

<b>Institution: Queen Mary University of London</b>		
<b>Unit of Assessment: 3</b>		
<b>Title of case study: 'One-stop' diagnosis: Vastly improved prognosis for Behçet's Syndrome</b>		
<b>Period when the underpinning research was undertaken: 2012 - present</b>		
<b>Details of staff conducting the underpinning research from the submitting unit:</b>		
<b>Name(s):</b>	<b>Role(s) (e.g. job title):</b>	<b>Period(s) employed by submitting HEI:</b>
1) Farida Fortune	1) Professor of Medicine in relation to Oral Health	1) 04/2005 - present
2) Lesley Bergmeier	2) Reader in Oral immunology	2) 11/2006 - 12/2017
3) Eleni Hagi-Pavli	3) Senior Lecturer in Oral Biology	3) 04/2007 - present
4) Steve Higgins	4) Clinical Psychologist	4) 12/2013 - present
5) Angray Kang	5) Reader in Molecular Cell Biology	5) 04/2011 - present
6) Nardos Wakjira	6) Senior Dental Nurse	6) 05/2012 - present
7) Harry Petrushkin	7) Ophthalmology Fellow	7) 07/2012 - 06/2015
8) Fabian Flores Borja	8) Lecturer in Oral Immunobiology	8) 10/2018 - present
<b>Period when the claimed impact occurred: 2014 - present</b>		
<b>Is this case study continued from a case study submitted in 2014? N</b>		
<b>1. Summary of the impact</b> (indicative maximum 100 words)		
<p>As a result of Queen Mary research, UK patients with the debilitating Behçet's Syndrome are now able to access a novel, integrated programme of diagnostics and disease management that has notably improved both clinical outcomes and patients' quality of life. By pioneering a multi-disciplinary, patient-focused model of care for this autoinflammatory condition, Queen Mary's Prof. Fortune has created an approved drug pathway for Behçet's and identified effective treatment for two of the syndrome's symptoms: oral ulceration and blood clotting. Fortune's work led to the formation of the Behçet's Syndrome Centres for Excellence (BCE), a 'one stop clinic' for treatment which has transformed patient care and achieved hugely positive clinical outcomes — such as cutting diagnosis time for the disease from 14 years to 1 and reducing the prevalence of serious complications such as disability and visual impairment (the latter of which saw a 94% reduction from 2014-2019). These changes have drastically improved patients' health, prognoses, and quality of life, and facilitated both direct and indirect cost savings to patients and the NHS of GBP15,878,551 (2011-2020).</p>		
<b>2. Underpinning research</b> (indicative maximum 500 words)		
<p>Behçet's Syndrome is a chronic, systemic condition that causes inflammation of blood vessels and tissues. It affects an estimated 0.64 per 100,000 individuals in the UK [3.1], with patients frequently suffering from severe oral ulceration that may progress to affect any organ in the body with debilitating consequences: skin lesions, swollen eye tissue (uveitis) and subsequent blindness, severe joint pain, strokes and blood clotting.</p> <p><i>Towards a better understanding of the condition</i></p> <p>Research by Queen Mary has helped reveal the mechanisms behind Behçet's Syndrome. Prof. Fortune and her team are part of the international group that completed the first Behçet's genome-wide association study in 2010 [3.2] — an approach that scans genomic markers across many individuals to identify genetic variants associated with the condition. The data confirmed the major role of the antigen HLA-B51 in susceptibility to Behçet's Syndrome; another region upstream which subsequently led to the discovery of epistatic interactions between this antigen (HLA-B51) and the enzyme ERAP1, which is associated with immune responses and genes that trigger inflammation.</p> <p><i>An effective 'one stop clinic' for patients</i></p> <p>The Queen Mary team's research, led by Fortune, has also found that many Behçet's patients suffer from complex symptoms, poor patient experience, substandard care, and a generally reduced quality of life. Patients typically undergo multiple appointments in different facilities,</p>		

where isolated symptoms may be treated with inaccurate diagnoses and result in poor clinical outcomes. Fortune's work [3.1] led to the establishment of the Behçet's Syndrome Centres of Excellence (BCE) in London, Birmingham and Liverpool, and the multidisciplinary clinics (MDCs) within these three, in 2012. The BCE have improved patient care while also achieving predicted annual cost savings of approximately GBP18,800 per patient [5.8], and now act as a 'one stop clinic' for 900 fully consented patients from both the UK and overseas [3.1]. The Centres play a leading role in Behçet's research, and have provided Fortune's team with recorded clinical outcomes, patient samples, and evidence of how Behçet's impacts patients' psychosocial wellbeing, employment situation, and levels of fatigue [3.3, 3.4]. Standardised oral and genital clinical severity scores have also been developed and are now used internationally [3.5].

#### *Championing patient-centred research*

By developing a model to address the multiple and varying needs of the patient and embedding this holistic approach into all education and training initiatives, Queen Mary has advanced patient-centred research for Behçet's and created a multi-disciplinary, integrated care approach to disease diagnostics. Patients are reviewed by experts from multiple clinical specialities — oral medicine, immunology, rheumatology, gastroenterology, ophthalmology and neurology, alongside a clinical psychologist and non-medical support worker — and all clinical outcomes are reviewed regularly by BCE MDCs. Fortune and the BCE have also produced an agreed 'Drug Pathway' of systemic therapy and biologics that is centrally funded and delivered locally to patients.

#### *Improved drug treatments for thrombosis*

Behçet's patients suffer from recurrent clotting throughout the body — even when treated with anticoagulants. Fortune's team identified why clotting occurs in this condition, finding it to be due to platelet activation [3.7] and confirming that anticoagulant drugs would be ineffective. Treatment guidelines for blood vessel clotting were thereby changed to instead involve immunosuppressives (to suppress inflammatory 'flares' and endothelial swelling) and antithrombotics (which, rather than inhibiting particular coagulation pathways, instead inhibit platelet activity and thrombi — as required for the mechanism Fortune observed in Behçet's).

### **3. References to the research** (indicative maximum of six references)

- [3.1] Bernabe, E., Marcenés, W., Mather, J., Phillips, C., & Fortune, F. (2010). Impact of Behçet's syndrome on health-related quality of life: influence of the type and number of symptoms. *Rheumatology*, 49 (11), 2165-2171. <https://doi.org/10.1093/rheumatology/keq251>
- [3.2] Remmers, E. F., Cosan, F., Kirino, Y., Ombrello, M. J., Abaci, N., Satorius, C., Le, J. M., Yang, B., Korman, B. D., Cakiris, A., Aglar, O., Emrence, Z., Azakli, H., Ustek, D., Tugal-Tutkun, I., Akman-Demir, G., Chen, W., Amos, C. I., Dizon, M. B., Kose, A. A., Azizlerli, G., Erer, B., Brand, O. J., Kaklamani, V. G., Kaklamanis, P., Ben-Chetrit, E., Stanford, M., Fortune, F., Ghabra, M., Ollier, W. E., Cho, Y. H., Bang, D., O'Shea, J., Wallace, G. R., Gadina, M., Kastner, D. L., Gül, A. (2010). Genome-wide association study identifies variants in the MHC class I, IL10, and IL23R-IL12RB2 regions associated with Behçet's disease. *Nature Genetics*, 42 (8), 698-702. <https://doi.org/10.1038/ng.625>
- [3.3] Senusi, A., Higgins, S., & Fortune, F. (2018). The influence of oral health and psychosocial well-being on clinical outcomes in Behçet's disease. *Rheumatology International*, 38 (10), 1873-1883. <https://doi.org/10.1007/s00296-018-4117-y>
- [3.4] Senusi, A. A., Ola, D., Mather, J., Mather, J., & Fortune, F. (2017). Behçet's syndrome and health-related quality of life: influence of symptoms, lifestyle and employment status. *Clinical and Experimental Rheumatology*, 35 (Suppl 108), 43-50.
- [3.5] Senusi, A., Seoudi, N., Bergmeier, L. A., & Fortune, F. (2015). Genital ulcer severity score and genital health quality of life in Behçet's disease. *Orphanet Journal of Rare Diseases*, 10 (1), 117. <https://doi.org/10.1186/s13023-015-0341-7>
- [3.6] Hasan, M., Bergmeier, L. A., Petrushkin, H., & Fortune, F. (2015). Gamma delta ( $\gamma\delta$ ) T cells and their involvement in Behçet's disease. *Journal of Immunology Research*, 2015. <https://doi.org/10.1155/2015/705831>

[3.7] Macey, M., Hagi-Pavli, E., Stewart, J., Wallace, G. R., Stanford, M., Shirlaw, P., & Fortune, F. (2011). Age, gender and disease-related platelet and neutrophil activation *ex vivo* in whole blood samples from patients with Behçet's disease. *Rheumatology*, 50 (10), 1849-1859. <https://doi.org/10.1093/rheumatology/ker177>








**Evidence of quality of the research:**

[EQR.1] Fortune, F. [Co-applicant]. (2018-2021). *Acacia project*. GBP1,500,000.  
 [EQR.2] Fortune, F. [Co-applicant]. (2014-2018). Optimal utilization of biologic drugs in Behçet's Disease: a stratified medicine approach [12/205/46]. *NIHR Efficacy and Mechanism Evaluation Programme*. GBP601,396.

**4. Details of the impact** (indicative maximum 750 words)

Queen Mary has worked with the Behçet's Syndrome Centres for Excellence (BCE) since their inception in 2012, and has advanced treatment, diagnosis, awareness and understanding of the debilitating disease through a combination of laboratory- and patient-focused research.

**Key impacts of Queen Mary's work on Behçet's Syndrome**

 <p>Improved quality of life</p>		<p>Improved patient care, satisfaction, and experience</p> 
<p>Reduced diagnostic time</p> 	<p>Improved physical health</p> 	<p>Improved psychosocial health</p> 
<p>Reduced cost for both patients and the NHS</p> 		
<p>New clinical guidelines and an internationally recognised model of care</p> 		

**Improving patients' quality of life: Better diagnostics, health, and clinical outcomes**

Queen Mary has provided significant quality-of-life improvements for UK patients with Behçet's Syndrome [5.1]. This is largely due to the establishment of the BCE, which was driven and facilitated by Queen Mary, and the subsequent and ongoing collaboration between the Centres and the university. Fortune is Clinical Lead for the London BCE; the BCE have Centres in London, Birmingham and Liverpool, and have been described by patients as "a blessing" [5.2].

*Rapid diagnosis — from 14 years to just 1*

Before 2012, the average time to diagnosis for Behçet's in the UK was 14 years. As a result of Queen Mary research, the BCE has reduced this to just 4.5 years (in 2018) [5.1]. Data from 2019 again shows improvement in most cases, with the London BCE in particular, the Centre Fortune works most closely with, achieving diagnoses in just one year [5.1].

*Improved physical health for patients*

The number of patients presenting with *visual impairment* has reduced annually since opening the London BCE — from 79 patients in 2015 to 22 in 2016 and 12 in 2017. Data for 2019 revealed that only 5 patients had increased visual impairment after attending the London BCE. No BCE patient has lost their sight due to Behçet's since the Centres' establishment [5.1]. *Joint pain* is another significant symptom that impairs quality of life; since the creation of the BCE, clinical outcomes related to joint-disease-related pain have reduced by 50% [5.1]. The most frequent symptom of Behçet's Syndrome is severe *oral ulceration*. Fortune's team developed and introduced oral health training and a bespoke mouthwash, Triorasol. This has transformed patient

experience [5.3] and had a statistically significant and positive impact on health-related quality of life [3.4]. In a study comprising of 261 Behçet's patients, Triarasol significantly reduced oral ulceration severity scores (OUSS), prevented or minimised the formation of intraoral scarring and showed a comprehensive positive effect on Behçet's outcomes [5.3]. In 2019, the Care Quality Commission deemed the dental hospital's service care 'outstanding' [5.4].

#### *Improved psychosocial health for patients*

As a result of Queen Mary's establishment and collaboration with the BCE, patients now experience reduced anxiety and depression. The BCE records Behçet's impact on the psychosocial health of patients (and vice versa, by assessing how increasing anxiety is associated with inflammation). Every time they attend the clinic, each patient is scored using Generalised Anxiety Disorder, Patient Health, and Mental Wellbeing questionnaires to assess their depression, anxiety and mental wellbeing, and evaluate the need for any emergency intervention and support. On starting this psychology service, a patient with 5 self-directed emergency appointments experienced decreased disease activity within 6 months, demonstrating the value of psychological support with systemic medication that improves anxiety, depression and clinical outcomes in treating Behçet's Syndrome [3.3].

To alleviate feelings of isolation, the BCE works closely with the society 'Behçet's UK' to improve access to patient support groups. Society membership increased from 423 in 2012 to 1,114 in 2019. There are also 7 new support groups across England that provide improved signposting for additional help for patients, including introductions to counsellors within the patient's primary care trust and assistance with the benefits system. In the BCE, the inclusion of psychological care has considerably impacted the Behçet's patient cohort seen in London, with 441 of 845 'Very Highly Vulnerable' patients actively accessing care at any given time.

#### **Improving clinical care with a '*patient knows best*' approach**

To maintain a high level of patient care and support, the London BCE works closely with patients and clinicians in hospitals and the community. As one patient says, "the service is holistic, and [the] continuity of staff and doctors who know each other individually on a personal basis...facilitates much better patient care" [5.2]. The adoption of a 'patient knows best' strategy has been successful, with patient satisfaction scores of over 99% [5.1]. Patients are given many opportunities to provide feedback (via clinic attendance, questionnaires and annual education days), with this feedback driving continuous service improvement and informing best practice. Additionally, Queen Mary facilitates greater awareness and education on Behçet's by hosting an annual national 'Behçet's in a day' workshop, which provides training and updates on new research and treatment in the disease for 40–80 attendees.

#### **Informing and optimising clinical guidelines and practice**

Queen Mary research demonstrated that gender, age and disease severity affect the activation of platelets and white blood cells in Behçet's Syndrome [3.7]. This directly drove the European League Against Rheumatism (EULAR) to update its guidelines in 2018, and therefore impacted subsequent clinical practice. Fortune was a member of the international review committee. Patients formerly treated with the anticoagulant warfarin are now treated with antithrombotic, immunosuppressive, anti-inflammatory (aspirin) and anti-platelet drugs [5.5]. The use of antithrombotics and immunosuppressives were presented at the International Conference on Behçet's Disease in 2016 [5.6].

#### **Reducing costs for patients and the NHS by over GBP15,800,000**

In 2011, 'Behçet's UK' employed an independent health economist to review the then-current service model for delivery of care to Behçet's patients. In 2019, the same firm was commissioned to ascertain whether Queen Mary's MDC model was cost-effective. The review confirmed that the London BCE has brought significant cost savings — direct and indirect — since 2011 [5.7].

**From 2011–2020, for treatment of 845 patients with Behçet's Syndrome at the London BCE:****Achieving international recognition of a new model of care**

The BCE model was validated by the EU Commission's rigorous audit process at the London Centre in September 2018, receiving an excellence rating of 97.2% for clinical service, research and education [5.8]. Through her research and key role in establishing and leading the BCE, Fortune and her team have demonstrated that a 'one drug regime fits all' strategy for clinical management is inappropriate for Behçet's, and is neither beneficial to patients nor a cost-effective use of treatment resources. Instead, the MDCs have enabled effective application of appropriate, patient-tailored treatment, with timely escalation of therapy according to individual clinical need, thus, improving current care while reducing the risk of patients developing complications.

**5. Sources to corroborate the impact** (indicative maximum of 10 references)

- [5.1] CQUIN. (2020). *CQUIN report outcomes (2014-2020)*.
- [5.2] Patient Service Feedback. (2016-2018). London Behçet's Syndrome Centre of Excellence.
- [5.3] Senusi, S., Kang, A., Buchanan, J., Adebawale, A., Aloraini, G., Stanford, M. & Fortune, F. (2020). New mouthwash: An efficacious intervention for oral ulceration associated with Behçet's disease. *British Journal of Oral and Maxillofacial Surgery*, 58 (8), 1034-1039.  
<https://doi.org/10.1016/j.bjoms.2020.07.027>
- [5.4] Care Quality Commission. (2019). *Barts Health NHS Trust – Inspection Report*.
- [5.5] Hatemi, G., Christensen, R, Bang, D., Bodaghi, B., Celik, A. F., Fortune, F., Gaudric, J., Gul, A., Kötter, I., Leccese, P., Mahr, A., Moots, R., Ozguler, Y., Richter, J., Saadoun, D., Salvarani, C., Scuderi, F., Sfrikakis, P. P., Siva, A., Stanford, M., Tugal-Tutkun, I., West, R., Yurdakul, S., Olivieri, I. & Yazici, H. (2018). 2018 update of the EULAR recommendations for the management of Behçet's syndrome. *Annals of the Rheumatic Diseases*, 77, 808-818.  
<http://dx.doi.org/10.1136/annrheumdis-2018-213225>
- [5.6] Clinical and Experimental Rheumatology. (2016). *The Effect of Medication on The Treatment Outcomes of Behçet's Disease, 17th International Conference on Behçet's Disease*.  
<http://www.allmeetingsmaterita.it/behcets/wp-content/uploads/2015/09/Abstracts-Book-17th-ICBD-2016-Matera-Italy.pdf>
- [5.7] TrueCue. (2020). *Heath Economic Impact Analysis for BCE*.
- [5.8] European Commission. (2018). *Healthcare Providers Assessment Report*.