsory education time. Previously students in England were able to leave full time education the summer following their GCSE examinations. However, since 2015 the law has changed and teenagers must be in some form of education, training or apprenticeship until they are 18 years old (Department for Education, 2016a). This change to education may have meant students need to become more focused on their future and this has potentially made teenage pregnancy less acceptable among peers.

As a nation and as a society, it can be argued that we owe it to our young people to fully educate them about sex and relationships education. Teenage pregnancy has numerous implications including 'adverse health, education and economic outcomes for both mother and child' (Vincent, 2007). In addition, many teenage mothers experience homelessness, poor mental and physical health

and lower educational attainment (Kiernan, 1995; Wellings et al, 1996, Corcoran, 1998 and Berrington et al 2005). These potential outcomes for teenage mothers spread further than the individual and have an impact on those around them as well as the wider economy and society. For these reasons, as well as from a moral standpoint, students should be educated within school with regards to SRE. Ofsted (2002) reported that ‘reducing the incidence of teenage pregnancy is not the only purpose of education about sex and relationships, but it is a very important one’. In contrast to this, there is some evidence that improving SRE and making it compulsory across all schools would not reduce teenage pregnancy rates. As DiCenso et al (2002) found, ‘interventions were largely unsuccessful in delaying the initiation of sexual intercourse, improving the use of birth control or reducing the number of pregnancies’. Here DiCenso et al are referring to their study which looked at the effectiveness of intervention strategies such as sex education, school clinics, community based programmes and family planning clinics. The study utilised data from across North America, Australia and Western Europe. This comprehensive study suggests similar findings would be applicable to British schools. However, Bonnell’s (2007) research found that schools do play a pivotal role in preventing teenage pregnancy, concluding that ‘Young women who feel supported by their schools and feel confident about their future careers are less likely to view early parenthood as a way of finding meaning and gaining respect from their peers and communities’.

Conclusion

Sex and relationships education is an important aspect of teenagers’ development. There are currently many shortcomings in the way SRE is delivered, particularly the lack of consistency between schools. Despite the fact the SRE is compulsory in state maintained schools, this reflects a relatively low proportion of all educational establishments. If SRE was set out in the national curriculum in the same manner as other subjects, with a detailed specification for teaching, this would encourage uptake at academies, free and private schools. If SRE is to be recognised with the respect it deserves it will need to be given the appropriate timetabling considerations, which will alleviate many of the problems with teaching, as identified by experienced teachers. SRE should be taught by teachers, with consideration for many of its aspects, such as consent, LGBTQ+ relationships and the emotional needs and communication of teenagers, which are currently lacking in many schools sex and relationships education. While there is some conflicting evidence as to the effectiveness of school led SRE, I firmly believe that educating teenagers so that they may make informed decisions

should be the responsibility of the school, although that is not to say that it shouldn't be supplemented by parental education. Sex and relationships education in the United Kingdom does need reform; there is great inequality in the way it is currently delivered and we owe it to our young people to educate them adequately in these matters. Legislation aiming to make SRE compulsory for all secondary schools, including free schools, academies and private schools in the United Kingdom is currently being examined by the British Government. Justine Greening's recent announcement of proposed plans for compulsory age appropriate relationships and sex education could be implemented from September 2019 (House of Commons Library, 2017).

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What is Transcranial Magnetic Stimulation?

A brief overview

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Introduction

In 1985, about 150 years after Michael Faraday had discovered electromagnetic induction, Anthony Barker and colleagues successfully stimulated the human motor cortex using magnetic pulses and measured electrical activity in the moving responding muscle. Since then, there have been numerous studies using Transcranial Magnetic Stimulation (TMS). This article gives a brief overview of how this (neuro-cognitive) method works and delineates examples of what it is used for.

Technical principles

With TMS, a magnetic pulse of usually up to 2 Tesla is produced when an electrical current of up to about 8 kiloampere is generated by a capacitor and discharged into a coil that is made up of wires and typically circular or figure-of-eight shaped. When the coil is placed on the scalp (see Figure 1), with the magnetic pulse changing at a rapid rate, an electric field is induced in that part of the cortex that is underneath the coil, and neuronal activity or changes in resting potentials in a large number of neurons are in turn elicited. As a result, normal brain activity is transiently interrupted, and the greatest effects of TMS on behaviour are observed close to the time of pulse onset (Walsh and Cowey, 2000; Walsh and Rushworth, 1999).

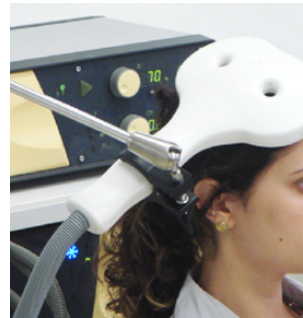


Figure 1: Example of a TMS setup².

Typical application protocols

Magnetic stimulation can either be applied in the form of single pulses, paired pulses, or in the form of repetitive pulses, so-called rTMS. While in single pulse mode the stimulation is delivered at one precise point in time, in paired-pulse TMS two pulses are delivered sequentially, either to a single cortical area using one coil or to two different areas using two different coils (Walsh and Rushworth, 1999). In repetitive pulse mode, a repeated train of pulses is applied at rates of up

²Taken from <https://commons.wikimedia.org/wiki/File%3ANeuro-ms.png>, By Baburov (Own work) [CC BY-SA 4.0 (<http://creativecommons.org/licenses/by-sa/4.0>)], via Wikimedia Commons. The image section was modified.

to 50 Hz (or higher) for between a few seconds and several minutes.

The choice of stimulation parameters such as intensity, frequency and inter-train interval are critical in determining whether the effects of stimulation are excitatory or inhibitory (O'Shea and Walsh, 2007; but see also Nevler and Ash, 2015, for various other relevant factors). In fact, it is likely that both a brief activation and a brief inhibition are induced by TMS but that they occur in differing amounts and in differing time courses depending on the specific context and parameters (Hallett, 2007). With single pulse TMS, facilitatory effects have mainly been found in research on phosphene perception or on producing specific muscle contractions (see Walsh and Rushworth, 1999). In the context of undertaking a specific task, however, TMS application usually decreases the neuronal signal-to-noise ratio, resulting in delayed or disrupted performance (Walsh and Cowey, 2000; Walsh and Rushworth, 1999). One prominent example of this are early TMS studies that examined the timing of critical processes in visual perception. They found that TMS applied to the occipital cortex 80-100 ms as well as in an earlier time window after the onset of a visual letter array impaired identification of the letters (Amassian et al., 1989; Corthout, Uttl, Walsh, Hallett, and Cowey, 1999), yet later on heterogeneous results were reported and the evidence debated (de Graaf, Koivisto, Jacobs, and Sack, 2014; Kammer, 2007; Tapia and Beck, 2014). More recently it has been noted that the current level of (pre-)activation of the brain region that is stimulated (and thus the exact timing of the stimulation before or during a certain task) seems furthermore critical in determining whether performance is facilitated or inhibited (Nevler and Ash, 2015; Rossi and Rossini, 2004).

Experimental considerations

An area for stimulation can be identified in different ways, such as by using the skull shape, brain anatomy, functional correlations detected by Functional magnetic resonance imaging (fMRI), or functional effects like motor responses. As different coil orientations or angles can induce different effects, placement of the coil requires particular attention (see Hallett, 2007). In order to make statements about the specificity of the obtained effects of TMS (and to draw valid conclusions), having an appropriate control condition or site is crucial. This is particularly important with TMS, as it can lead to face twitches, eye blinks and auditory clicks and sensations on the scalp as side effects (Corthout, Hallett, and Cowey, 2011; Epstein, 2008; Walsh and Rushworth, 1999). However, these side effects may be difficult to completely control for in some experimental designs. Depending on the research question and the experimental design, there

are different ways to choose a control condition or site. For example, a control site can be a brain region that is thought to be related to a different cognitive function. Alternatively, in order to gain more precise information about the spatial layout of the brain and test where stimulation produces an effect in a specific task and where it doesn't, several control sites that are close to one another can be chosen (Walsh and Cowey, 2000; Walsh and Rushworth, 1999). On the other hand, in order to show that two processes can functionally be dissociated in space or time, a task control is needed (Walsh and Cowey, 2000). Especially in clinical research settings, sham stimulation is usually used as some sort of placebo condition and specific sham TMS coils have been developed in the recent years for this purpose (see Epstein, 2008).

TMS in research and practice

When investigating brain-behaviour relationships TMS displays some advantages over other methods. While it is more economical than fMRI or Positron emission tomography, which record brain activity correlated with some cognitive or behavioural event, TMS can be used to make inferences about the *necessity* of a brain region for (particular) cognitive processes (Walsh and Rushworth, 1999). Aside from investigating deeper medial cortex and subcortical structures (e.g., Walsh and Cowey, 2000), TMS also displays advantages over lesion studies with neuropsychological patients. Firstly, these patients often possess large, ill-defined lesions, meaning that assigning specific brain regions to certain cognitive functions can be difficult. With TMS, however, distinguishable effects may already be observable by stimulating scalp sites as little as about 1 cm (or less) apart from each other (Walsh and Rushworth, 1999), although it should be noted that the current induced by TMS spreads beyond the cortical area that is underneath the coil (e.g., Maccabee, Eberle, Amassian, Cracco, and Rudell, 1990). Secondly, the damaged brain of neuropsychological patients might have reorganized itself since the time of the stroke or accident (in a form of synaptic plasticity) or the subject may have acquired other compensatory strategies (Robertson and Murre, 1999). In contrast, TMS causes only a very brief, reversible (and repeatable) disruption in cortical function. It is therefore specifically suited for determining whether the contribution of a cortical area is essential for performance and thus for testing theories of the functions of different brain regions (yet it should be noted that in patients with focal lesions oftentimes more profound, selective cognitive effects can be observed). Additionally, also due to its high temporal resolution, TMS can be used to investigate the precise moment at which a certain cortical area critically contributes to performance in a

specific task and to investigate the ordering of component (cognitive) processes and their interactions (Pascual-Leone, Walsh, and Rothwell, 2000; Walsh and Rushworth, 1999). From a clinical perspective, single and paired-pulse TMS applied to motor-associated areas may help to detect impairments of central motor conduction in corticospinal or corticobulbar pathways and may thereby assist in the clinical diagnosis of several neurological disorders that involve motor dysfunction (Chen et al., 2008; Groppa et al., 2012; Rossini et al., 2015). Moreover, since rTMS seems to produce certain effects that persist for some time after the stimulation, possibly due to long-term potentiation and long-term depression of synapses in the central nervous system (Hallett, 2000; Nevler and Ash, 2015; see also Ridding and Rothwell, 2007), researchers have started to investigate its usefulness for the treatment of several neurological and psychiatric disorders when applied over multiple sessions. These include depression, schizophrenia, and neurodegenerative diseases, amongst others (for an overview of studies see for example Elder and Taylor, 2014; Hallett, 2007; Haraldsson, Ferrarelli, Kalin, and Tononi, 2004; Lefaucheur et al., 2014; Schutter, 2009). However, individual studies vary in the outcomes and the sizes of effect they report, with effects overall being rather modest and short-lived. Therapeutic effectiveness seems to depend not only on the exact site of stimulation but also on intensity and the precise pattern of pulses, among many other factors (e.g., Elder and Taylor, 2014; Hallett, 2000; Lefaucheur et al., 2014). Further and more detailed characterization of rTMS application and its subsequent effects on individual patients, possibly in combination with other forms of therapy, as well as technical developments and careful application guidelines and restrictions are needed before potential wider therapeutic use is seen.

Concluding remarks

Overall, TMS displays methodological advantages as well as certain challenges and limitations in research and practice, and various ethical concerns should also be considered and addressed before using this method. Whilst the discussion of these is beyond the scope of this short summary, the reader is directed to reviews of application guidelines and potential risks that have been published elsewhere (see for example Cabrera, Evans, and Hamilton, 2014; Horvath, Perez, Farrow, Fregni, and Pascual-Leone, 2011; Illes, Gallo, and Kirschen, 2006; Rossi, Hallett, Rossini, and Pascual-Leone, 2009; Oberman, Edwards, Eldaief, and Pascual-Leone, 2011; Maizey et al., 2013). Yet, TMS has contributed remarkably to several lines of research in the recent years, particularly to the understanding of perception, attention, awareness, motor control, and plasticity.

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What matters to children in care?

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Residential care tends to be regarded as a last resort compared to foster care whereas adoption is regarded as 'golden standard' due to its permanency character (McSherry, Fargas Malet, Weatherall, 2016; UN General Assembly Resolution, 2009). This article reveals the views of 39 Romanian care leavers and adoptees about their adoption experience and it argues that the quality of placement is more important than the type of placement.

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Introduction

Soon after the end of the Cold War (1989), Romania became known to the world for the extremely precarious conditions in which children in residential care lived. As images were broadcast all over the developed world, people reacted instantly (Kligman, 1998; Watkins, 1994).

With little knowledge of the root causes, thousands of people went to Romania to bring aid to institutions or to 'save' (i.e. adopt) a Romanian 'orphan' (Dickens, Serghi, 2000). In less than one year 7000 children were adopted from institutions or from poor families (DCI and ISS, 1991; Kligman, 1998). Yet many of the children, they were to learn, were not orphan. Such a quick emotional response in a country ridden with extreme poverty, at a time when its institutions and legislation were being contested, led to corruption and child trafficking. The media reports also drew researchers' interests. Neuroscience scholars saw in the children reared in institutions a unique opportunity to explore long term impact of physical and emotional deprivation in early life. UK and Canada initiated longitudinal studies comparing the Romanian adoptees with UK, respectively Canadian born adoptees (Rutter, Sonuga-Barke, Castle, 2010; Le Mare, Audet, 2006).

Meanwhile, the children have grown up. Not all of them left the country. Amongst those who remained, some were adopted in Romania, others remained in residential care or were later placed in foster care or small group homes when such alternatives became available in Romania. The country's transition from a communist state to democracy and market economy which culminated with the accession to the European Union in 2007 ran in parallel with their upbringing. During this time, the country received criticism, recommendations and sometimes contradictory demands on how to address the institutionalised children issue. Intercountry adoption was a notorious example of this (Neagu, 2015). Reform of the child protection sector was a condition for the country's accession to the European Union and it entailed change of legislation and introduction of alternative services to large institutions, such as small group homes and foster care placements. This is the context of the research project.

Remembered childhoods and what one can learn

One important criterion to understand the quality of the child protection services is the feedback of those who benefitted from them. By undertaking 39 life history interviews with Romanian care leavers (young people with large residential care or foster care experience) and adoptees who are now in their 20s, I have attempted

to capture their memories of being in residential care¹, foster care, domestic or intercountry adoption and the challenges they faced in their transition to adulthood from these different types of placement.

According to Article 12 of the UN Convention on the Rights of the Child, 'the child who is capable to forming his or her own views' has the right 'to express those views freely in all matters affecting the child...the views being given due weight in accordance to age and maturity' (UNRC 1989). This is a particularly important provision for children in care. The extent to which their opinions were taken into account by their carers, foster carers or adoptive parents, or professionals that came in contact with them was an important aspect of their childhood. Other key aspects were to what extent the interviewees felt safe, felt that their basic needs (such as food, health, education) were satisfied and how they recalled their school experience.

Preliminary findings indicate that the type of placement is not a guarantee of its quality. Good placements were those in which children felt safe, were listened to and appreciated for who they were. Having information about their history came across as an important aspect for most interviewees regardless the type of placement they were in. When those who entered care at a later age had been given explanation why it was good for them to go into care, they tended to recall adapting easier to the new setting, compared to those who were taken into care (or moved to a different placement) at short notice. Although there was little or no concern of the child protection services to facilitate the children's contact with their parents, children had a better response to their demand to know their families if they were in residential care, compared to foster care or adoption. In these cases, contact depended also or mainly on the cooperation of the foster or adoptive parents.

Many of the interviewees recalled being bullied or stigmatised by other children in school either because of their perceived race or in relation to their care or adoptee status. This occurred in all types of placement but it varied: it was predominant in primary or middle school years, in schools where the majority of children were from families with a privileged socio-economic status and in schools where they were the only or one of the very few children in care in that setting. Abuse and degrading treatment (either from peers or staff) was reported by most research participants who grew up in large residential

¹Large residential institutions in Romania in the 1990s would host over 100 children, in some cases as many as four or five hundred children. During the reform process (early 2000s), the number of children was reduced to an average of 40 children/institution, many other children being placed in foster care or family type homes (up to 12 children/home). Since 2005, it is illegal in Romania to place children under three in residential care.

institutions although not all of them were directly affected by it. Physical and/or emotional abuse was reported in some cases also in the other types of placement.

Despite this, most of the interviewees managed to achieve independent living. To what extent they live a life of their choice is a different matter which is beyond the scope of this article.

Conclusion

This research brings forward the voices of 39 Romanian people who entered adulthood being in residential care, foster care, domestic adoption or intercountry adoption. Findings suggest that good or poor care experiences, as perceived by the research participants, are not necessarily related to the type but to the quality of the placement they were in; that the ways in which children are treated has impact on outcomes in adult life and that knowing their birth families or having knowledge of their histories before entering care is important to them. The consultation of children prior to entering care or while they were in care about aspects which concerned them was regarded as beneficial and those placements were mostly recalled as good ones. These findings might be an inspiration for further research and for improving policy and decision-making by creating mechanisms for children in out of home to be better heard while they are in care.

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CRISPR/Cas9: A revolution in genetic disease treatment?

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Genetics and the human body

Cystic Fibrosis, Hutchinson-Gilford progeria syndrome, HIV/AIDS. All potentially deadly diseases with a direct genetic cause, and all with the ability to be treated or even cured using revolutionary genome editing technology.

Our genome, inherited from our parents at conception, contains all the instructions necessary to form a fully functioning human body (Encode Project Consortium, 2012). Some traits, such as blood type, are determined by a single gene (and are known as monogenic traits). The vast majority of other biological traits are the result of interactions between multiple genes, and are therefore known as polygenic traits (Hinney et al., 2010).

In order to maintain a human body with fully functioning metabolism, organs etc, which is also adaptive (an example being melanin production in skin on exposure to strong sunlight), some genes must be continually expressed, whilst others are expressed only under certain conditions.

In the case of protein production, the DNA of genes is copied (also known as transcribed) to produce a molecule known as messenger ribonucleic acid (mRNA) (Clancy and Brown, 2008). This mRNA (which may itself be further tailored, or spliced, depending on the protein required) then undergoes translation in which a ribosome enzyme uses the message encoded in mRNA to form a protein, which can then carry out cellular functions (Clancy and Brown, 2008).

The human genome (approximately 3.2 billion ‘base pairs’, the building blocks of double stranded DNA, in length) encodes an estimated 20,000 protein coding genes (Ezkurdia et al., 2013). For the most part, it is the differential expression across cells of the protein coding genes that gives rise to different tissues and organs.

It is worth noting that the genetic principles outlined above govern not only humans, but all other animals and plants and, in a slightly altered fashion (in the sense that their genomes are simpler) prokaryotic organisms such as bacteria (Clancy and Brown, 2008).

Genes, human disease and genome editing

Not all human bodies formed function healthily, and many develop disease over time. Whilst many common diseases, such as diabetes, heart disease and cancers, may be very complex in their underlying aetiology, there exist some in which single gene alterations or ‘genomic events’ (in the case of HIV/AIDS) have serious consequences (see Table 1).

The diseases described in Table 1 are severe and, whilst palliative medica-

tions are available, no established cure exists for any (Doitsh and Greene, 2016, Gonzalo et al., 2017, Kunzelmann and Nitschke, 2000). However, the relative simplicity of the underlying causes of these diseases in relation to polygenic or lifestyle diseases (such as diabetes and heart disease) means curative solutions are easy to imagine. Undo the $\Delta F508$ deletion in CF, change a single gene base in HGPS, or remove the HIV genome in HIV/AIDS and the burden of these diseases is removed from the sufferers, who, combined, number 36.8 million worldwide (estimated from Cystic Fibrosis Foundation, World Health Organisation and Gonzalo et al., 2017).

In the case of human disease, the above examples are cases in which genome editing (GE) technology has the potential to make a revolutionary impact. The underlying principle of GE is simple: to insert, delete or replace DNA at a targeted location (Ma and Liu, 2015). The latter refers not only to genomic location (i.e. targeting a specific genomic locus), but can also refer to specific cell types (i.e. targeting airway epithelial cells, where the effects of CFTR mutation are most severe - Kunzelmann and Nitschke, 2000). In terms of curative solutions discussed above, it is easy to see why a reliable GE technology would be so powerful in the treatment of these diseases.

The (r)evolution of genome editing

GE is by no means a new idea. DNA binding proteins such as Transcription-Activator Like (TAL) effector proteins and Zinc Finger containing proteins have been coupled to nucleases (enzymes cleaving DNA) to generate Zinc Finger Nuclease (ZFN) and TAL Effector Nuclease (TALEN) GE tools. However, the inherent protein guided nature of these tools makes them difficult to design, produce and validate, limiting their adoption (Ma and Liu, 2015).

To spur GE on and enable its widespread use, a technology was required which was inexpensive, easy to use, and could be tested and validated in a wide variety of biological systems. Here, we come to CRISPR/Cas9. CRISPRs (Clustered Regularly Interspaced Short Palindromic Repeats) are repetitive DNA sequences originally observed in *Escherichia coli*, but have since been found to be widespread in bacteria and archaea. It was later observed that many sequences of DNA in CRISPR regions seemed to be of viral origin. These regions were found to be actively transcribed, and to be associated with Cas (CRISPR-associated) proteins, which can unwind and cut DNA (Sontheimer and Barrangou, 2015). Experiments in 2007, using the *Streptococcus thermophilus* bacterium and infection with bacterial viruses (known as phages) revealed that the CRISPR/Cas system encodes a previously uncharacterised adaptive immune system in bacteria

Disease	Cause	Effects
CF	Mutation in cystic fibrosis transmembrane conductance regulator (CFTR) gene, the most common of which ($\Delta F508$) deletes a single amino acid in the protein (Kunzelmann and Nitschke, 2000)	Persistent airway inflammation, coughing, wheezing, chest infections, bowel obstruction, infertility (Kunzelmann and Nitschke, 2000)
HGPS	Point mutation (single base change) in the LMNA gene replacing cytosine in position 1824 with thymine (Gonzalo et al., 2017)	Premature ageing, atherosclerosis, kidney failure, loss of eyesight, heart failure. Life expectancy averages 14.6 years of age (Gonzalo et al., 2017)
HIV/AIDS	Infection with Human Immunodeficiency Virus. This retrovirus inserts its own genome into cells of the human body, causing them to become factories for new HIV virions (viral particles), which are able to destroy crucial immune cells known as CD4+ T cells (Doitsh and Greene, 2016)	Acquired Immunodeficiency Syndrome (AIDS) – immune system failure, with increased susceptibility to cancers, tuberculosis and opportunistic infections. (Doitsh and Greene, 2016)

Table 1: Examples of some monogenic or single ‘genomic event’ diseases. It should be noted that, for CF and HGPS, multiple other potential genetic aberrations can lead to disease but, for the purposes of this article, only the most common were listed. CF = Cystic Fibrosis, HGPS = Hutchinson-Gilford Progeria Syndrome, HIV/AIDS = Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome.

(Barrangou et al., 2007) whose mechanism is outlined below.

Invading phages and other pathogens carry DNA. Segments of this invading DNA can be captured by the bacteria and inserted into their own genomes in CRISPR regions. These sequences can then be copied (transcribed) to generate a type of RNA, known as crRNA (CRISPR-RNA), which associates with Cas proteins. The crRNA/Cas complex can target the invading foreign DNA. On correct targeting of the foreign DNA, the Cas protein acts as a pair of ‘molecular scissors’, cutting the invading pathogen DNA, rendering it inactive and disabling the pathogen. This cleavage does not occur in the CRISPR regions. The overall result of this is the selective cutting of foreign DNA, along with a genome-encoded ‘memory’ of infection (essentially a type of vaccination) in the intact CRISPR regions (reviewed in Amitai and Sorek, 2016).

This system can be thought of as one which allows the pathogen-infected cell to ‘post’ (using the crRNA as an address label and stamp) a pair of scissors to the pathogen. On reaching its address the scissors destroy the pathogen’s DNA before it has a chance to damage the host cell. A copy of the address label and stamp remain in the host’s DNA so that, if the pathogen invades again, another scissor-containing letter can quickly be dispatched. It was rapidly realised that this system could form the basis of an ideal GE technology. Expression or delivery of a Cas protein (Cas9 from *Streptococcus pyogenes* is frequently used) along with an appropriate single guide RNA molecule (sgRNA) can, in theory, allow targeting of genes in any cell type (Ma et al., 2014). The Cas9 protein is simple to produce in the laboratory, and sgRNAs can easily be designed to target any gene of interest (both advantages over ZFNs and TALENs) (Doudna and Charpentier, 2014).

Molecular mechanisms in genome editing

Thus far we have seen that CRISPR/Cas9 represents the most tractable GE technology currently available to researchers. However, how does inducing a break in DNA at a targeted location allow genome editing to occur? The answer to this lies in the methods cells can use to repair breaks in their DNA.

Used ‘off the shelf’, the CRISPR/Cas9 system can be used to induce a double strand break in a targeted location in host DNA upon introduction of the components (Cas9 and sgRNA) into the cell (see Figure 1) (Doudna and Charpentier, 2014). Unless repaired, double stranded DNA breaks are likely to be lethal to the cell in question. Using the example of human cells, there are two main pathways that can be used for DNA repair, and this is where the results of genome editing become apparent. The first pathway is known as Non-Homologous End Joining (NHEJ), in which the cut ends of the DNA are simply

re-ligated. However, NHEJ often results in small insertions or deletions (known as indels) in the targeted DNA region, resulting in loss of function of the gene (see Figure 1) (Aparicio et al., 2014). In the case of HIV/AIDS, targeting the viral genome in this way could inhibit the production of functional virions (Spragg et al., 2016).

The second possibility is alteration of a targeted gene using the Homology Directed Repair (HDR) process (Aparicio et al., 2014). In this case, CRISPR/Cas9 is used as before, but with the additional supply of a replacement section of DNA, which has some similarity (homology) to the target sequence. This is likely to merge (recombine) with the targeted DNA region on double strand break formation, and can therefore result in the introduction of the replacement DNA, essentially forming a functional edited gene (see Figure 1) (Shen et al., 2017). In the cases of CF and HGPS (see Table 1), this HDR CRISPR/Cas9 method could be used to ‘correct’ the faulty genes causing the disease permanently (Schwank et al., 2013, Liu et al., 2011). A visual overview of this GE technology and the possible DNA repair pathways causing editing effects is presented in Figure 1.

Since its discovery, the CRISPR/Cas9 system has progressed rapidly as a GE tool (at the time of writing, over 5500 scientific papers had been published on the subject of CRISPR – PubMed 2017). Multiple human and mouse cell types have provided proof of concept of CRISPR/Cas9 as a successful system (Moreno and Mali, 2017). In addition to this, multiplexing of CRISPR/Cas9 has also been demonstrated, where multiple sgRNAs are used to guide Cas9, leading to simultaneous editing of genomes at multiple locations (Cong et al., 2013), with high efficiency.

Treating disease with genome editing

In terms of disease treatment, two main approaches can be taken; *in vivo* or *ex vivo* genome editing (see Figure 2). In the case of CF research, Schwank et al., (2013) were able to demonstrate the use of CRISPR/Cas9 in an HDR GE approach to repair the faulty CFTR gene in intestinal stem cells harvested from CF sufferers. This was able to return the cells to a ‘healthy’ phenotype *in vitro*, although was not subsequently used *in vivo*. A similar approach has been shown to be successful in the case of HGPS, using patient fibroblast cells which were harvested and de-differentiated to the induced pluripotent stem cell (iPSC) state before treatment (Liu et al., 2011). iPSCs have the ability to differentiate back into multiple tissue types (Liu et al., 2011), and could in theory (as shown in figure 2) be used for transplantation of disease free genome edited tissues back into patients. Disruption of the HIV genome using cells harvested from patients

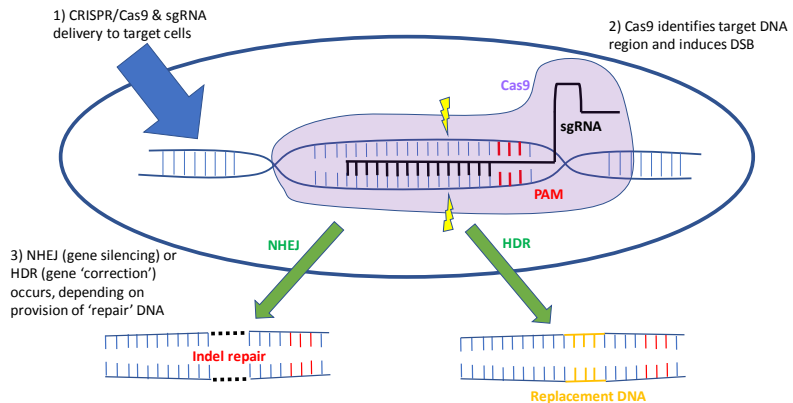


Figure 1: A guide to CRISPR/Cas9. Once the CRISPR/Cas9 GE 'toolkit' is delivered to target cells (section 1), sgRNA guides Cas9 to the targeted DNA site and double strand cleavage occurs (section 2, and represented by two lightning bolts), dependent on the presence of a common PAM sequence. Following this, DNA repair via NHEJ (indel repair, indicated by the dotted black lines) or HDR pathways occurs (with replacement DNA shown in yellow), resulting in editing of the targeted genomic region as required (section 3). Further detail on delivery on CRISPR/Cas systems can be found below. Note that the Cas9 protein and host genome inside the targeted cell (delineated as a blue oval) is not shown to scale. DSB = Double Strand Break, sgRNA = Small Guide RNA, PAM = Protospacer Adjacent Motif, NHEJ = Non-Homologous End Joining, HDR = Homology Directed Repair.

has also been successfully demonstrated *in vitro*, and is an important first step in establishing GE as a possible treatment for HIV/AIDS (reviewed in Spragg et al., 2016).

Genome editing – off-target effects and delivering therapy: opportunities and challenges

Whilst CRISPR/Cas9 GE has proven itself as a powerful *in vitro* tool, with the potential for application in the treatment of multiple diseases, there remain key barriers to its *in vivo* usage, the most important of which are off target effects (i.e. cutting DNA in the wrong place) and safe, effective delivery. Off target effects are present in all GE technologies characterised to date (Dorson and Border, 2016). Off target effects are clearly a major concern in therapeutic application; should a CRISPR/Cas9 GE construct accidentally target an oncogene (genes which can cause cells to become cancerous), then tumour formation may result (Cho et al., 2014). In a revolutionary (and controversial) recent study, Liang et al. (2015) described the use of the CRISPR/Cas9 system in human embryos. Many have called for a moratorium on such work (Lanphier et al., 2015), due in part to ethical concerns relating to ‘designer babies’ as well as the issue of consent where an embryo is concerned. Although tripronuclear embryos were used, fertilised by two sperm and therefore non-viable, the work highlighted the off-target issue. The researchers used a construct targeting only the Beta-globin gene, mutations in which can cause blood disorders such as beta thalassemia and sickle cell disease. However, off target mutations generated by the CRISPR/Cas9 construct were numerous, pointing to a potentially serious safety concern in the use of this technology for disease treatment.

To combat this, researchers have experimented with both ‘nickase’ Cas9 variants (which cut only one strand of DNA on binding, therefore requiring two Cas9 nickases with different sgRNAs to induce a single double strand break) and ‘dead’ Cas9 (dCas9) variants (inactive but fused to a different nuclease) as well as alterations in sgRNA structure (Moreno and Mali, 2017). These have been able to improve accuracy in targeting, but further work must still be done before off target effects are deemed at low enough frequency for safe use.

In terms of *in vivo* therapy, which could be required in the case of HIV/AIDS treatment, where the HIV virus is able to infect multiple cell types, there exist further challenges in terms of delivery of the system. Whilst the direct use of proteins and RNA to administer the CRISPR/Cas9 system has been tested in cells and animal models, these are quickly broken down in the body (Moreno and Mali, 2017), and thus have a limited window of effectiveness (see Table 2). A more

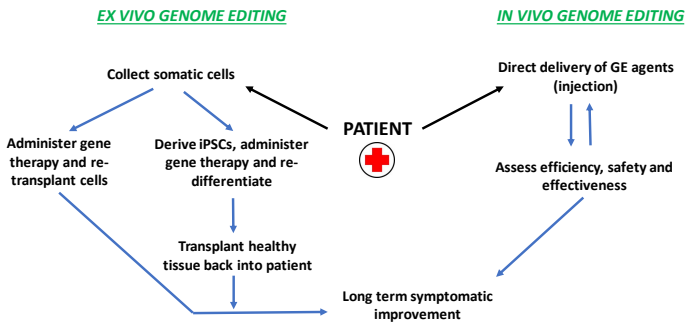


Figure 2: In vivo and ex vivo gene therapy workflows. Ex vivo genome editing for gene therapy (left) involves somatic (non-gamete) cell harvesting from patients. These cells may be directly subject to gene therapy before transplantation back into the patient. Alternatively, they may be used to derive iPSC cells which undergo gene therapy before differentiation into desired cell or tissue types prior to transplantation. In vivo genome editing (right) for gene therapy involves direct administration of the required agents to a patient (in this case CRISPR/Cas systems). Depending on efficacy and duration of activity, re-administration may or may not be required at a later date. If successful, both routes could lead to long term symptomatic improvement. iPSC = Induced Pluripotent Stem Cell, GE = Genome Editing.

effective approach would be delivery of the DNA encoding the components of the GE system, such that it is expressed *in vivo*, providing a longer-term window of effectiveness. Retroviruses, lentiviruses, adenoviruses and adeno-associated viruses (AAVs) are naturally able to deliver genetic information into mammalian cells (Schmidt and Grimm, 2015). Whereas retroviruses and lentiviruses insert their genetic material into the host genome (HIV is a retrovirus), the genomes of adenoviruses and AAVs remain in the host cell without integration (see Table 2) (Moreno and Mali, 2017). AAVs have become a preferred gene therapy delivery vector, due to a variety of favourable characteristics, outlined in table 3. Indeed, they are already under investigation in clinical trials (Mendell and Rodino-Klapac, 2016). However, the package size able to be delivered to target cells *in vivo* by AAVs is limited to 4.7kb (kb = kilobase pair, 1kb being 1000 base pairs of DNA, see Table 2). Whilst the DNA required to encode Cas9 is only 4.2kb, sgRNA coding sequence and other factors necessary to drive expression must also be delivered (Moreno and Mali, 2017). To combat this space limitation, researchers have experimented with smaller versions of Cas9 from different bacterial species, but these often require more complex PAM sequences for recognition of their cut site (Ran et al., 2015, see Figure 1). Current work is aiming to engineer the Cas9 proteins to reduce the stringency of this PAM requirement in smaller versions of the nuclease (Zetsche et al., 2015).

Lentiviruses are another possible option, and have a much larger package size of 9.7kb (see Table 2). Additionally, their ability to infect specific cell types is easily altered via engineering the viral envelope proteins to target certain cell type receptors, yielding a cell type specific delivery of the GE tool (Moreno and Mali, 2017). Lentiviruses are a proven tool for CRISPR/Cas9 delivery in both *ex vivo* and *in vivo* (experiments with mice) settings (Naldini, 2015). A drawback of lentiviruses is their genomic integration. As oppose to AAVs, where DNA is delivered to the cytoplasm or nucleus and is expressed without integration, lentiviruses randomly integrate their genomic package into the host genome. This integration poses a risk of ‘insertional mutagenesis’, where random insertion of the viral DNA disrupts host cell genes, with the potential to perturb cellular function or even generate cancerous mutations (Moreno and Mali, 2017). Currently under investigation are integrase (enzymes that catalyse the integration of DNA) deficient lentiviruses (Wang et al., 2016), but further work must be done to characterise the immunogenicity of these delivery vectors, as well as any continuing integration risk.

Delivery method	Active timeframe	Risk of insertional mutagenesis?	Immunogenicity	Package size
Retroviruses	Long term	Yes (oncogenic)	Low	8.5kb
Lentiviruses	Long term	Yes (oncogenic)	Low	9.7kb
Adenoviruses	Medium term	Low	High	8.0kb
AAVs	Medium term	Low	Low	4.7kb
Proteins	Transient	No	Under investigation	N/A
RNA	Transient	No	Low	N/A

Table 2: Gene therapy delivery methods. Active timeframe of therapy after delivery, risk of insertional mutagenesis, immunogenicity and package carrying size is given for six commonly discussed gene therapy delivery vectors. AAVs = Adeno-associated viruses. Adapted from Moreno and Mali (2017).

Future avenues for CRISPR/Cas9

This review has sought to explain the CRISPR/Cas9 system in the context of genome engineering for the treatment of human diseases. It should also be noted, however, that CRISPR/Cas systems have potential uses ranging far beyond human clinical therapy. These include biomedical research, generation of disease resistant agricultural animals (Reardon 2016), enabling animal based production of human organs (Reardon, 2015), production of higher yield crops (Khatodia et al., 2016) and many more, where CRISPR/Cas GE is already making an enormous impact. Although basic characterisation of CRISPR/Cas systems has progressed rapidly since its discovery and first demonstration as a GE tool a mere decade ago, there remain key challenges to its *in vivo* human usage, including off target mutations and characterisation of suitable delivery methods. Additionally (and especially in the case of potential embryo GE), key ethical questions remain as to the extent to which we regulate for genome editing in humans. However, despite these challenges CRISPR/Cas GE systems hold great potential as a tool of the future and are likely to develop into a truly life-changing biotechnology.

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Proposing a new division within placebo

The mimicebo effect

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The placebo effect is the phenomenon of inert treatments eliciting positive outcomes, whereas the more recently described Nocebo effect is the antithesis, where negative outcomes are elicited. These effects are able to act alongside pharmacological mechanisms and can be triggered purely by the suggestion of benefit or harm. Literature suggests that these phenomena are a fusion of expectation and non-expectation based effects. I propose that the non-expectation aspects are distinct from expectation aspects, with a different basis in physiology. A distinct subset of classical conditioning, consisting of extinction-resistant subconscious chemical conditioning in the absence of affect, which I have named the mimicebo effect, gives rise to these non-expectation aspects. The notion of placebo and nocebo as having two distinct components may provide a better understanding of an often misunderstood and confusing group of processes. Further, it will enable a more effective investigation of the physiological basis of these phenomena as it will encourage researchers outside of the field to start thinking about the distinct pathways and components involved. This will help to provide insight into situations where these effects are especially important, such as clinical trials.

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Introduction

The placebo effect describes the phenomenon in which inert treatments can elicit positive outcomes. John Haygarth first demonstrated the placebo effect in 1799 when he showed that Perkins tractors (metal rods that ‘drew out disease’) had positive responses on patients but that these responses were indistinguishable from the responses elicited by dummy wooden rods [1]. Haygarth demonstrated both how the placebo effect can make genuinely ineffective treatments seem efficacious, rendering these phenomena the scourge of clinical trials, and how expectation of benefit can influence outcomes. The more recently described nocebo effect [2] is the poorly characterised antithesis of the placebo effect, where negative outcomes are caused by negative expectations. These processes not only contribute to properties of sugar pills, but also act alongside pharmaceutical mechanisms of actual medication and in situations involving suggestions about outcomes. Furthermore since the 1978 discovery of placebo analgesia being blocked by naloxone [3], an opioid receptor antagonist, it has become apparent that the placebo effect is really ‘a psychobiological phenomenon occurring in the patient’s brain’ [4]. We now know that diverse mechanisms underlie nocebo and placebo effects in pain, but also a plethora of other conditions like anxiety, Parkinson’s disease (PD) and additionally influence immune function.

The placebo effect has been separated into outcomes caused by expectation of the treatment outcome and outcomes caused by conditioning through previous exposure to treatments [5]. Classical conditioning describes a form of learning that involves the formation of an association between a stimulus and response typically associated with Pavlov’s dogs. Here the repeated presentation of food (unconditioned stimulus) with a bell (conditioned stimulus) caused the two to become associated and thus let the bell alone cause the dog to salivate (conditioned response). Effects caused by conditioning have partially been shown to be expectation-independent, with distinct differences from the expectation-based effects. I propose that this expectation-independent aspect of placebo, which I now call the mimicebo effect (from *mimiceo* – I shall mimic), stems from mimicry of an agent’s original actions. In contrast the remaining mechanisms contributing to placebo and nocebo effects are two sides of a coin, stemming purely from positive and negative expectations. The mimicebo effect is devoid of the moral connotations associated with the ‘positive’ placebo effect or ‘negative’ nocebo effects. The mimicebo effect occurs independently of these expectation-based phenomena.

At the moment, the placebo effect is in fact a merging of two different effects, and this can obfuscate underlying principles. Current understanding of

the placebo does not clearly account for the fact that there are two distinct groups of effects involved. These two groups can come about differently and thus need to be dealt with differently, whether to minimise their impacts in a clinical trial or to maximise their benefits in clinical practice. This new classification will improve understanding of this rather mysterious group of effects.

The mimicebo effect is a distinct subset of classical conditioning consisting of subconscious chemical conditioning in the absence of affect; that is, conditioning stems from direct action conditioned response when it is presented without the conditioning stimulus. Indeed, the more times the extinction of conditioned immunosuppression (i.e., suppression of immune responding) was attempted in mice by presenting the conditioned stimulus alone, the greater the resulting immunosuppression. This is an abrupt reversal of traditional conditioning, where we would expect a reduction. To reference Pavlov again, ringing the bell without providing food should lead to reduced salivation on ringing the bell [6]. This reversal occurs due to reward being internally (intrinsically), rather than externally (from the environment), driven and so once conditioned, the mimicebo response is powerful enough to reinforce its own conditioning (Figure 2). The inert treatment has been imbued with the power to make the patient feel better through psychobiological mechanisms and so continues to reinforce the conditioning. This means that the conditioned effect is indistinguishable from the unconditioned effect. The mimicebo effect is a distinct subset of classical conditioning consisting of subconscious chemical conditioning in the absence of affect; that is, conditioning stems from direct action.

All three effects, while artificially separated for the purpose of discussion, are actually running concurrently and act together to give the final placebo outcome. For example, antidepressant treatment may decrease depression (mixture of genuine and placebo effects) and simultaneously cause a headache (nocebo effect).

The Mimicebo Effect

The proposed mimicebo effect can be most convincingly demonstrated in situations where the placebo and nocebo expectations have no influence; this occurs during experiments involving drugs, which can alter hormonal levels. Injection of sumatriptan, a medication used to acutely treat migraines, results in growth hormone increases and cortisol decreases. Giving sumatriptan injections to form an association between injections and sumatriptan, enabled inert saline injections to cause these same growth hormone rises and cortisol decreases [7]. These hormonal changes are unaffected by verbal suggestions of either hormonal

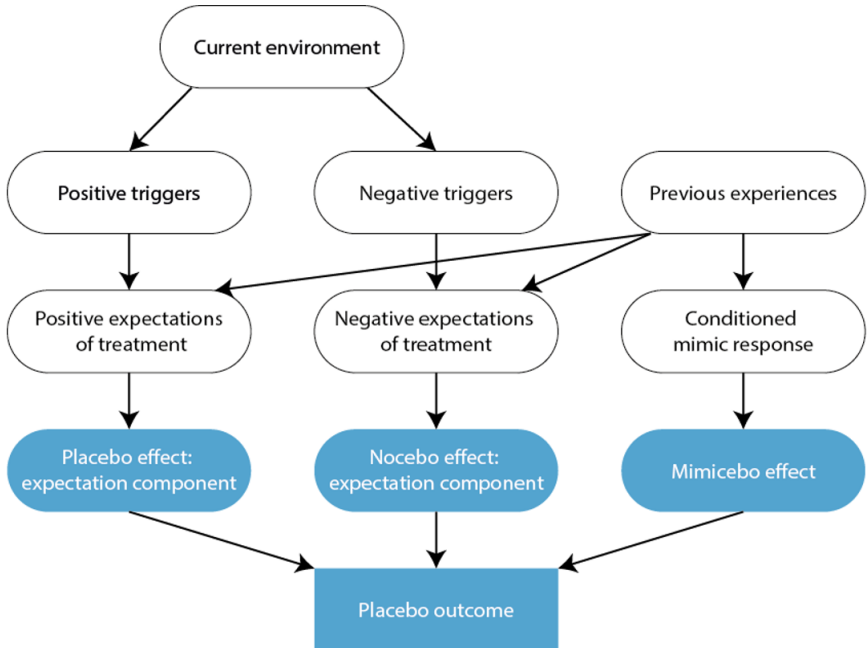


Figure 1: The figure depicts the three distinct pathways underlying the placebo outcome. The outcome of every treatment is a combination of the genuine action of a treatment (pharmacological, surgical etc.) and the 'Placebo outcome' which comes from the combined action of these three effects. Positive or negative triggers, such as verbal instruction or open interruption of treatment, trigger expectations that cause placebo or nocebo effects, which work alongside expectations from experience and the mimicry response caused by that conditioning.

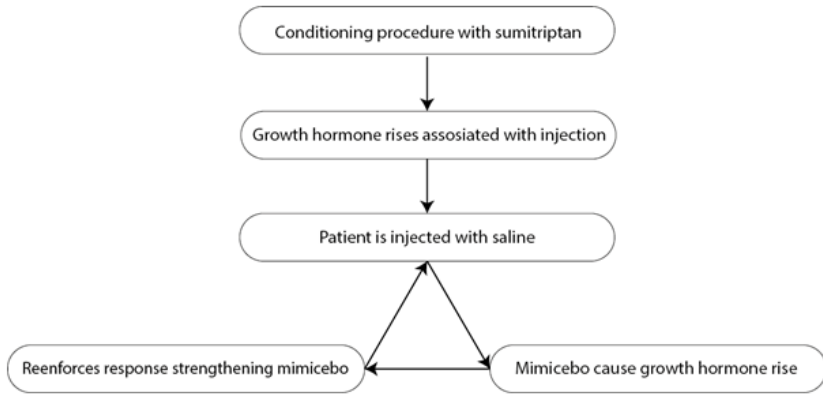


Figure 2: Demonstrates how internally driven reward enable mimicebo to be resistant to extinction. The initial conditioning procedure acts like the first sphere in a Newton’s Cradle and provides the impetus for the association to be sustained without further input.

increases or decreases [7]. This insensitivity to expectation demonstrates the stark differences between mimicebo and expectation-based effects. The mimicebo effect is shown in its purest form to be unencumbered by expectation and thus unaffected by suggestion.

However, even in more complex situations when expectations and mimicebo effects are acting concurrently, the different properties of the processes can be observed. I propose that the mimicebo effect mimics the actions of the drug or procedure being conditioned. Therefore the mimicebo effect should be treatment-specific, changing as the treatment changes. In contrast, as placebo and nocebo effects are expectation-induced changes, they should remain unchanged for each specific condition, for example ischaemic pain (pain relating to reduced blood flow), regardless of the treatment.

The above proposal has been demonstrated in analgesia. Giving participants inert injections after conditioning with analgesic injections induces analgesia through a combination of mimicebo and placebo effects. Benedetti’s group examined the influence of expectation and conditioning with opioid and non-opioid analgesics in ischaemic pain, where participants squeezed a handspring exerciser with a tourniquet to cut off blood supply. The researchers showed that regardless of the type of analgesic, the expectation element of analgesia could be eliminated with naloxone, an opioid receptor antagonist [8]. In contrast,

when expectation was eliminated after preconditioning by telling patients the last injection was an antibiotic to ensure sterility, with no influence on pain, analgesia persisted. This analgesia produced by conditioning without expectation could only be antagonised by naloxone when morphine was the conditioning agent [8]. The conditioning effect produced by the NSAID (non-steroidal anti-inflammatory drug) ketorolac was naloxone-insensitive and was later shown to be blocked by rimonabant, a cannabinoid receptor type 1 (CB1)-specific antagonist [9]. Cyclooxygenase type II (COX-2), one of the targets of NSAIDs, has been shown to be involved in endocannabinoid processing within the body [10]. This clearly shows that while the placebo effect is mediated by opiates across different treatments, the mimicebo effect is only mediated by opiates when opiates are used for analgesia, thus a demonstration of mimicry. Altering the treatment alters the physiological basis of the mimicebo effect. Furthermore, responses to placebo analgesia were correlated with sensitivity to initial analgesia, thereby demonstrating how the mimicebo response mimics the initial action of the original agent. Once again, persistence of only the mimicebo component when patients are told they are receiving a saline injection demonstrates that it is not affected by expectation.

In situations such as pain, negative expectation-based effects are dominant over mimicebo effects. NSAID conditioning-induced analgesia is completely antagonised when the patients are told to expect more pain. Indeed this procedure results in significant hyperalgesia, i.e. increased sensitivity to pain [7]. Benedetti et al [7] concludes that the analgesia is thus purely expectation-based. However, this hyperalgesia is slightly lower than the hyperalgesia experienced in the nocebo condition without preconditioning. This suggests that the mimicebo effect is still present and damping down the effects of nocebo expectation but that it is just being 'overpowered' by the expectation. Indeed the sheer potency of expectation in increasing pain is evidenced by the nullification of remifentanyl's (an opioid agonist) analgesic properties upon participants being told that painkiller application has stopped and that they should expect an increase in pain [11]. Thus, in the case of analgesia, the mimicebo effect is less powerful, but still not abolished by expectation.

Mimicebo effects can also be seen in immune function. Conditioning procedures where cyclosporin A capsules were associated with a flavoured drink (strawberry milk with lavender oil) enabled placebo pills paired with the same drink one week later to cause immunosuppression in participants. These placebo pills were able to reduce the production from genes, by reducing mRNA expression, of several factors important in the inflammatory response (IL-2 and IFN- γ) as well as white blood cell proliferation [12]. A control group

who received placebo pills paired with the drink throughout the whole study experienced no changes. The power of the mimicebo effect is demonstrated by the fact that in mice conditioning an association between saccharin and cyclosporin A, a calcineurin inhibitor enabled saccharin alone to cause inhibition of calcineurin in mouse splenocytes [13]. Calcineurin is a key protein in modulating the action of T cells within the body.

In other research, human participants received a novel flavoured drink as the conditioned stimulus, paired with an antihistamine as the unconditioned stimulus. Participants re-exposed to the novel drink, paired with a placebo pill, showed reduced subjective total symptom scores, skin prick test sensitivity (i.e. degree of allergic response) and basophil activation (as measured by a Basophil Activation Test). Basophils are a type of white blood cell whose activation indicates an allergic reaction [14]. However participants re-exposed to the placebo pill with water only, thus removing the conditioned response, had reduced subjective total symptom scores and skin prick test results but not basophil activation [14]. This suggests that the basophil activation is exclusively a mimicebo effect. Unfortunately these studies did not examine whether a suggestion of ineffectiveness could influence the response. This mimicebo theory could be tested by rerunning the experiment with the inclusion of this suggestion. From this, it would be expected that the suggestion of ineffectiveness would remove the placebo expectation effects without affecting the mimicebo effects; that is, the decreased basophil activation would persist.

The method of this mimicebo immunosuppression has been explored in animal studies. The insular cortex and amygdala have been shown to be important in taste-visceral associative learning in animals. Lesions to the insular cortex prevented both the learning and evocation of the immunosuppressive responses, whereas amygdala lesions only prevented the initial learning stage [15, 16]. However, responses to inert treatments have been observed during clinical trials, such as irritable bowel syndrome [17] or relapsing remitting multiple sclerosis [18], where these taste-visceral associations presumably would not be triggered. It is not clear if these observed outcomes are mediated by the same areas as taste-visceral associative learning or whether they represent expectation-based immune modulation. Expectation effects are thought to be linked to direct nervous links between peripheral immune organs and an area of the brain called the hypothalamus. Complicating matters is the fact that the insular cortex, discussed earlier, is heavily involved in regulating this hypothalamic-immune connection. This suggests that the integration of expectation-based effects and conditioning may occur at the level of the hypothalamus [19].

Most examples of the mimicebo effect are contributions to placebo effects,

although some actions, such as immunosuppression, could be part of unwanted nocebo side effects of a medication. This is due to the ethical restrictions regarding the conditioning of negative effects in humans. Additionally, the occurrence of side effects when inert pills are taken render it difficult to distinguish between outcomes due to conditioning and outcomes due to expectation resulting from warnings about possible effects. One example of a definite negative conditioned symptom is anticipatory nausea and vomiting, a condition that 25 percent of chemotherapy patients get by their fourth treatment cycle, where nausea from treatment is associated with environmental details such as the smell or sight of the ward. This results in environmental triggers causing nausea and vomiting before chemotherapy is received [20]. However, it is important to consider that conditioning may not only contribute to this anticipatory effect but may also contribute to nausea and vomiting experienced post-treatment via the mimicebo effect. Attempts to prevent this type of conditioning (for example by varying the treatment environment) may help to ameliorate both anticipatory and post-treatment vomiting and nausea.

Expectation Effects: Placebo and Nocebo

Nocebo effects have been shown to result from negative expectations in experiments using hidden and open interruption of treatments. Patients post-surgery who were on morphine or diazepam were taken off their medication. Half were informed that their medication was being switched off, an open interruption. The other half of patients was taken off their medication without their knowledge. Patients who didn't know they were being switched off their medication had no increase in state anxiety and had a much slower and smaller rise in their reported pain [21]. A similar result was observed in Parkinson's patients who had a much reduced return of slowing of hand movement velocities when their deep brain stimulation (DBS), a neurosurgical treatment commonly used to treat PD, was decreased without their knowledge [21]. This rationale also applies to the placebo effects where open injection of diazepam decreased anxiety but hidden injections did not alter anxiety [21]. It has been shown using positron emission tomography (PET) scans that Parkinson's patients respond to placebo pills with higher hand movement velocities, due to increased dopamine release in their basal ganglia, a group of brain cells involved in voluntary motor control [22,23].

Expectation can be manipulated by associating different faces with stimuli eliciting varying levels of pain. Faces associated with high and low pain were able to cause hyperalgesia and analgesia, respectively, when presented again with a standardised pain stimulus [24]. Recent evidence has indeed demonstrated that

these expectations are able to produce placebo and nocebo effects even when presented subliminally [24]. It is important to note that despite this being a conditioning procedure, it is expectation that is being manipulated in the absence of chemical conditioning, indicating that this is not a mimicebo effect. This work, however, raises important considerations about the clinical environment where hundreds of subliminal cues by the clinician and environment could affect outcome.

In addition to experiments demonstrating that placebo analgesia can be blocked by naloxone [3, 8, 25] a seminal experiment by Benedetti's lab was able to unpick the physiological basis of the expectation component of the nocebo effect. This experiment used the same ischaemic pain technique as their placebo experiments. Participants given a pill that they were told would cause hyperalgesia rated their pain as significantly worse and had raised plasma ACTH (adrenocorticotrophic hormone) and cortisol (stress hormones), compared to those given no instruction. Both benzodiazepines, a class of drugs used to treat anxiety, and proglumide, a Cholecystokinin receptor (CCK) antagonist, blocked this nocebo hyperalgesia but did not influence baseline pain sensation. Whereas anxiolytic benzodiazepines blocked both the hyperalgesia and the stress hormone rises, proglumide blocked only the hyperalgesia [26]. This seems to indicate that CCK release stemming from anxiety caused nocebo hyperalgesia in ischaemic pain (Figure 3). Interestingly proglumide is also able to potentiate the placebo effect which seems to suggest that nocebo and placebo responses may directly antagonise one another, at least in the case of pain [27]. This suggestion was reinforced by recent work which demonstrated that in the case of high altitude headaches, placebos are only effective when nocebo suggestions have been introduced but are ineffective at removing baseline headaches [28].

A thought experiment allows us to see the importance of the mimicebo effect in clinical trials. Consider a double-blind placebo controlled trial regarding sumatriptan's ability to alter growth hormone in treatment-naive patients. Placebo pills would do nothing, as expectation does not produce hormonal changes, while sumatriptan would increase growth hormone. This would lead to the conclusion that sumatriptan is an effective drug. If however the patients had been injected with sumatriptan previously, the differences might be insignificant due to a large mimicebo effect response of the inert treatment. In clinical trials, conditioning of responses may often occur in participants because they are infrequently completely naive to treatment. This may confound results, causing drugs that have genuine physiological effects seem as though they are ineffective, the opposite sort of error to those that these phenomena are traditionally associated with. For example, there has been an extensive debate on the contribution of placebo

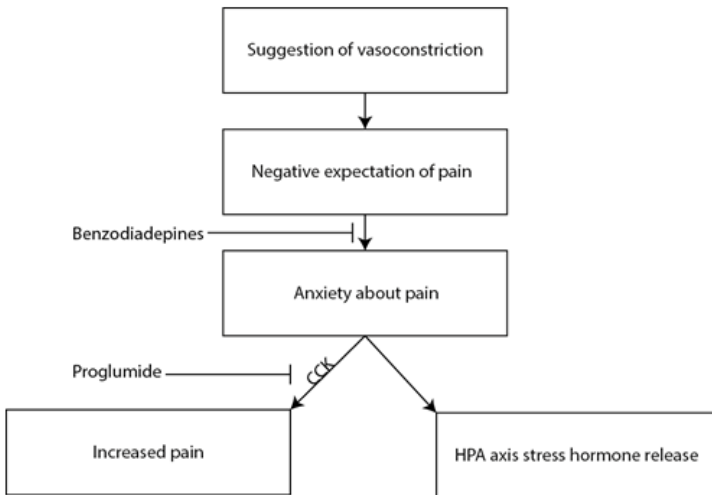


Figure 3: The physiological basis of the effects observed in nocebo hyperalgesia. Benzodiazepines are able to block the increases in pain, ACTH, and cortisol rises caused by the nocebo procedure whereas proglumide blocks just pain. This indicates nocebo expectation of hyperalgesia causes pain through anxiety-linked upregulation of CCK signalling.

effects to antidepressant action, with some meta-analyses claiming placebo effects constitute as much as 75 percent of the treatment outcomes [29, 30]. Although the validity of the methods used in these analyses, is still debated [31, 32] one possible explanation of the large observed placebo effect is that patients previously exposed to antidepressant therapies exhibit a large response to inert treatment due to a large mimicebo effect. Although this is speculation, it could help explain high placebo responses despite what clinicians view as a powerful therapeutic tool.

Brain Imaging

Functional magnetic resonance imagery (fMRI) and PET studies have been used to investigate placebo analgesia, demonstrating mediation by opioids. PET scans showed that the rostral anterior cingulate cortex (rACC) and right lateral orbitofrontal cortex were both activated in both placebo and opiate analgesia; these areas are involved in cognitive processing, emotion and decision making.³³ Placebos also triggered downstream regions such as the periaqueductal grey (PAG), known to mediate analgesia [16,33]. Naloxone prevented placebo-induced coupling of the rACC and PAG [34]. Unfortunately brain scan studies have not yet looked to separate expectation and mimicebo effects. Future research could compare the activation profiles of conditioning followed by an open injection of saline to expectation-induced analgesia without conditioning to help validate this division between the mimicebo and placebo effects.

Clinical Use

Potential clinical use for these effects can be exploited in three ways.

Firstly, the potential of fully understanding how and why placebo and nocebo effects come about would enable doctors to streamline how they design and deliver medication. This is already to some degree being done. For example, previous research has shown that blue capsules are more effective than red capsules at causing a sedative effect [35]. More insight into placebo outcomes enables optimal design of medication. This area however has obviously limited potential, permitting the optimisation of existing medication but with no new areas of possibility being opened.

Secondly, medications that either potentiate placebo effects or negate nocebo effects could be used to try to optimise existing medications. For example, proglumide was able to block the nocebo hyperalgesia response [26]. If we could find drugs that were able to block troubling nocebo effects of commonly used

medications, it would open the door for co-prescription in order to minimise these side effects. For instance, if we were able to find the biological chemical correlate of anticipatory nausea and vomiting (ANV), it would enable doctors to administer a drug either during the initial treatment phase, or after ANV developed, in order to stop this immensely troubling phenomenon. However, since one should avoid whenever possible prescribing drugs to treat the effects of other drugs, this area would be limited to extremely troubling side effects, such as ANV, which can interfere with life-saving treatment.

Finally, placebo tablets have the potential to be used as medicines in their own right. Many times, medicines are declared ineffective compared to placebo and abandoned once deemed useless. Often lost in this is how radically effective placebos can be. As this review has shown, although these effects come from within, they stem from genuine pharmacological phenomena in the body that are in many cases indistinguishable from so-called ‘real’ medications. We should not be left behind by a false dualist interpretation of these effects.

However, giving placebo tablets as medications raises important ethical questions, as the interpretation and conditioning of the patient play an important role in the efficacy of placebo. A study by Ted Kaptchuk is a first foray into these questions. In the study, patients with irritable bowel syndrome (IBS) were given placebo tablets, and placebos were truthfully described as inert or inactive pills, like sugar pills, that did not contain any medication. Furthermore, patients were told that ‘placebo pills, something like sugar pills, have been shown in rigorous clinical testing to produce significant mind-body self-healing processes’ [36]. This study found that giving placebo resulted in significant improvements in patients’ symptoms compared to no treatment as measured by the IBS Global Improvement Scale – where patients rate how bad they think their IBS is and how it is affecting them. This study acts as a proof of concept as to how placebos can be ethically used as medications to improve people’s lives.

Conclusion

I have shown how there are distinct expectation-dependant and expectation-independent aspects with placebo and nocebo. These aspects are different and have a distinct theoretical basis. Incorporation of the mimicebo classification into our understanding of placebo and nocebo effects would help to clarify what is often a poorly understood area. Of course, in most real-life situations the dividing lines are often blurred, as outcomes are often a mixture of mimicebo, placebo and nocebo effects. However, Figure 4 shows how this theoretical division enables the physiological basis of outcomes to be clearly illustrated by using

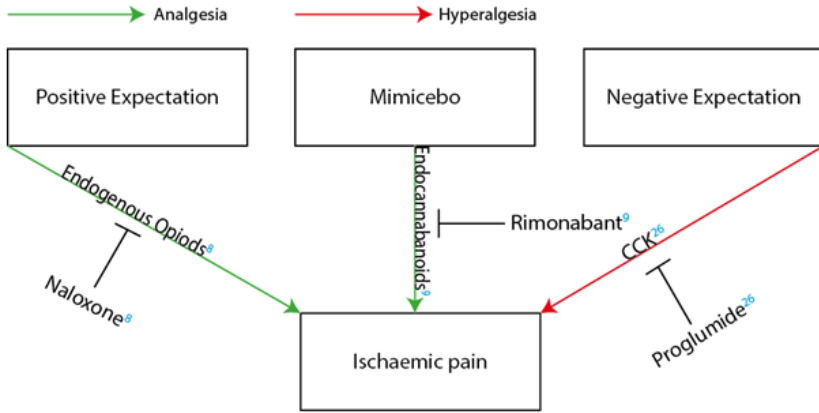


Figure 4: A complete physiological map of Placebo, Nocebo and Mimicebo effects in Ketorolac/Ischaemic pain. A map can be created for each drug-effect interaction. The Placebo and Nocebo effects are effect specific, the Mimicebo effect is drug specific.

the example of the interaction between NSAIDs and ischaemic pain. Thinking of this phenomenon as three separable effects that interact to produce a ‘placebo outcome’ allows us to describe these effects in a way that reflects their underlying basis, which will aid understanding of these important effects. This will enable optimal utilisation within clinical practice, perhaps by purposely conditioning wanted mimicebo effects, and will facilitate understanding of how mimicebo effects can effect clinical trials.

Acknowledgments

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The Despot's Accomplice

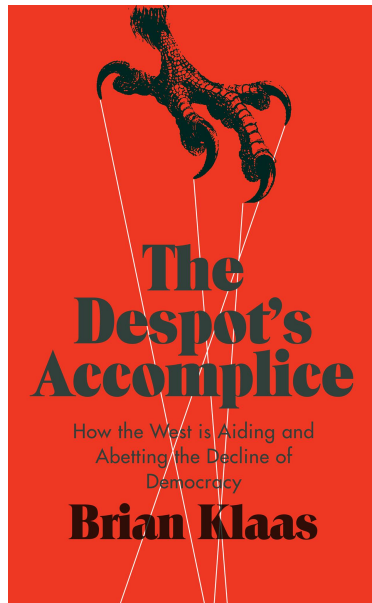
How the West is Aiding and Abetting the Decline of Democracy

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Book Excerpt¹



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For the first time since the end of the Cold War, the world is losing faith in democracy. Between Donald Trump's rise in American politics and the predictable but self-inflicted 'Brexit' economic shockwave, many are now openly asking what was previously an unthinkable question in the West: can people really be trusted with self-government? Is it time to ditch democracy and try something else?

After the Soviet Union fell, democracy expanded at an unprecedented rate. Today, global democracy has receded slightly every year since 2006; in other words, there has been no democratic forward progress for the last decade.

At the other end of the spectrum, powerful authoritarian regimes are becoming more authoritarian. Across multiple indexes and measures, democracy is steadily declining at worst and stagnating at best. Unless the trend is reversed, anyone born in 2016 will be, on average, less free than someone born during the 1990s. These declines are not an accident; they are the battle scars of a struggle between the rule of the people and the rule of despots and dictators. Right now, the people are losing.

However, the democratic sky is not falling. The world remains more democratic than it has been at almost any time in human history. Many countries that were bastions of authoritarian repression just a few decades ago are now democracies. Nonetheless, the recent retreat of democracy is serious cause for concern. This is not a theoretical philosophical debate. Billions of people remain trapped in unresponsive, unaccountable regimes where ruthless oppression is common.

As many despots have rolled back democracy or refused to embrace it, they have found an unlikely accomplice: the West. Western governments, in London, Paris, Brussels, and most of all Washington, have directly and indirectly aided and abetted the decline of democracy around the globe. This unfortunate truth comes despite the stated goals of all Western governments and despite the personal principles of almost everyone in those governments. Overwhelmingly, Western elites genuinely believe in democracy. They want democracy to spread. Moreover, Western governments have been, are, and will continue to be the biggest force backing democracy in the world. But their current approach is backfiring. ...For the moment, though, the West is suffering an acute case of democracy promotion fatigue. Its leaders have less of a stomach for the short-term risks it presents than they used to. This feeling has only intensified in recent years as prolonged debacles in Ukraine, the Arab Spring, Libya, Afghanistan, and Iraq have replaced stable authoritarian regimes with violent chaos. As a result, democracy promotion has been knocked down several rungs on the priority list of Western governments as they set foreign policy agendas. It's perfectly

understandable. After all, failed transitions to democracy in places like Libya after botched interventions are indeed tragedies. Yet it would be a greater tragedy to doom the next generation to the rule of despots, dictators, and thugs, simply because this generation of political leaders is unwilling to make smart but difficult choices to support democracy consistently across the globe. Instead of running away from the challenge, Western governments need to learn from their mistakes and redouble their efforts. They need to stick to their principles and challenge despots, rather than aiding them in pursuit of nearsighted pragmatism. This will not be easy; there are few lowhanging authoritarian fruits just waiting to be plucked. Nor is there any guarantee that toppled despots will be replaced by genuine democrats. But the current approach needs to change, in order to give democracy a fighting chance.

I discovered a strange cast of characters on the frontlines of this battle for global democracy. Their voices are important but are rarely heard in the West. So, over the last five years, I have crisscrossed the world exploring local struggles for democracy to understand why the world is becoming less democratic and what can be done to reverse the trend.

I lived for months at a time in many different countries. Some seemed superficially democratic but were nonetheless home to toxic politics and broken societies. Dictators or juntas governed others. I had poetry read to me by a general in Madagascar who spoke of the glory days when he kidnapped politicians. I sipped mango juice with ex-rebels and was robbed at machete point in post-conflict Côte d'Ivoire. I was tailed by the KGB in Belarus as I spoke to presidential candidates bravely challenging Europe's last dictator. I had tea with a failed coup plotter's family in Zambia and coffee with generals in Thailand's junta café.

These were surreal experiences. But the crisis of democracy in the twenty-first century is all too real for the billions of people around the world who live either under the unforgiving yoke of a dictator or the illusion of freedom in what I call 'counterfeit democracies' – countries that claim to be of the people, by the people, and for the people, but are really none of the above. A minority of the global population lives in true democracies, where people can meaningfully participate in decisions being made about their lives, where the laws matter more than the whims of strongmen, and where citizens have a real choice in electing leaders to represent them. The true criminals in this heist against democracy are dictators and counterfeit democrats – the dictatorial wolves cloaked in democratic sheepskins. But the West is also an accessory to the crime, inadvertently robbing pro-democracy forces abroad of a path to power. Governments in Washington, London, and Brussels pick the side of the despot all too often, as they chase

competing short-term economic and security – and ultimately pyrrhic – victories. This approach undermines long-term Western interests, batters global democracy, and keeps billions oppressed with little hope for better governments.

If the West is doing so much damage, should Western governments even try to make the world more democratic? If so, how? After all, domestic factors are critical to democratisation. Perhaps it's none of our business. Countries often democratize without a nudge from the outside. Moreover, many key barriers to democratisation are difficult to remove or overcome: dynastic oil monarchies, poor countries with weak political institutions, and single-party states that manage strong economic performance are all less likely to democratize. But scholars have also shown that links to the West are a crucial aspect of democratisation across all types of countries. How, then, can Western governments maximize the probability that a given country will become genuinely democratic?

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Questions

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