Institution: Royal Holloway, University of London

Unit of Assessment: 3 Allied Health Professions, Dentistry, Nursing and Pharmacy

Title of case study: Transforming cognition with the global multiple sclerosis community

Period when the underpinning research was undertaken: 2011-2019

Details of staff conducting the underpinning research from the submitting unit:

Name(s): Dawn Langdon	**Role(s) (e.g. job title):** Professor	**Period(s) employed by submitting HEI:** 1999-date
Period when the claimed impact occurred: 2013-2020		

Is this case study continued from a case study submitted in 2014? N

1. Summary of the impact

2,300,000 people worldwide live with multiple sclerosis (MS) and cognitive difficulties profoundly impact their disease management, employment, and quality of life. Langdon led the development of the Brief international Cognitive Assessment for MS (BICAMS) and pioneered its introduction, reducing the cost, time and training required for cognitive assessment in MS, thereby increasing awareness and access to appropriate care. BICAMS has been validated in 24 countries, and globally 11,000 patients are routinely assessed every year on BICAMS. BICAMS has increased the skills of health care professionals in assessing MS cognition, and facilitated cognition as an outcome in major treatment trials.

2. Underpinning research

MS cognitive impairment has been a "hidden symptom", rarely included in clinical care or drug trials. The resulting disability was often wrongly attributed to physical symptoms. There was no feasible cognitive measure that was psychometrically robust, practical, and validated internationally. Langdon's research developed a measure that could be completed in 15 minutes, addressing the key MS cognitive deficits (attention and memory). The test requires only papers, pen and stopwatch, it can be administered by most health professionals and was suitable linguistically and culturally for translation globally. This resulted in an international currency for MS cognition, which has facilitated clinical and research work across the world, enhancing awareness, assessment and management.

Langdon secured funding for, and convened, the three BICAMS committee meetings (Toronto 2011, London 2012 and Bordeaux 2012), comprising the 12 leading international MS cognition experts (neurologist and neuropsychologists), which she co-chaired. This was the fundamental driver in developing and publishing the BICAMS battery and international validation recommendations (**R1, R2**). This research was used to develop a review process to select scales, from a complex and chaotic literature that could be combined to realise a feasible, valid and international MS cognitive assessment. Based on their combined research and international trial experience, Langdon's expert committee identified psychometric and pragmatic parameters essential for scale selection. This unique and novel approach took account of both the science (reliability, validity and sensitivity) and the practicalities (ease of administration, patient congeniality, translation stability). 200 key papers were selected by consensus and scales rated on the six parameters. Three scales were identified to assess attention, and verbal and visual memory.

Their resulting recommended battery (**R1**) can be completed in 15 minutes, without needing special assessor training. The committee also published an international validation protocol, to guide national validations (**R2**). Subsequently, 30 countries have joined the national validation pipeline. 24 have published to date in peer-review clinical neurology journals. Langdon has

offered guidance and support as required, recognised in her co-authorship of eight of the validations. These national studies have demonstrated the validity and reliability of BICAMS in different cultures and language groups, and that it has the same sensitivity to cognitive impairment as the lengthy, complex and expensive "gold standard" batteries. BICAMS thus provides a feasible, accurate and quick cognitive assessment for routine clinical use.

Subsequently 100 peer review papers in clinical neurology journals, on 9 of which Langdon is an author, have demonstrated the further validity of BICAMS in relation to physical disability and brain pathology (criterion validity), and everyday functioning including employment (ecological and external validity). These have confirmed Langdon's original recommendations and supported adoption in clinical practice (**R3, R4**).

More recent research (**R6**), involving patient partnership and surveys, explored how to enhance the relationship between health professionals and MS patients. Key areas were identified: fostering positive relationships with the patient community; providing patients with up to date and reliable information (mindful of the prevalence of unreliable online information about MS), appropriate for cognitive difficulties; and ensuring patient input to co-produce future patient trials and surveys. Langdon's research, with funding from Merck KGaA, including sponsored open access for all publications, has helped to pioneer a model for patient involvement in close partnership with health professionals.

3. References to the research

The following articles are all published in highly regarded journals and with established academic publishers, all have been peer reviewed, and include grant funding from multiple sources including pharmaceutical providers.

(R1) Langdon DW, Amato MP, Boringa J, Brochet B, Foley F, Fredrikson S, Hämäläinen P, Hartung HP, Krupp L, Penner IK, Reder AT, Benedict RH. Recommendations for a Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS). *Mult Scler*. 2012 Jun;18(6):891-8. Doi: 10.1177/1352458511431076 (560 citations).

(R2) Benedict RH, Amato MP, Boringa J, Brochet B, Foley F, Fredrikson S, Hamalainen P, Hartung H, Krupp L, Penner I, Reder AT, Langdon D. Brief International Cognitive Assessment for MS (BICAMS): international standards for validation. *BMC Neurol*. 2012 Jul 16;12:55. Doi: 10.1186/1471-2377-12-55 (254 citations).

(R3) Corfield F, Langdon D. A Systematic Review and Meta-Analysis of the Brief Cognitive Assessment for Multiple Sclerosis (BICAMS). *Neurol Ther*. 2018 Jun 19. Doi: 10.1007/s40120-018-0102-3 (28 citations).

(R4) Smerbeck A, Benedict RHB, Eshaghi A, Vanotti S, Spedo C, Blahova Dusankova J, Sahraian MA, Marques VD, Langdon D. Influence of nationality on the Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS). *Clin Neuropsychol*. 2018 Jan;32(1):54-62. Doi: 10.1080/13854046.2017.1354071 (15 citations).

(R5) Yeandle D, Rieckmann P, Giovannoni G, Alexandri N and Langdon D Patient Power Revolution in Multiple Sclerosis: Navigating the New Frontier *Neurol Ther*apy. 2018. Dec 7 (2): 179-187. Doi: 10.1007/s40120-018-0118-8 (11 citations, 2,399 downloads - this paper, with an MS patient as first author, reported a live international symposium chaired by Langdon, involving neurologists and patients debating how shared decision-making and patient engagement could improve health care, including cognition).

Pharmaceutical investment
Langdon, DW. EUR13,000 from Bayer Healthcare for development and maintenance of BICAMS.net, December 2010.

Langdon, DW. EUR40,000 from Bayer Healthcare to sponsor BICAMS initiative, largely for funding international committee meetings, November 2011.

Langdon, DW. GBP53,000 from Bayer Healthcare for BICAMS validations. December 2012.

Langdon, DW. IPAD BICAMS. GBP118,960 from Novartis Pharma AG, October 2014.

Langdon, DW. BICAMS UK first adopters. GBP25,114. Novartis UK. October 2015.

4. Details of the impact

MS cognition has been the "dark matter" of the condition, with an inferred ubiquitous, negative impact, but without a tangible presence that could be measured, understood or addressed by health services. Langdon met this challenge by delivering a psychometrically sound and feasible international measurement technology, in collaboration with MS patients, health professionals, MS charities, pharmaceuticals and the global MS community. BICAMS has transformed awareness, assessment and management of MS cognition, thereby transforming the care and quality of life of people living with MS worldwide.

First, the patient community recognises how BICAMS has **improved awareness and increased access to care,** identifying and validating those 'missed' by existing health care. As a leading US-based MS advocate and award-winning author of *Facing the Cognitive Challenges of Multiple Sclerosis*, Jeffrey Gingold acknowledged, "Her research work is exceptionally relevant and helpful to people with MS. It is hope and validation" adding "The BICAMS project is truly remarkable and is a **game-changer for the MS community**." (S4, testimonial 31st October 2019). 2,131 people with MS have participated in published BICAMS validation studies globally and a further 13,102 in other published BICAMS scientific studies, indicating its importance to them. The NMSS (American MS Society) funded a project and publication about MS cognition which recommended BICAMS (**S1,** testimonial 28th October 2019).

Second, leading MS charities used BICAMS in their funded trials. MS Societies in the UK and US funded MS-Stat 2 with GBP6,000,000 and the Canadian MS Society funded CogEx with USD5,000,000, together involving over 1,500 patients. Testimonials from other MS patient advocates acknowledge BICAMS' **fundamental contribution to public health improvement** and Langdon's ability to bring together key beneficiaries across charitable, health and care sectors internationally. (**S4, S5**, **S6**). Importantly, they also highlight how Langdon's research has facilitated change by actively incorporating the views and experiences of MS patients. As MS advocate, David Yeandle noted "The importance of this paper appearing in a peer review clinical neurology journal was that it emphasised that shared decision making and patient engagement were essential for optimum MS patient care" (**S5,** testimonial,5th November 2019). This point about Langdon's research being a catalyst for research network development was emphasised by Sara Joiner, an MS Trust trustee who noted, "Her work on the BICAMS scale has led to the recruitment of 30 countries to the project [i.e. BICAMS], meaning that quick, accurate cognitive assessment is now available to so many more people with MS and so many more MS health professionals are more aware of cognitive issues and able to tackle them" (**S6**, testimonial, 4th November 2019). Langdon's commitment to sharing her research with all possible beneficiaries was acknowledged by another American-based patient advocate, Jeffrey Gingold "I invited her to write the foreword to the second edition of my book "Facing the Cognitive Challenges of Multiple Sclerosis [published by Demos Health]" (**S4**, testimonial 31st October 2019).

Third, BICAMS is now recognised and formally **adopted in clinical practice around the world**. Between 2013 and 2020, 20 peer review papers in international clinical neurology journals, arbiters of clinical practise, recommended BICAMS for routine clinical MS cognition assessment. The American Academy of Neurology (AAN), the world leader in setting standards for clinical care, recommended BICAMS in their Quality Measurement Sets for MS in both 2014 and 2020. The Canadian Guidelines for MS Treatment endorsed BICAMS in 2020. Six leading UK MS clinics have been recruited as BICAMS First Implementers (funded by Novartis UK). Over **10,000 health professionals globally** have chosen to attend Langdon's lectures on BICAMS and MS cognition.

BICAMS is being translated and validated in thirty countries (24 formally published to date) in Asia, the Middle East, Europe, and North and South America. The international MS community has allocated resources equivalent to over GBP3,000,000 to validate BICAMS between 2013 and 2020, signalling the importance with which BICAMS is viewed, for improving MS patient care and health professionals' MS cognition skills. Cognition management is now possible for 1,000,000 patients in countries with completed national validations (almost half the global MS population of 2,300,000). **188 centres globally have registered with the BICAMS website**, which includes access to real time calculation of national norms for individuals. Over 11,000 patients are known to be assessed on BICAMS annually around the world. As Professor Ralph Benedict, Professor of Neurology and Psychiatry, University of Buffalo, New York noted "BICAMS is the core of our clinical test battery…BICAMS is brief and sensitive and enables us to reach a much broader base of patients…" and crucially is more likely to be judged affordable by the US health care industry and patient self-funders (**S2,** testimonial 7th June 2019).

Fourth, the pharmaceutical industry has embraced BICAMS, funding Langdon to promote: (1) international validations; (2) software development for IPAD BICAMS; and (3) the UK First Implementer project. In total, Langdon's initial research generated a total of GBP244,000 pharmaceutical sector investment in further development of BICAMS between 2013 and 2020. The BICAMS battery is being used by global pharmaceuticals such as Merck to measure cognition as a treatment outcome in ongoing trials of new MS therapies (CLARIFY, ENSEMBLE, CASTING, CONSONANCE). Langdon's consultancy on BICAMS for pharma have generated approximately GBP200,000 income between 2013 and 2020 and this external work has been devoted to ensuring further development and implementation of BICAMS. As Dr Davorka Tomic World-Wide Brand Medical Director, Neuroscience Franchise, Novartis Pharma AG acknowledged "**BICAMS has changed the way that the pharmaceutical industry thinks about MS cognition**…Global pharma rarely included recognition as an outcome measure in clinical trials, because it was viewed as too unreliable and difficult to manage…**BICAMS has become an international brand with wide global recognition**" (**S3**, testimonial 13th June 2019).

Fifth, BICAMS has been acknowledged as **transforming professional awareness and practice**. The feasibility of BICAMS, and validation studies in so many languages, made a raft of MS cognition research projects possible. BICAMS has created a growing cadre of MS neurologists and health professionals around the world with increased awareness, tools, skills and knowledge of MS cognition. This has enhanced their professional development and benefitted MS patients. As Professor Alan Thompson, Dean of UCL's Faculty of Brain Sciences acknowledged, "**BICAMS has changed the way that the international MS community engages with cognition…I consider the development of BICAMS to be one of the most important advances in the MS world over the last decade, particularly in relation to improving the management of those affected by MS.**" (**S1**, testimonial 28th October 2019).

5. Sources to corroborate the impact
(S1) Testimonial from Professor Alan Thompson, Dean of Faculty of Brain Sciences, UCL, dated 28th October 2019.
(S2) Testimonial from Professor Ralph Benedict, Department of Neurology, Jacobs School of Medicine and Biomedical Sciences, University of Buffalo, New York, USA, dated 7th June 2019.
(S3) Testimonial from Dr Davorka Tomic, World-Wide Brand Medical Director Neuroscience Franchise Novartis AG, Switzerland, dated 13th June 2019.
(S4) Testimonial from Jeffrey Gingold, US-based MS advocate, author and lawyer, dated 31st October 2019.
(S5) Testimonial from David Yeandle OBE, MS Ambassador and Member of the Council of the Pensions Policy Institute, dated 5th November 2019.
(S6) Testimonial from Sara Joiner, MS Trust trustee and MS patient, dated 4th November 2019.