Institution: Liverpool John Moores University (LJMU)		
Unit of Assessment: UOA17		
Title of case study: Improving patient outcomes through better project management of clinical trials		
Period when the underpinning research was undertaken: 1st January 2005 - 31st December 2018		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s):	**Role(s) (e.g. job title):**	**Period(s) employed by submitting HEI:**
David Bryde	Professor of Project Management	1st September 1991-date
Christine Unterhitzenberger	Lecturer/Senior Lecturer in Project Management	1st September 2016 - 31st October 2018
Period when the claimed impact occurred: 1st September 2013 – 31st December 2020		
Is this case study continued from a case study submitted in 2014? N		

1. Summary of the impact

The research influenced the project management (PM) of clinical trials. The global pharmaceutical R&D spend is $125-$160 billion annually and of that at least $20 billion is wasted annually due to management failures associated with clinical trials. The research has devised new PM approaches, enhancing PM knowledge and capability, contributing to cultural change, by changing attitudes towards the efficacy of PM in clinical trials. It has led to cost and time efficiencies in the PM of specific clinical trials. For example, on one project detailed in the case study a cost saving of 80,000 GBP was reported during the clinical trial phase, with a time saving of 10 days, which by conservative estimates equates to a saving of at least 6m GBP on the overall cost of the drug development process. The efficiencies, which are in the form of reduced delays against schedule and elimination of wasteful activities, have a direct beneficial impact on patients through faster time to market of drugs, which can then also be more competitively priced if the associated development costs are reduced.

2. Underpinning research

To improve the management of clinical trial projects, Prof Bryde carried out research, with both academic and external academic and industrial partners, on addressing management challenges arising from the dominant business model in the pharmaceutical industry. In this model pharmaceutical (pharma) companies, who act as the client, outsource the project management of clinical trials to Clinical Research Organisations (CROs), who act as the supplier.

In-depth interviews with PM practitioners, coupled with observations, expert opinion and literature review, identified the limitations of current clinical trial PM and resulted in the formulation of a new approach. This approach provided a model whereby outputs from a project were more closely aligned to the needs of the pharma client and the CRO supplier through deliverable-based planning. It also provided a new method to monitor progress, based on outputs rather than activities and milestones, and a novel treatment of costing the PM function based on meeting deliverables rather than PM being conceived as being a time-based activity, as was traditionally the case (Output 1). Interest in the research led to the Institute of Clinical Research (ICR) commissioning a book to disseminate the work to the practitioner community (Output 2). This research happened in 2005-2007. This first phase of research provided the scaffold for the next phase, described in the next section.

A second phase to the research related to developing Earned Value Analysis (EVA)-based methods which, when combined with the novel deliverable-based planning methods that had

previously been developed by Prof Bryde, further improved clinical trials PM. This improvement was achieved by using EVA-based methods to help reconcile opposing perspectives and address agency-related issues between pharma and CRO, in terms of achieving mutually beneficial outcomes from a clinical trial i.e. the pharma seeking a drug safely tested in a timely and cost effective manner and the CRO seeking to make an acceptable profit margin from the contract. This strand of research occurred between 2008 and 2014. Conditions for success of EVA in clinical trials were identified, derived from an analysis of the performance of two cases; one of which utilized EVA effectively and one that did not. A framework of EVA conditions of success established a number of design-related and operation-related conditions that lead to beneficial outcomes for both pharma and CRO, by addressing adverse agency-related characteristics in the project environment (Output 3).

Finally, building on the outputs of the research in the previous two phases, research undertaken in 2013-2018 involved a multiple case study design. Four project cases were analysed in detail: two from the construction industry and two involving clinical trials. The focus of the analysis was on the management of the relationship between client and supplier. By looking at one project that succeeded from each industry sector, and one project that failed, the research produced a new and innovative framework, which enables pharma and CRO to work together to mitigate for relational project risk and hence deliver successful outcomes. The CURED framework – which is an acronym for the CURED capability nodes of Contract, Understanding, Resources, Education and Delegation – provides a route map for collaborative working on clinical trials (Output 4). This research was part-funded by a grant from the Association of Project Management (APM) from their 2016/17 Research Fund, which is a competitive call for proposals and in 2018 the APM published online via their members website a white paper of the research findings (Output 5). The CURED Framework was foundational to a case study written by Dr Christine Unterhitzenberger, a co-author of output 4 and 5, which won the Decision Sciences Institute/Project Management Institute Best Instructional Case Writing Competition 2019.

3. References to the research

1. Bryde, D.J& Joby, R. (2007) “Product-based planning: the importance of project and project management deliverables in the management of clinical trials”. R&D Management, 37 (4), 363-377. DOI: 10.1111/j.1467-9310.2007.00482.x.
2. Bryde, D.J. & Joby, R. (2007). “Outsourcing Clinical Research Projects”. The Institute of Clinical Research, Marlow, Bucks. ISBN 13:9 781905 238057 https://www.amazon.com.au/Outsourcing-Clinical-Research-Projects-Roger/dp/1905238053. Authored book
3. Bryde, D.J., Unterhitzenberger, C. & Joby, R. (2018). “Conditions of success for earned value analysis in projects”. International Journal of Project Management, 36 (3), 474-484. DOI: 10.1016/j.ijproman.2017.12.002.
4. Bryde, D.J., Unterhitzenberger, C. & Joby, R. (2019). “Resolving agency issues in client-contractor relationships to deliver project success”. Production Planning & Control, 30:13, 1049-1063, DOI: 10.1080/09537287.2018.1557757.
5. Bryde, D., Joby, R., Taylor, S. & Unterhitzenberger, C. (2018) “Research Summary - Effective Relationship Management in Outsourced Projects”. Association of Project Management, High Wycombe, Bucks. https://www.apm.org.uk/resources/find-a-resource/research-series/resolving-agency-issues-in-client-contractor-relationships/. Summary report on research commissioned/funded by external organisation.

Research outputs 1,3 and 4 have been through a rigorous peer-review process.

4. Details of the impact

Efficiencies in the management of clinical trials have a massive impact on the overall success of the drug development cycle. Faster time to market of drugs means earlier administration of effective new treatments for diseases. It also means that pharma have more time to sell a drug under patent and hence they can be more competitive in their pricing (Association of British Pharma Industry). Data shows that 70% of clinical trials are more than one month behind schedule, with such delays costing pharma between 600,000 GBP and 7m GBP for each day that a clinical trial delays a drug's development or launch (Journal of Clinical Research Best Practice). Hence, the contribution of the underpinning research to improved PM practices and PM policy in undertaking clinical trials, documented below, has significant societal and economic impact.

THE PM PRACTICES OF PHARMACEUTICAL AND CLINICAL RESEARCH ORGANISATIONS

H. LUNDBECK A/S

In 2019 staff at H. Lundbeck A/S (HLU), an international pharmaceutical company with headquarters in Copenhagen, Denmark, used the research findings from Outputs 4 and 5 as the driver to *"re-evaluate our entire governance Metrices and KPIs. I have used your CURED framework…"* (Kristine Dalsgaard Cohen) [Source 1] The research enabled them to assess their preferred providers/strategic partnerships and internally benchmark the performance of different CROs. *"We have an internal workstream on the Metrics/KPI launched in Q3. As the Metrics/KPIs not only should allow us to measure the collaboration between HLU/CROs, but also give us a chance to compare internally between the various CRO collaborations.... Some kind of 3 dimensional approach"* [Source 1].

LEO PHARMA A/S

LEO Pharma A/S, a multinational Danish pharmaceutical company, utilised the research from Outputs 1 and 3 on a phase III clinical trial that started in 2014 to gain cost and time efficiencies. The project had a contract value of 16,000,000 GBP over 3 years. The client was in Denmark and the Clinical Research Organisation [CRO] project managing the clinical trial was in the UK. In the first year of the project, the client identified a saving of 80,000 GBP through the elimination of change orders. Comparable projects generated 3-4 change orders per annum and dealing with these orders cost the client 40,000 GBP, based on 10 days of PM time costed at 1,000 GBP per day and the same amount for the Clinical Research Organisation [CRO]. The trial saved a further 10 days on the schedule in year 1 through improved PM [Source 1].

BLAU FARMACEUTICA

The research [Outputs 1 and 2] has led to the development of a new procedure used in Blau Farmaceutica, a pharmaceutical company in Brazil since 2018. The company has incorporated the novel PM method developed from the research i.e. client/CRO aligned deliverable-based planning and Earned Value Analysis approach for monitoring and control - into their Standard Operating Procedures (SOPs) in respect of CRO and other Clinical Research Vendor selection.

"Outsourcing Clinical Research projects" [Output 2] *really helped me to understand the overall outsourcing process. I cannot express how much I appreciate it! The indicators and examples given are really well defined, which helps the selection process become less subjective, more technical and focused on what really matters. With the addendum to ICH's E6 guideline, the pharmaceutical industry needs to establish increasingly robust processes for the CROs selection and oversight as well as other clinical research vendors and your book definitely helped me in the attempt to translate this into a clear and concise procedure* [Output 1], *according to my local reality"* [Source 2].

GSK VACCINES

In November 2019 the Strategic Partnership Management Group, Vaccine Division of GSK, headquarters in Brussels, Belgium and offices in Italy and the US invited Prof Bryde to disseminate the CURED framework [Output 4 and 5] to over 70 staff worldwide from the HQ and regional offices, some who attended physically and others by WebEx, as part of an awareness raising initiative relating to the need to manage relational risk when outsourcing work.

Laura Lulli, Strategic Partnership Manager, GSK, Italy [Source 3], collated feedback from the presentation, which included the following:

"The analysis of causes of success and failures for the presented cases [Output 4 and 5] was particularly relevant to the audience and eye-opening at the same time: the presentation triggered a lot of questions and reflections among the attendees".

After the dissemination, Shirley Pullan, Strategic Partners & Resourcing Strategy Manager, GSK Belgium stated: *"I believe it really cemented for our internal customers, the importance of relationship building. A message that we state repeatedly but often is not heard"* [Source 4].

THE WORK OF CONSULTANTS

Th3rdcurve.co.uk LTD.

Th3rdcurve are a consultancy to the project controls and PM professions, advising the leading programmes organisations and governments on their PM approaches. The th3rdcurve have used the CURED framework and its underpinning research as the basis for developing a consultancy offering targeted at the clinical trial sector. They have invested significant resources into developing a five stage process involving 1) health-check 2) diagnosis 3) treatment 4) care and 5) immunity that operationalises the CURED capability nodes (Outputs 4 and 5) to provide insight into PM performance, benchmarking data similar projects and evidence of growth in PM maturity.

"The CURED research represents a step change in the way th3rdcurve will realise true business capability for our clients. Working in partnership with LJMU has allowed us to codify impact into our future and we will continue to work closely with David [Prof Bryde] and the team in 2020". Simon Taylor, Founder and COO, th3rdcurve.co.uk [Source 5].

R & N. R. CONSULTING LTD.

Between 1st September 2013 and 31st December 2020, R&R Consulting used Outputs 1 – 5 to design and deliver unique and differentiated research-informed PM training offerings that proposed new and innovative approaches to the management of clinical trials.
As testified by R. Joby, Senior Consultant at R&R:

"An important part of the business conducted by R. & N.R. Consulting Ltd. is project management training. There are two courses where the research conducted by Liverpool JM University (LJMU) has had a major input into the content and the approach. The three-day Project management course sponsored by the Institute of Clinical Research (ICR) and the two-day courses on the successful management of CRO budgets. Both courses are run on a regular basis dictated by demand. The research on relational risk, dealing with the problems associated with principal agent theory and the development of the CURED Framework have fundamentally changed the emphasis of these courses. Whereas once these courses had their foundations in the Association for Project Management Body of Knowledge it is now firmly in the CURED framework" [Source 6].

This focus enabled R & N. R. to secure 52 contracts, with a total contract value of 90,706 GBP with clients in France, UK, Germany, Switzerland, Russia and the US. They delivered training to 415 delegates and the value of the training to the clients was 295,251 GBP based on daily rates per delegate charged.

Course feedback testifies to the significant change in knowledge, capability and behaviours i.e. the knowledge enabled the: *"… improving of activities v deliverables on budgets"* [Output 1] and *"introducing new ways of tracking budgets/improve communications"* [Output 3] [Source 7].

CLINICAL TRIAL PROJECT MANAGEMENT POLICY AND PRACTICE

INSTITUTE OF CLINICAL RESEARCH (ICR)

In August 2019, Prof Bryde had an initial conversation with Alison Messom, Chairman of the Board of Directors of the ICR and some of the ICR staff about next steps in relation to disseminating the research. The suggestion was made in the meeting to write a Code of Practice (CoP) that the ICR would endorse through use of their logo and inclusion on their website. Prof Bryde was then invited to present this proposal to members of the ICR Board in February 2020, at which point approval was given. The CoP was developed by Prof Bryde, in collaboration with two industry practitioners: R. Joby and S. Taylor. Titled "A code of practice to aid successful delivery of clinical research projects", it is structured around the CURED Framework [Outputs 4 and 5]. The CoP was formally launched via an ICR online webinar on 8th December 2020. The ICR has over 1,000 members, all of whom are involved in the management of clinical trials, from across the globe, including UK, Europe, US and Africa. Alison Messom stated that the proposed model in the CoP provides a platform for further research which is *"key to improve and benefit the successful conduct and completion of clinical trials"* [Source 8].

THE PHARMACEUTICAL CONTRACT MANAGEMENT GROUP

The Pharmaceutical Contract Management Group (PCMG) – an association with 130 named members across the spectrum of companies in Europe involved in the outsourcing management of clinical trials, testify to the impact in terms of providing practitioners with evidence to do things differently. In the words of the Chair of the Project Management Special Interest Group of the PCMG *"the work that you have been doing has encouraged smarter outsourcing but with a results-based focus, and if outsourcing is to be credible it has to be able to deliver results. And what you've provided is, it's more than a framework, it has provided people with something to go into their management and say, look, there's a better way of doing this"* [Source 9].

5. Sources to corroborate the impact

S1. Kristine Dalsgaard Cohen, Principal Outsourcing Manager, Lundbeck, Denmark and Principal Outsourcing Manager, LEO Pharma A/S, Denmark [2014/15].
S2. Regiane Braga, Clinical Research Analyst, Blau Farmaceutica, Brazil.
S3. Laura Lulli, Strategic Partnership Manager, GSK, Italy.
S4. Shirley Pullan, Strategic Partners & Resourcing Strategy Manager, GSK Belgium.
S5. Simon Taylor, Founder and Chief Operating Officer, th3rdcurve Ltd, London, UK]
S6. Roger Joby, Founder and Senior Consultant, R&S Consulting Ltd, Reading, UK
S7. Erika Brennan, Clinical Trials Manager, Vitaflo, UK
S8. Alison Messom, Chairman of the Board of Directors, Institute of Clinical Research.
S9. Richard Schaife, Chair of the Project Management Special Interest Group of the Pharmaceutical Contract Management Group (PCMG), UK.