BURNOUT IN MEDICINE

A NOVEL APPROACH EXPLORING THE IMPACT OF UNCERTAINTY AND THE USE OF BIOMARKERS AS A MEASUREMENT TOOL

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Dedicated to my parents,

DR PAUL AND MRS MARIE-LOUISE SIMPKIN,

my greatest source of inspiration.

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"Victory has a hundred fathers, and defeat is an orphan," President Kennedy once observed. And so it is with this thesis. Any successes are the result of the support given to me. Any failings are my own.

DECLARATION

I hereby declare that the work presented in this thesis is my own and all contributions from other sources have been appropriately acknowledged and cited. The content is solely the responsibility of the authors and does not necessarily represent the official views of the University of Oxford and its affiliated academic health care centres.

THESIS ABSTRACT

Burnout constitutes a significant challenge for healthcare organisations not only in respect to individual wellbeing but also in terms of the catastrophic downstream implications to patient safety, patient satisfaction, and quality of care. This DPhil, divided into three parts, aims to explore burnout in healthcare professionals, an accelerating phenomenon that is hotly discussed but minimally understood, with a focus on the impact uncertainty has and an exploration into the novel use of neurohormones as potential biomarkers of wellbeing.

Part I: Exploration of concepts: burnout and uncertainty
Chapter 1 presents a selective overview of the broad context of burnout in healthcare, reporting existing literature on the impact of burnout—to physicians, to patients, and to healthcare organisations—and considering the challenges that pertain to burnout research, particularly relating to challenges in measurement. Chapter 2 explores the presence of uncertainty in the healthcare environment looking at what impacts an individual's tolerance of uncertainty and how the reaction affects provider- and patient-centred outcomes. Chapters 3 and 4 present two observational studies exploring drivers of satisfaction at work for faculty in an academic medical centre, with an analysis of the interplay between burnout and uncertainty in the clinical environment. Chapter 5 presents a study that looks at how language used in clinical hand-over affects sense of uncertainty in the receiving clinician, demonstrating how language variation can influence emotional perception of uncertainty.

Part II: Exploration of biology: exploration into use of biomarkers to measure burnout
Chapters 6 and 7 explore the novel use of cortisol and oxytocin levels as potential biomarkers of stress and burnout in clinical faculty at a large teaching hospital.

Part III: Exploration of interventions to reduce burnout and strategies to embrace uncertainty
Chapter 8 presents an interprofessional intervention study looking to reduce burnout through self-facilitated groups meeting monthly for three months. This study re-affirms the importance of the findings presented in this thesis and points to the need for more interventions aimed at enhancing trainee and faculty wellbeing. Chapter 9 synthesises current literature on tolerance of uncertainty alongside findings of the thesis, self-experience, and experience of colleagues and students in a narrative review to identify strategies to help clinicians thrive in the face of clinical uncertainty.

Finally, Chapter 10 presents an overview of the key findings from each study, their methodological strengths and limitations, directions for future research, and implications for clinical training, the measurement of wellbeing initiatives, and patient care.

THESIS-RELATED PUBLICATIONS AND PRESENTATIONS

CONFERENCE PRESENTATIONS:

1. **Simpkin AL**, Hata S, Logan M, Armstrong K. Increasing Connection Between Physicians to Enhance Joy in Practice and Prevent Burnout: An Intervention for Fellows. Society of General Internal Medicine (SGIM) Annual Meeting, Denver CO; 2018. Poster presentation.
2. **Simpkin AL,** Emergency Department to Inpatient Handoff: Does Language affect Medical Students Sense of Uncertainty? International Association for Medical Education (AMEE), Basel, Switzerland; 2018. Oral Research Presentation.
3. **Simpkin AL,** Zahra Smyth F, Janczukowicz J, Selleger V. A Toolkit to Embed the Humanities in Healthcare Professions Education. International Association for Medical Education (AMEE), Basel, Switzerland; 2018. Workshop.
4. **Simpkin AL**, Hata S, Logan M, Armstrong K. Increasing Connection and Engagement: A Study of Peer-Led Reflection Groups for Fellows. Society of General Internal Medicine (SGIM) Annual Meeting, Washington DC; 2019. Poster presentation.
5. **Simpkin AL**, Hata S, James K, Berkowitz L. Burnt Out and Yet Engaged: Are we Asking the Right Questions in Faculty Wellness Research? American College of Obstetricians and Gynecologists and Council on Resident Education in Obstetrics and Gynecology annual national meeting, New Orleans, 2019. Oral Research Presentation.
6. **Simpkin AL**, Berkowitz L. A Tale of Two Attributes: Resilience and Tolerance of Uncertainty in an Ob-Gyn Learning Environment. American College of Obstetricians and Gynecologists and Council on Resident Education in Obstetrics and Gynecology annual national meeting, New Orleans, 2019. Workshop.

INVITED TALKS:

1. **Simpkin AL.** Embracing Uncertainty in an Era of Big Data. Invited Lecture at the Quarterly Teaching, Investment, Education Seminar, Farallon Capital, California, 2017.
2. **Simpkin AL.** Embracing Uncertainty in Healthcare. Invited Keynote at the Coping with Workplace Stress & Burnout Symposium, Intensive Care Society, London, UK, 2017.
3. **Simpkin AL.** Embracing Uncertainty in Medicine. Invited Keynote at the Diagnostic Error in Medicine International Conference, Society to Improve Diagnosis in Medicine, Boston, 2017.
4. **Simpkin AL.** Uncertainty: It's Okay to Think Outside the Box! Invited Lecture at the Connecticut Children's Medical Centre, Hartford, CT, 2018.
5. **Simpkin AL.** Reaction to Uncertainty: A Blindspot for Diagnostic Error. Invited Lecture at the Julia Berg Memorial Lecture, University of Minnesota Masonic Children's Hospital, Minnesota, 2018.
6. **Simpkin AL.** Embracing Uncertainty to Alleviate Burnout: Lessons from Frontline. Invited Lecture at the NE Regional Conference MA Medical Society Alliance and MA Medical Society, Boston, 2018.
7. **Simpkin AL.** Embracing Uncertainty: Pioneering the Possible. Invited Lecture at the Harvard Medical School Sharing Struggles and Building Resilience Series, Boston, 2018.
8. **Simpkin AL.** Embracing Uncertainty: A Key to Wellbeing? Invited Grand Rounds at the Massachusetts Eye and Ear Hospital, Boston, 2018

9. **Simpkin AL.** Embracing Uncertainty: An Antidote to Burnout? Invited Grand Rounds at the Department of Neurology, MGH / Annual Medical Education Grand Rounds, 2018.
10. **Simpkin AL.** How Far Can We Push the Limits of the Human Brain? Invited Lecture at the Lincoln Leads lecture series, Lincoln College, University of Oxford, UK, 2019.
11. **Simpkin AL.** Uncertainty in the Emergency Department. Invited Lecture at the Boston Children's Hospital, Emergency Department Fellows, Boston, 2019.
12. **Simpkin AL.** Uncertainty in Clinical Medicine: Survival Strategies. Invited Lecture at the Newton-Wellesley Hospital, Noon Conference for Residents, Massachusetts, 2019.
13. **Simpkin AL.** Uncertainty Ahead? Survival Strategies. Invited Lecture at the Boston Children's Hospital, Cardiology Department Fellows, Boston, 2019.
14. **Simpkin AL.** Embracing Uncertainty: Why and How. Invited Keynote at the Boston Children's Hospital, Community Faculty, Annual Retreat, Boston, 2019.
15. **Simpkin AL.** Medical Education Research—Pinpointing Uncertainty. Invited Lecture at the Hospital Medicine Unit Faculty monthly teaching series, MGH, Boston, 2019.
16. **Simpkin AL.** Embracing uncertainty—why and how. Invited Visiting Professor Grand Rounds at the Maine Medical Centre, Portland, Maine, 2019.
17. **Simpkin AL.** Uncertainty—impact on course design, assessment and evaluation. Invited Lecture for the Postgraduate Certificate in Teaching Evidence-Based Practice run jointly by the Centre for Evidence-Based Medicine and Department for Continuing Education, University of Oxford, 2020.

PEER-REVIEWED JOURNAL PAPERS THAT APPEAR IN CHAPTERS:

1. **Simpkin AL**, Armstrong K. Communicating uncertainty: a narrative review and framework for future research. *JGIM* 2019; 34(11): 2586-2591 Doi: 10.1007/s11606-019-04860-8 (Chapters 2 and 9)
2. **Simpkin AL**, Chang Y, Yu L, Campbell EG, Armstrong K, Walensky RP**.** Job satisfaction and feeling valued in academic medicine: findings from a faculty survey. *JAMA Int Med. 2019; 179(7):992-994.* doi:10.1001/jamainternmed.2019.0377 (Chapter 3)
3. **Simpkin AL**, Hata S, Logan M, Armstrong KA. Stress from uncertainty predicts resilience and engagement among subspecialty medicine fellows. *International Archives of Internal Medicine* 2020; Doi: 10.23937/2643-4466/1710023 (Appendix 4.1)
4. **Simpkin AL,** Murphy Z, Armstrong K. A randomised experimental study to assess the effect of language on medical students' anxiety due to uncertainty. *Diagnosis. 2019; 6(3): 269-276* (Chapter 5)
5. Gheihman G, Johnson M, **Simpkin AL.** Twelve tips for thriving in the face of clinical uncertainty. *Medical Teacher* 2019. Doi: 10.1080/0142159X.2019.1579308 (Chapter 9)

SUBMITTED PAPERS THAT APPEAR IN CHAPTERS:

1. Wilson-Scholin HCP, Abrams SJ, **Simpkin AL.** Why do junior doctors leave their training programs in the NHS to train overseas? *Submitted to the British Medical Journal* 2020 (Chapter 1)
2. **Simpkin AL**, Hidure M, Lehrhoff S, del Carmen MG, Armstrong KA, Wasfy JH. Factors associated with physician tolerance of uncertainty at a multispecialty academic physician practice organisation. *Submitted to JAMA* 2020 (Chapter 2 and 4)

3. Berkowitz LR, Dzara K, **Simpkin AL**. Building your "educational peloton": cycling together for success during uncertain times. *Submitted to Teaching and Learning in Medicine* 2020 (Chapters 2 and 9)
4. **Simpkin AL**, Hata S, Emptage N, Berkowitz LR, Armstrong KA. Biomarkers of clinician burnout. *Submitted to Psychoneuroendocrinology* 2020 (Chapter 7)
5. Hata S, Berkowitz LR, James K, **Simpkin AL.** An interprofessional group intervention to promote faculty wellbeing and engagement: a randomised clinical trial. *Submitted to American Journal of Obstetrics and Gynecology* 2020 (Chapter 8)
6. Devaraj LR, Cooper C, **Simpkin AL**. Creating psychological safety on medical teams: a narrative review with strategies for success. *Submitted to Journal of Hospital Medicine* 2020 (Chapter 9)

OTHER PEER-REVIEWED JOURNAL PAPERS OF RELEVANCE:

1. Gheihman G, Cooper C, **Simpkin AL.** Everyday resilience: practical tools to promote resilience among medical students. *JGIM* 2019;34(4):498-501. Doi: 10.1007/s11606-018-4728-8
2. Brunsberg KA, Landrigan CP, Garcia BM, Petty CR, Sectish TC, **Simpkin AL**, Spector ND, Starmer AJ, West DC, Calaman S. Association of pediatric resident depression with harmful medical errors on inpatient services. *Academic Medicine.* 2019; 94(8): 1150-1156. Doi: 10.1097/ACM.0000000000002778.
3. Ganguli I, **Simpkin AL**, Colla CH, Weissman A, Mainor AJ, Rosenthal MB, Sequist TD. Why do Physicians Pursue Cascades of Care After Incidental Findings? A National Survey. *J Gen Intern Med*. 2019; Jul 25. Doi: 10.1007/s11606-019-05213-1
4. Ganguli I, **Simpkin AL**, Lupo, C, Weissman A, Mainor AJ, Orav EF, Rosenthal MB, Colla CH, Sequist TD. Cascades of Care Following Incidental Findings: A US National Survey of Physicians. *JAMA Open Network.* 2019; Oct 2;2(10):e1913325. Doi: 10.1001/jamanetworkopen.2019.13325.

NON-PEER REVIEWED PUBLICATIONS:

1. Wilson H, **Simpkin AL.** Why are so many doctors quitting the NHS? It's time to ask the right questions. *BMJ Opinion,* 2019; In *BMJ* print edition, March 2019
2. **Simpkin AL.** Promoting resilience in academic medicine. *Journal of HMS Academy* 2019; 1(1)
3. Wilson H, **Simpkin AL.** Why are so many doctors quitting the NHS? We have begun to ask the right questions. *BMJ Opinion,* 2020
4. **Simpkin AL.** Embracing uncertainty: could there be a blueprint from covid-19? *BMJ Opinion* 2020
5. **Simpkin AL**. Escaping the Broom Cupboard—Promoting a Culture of Openness in Healthcare. *BMJ. Accepted for publication. 2020*

PODCASTS:

1. **Simpkin AL.** Uncertainty in Medicine. Internal Medicine Reasoning Series: Episode 38
2. **Simpkin AL.** Uncertainty in Med Ed. Educator's Podcast Series. April 26, 2019
3. **Simpkin AL.** Embracing uncertainty—why and how. MD Advantage Podcast Series. December 2019

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LIST OF ABBREVIATIONS

A&E	accident and emergency department
AAPOR	American Association for Public Opinion Research
ACGME	Accreditation Council of Graduate Medical Education
ACN	acetonitrile
ANOVA	analysis of variance
ANS	autonomic nervous system
BMI	body mass index
CI	confidence interval
CNS	central nervous system
CRP	C-reactive protein
CSF	cerebrospinal fluid
CV	coefficient of variation
DOG	Department of Obstetrics and Gynaecology
DOM	Department of Medicine
DP	depersonalisation
EBM	evidence-based medicine
EE	emotional exhaustion
ELISA	enzyme linked immunosorbent assay
EMR	electronic medical record
FAA	Federal Aviation Administration
FY2	foundation year 2
GMC	General Medical Council
GPCR	G protein-coupled receptor
HDL	high-density lipoprotein
HMS	Harvard Medical School
HPA	hypothalamic-pituitary-adrenal
ICD	International Classification of Disease

IMG	international medical graduates
LC-MS/MS	liquid chromatography-tandem mass spectrometry
MBI	Maslach Burnout Inventory
MBI-GS	Maslach Burnout Inventory-General Survey
MCAT	Medical College Admission Test
MGH	Massachusetts General Hospital
MGPO	Massachusetts General Physicians Organisation
NHS	National Health Service
NIH	National Institute of Health
ob-gyn	obstetrics and gynaecology
OR	odds ratio
PA	personal accomplishment
PCP	primary care practice
PSS	perceived stress scale
PVN	paraventricular
PSA	prostate specific antigen
RR	rate ratio
SAM	sympathetic adrenomedullary
SON	supraoptic
SPE	solid-phase extraction
TFA	trifluoracetic acid
TICS	Trier Inventory for the Assessment of Chronic Stress
UK	United Kingdom
US	United States
WHO	World Health Organisation
WHR	waist-to-hip-ratio

Note: I use the term “physician” in this thesis to represent medical practitioners across all medical and surgical specialties and to include those in training roles.

IN BROKEN IMAGES

by Robert Graves

He is quick, thinking in clear images;
I am slow, thinking in broken images.

He becomes dull, trusting to his clear images;
I become sharp, mistrusting my broken images,

Trusting his images, he assumes their relevance;
Mistrusting my images, I question their relevance.

Assuming their relevance, he assumes the fact,
Questioning their relevance, I question the fact.

When the fact fails him, he questions his senses;
When the fact fails me, I approve my senses.

He continues quick and dull in his clear images;
I continue slow and sharp in my broken images.

He in a new confusion of his understanding;
I in a new understanding of my confusion.

PART I

EXPLORATION OF CONCEPTS: BURNOUT AND UNCERTAINTY

CHAPTER 1: AN OVERVIEW OF BURNOUT IN HEALTHCARE

"The cause is hidden; the effect is visible to all."
Ovid

1.1 INTRODUCTION

Burnout has become a big concern within healthcare. Well established as a global predicament with catastrophic consequences for the health and wellbeing of healthcare providers and patients, it is the zeitgeist of the 21st century. Worryingly, burnout appears to be a crisis that is accelerating; an international epidemic affecting professionals, patients, organisations, and society[1-7]. Although the research and commentary literature on burnout has exploded over the last 40 years, drawing attention to an important occupational hazard, there are considerable conceptualisation and measurement issues that threaten our understanding and efforts to ameliorate this phenomenon.

We live in an age where uncertainty is rife—present both in and out of the workplace. Nowhere is its presence more prominent than in the healthcare environment. It manifests in the processes of diagnosis, prognosis, and therapeutics, and in the complexities of healthcare coordination. Despite the alluring call of certainty suggested by terms like "precision medicine" and "molecular genomics", and the promise of ever-more targeted therapies, the ironic reality is that with more information at our fingertips, uncertainty only continues to rise. Yet, strong defences against, and denial of, uncertainties are consistent observations made by sociologists studying the process of medical training. It makes most of us—physicians and patients—deeply uncomfortable. Stress from uncertainty is

increasingly recognised to be a likely catalyst of burnout in healthcare[8,9], and doctors' maladapted responses to uncertainty are known to contribute to work-related stress[10-12].

This thesis aims to explore burnout in healthcare professionals, with a focus on the impact that uncertainty has on this domain. The first part of the thesis will explore drivers of satisfaction at work with an analysis of the interplay between burnout and uncertainty for physicians in the clinical environment, and an experimental study to assess how stress from uncertainty can be affected by language used in the clinical domain. Recognising that particular concern in the field comes from how best to measure burnout, the second part of the thesis will explore the novel use of cortisol and oxytocin levels as potential biomarkers of stress and burnout. The third part of the thesis will examine an intervention to reduce burnout and increase engagement and tolerance of uncertainty and will conclude with a review of the findings presented along with implications for training and suggestions for curricular approaches and future research to embrace uncertainty, reduce burnout, and ultimately maximise workforce wellbeing and minimise error and harm in clinical settings.

This chapter provides a general overview of the broad context of burnout in healthcare. It starts by exploring the history and definition of burnout and continues with a more extensive presentation of the existing literature on the impact of burnout—to physicians, to patients, and to healthcare organisations—and the current thoughts on potential drivers of burnout, introducing the concept that reaction to uncertainty may be a critical, and overlooked, driving force. The chapter will conclude with a consideration of the challenges that pertain to burnout research, particularly relating to challenges in measurement.

1.2 THE CONCEPT OF BURNOUT

The concept of burnout in healthcare emerged in the late 1960s as a way to describe the emotional and psychological stress experienced by clinic staff caring for vulnerable patients in free clinics. Herbert Freudenberger[13], a psychiatrist who worked in substance abuse in a free clinic in New York, and Christina Maslach[5], a social psychologist who was studying emotions in the workplace, began exploring this phenomenon—a work-related syndrome involving emotional exhaustion, interpersonal disengagement and a sense of reduced personal accomplishment[14]. Freudenberger wrote that burnout often occurred in contexts requiring large amounts of personal involvement and empathy, primarily among "the dedicated and committed". Over the next 40 years, Maslach systematically studied and defined burnout, developing the Maslach Burnout Inventory (MBI)[14], which emerged from the earlier qualitative research and is still considered to be the gold standard measure[15].

Healthcare workers were not alone in developing this psychological syndrome. During the 1960s and 70s, air traffic controllers reported poor training environments, inadequate equipment, rapidly changing shift patterns, long shifts without breaks, fatigue, monotony due to automation, and challenges arising from human-machine interfaces. After a series of fatal mid-air collisions linked to human error, the Federal Aviation Administration (FAA) commissioned a prospective cohort study in 1973 from Boston University School of Medicine[16]. This landmark study is one of the first investigations into workplace burnout, following 416 air traffic controllers over three years and identifying burnout, increased incidence of hypertension, and signs that controllers developed overt psychiatric problems over the course of the study.

1.3 DEFINING BURNOUT

Burnout is defined as a psychological syndrome emerging as a prolonged response to chronic emotional and interpersonal stressors on the job. It is characterised in the ICD-11, the World Health Organisation's International Classification of Disease, as "not a single event but a process in which everyday stresses and anxieties gradually undermine one's mental and physical health", referring specifically to phenomena in the occupational context. The three key dimensions of this response are an overwhelming exhaustion, feelings of cynicism and detachment, and a sense of ineffectiveness and lack of accomplishment[17]:

- **Emotional exhaustion (EE):** represents the basic individual stress dimension of burnout and refers to feelings of being overextended and depleted of one's emotional and physical resources;
- **Cynicism (or depersonalisation (DP)):** represents the interpersonal context dimension of burnout and refers to a negative, callous, or excessively detached response to various aspects of the job;
- **Reduced efficacy or personal accomplishment (PA):** represents the self-evaluation dimension of burnout and refers to feelings of incompetence and a lack of achievement and productivity at work.

The work of Maslach and colleagues has consistently supported a theory of burnout that must include both high EE and DP, although there has been recent work that calls into question the centrality of low PA[14,18,19]. As the majority of burnout research uses the criteria outlined by the MBI, the way in which Maslach conceptualises burnout is central to how we view that research. Maslach has long argued against the tendency among

clinical researchers to classify individuals as “burned out” or “not burned out” as she believes that burnout ranges along a continuum of low to high.

It can be hard to differentiate between exhaustion, fatigue, and burnout. Exhaustion is a shorter-lived form of fatigue that can be experienced emotionally, mentally, and physically. Periods of exhaustion build up to form longer-experienced fatigue or can contribute to burnout. Although burnout manifests in our mental health, it is not considered to be a mental illness, but rather a form of chronic workplace stress that has not been successfully managed. It is important, however, to differentiate it from too much stress—too many pressures that demand too much of you physically and mentally. While excessive stress can feel like you are drowning in responsibilities, burnout is about “not enough”—feeling empty and mentally exhausted, devoid of motivation, detached, and beyond caring. And, while you are usually aware of being under a lot of stress, you do not always notice burnout when it happens.

1.4 PREVALENCE OF PHYSICIAN BURNOUT IN HEALTHCARE

Physician burnout is now recognised as a global healthcare predicament and public health crisis. In the United States (US), where most of the research has been conducted, physicians are at significantly increased risk for burnout relative to workers in other fields with approximately half of practicing physicians affected (Figure 1.1)[20].

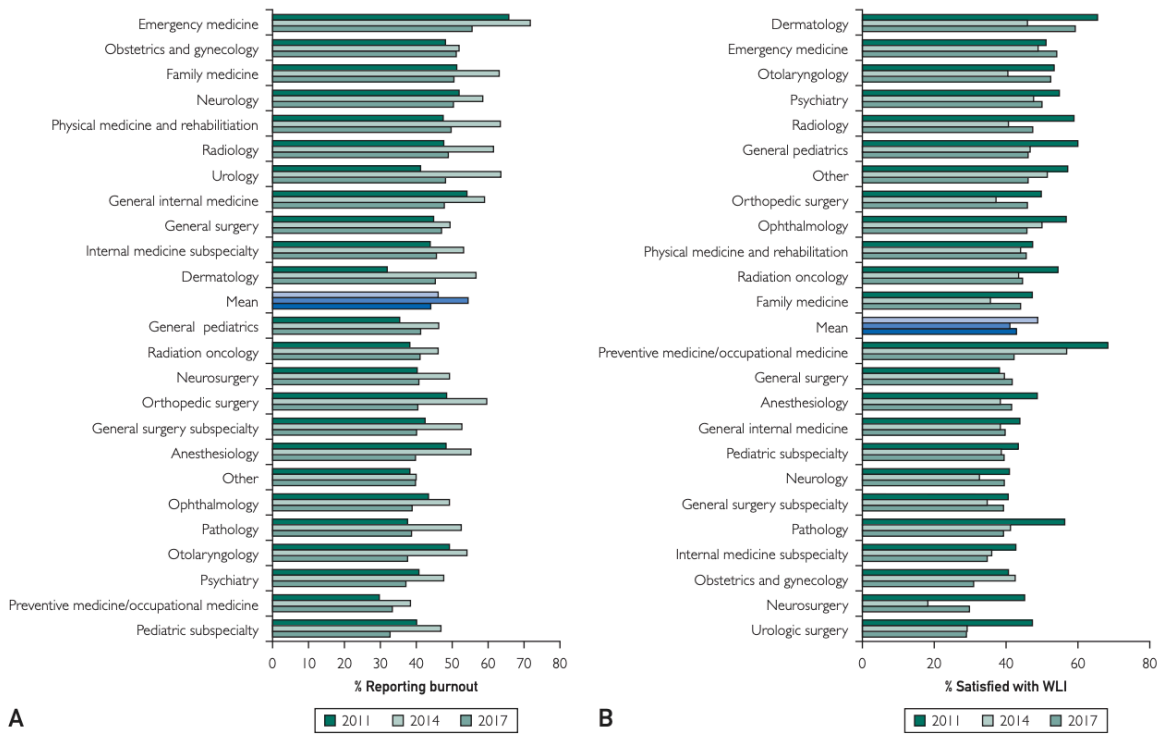

Figure 1.1 Burnout (A) and satisfaction with work-life integration (WLI) (B) by specialty, 2017, 2014, and 2011 from "Changes in Burnout and Satisfaction with Work-Life Integration in Physicians and the General US Working Population Between 2011 and 2017" by Shanafelt TD, West CP, Sinsky C et al. In Mayo Clin Proc, 2019; 94(9): 1681-1694[20]

More worryingly, burnout appears to be on the rise among medical students and trainees[21-23], with rates in resident physicians ranging from 27% to 75%, and described as being higher than consultant physicians[24,25]. A 2018 meta-analysis of over 16,000 medical students worldwide found that 44% suffered from burnout[26]. Similar prevalence of burnout is seen in the United Kingdom (UK), with many suggesting that it may threaten the survival of the health service[27]. The latest report by the General Medical Council (GMC) lays out a crisis that has been unfolding for many years in healthcare professionals, with a terrifying increase in the number and proportion of UK graduates and international medical graduate (IMG) doctors leaving the profession, that is now seeing the workforce at breaking point[28]. Since 2011, when preliminary career-destination surveys were first conducted, there has been a downward trend in the number of Foundation Year 2 (FY2) doctors entering higher-training posts in the UK, from 71.3% of FY2 doctors in 2011 to 37.7% in 2018 reporting immediate

entry into specialty training[29]. The GMC describes it as the most critical juncture in the history of the National Health Service (NHS) and one that deserves our utmost attention.

1.5 IMPACT OF BURNOUT

Rising rates of burnout are felt to represent an international public health crisis with negative impacts on individual physicians, patients, and healthcare organisations. Whilst it is difficult to fully measure and quantify, studies suggest that burnout may erode professionalism, influence quality of care, increase the risk for medical errors, and promote early retirement[30-35]. In short, the impact on the healthcare service is huge.

1.5.1 Impact of burnout on physicians

Although the practice of medicine can be incredibly meaningful and personally fulfilling, it is also demanding and stressful, with many experiencing burnout. This has adverse personal and professional consequences for physicians and trainees including contributing to broken relationships, problematic alcohol use[36], depression[37-39], and suicidal ideation[40-42] (Figure 1.2). Trainee depression and suicide are well-known concerns in the medical community that have not been adequately addressed. The connection with burnout is concerning as physicians are already at increased risk of suicide compared to the general population, with the suicide rate amongst male physicians being 40% higher than other males in the population and the suicide rate amongst female physicians being 130% higher than other females in the population[43]. In study after study over the past two decades, rates of depression among physicians and trainees have been consistently elevated over general population rates[43-49].

Unfortunately, physicians are slow to seek help[50,51] because of fears of judgment, stigma[52], and punitive actions[43]. They are less likely than the general population to receive appropriate treatment despite seemingly better access to care[53-55] and, despite their training, often fail to recognise that depression is a significant illness that requires treatment[53]. Physician burnout is also associated with increased risk of motor vehicle crashes and near-miss events, even after adjusting for fatigue[56].

BURNOUT	
PERSONAL REPERCUSSIONS	**PROFESSIONAL REPERCUSSIONS**
Broken relationships	Decreased quality of care and increased medical errors
Alcohol and substance use	Decreased patient satisfaction
Depression	Decreased productivity and professional effort
Suicide	Physician turnover

Figure 1.2 Personal and professional repercussions of physician burnout adapted from "Executive Leadership and Physician Wellbeing: Nine Organisational Strategies to Promote Engagement and Reduce Burnout" by Shanafelt TD and Noseworthy JH. In Mayo Clin Proc, 2017; 92: 129-46[57]

1.5.2 Impact of burnout on patient care

Cross-sectional studies have linked physician burnout with suboptimal and ineffective patient care practices[58-61], as well as with a doubled risk of medical error[33] and a 17% increased odds of being named in a medical malpractice suit[62]. Additional studies have found higher standardised patient mortality ratios in physicians with higher levels of emotional exhaustion working in intensive care units[63]. Increased physician depersonalisation levels have been shown to relate to longer recovery times for hospitalised patients post discharge[64]. Studies have also reported significant correlations between physician burnout and decreased patient satisfaction with their hospital care[1,59,64-68] and between physician job satisfaction and patient-reported adherence to medical advice[69,70]. A recent meta-analysis, that included 47 studies on 42,473 physicians, demonstrated that physician burnout was associated with an increased risk of patient safety incidents (OR, 1.96; 95% CI, 1.59-2.40), poorer quality of care due to low professionalism (OR, 2.31; 95% CI, 1.87-2.85), and reduced patient satisfaction (OR, 2.28; 95% CI, 1.42-3.68)[71].

1.5.3 Impact of burnout on healthcare organisations

Physician burnout has been shown to correlate with decreased productivity[1], and increased risk of leaving clinical practice[72,73]. A longitudinal study of physicians using the single-item MBI-based measures reported that each 1-point decrease in job satisfaction between 2011 and 2013 was associated with a 28% and 67% greater likelihood, respectively, of reduction in professional effort and work hours over the ensuing year according to payroll records[2]. Extrapolating this to the national level in the US results in lost productivity annually that is estimated to equate to the loss of the graduating classes of seven medical

schools[74]. These practice changes risk reducing patient access to physician care, further straining healthcare systems already struggling to meet the needs of the populations they serve[75]. Physician turnover also results in significant financial implications for healthcare organisations[76-78], with recent estimates of the organisational cost to replace a physician between $500,000 and $1,000,000[76,79]. In addition, burnout may increase healthcare expenditures indirectly via higher rates of medical errors[33,68,80] and malpractice claims[33,62,81], absenteeism, and lower job productivity[1,82,83] (Figure 1.2).

1.6 WHAT IS DRIVING BURNOUT?

A multitude of factors have been put forward to try to explain what is causing the burnout crisis—some work-related factors at the individual and organisational levels, as well as more personal factors which may leave some physicians predisposed to burnout. Academic medical centres have a tripartite mission to provide high quality clinical care, to advance knowledge through research, and to train the next generation of healthcare providers. External factors and competing pressures from these domains are often blamed for the rising discontent[84].

1.6.1 Nature of the work

Although there are substantial differences by specialty, physicians at the front line of care report the highest rates of burnout[30]. While a physician's job can be incredibly fulfilling, it is a role fraught with tremendous responsibility alongside stress from accountability and concern for patient outcomes, changes in healthcare delivery and financing, increased competition for declining pools of funding for research and scholarly work, and expectations

for innovative learning to be adopted into practice[85]. It is perhaps, therefore, unsurprising that work-related stressors have been shown to drive physician burnout[14,57,86,87].

In particular there has been recent focus on moral distress as a root cause of clinician burnout. Clinician moral distress, originally defined by Jameton as the inability to act according to an individual's ethical beliefs due to structural or hierarchical constraints, can be prevalent in the high-stakes healthcare environment[88]. Doctors share with military personnel a risk of suffering what is termed 'moral injury'[89,90] which refers to the emotional and psychological damage that is suffered by people who repeatedly witness, or participate in, acts that contravene moral expectations. These include situations in which the individual is causing suffering; where there is a proximity to death; and where there is a need to function within highly complex, uncertain, and unpredictable situations. Modern medicine has advanced to the point where we can support multiple organ systems simultaneously and sustain life when the benefits of treatments to overall survival and quality of life are not always clear[91]. Failing to meet patients' best interests can have a profound impact on physician wellbeing.

Additional factors include changes to junior doctors' salaries, hours-worked, a reduced investment in training, inflexibility with schedules, altered work flows and patient interactions, lack of consistent teamwork, and an understaffed service[15,28,92-96]. High job demands in conjunction with lack of control and profound inefficiencies in the practice environment, together with increased performance measurement with endless quantification and comparison of the measurable aspects of care delivery, are eroding physician autonomy and compromising the art of medicine[97]. But perhaps what underpins it all, driving the discontent and dissatisfaction, is a lack of feeling respected, valued and supported, with the

current healthcare environment at risk of taking for granted the human capital which forms the foundation of the system.

1.6.2 Individual factors and attributes

Although gender is not considered an independent predictor of burnout after adjusting for age and other factors, some studies have found female physicians to have 20-60% increased odds of burnout[98-102]. Younger physicians also appear to be at increased risk of burnout symptoms, with those less than 55 years old at more than double the risk of those older than 55[103]. Individual characteristics, such as personality and interpersonal skills, and personal experiences may influence how physicians cope with stress[104-107]. Personal characteristics associated with burnout include being self-critical, engaging in unhelpful coping strategies, sleep deprivation, over commitment, perfectionism, neuroticism, idealism and work-life imbalance, and an inadequate support system outside the work environment (e.g. having no spouse, partner, or children)[108]. However, individuals who choose to become physicians do not appear to be inherently more vulnerable to stress and burnout, emphasising the importance of work-related, organisational and healthcare system factors in the current burnout crisis[57,109].

1.6.3 Reaction to uncertainty

Clinical practice all too often entails serial contact with suffering and extreme emotions, often for long hours, dogged by the ever-present risk and consequence of errors; though solutions are few, expectations are high. It is an environment rife with uncertainty, yet the educational pathways and training do not prepare doctors for this reality[8,110]. Early stages of medical training—with a predominance of multiple-choice questions with "right"

answers—inculcate a notion that there is one absolute truth or single best answer in medicine. This suggests an element of certainty that often does not translate from the textbook and classroom to the real-world bedside. An unintended consequence of this educational approach is that not knowing the best answer can become a fear-inducing mark of incompetence for physicians. Indeed, studies link intolerance of uncertainty (as defined by heightened anxiety and feeling "stumped" or "helpless") to burnout, ineffective communication strategies, cognitive biases, and inappropriate resource use[111-113]. The human brain is hardwired to perceive reward from certainty and discomfort from increasing levels of uncertainty[114,115]. We have elaborate cognitive and emotional drives to eliminate it from our decision-making process[116]. Indecision and anxiety related to uncertainty can lead to depression or other mental health problems that undermine physician wellness and resilience[9]. Unfortunately, the healthcare environment is a breeding ground for uncertainty, arising from hard-to-predict disease processes, ambiguous laboratory and imaging findings, and from healthcare outcomes that are far from binary[8]. As uncertainty borders the edge of our knowledge, it is only likely to increase in the years ahead.

1.6.4 Wider changes in healthcare environment

The healthcare environment has changed in unprecedented ways over several decades, with an ageing population with increased complexities and co-morbidities, and advances in healthcare delivery. Recently, there has been a shift from viewing burnout as an individual problem to a problem of the healthcare organisation as a whole, rooted in issues related to working environment and organisational culture[117]. The fact that almost 1 in 2 physicians has symptoms of burnout implies that the origins of this problem are rooted in the environment and care delivery system rather than in the personal characteristics of a few

susceptible individuals. Inefficient work processes and environments (e.g. requiring physician-entered comprehensive documentation and electronic instruction communication, and other tasks not maximising the time physicians spend working at the top of their licence) contribute to burnout symptoms[99,118,119]. For each hour of clinical face time that physicians spend with patients, an additional two are consumed by administrative and clerical work, with increases in time spent in front of computer screens treating the "iPatient" in the electronic medical record (EMR) at the expense of personal patient encounters and time at the bedside[118,120-122]. Excessive workloads (e.g. long work hours, frequent overnight call duties, and high work intensity), work-home conflicts, loss of support from colleagues and deterioration in control, autonomy and meaning at work have each been associated with burnout amongst physicians[30,31,38,65,72,99,123]. While the modern, high-technology local work environment—featuring electronic health records, computerised physician order entry, patient portals, and around-the-clock remote computer access to patient records, test results, and current inpatient status—promised to lighten workload, it is increasingly recognised as a major cause of physician dissatisfaction and burnout. What has not been examined is the related concept of feeling valued and respected, or the importance of feeling that the work environment is sociable and supportive—this may be threatened by the advent of impersonal technologies and may be important in understanding what affects satisfaction at work. Organisational factors (e.g. negative leadership behaviour and limited interprofessional collaboration, opportunities for advancement and social support for physicians) also influence burnout[124,125].

1.7 THE MEASUREMENT OF BURNOUT

Over the last several years, many national organisations have called for healthcare systems to take both programmatic and institutional responsibility for prioritising healthcare professionals wellbeing[126,127]. However, this effort has been hampered by lack of agreement about how burnout should be measured, in part because of inadequate understanding of the pathophysiology of burnout[95]. To date, the gold standard of burnout measurement is the MBI[14], but a recent review of burnout studies[15] highlighted substantial limitations to the MBI including concerns about heterogeneity of results and applicability of the underlying conceptual framework[128]. Multiple experts have emphasised the importance of advancing the current approach to conceptualising and measuring burnout[15,95,128].

1.7.1 Self-reported burnout

1.7.1.1 The Maslach Burnout Inventory

The most widely accepted standard for burnout assessment is the MBI, which includes a Human Services Survey applicable to healthcare professionals[14]. This instrument is comprised of 22 items, across three domains (emotional exhaustion (EE); depersonalisation (DP); and personal accomplishment (PA)) each scored from 0 to 6 based on self-reported frequency of the feeling addressed by each item.

The MBI defines burnout as scoring in the high range (27 or more points) on EE, in the high range (13 or more points) for DP, and in the low range (31 or fewer points) for PA among professionals who serve people who suffer. The length of the MBI presents challenges for its use in surveys due to its length, and consequently single-item measures

of burnout have been developed by confirming the concurrent validity of two items (one for EE and one for DP) relative to the full MBI[129]. However, although the psychometric properties of several of the many adapted versions of the MBI may appear robust compared with the full instrument, they may be lacking in clinical meaning.

1.7.1.2 Measurement issues of the Maslach Burnout Inventory

There are measurement issues that are specific to the MBI itself. First, the MBI does not consider non-professional confounders of burnout such as childcare demands, the schedule and support of spouse or partner, life events, and financial concerns. Second, the MBI was not normed on physicians-in-training and included only a small normative sample of 43 attending physicians. The convergent and discriminant validity studies were based on mental health workers, legal aid employees, attorneys, police officers, probation officers, ministers, librarians, and agency administrators and were not, therefore, validated in the physician population[128]. Importantly, there is no established understanding of the pathophysiology of burnout or agreement on how it should be measured[95].

1.7.1.3 Measurement issues with self-reported surveys

As with all self-reported scales, they are subject to the inherent selection and reporting biases that often occur in survey studies, with participants potentially susceptible to social desirability bias. In addition, self-reported studies are inherently biased by the person's feelings at the time they filled out the questionnaire. Survey fatigue often affects participation, especially in an age where respondents are often overwhelmed with the number of surveys they are asked to take. Statements pertaining to burnout risk capturing individual perceptions as opposed to physiological changes, which are perhaps more

important to ascertain with regard to negative health consequences (metabolic, cardiovascular, mental health etc.) and it has been suggested that they may be lacking in clinical meaning[95].

1.7.1.4 Methodological variability in survey studies of burnout

A recent meta-analysis by Rotenstein and colleagues[15] identified 182 studies of burnout prevalence and demographic correlates in 109,628 physicians from 45 countries. The investigators found so much heterogeneity in the study design, in the methods of measuring burnout across a wide range of cultures and health systems, in the response rates, in target populations, and in the outcomes that reaching any conclusions about the prevalence of burnout or its effect was impossible. In addition, there was substantial heterogeneity within each instrument, raising concern about the validity of the instruments used. The authors abandoned a formal meta-analysis as a viable approach to present the data. Of the 182 studies, 156 used one of several variations and scale cut-offs from the MBI and the remainder used several variations of other instruments. In total, 142 different definitions of burnout were used, with reported range of burnout prevalence 0% to 80.5%. This review identified a lack of consensus on how the burnout construct is used to measure physicians' exposure and response to occupational stress calling into question whether any prevalence estimate cited for burnout can be meaningfully interpreted. Yet, the self-reported symptom of burnout has rapidly become an accepted marker for an epidemic of physician dissatisfaction and potential self-harm described as a national crisis.

1.7.2 Biomarker measurement of burnout

While efforts have attempted to simplify measurement strategies with burnout regarded as a one-dimensional construct assessed through single-item measures, the reality is that the underlying neurophysiological changes are likely to be more complex—people experiencing burnout are not simply exhausted or overwhelmed by their workload. They also have lost a psychological connection with their work, which has implications for their motivation and their identity. There is likely to be heterogeneity in the "phenotype" of burnout. Recognising and identifying this heterogeneity may help as we look to develop interventions.

The criteria for ideal biomarkers recommend the provision of non-invasive biological samples, such as easily accessible external body secretions. Diverse data relating to the identification of various types of physiological stresses, and their associated molecular and systemic mediators, are still accumulating. Research studying the plausible pathophysiological mechanisms has primarily focused on dysregulation of the hypothalamus-pituitary-adrenal (HPA) axis and immune functions. Hopefully, future advances will provide us with precise, multidimensional biological molecules that can address many of the current measurement deficiencies in the field of burnout.

1.7.2.1 Cortisol

As burnout and stress are conceptually linked, neuro-hormonal changes in response to stress, such as cortisol levels, may provide a novel avenue for understanding the pathophysiology of burnout and for improving measurement using biomarkers. Physiological stress responses, mainly triggered through the sympathetic adrenomedullary

(SAM) system and the HPA axis, result in the release of glucocorticoids, specifically cortisol[130], which has become the "gold standard" biomarker by which to evaluate systemic fluctuations of the HPA axis. In addition to measuring cortisol in blood or saliva, which reflects acutely circulating hormone concentration with diurnal variation that may limit usability, measuring cortisol in hair for cumulative long-term stress exposure has recently started[131]. Making use of the continuous incorporation of lipophilic substances, such as steroid hormones, into the growing hair, hair cortisol concentrations are assumed to provide an easily obtainable index of cortisol levels integrated over the extended period of hair growth, i.e. several months[132].

1.7.2.2 Oxytocin

Over the last few decades, oxytocin—a neuropeptide synthesised in the paraventricular nucleus and supraoptic nucleus of the hypothalamus and released into both the central and peripheral circulation—has received increased attention for its role in social functioning. Trust is an adaptive mechanism essential to building social relationships. Oxytocin increases in situations with high trust or bonding[133], and stress, uncertainty, and isolation all work against the development of a trusting disposition. Later in the thesis, we will introduce the idea that oxytocin may be a useful biomarker by which to measure the physiological basis of pro-social behaviour which may mitigate the impact of burnout on healthcare outcomes.

1.7.2.3 Autonomic nervous system activity

The autonomic nervous system (ANS) plays a crucial role in both the biological stress process and the manifestation and maintenance of stress-related symptoms. While there are

a number of ANS markers that are indicative of autonomic activation, different markers have been found to reflect different aspects of ANS activity, and as such their use is dependent on the specific mechanism under study. Heart rate variability, for example, is a widely used laboratory assessment of cardiovascular functioning, since it reflects the input of sympathetic and parasympathetic control of the heart[134]. However, technological and experimental complexities associated with the measurement of heart rate variability restrict its ability to assess ANS functioning across a wide range of settings and in different populations[135]. Likewise, other ANS markers such as the centrally synthesised catecholamines, noradrenaline, and adrenaline, require invasive blood or spinal fluid draws, which limit their use, particularly in real-world healthcare research settings.

1.7.2.4 Immune function

It is suggested that chronic psychological stress alters immune function and many studies have been undertaken to identify immunological diagnostic or prognostic biomarkers or to explore linking pathways between the neuroendocrine and immune systems in chronic stress-related diseases[136]. There are only a few studies, however, that have specifically evaluated immunological processes in burnout (e.g. C-reactive protein (CRP); leukocyte numbers in blood; and cytokines) with contradictory and inconclusive results[137].

1.8 INTERVENTIONS TO REDUCE BURNOUT IN PHYSICIANS

Although a variety of interventions have been studied, to date it is not clear which interventions may be considered effective. Interventions to reduce burnout in physicians can be classified into two main categories: physician-directed interventions targeting individuals and organisation-directed interventions targeting the work environment (Table

1.1)[138,139]. While interventions that are organisation-directed aim to achieve long-term changes through the reorganisation of the work environment, individual interventions can be adapted for those who are already in the process of burnout.

1.8.1 Physician-directed interventions

Physician-directed interventions typically involve mindfulness techniques or cognitive behavioural techniques to enhance job competence and improve communication skills and personal coping strategies. They have been shown to lead to only very small significant reductions in burnout, suggesting that solely intervening at the individual level may not be addressing the root of the problem. It has been suggested that physicians expected to deal with burnout individually and remotely from their practicing organisations might view physician-directed interventions as a personal responsibility (or blame themselves for being less "resilient") rather than as a shared resource to create a flourishing health care environment. Such an individualistic approach can ignore the sources of chronic stressors in the workplace such as incivility, staff shortages, austerity measures, and uncertainty, often beyond an individual's control. Of course, individually focused solutions are important to support overburdened staff but they are less likely to have longevity and sustainability than solutions that are team-based and organisationally embedded[71]. Indeed, they may even compound problems in the long run by reinforcing a dysfunctional coping approach that interprets failure as wholly personal[140]. There are both philosophical and pragmatic reasons underlying the predominant focus on the individual, including notions of individual causality and responsibility, and the assumption that it is easier and cheaper to change people than organisations[141].

1.8.2 Organisational-directed interventions

Organisational-directed interventions can involve simple changes to schedules and reductions in the intensity of workload or more ambitious changes to the operation of practices and whole healthcare organisations. These usually involve improved teamwork, changes in work evaluation, supervision to reduce job demand and enhance job control, and increasing the level of participation in decision-making. Those that combine several elements such as structural changes, fostering communication between members of the healthcare team, and cultivating a sense of teamwork and job control tend to be the most effective in reducing burnout[142]. However, such intense organisation-directed interventions are rare and not evaluated widely. Randomised studies of structural or organisational interventions have been uncommon, with very few reported in the literature to date[143]. Concerns about implementation and delivery costs of organisation-directed interventions, especially if they involve complex and major health care system changes, might explain their scarcity[117].

Despite the widespread awareness of the benefits of interprofessional collaborative practice, the literature is lacking in evidence-based interprofessional interventions that might enhance workplace engagement and reduce burnout for these faculty. Most studies of wellbeing interventions in healthcare have tended to focus on faculty who share the same professional role, such as physicians-only or nurses-only, rather than studying the inclusive interprofessional groups that make up most academic departments, in which physicians, nurse practitioners, and other allied health professionals work collegially together[144]. Which interventions offer the greatest value to physicians and their organisations remains unclear, as well as whether or not the processes involved in development and deployment of interventions could influence their effectiveness. For

example, relative to externally developed approaches, interventions for which physicians in the local work environment are engaged in design and implementation might heighten their sense of control and engagement, which might be expected to reduce burnout[145] (Table 1.1).

DRIVER	ORGANISATIONAL-LEVEL SOLUTIONS	INDIVIDUAL-LEVEL SOLUTIONS
Excessive workload	Fair productivity targets Duty hour limits Appropriate distribution of job roles	Part-time status Informed specialty choices Informed practice choices
Work inefficiency and lack of work support	Optimized electronic medical records Non-physician staff support to offload clerical burdens Appropriate interpretation of regulatory requirements	Efficiency and skills training Prioritise tasks and delegate work appropriately
Lack of work-home integration	Respect for home responsibilities in setting schedules for work and meetings Include all required work tasks within expected work hours Support flexible work schedules, including part-time employment	Reflection on life priorities and values Attention to self-care
Loss of control and autonomy	Physician engagement in establishing work requirements and structure Physician leadership and shared decision-making	Stress management and resiliency training Positive coping strategies Mindfulness
Loss of meaning from work	Promote shared core values Protect physician time with patients Promote physician communities Offer professional development opportunities Leadership training and awareness around physician burnout	Positive psychology Reflection/self-awareness of most fulfilling work roles Mindfulness Engagement in physician small-group activities around shared work experiences

Table 1.1 Common drivers and selected solutions for physician burnout, adapted from "Physician burnout: contributors, consequences and solutions", by West CP, Dyrbye LN and Shanafelt TD. In Journal of Internal Medicine 2018; 282: 516-529[103]

1.9 CHALLENGES IN APPROACH TO BURNOUT RESEARCH

Whilst there has been much focused attention from leaders in healthcare organisations and health professions' educational institutions to identify the causes and consequences of clinician burnout, and suggest interventions to support clinician wellbeing, there are myriad problems with current burnout research and its measurement that threaten the validity of conclusions and risk hindering progress in this critical domain. As we have explored above, a fundamental concern is in the heterogeneity of defining and measuring burnout.

1.10 CONCLUSIONS

"Never let a good crisis go to waste"
Winston Churchill

After nearly 50 years of the study of burnout, there are many proposed solutions to it but little evidence of their effectiveness[15,95]. Inadequate measurement approaches have hampered progress[15,95,128] and viewing burnout as a disease has hindered efforts to focus on the workplace values and culture that are potentially driving the state. There are many theories of physician burnout and a multitude of factors that have been put forward to explain the crisis that has unfolded. Pressures on humans to minimise or even dismiss uncertainty are large and growing and we have a culture that too often equates uncertainty with ignorance or failure[8]. Unfortunately, uncertainty is fundamental to medicine and, despite the remarkable trajectory of biomedical research over recent decades, it will always be rife in the healthcare environment. This has been particularly evident in recent months with the emergence of Covid-19, a virus that has swept the world without pause with a trajectory defined by uncertainty. It seems likely that Covid-19-associated

uncertainties will extend well into this decade and it will be increasingly necessary to eliminate the toxic fear and anxiety that has for too long been fuelled by our unhealthy reaction to uncertainty[146]. Striving to outsmart uncertainty would seem like a futile goal. Instead we should remind ourselves of Osler's maxim that "medicine is a science of uncertainty and an art of probability", and model comfort with uncertainty so that we can finally turn the tide on an unachievable ideal of complete determinism.

There is clearly something important and worrying happening to physician wellbeing on a global scale. What is not up for debate is a real need to enhance our understanding of the root causes driving this phenomenon, together with robust objective markers for measurement, to ensure we can develop strategies to revive the noblest profession and empower physicians to maximise their potential and provide high-quality care driving healthcare forwards. The next chapter will explore uncertainty in more detail and consider the impact that it has in medicine and specifically its role in burnout.

CHAPTER 2: UNCERTAINTY IN MEDICINE AND ITS ROLE IN BURNOUT

"Medicine is a science of uncertainty and an art of probability."
William Osler

2.1 INTRODUCTION

Although uncertainty is fundamental to medicine, the healthcare environment strives to minimise and dismiss it[8]. The quest to eliminate uncertainty in clinical decision-making has become central to biomedical research over the past 50 years, driving the emergence of evidence-based medicine (EBM), precision medicine, and most recently, biomedical artificial intelligence. Although advances in biomedical research will continue to improve the accuracy of information available for clinical decision-making, uncertainty in clinical medicine will always be rife. Indeed, as uncertainty borders the edge of knowledge, its presence in the healthcare environment is likely to increase, exponentially. The reality is that doctors continually have to make decisions on the basis of imperfect data and limited knowledge, which leads to diagnostic uncertainty, coupled with the uncertainty that arises from unpredictable patient responses to treatment and from healthcare outcomes that are far from binary[8].

Although individual tolerance of uncertainty varies based on genetic, experiential, and contextual factors, uncertainty discomforts most humans, who have cognitive and emotional drives to eliminate it from their decision-making process[116]. Future physicians will need to tolerate, learn, and practice in a new frontier of ever-expanding uncertainty. Doctors, however, often fear that by expressing uncertainty, they will project ignorance to

patients and colleagues, so they internalise and mask it. Stress from uncertainty is increasingly recognised as a likely driver of burnout in healthcare[8,9,113,147]. We are still strongly influenced by a rationalist tradition that seeks to provide a world of apparent security.

In this chapter we will explore the dimensions of uncertainty and consider the impact that it has in medicine and the concept that reaction to uncertainty (and perhaps more specifically intolerance of uncertainty) may be a critical, and much overlooked, driving force behind the burnout pandemic.

2.2 UNCERTAINTY IN MEDICINE

Osler's maxim that "medicine is a science of uncertainty and an art of probability"[148] remains as true today as it has in centuries past. Uncertainty in healthcare pertains to numerous unknowns: whether a patient has or will develop a particular condition; how that condition will evolve; to what extent a particular treatment is beneficial; and whether a patient is receiving the right care, in the right place, at the right time, from the right people. The sheer number and variety of these unknowns make uncertainty a ubiquitous problem in healthcare[149]. The increasingly rapid emergence of new medical technologies that is outpacing the development of evidence regarding benefits, harms, and implications, is resulting in uncertainty becoming a growing problem in healthcare[149]. In addition, the exponential increase of knowledge in health sciences, with a widening array of therapies and diagnostics fuelled by advances in immunology, genetics, and systems biology, brings further levels of complexity that can, ironically, amplify uncertainty. Patients are older, with more coexisting illnesses and more medications. They see more specialists and undergo more diagnostic testing, which leads to exponential accumulation of electronic

medical record (EMR) data. Every patient is now a "big data" challenge, with vast amounts of information on past trajectories and current states—detecting "the signal" from "the noise" becomes an increasing challenge. An emphasis on molecular genomics and precision medicine—terms which undoubtedly connote certainty—risks widening a gap between expectation and reality, for patients and physicians. Given the growth of access to information online and electronically, students can spend less time at the bedside in the greyscale world of medicine and more time in front of a screen – absorbing processed and general information, rather than immediate and often confusing realities. Their online experience may reinforce their sense of a black-and-white world where certainty is readily achievable — the antithesis of the perspective they will need to thrive in 21st century medicine[8]. As we move further into the 21st century, it seems clear that technology will perform the routine tasks of medicine for which algorithms can be developed. Our value as physicians will lie in the greyscale space, where we will have to support patients who are living with uncertainty[8]. Responding to the plethora of uncertainties that arise in the healthcare environment in an adaptive way is one of the most important challenges facing physicians and patients.

2.2.1 Acknowledgment of uncertainty and performance

Acknowledging uncertainty drives curiosity, preventing premature closure and enhancing performance and decision-making, but only up to a point. When acknowledgment of uncertainty gets too high—a threshold that differs between individuals—performance begins to decrease as anxiety increases and indecision accumulates and paralysis in decision-making ensues (Figure 2.1). On the one hand, the anxiety and frustration that even experienced physicians encounter when facing uncertainty may be constructive as it motivates physicians to continue to evaluate, ponder, and care for patients even when a

diagnosis or positive outcome is not readily apparent. However, it is important that the frustration and anxiety does not lead to disillusionment and burnout[150].

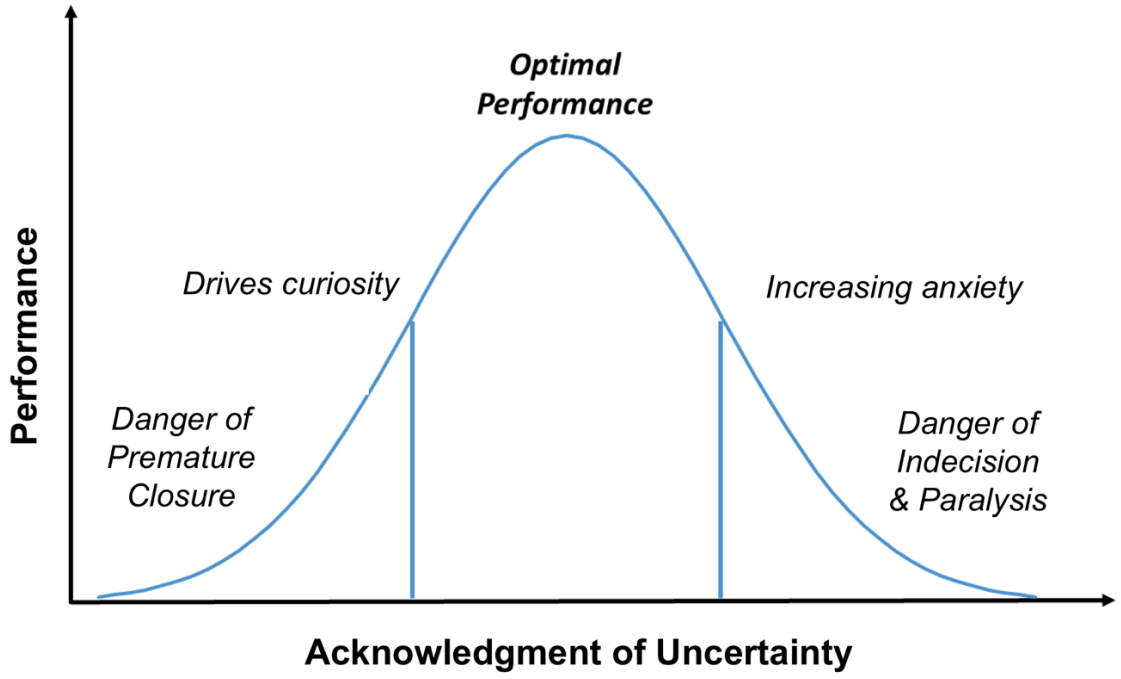

Figure 2.1: Acknowledgment of uncertainty and performance

2.3 DIMENSIONS OF UNCERTAINTY

Despite decades of research into uncertainty in a multitude of disciplines, it has proved challenging to develop a unified definition of uncertainty that encompasses the numerous types, sources, and manifestations of uncertainty. Broadly, uncertainty can be thought of as "the conscious awareness of being unsure, of having doubt, of not fully knowing"[149,151]. It is not simply the absence of knowledge as it usually occurs in the company of an abundance of information. All medical decision-making occurs under conditions of varying levels of uncertainty about diagnoses, optimal treatments, and prognoses—it is ubiquitous in healthcare[152].

Although often confused and deemed as interchangeable, uncertainty and ambiguity correspond to slightly different constructs[153]. It has been argued that ambiguity refers to the stimuli's properties—unpredictable, novel, complex, and/or insoluble; whereas uncertainty refers to the emotional state that has been provoked by the aversive or ambiguous stimulus[154,155]. In other words, ambiguity seems to precede uncertainty. Uncertainty relates to the conscious, metacognitive awareness of ignorance[151]. It is the overarching, superordinate construct, the seminal metacognition pertaining to some object and produced by some source. In contrast, ambiguity is the subordinate construct, one of uncertainty's principal sources, a property of information pertaining to its lack of reliability, credibility, or adequacy[152,156-158].

2.3.1 Aleatoric and epistemic uncertainty

Uncertainty has been recognised to have two major dimensions:

(1) **Aleatoric uncertainty** (from the Latin root *alea* for dice and gaming) relating to chance uncertainty, i.e., the inherent uncertainty due to random variability;[159]

(2) **Epistemic uncertainty** (from the Greek root *episteme*, meaning knowledge) relating to our incomplete knowledge that arises both from limitations in existing scientific knowledge about a medical question and limitations in the decision-makers ability to access and process effectively existing scientific knowledge.

Any scenario has a combination of these two dimensions. As an example, there is inherent variability in whether a patient develops a certain disease (aleatoric uncertainty), and inherent limitations in the provider's ability to diagnose the disease—in part because scientific knowledge about the disease is imperfect and in part because of imperfections in

the provider's access to, and use of, the existing knowledge (epistemic uncertainty). The different sources of uncertainty are not distinguished in the scales used to measure tolerance of uncertainty, although the two dimensions may nevertheless be experienced very differently. Table 2.1 outlines sources of uncertainty, categorised as aleatoric or epistemic uncertainty, in medical decision-making.

NATURE OF UNCERTAINTY	SOURCE OF UNCERTAINTY
Aleatoric, or chance, uncertainty ***(uncertainty due to random variability)***	Variation in disease incidence or outcomes across patients Variation in personal significance of particular risks: tolerability, scope, timing, or temporal impact Potential for future developments that may affect risk of disease or outcomes
Epistemic uncertainty ***(uncertainty due to incomplete knowledge)***	Inadequate scientific knowledge: • Uncertainty due to missing or inconsistent evidence • Uncertainty from translating population level findings to individuals Inadequate access to, and application of, existing scientific knowledge: • Uncertainty from ignorance of existing evidence • Uncertainty from complex or poorly understood evidence

Table 2.1: Sources of uncertainty in medical decision-making adapted from "Communicating uncertainty: a narrative review and framework for future research" by Simpkin AL and Armstrong KA. In Journal of General Internal Medicine, 2019; 34(11): 2586-2591[160]

2.4 REACTION TO—OR TOLERANCE OF—UNCERTAINTY

Uncertainty is a critical phenomenon in healthcare because of its many potential psychological effects, both negative and positive. Large bodies of research have demonstrated that uncertainty provokes fear, worry and anxiety, perceptions of vulnerability, and avoidance of decision-making. Individuals engage in a variety of different responses, depending on the specific context, to minimise the negative effects and maximise the positive effects of uncertainty. Understanding these individual differences in

people's responses to—or tolerance of—uncertainty is an increasingly important focus of research (Table 2.2). Crucially, any of these various responses can be either conscious and intentional or unconscious and reflexive. Tolerance of uncertainty represents the capacity to "close the gap between the normative ideal and the descriptive reality" of decision-making under uncertainty[161], and can be defined as "the set of negative and positive psychological responses—cognitive, emotional, and behavioural—provoked by the conscious awareness of ignorance about particular aspects of the world"[149]. An individual's "tolerance" of uncertainty is the balance between the positive and negative responses. The capacity of healthcare professionals and patients to tolerate uncertainty can affect individual wellbeing, and the extent to which both parties form therapeutic relationships, engage in shared decision-making, and ultimately influence health behaviours, the quality of healthcare, and health outcomes[149].

Positive	*Exemplary measure item*	Negative	*Exemplary measure item*
COGNITIVE			
Acknowledgment	*People who insist upon a yes or no answer just don't know how[162] complicated things really are*	**Denial**	*There's a right way and a wrong way to almost everything[163,164]*
Attraction	*I prefer a situation in which there is some ambiguity[165]*	**Aversion**	*The sooner we all acquire similar values and ideas, the better[162,166]*
Curiosity (wonder, fascination)	*The idea of taking a trip to a new country fascinates me[167]*	**Distrust**	*I would not have confidence in a medical test or treatment if experts had conflicting opinions[168]*
		Self-doubting	*Being uncertain means that I am not first rate[169,170]*
		Confusion	*When trying to solve a problem I often see so many possible options that it's confusing[171]*
		Doubt	*When I find myself in an uncertain situation, I tend to have doubts about what I am doing[172]*
		Catastrophising	*I often exaggerate the odds that the worst will happen when something unexpected occurs[172]*
EMOTIONAL			
Comfort (wellbeing, relaxation); **Enjoyment**	*It is more fun to tackle a complicated problem than to solve a simple one[162,163]*	**Discomfort** (unease, emotional upset, feeling overwhelmed	*It really disturbs me when I am unable to follow another person's train of thought[173,174]*
Excitement (passion, stimulation)	*I think a mid-life career change is an exciting idea[167]*	**Stress**	*Uncertainty makes me uneasy, anxious and distressed[169,170]*
		Worry/anxiety (nervousness/sense of vulnerability)	*Problems which cannot be considered from just one point of view are a little threatening[165]*
		Fear	*I fear being held accountable for the limits of my knowledge[175]*
		Depression (sadness)	*Thinking about uncertainty makes me feel depressed[167]*
		Anger (irritation, frustration)	*I find it frustrating when I can't find the answer to a clinical question[176]*
BEHAVIOURAL			
Approach (confrontation, pursuit, seeking)	*I often find myself looking for something new, rather than trying to hold things constant in my life[163,165]*	**Avoidance** (of the source of uncertainty)	*I avoid settings where people don't share my values[166]*
Function	*I think that I would learn best in a class that lacks clearly stated objectives and requirements*	**Dysfunction** (debilitation)	*When I am uncertain, I can't function very well[169,170]*
Adaptation	*I easily adapt to unfamiliarity[167]*	**Paralysis** (decision avoidance, hesitance, deferral)	*When it's time to act, uncertainty paralyses me[170,177]*
Deliberation	*When I feel uncertain about something, I try to rationally weigh up all the information I have[167]*	**Non-disclosure** (reluctance to acknowledge)	*I almost never tell other physicians about diagnoses I have missed[175]*
Disclosure (tendency to disclose)	*I always share my uncertainty with my patients[175]*	**Resignation** (non-perseverance)	*I tend to give up easily when I don't clearly understand a situation[167]*
		Control-orientation (problem-solving)	*I prefer to control everything in order to decrease uncertainties[172]*

Table 2.2: Multiple responses to uncertainty identified implicitly in measure items, adapted from "Tolerance of uncertainty: conceptual analysis, integrative model, and implications for healthcare" by Hillen MA, Gutheil CM, Strout TD, Smets EMA, Han PKJ. In Social Science and Medicine, 2017; 180:62-75[149]

2.4.1 Influence of personal and professional characteristics on tolerance of uncertainty

Tolerance of uncertainty is thought to be a state determined by situational or contextual factors[166,178], and therefore amenable to change through an educational and experiential process[179], though there is a likely influence from inherited personality traits and environmental influences that predispose individuals to specific psychological responses. In other words, applicants to medical school likely possess a predisposition to respond to uncertainty in a particular way, a response mitigated or reinforced by life experience[180]. The medical socialisation process is likely to exert a mediating influence on how graduating students deal with uncertainty. There are many opportunities through training to hone communication and decision-making skills in the face of uncertainty. It has been shown to improve over time and with experience[181].

The need for closure—the desire for any firm belief on a given topic, as opposed to uncertainty—is a fundamental motivation for human behaviour. Findings relating to associations between tolerance of uncertainty and sociodemographic characteristics have been inconsistent: some studies showing tolerance of uncertainty increases with older age[182-184]; some demonstrating tolerance is higher with younger age[185], and some showing no association[186]. Similar discrepancies have been found in studies looking at tolerance of uncertainty in association with gender[185,187-189]. Interestingly, tolerance of uncertainty has been shown to be greater in physicians who hold a graduate degree other than an MD[190,191].

One study demonstrated that trainees who classified as thinking (vs. feeling), extroverted (vs. introverted), and perceptive (vs. judging) had greater tolerance of uncertainty[188]. Tolerance of uncertainty has been consistently related to other personality traits such as authoritarianism, dogmatism, and openness to experience[164,192-195]. Further work is needed to ascertain how

differences in both individual personalities and situational factors interact in producing varying levels of tolerance of uncertainty. Although uncertainty is by definition always conscious, in their consequent responses to uncertainty people may have variable awareness of the extent to which their uncertainty is causing them to think, feel, or behave in particular ways.

2.4.2 Cultural influences on tolerance of uncertainty

Far from embracing the uncertainty inherent in our natural world, we have an educational system and cultural upbringing that focuses on certainty. Pressures on humans to minimise or even dismiss uncertainty are large and growing and we have a culture that too often equates uncertainty with ignorance or failure[8]. From early education, we give more weight to, and prioritise, certainty. Subjects that convey certainty, like science and mathematics, are often valued higher than the humanities that epitomise and celebrate uncertainty (such as drama, music, and art) in academic institutions. We instil a sense of a hierarchy with greyscale subjects lower down the pecking order. Even within the mathematics timetable, more time is spent on geometry and calculus than probability and statistics. In many walks of life, expressions of uncertainty are mistaken for admissions of weakness. We reward students for getting it "right" and create examinations that inculcate a notion that success equates to knowing the answer. To date, we have been in pursuit of unambiguous certainty.

Our drive for certainty makes sense from an evolutionary standpoint. Our natural discomfort with uncertainty is a legacy of our survival instincts—we are more comfortable with what is familiar and certain (it hasn't killed us yet), than the unknown, which could be dangerous. Certainty is rewarding and so we have evolved to steer towards it. Though we are now far from being in life-threatening situations in most of the spaces when we face uncertainty, our

response is the same as that which our ancestors evolved to avoid long ago. Embracing uncertainty is counter to our evolutionary instincts.

2.5 TOLERANCE OF UNCERTAINTY AND PROVIDER-CENTRED COGNITIVE AND BEHAVIOURAL IMPACT

Uncertainty has been implicated as a cause of anxiety for physicians and an important cause of variation in physicians' practice patterns and use of resources[196-199]. Yet, in many respects, the primary communication task of clinicians is the management of uncertainty.

2.5.1 Tolerance of uncertainty and cognitive impact

Tolerance of uncertainty has been associated with various practice-related attitudes of medical students with studies showing students with lower tolerance of uncertainty showed greater reliance on high-tech medicine, a more negative orientation towards patients' psychological problems, more Machiavellianism, and a preference for a structured work environment[200,201]. Evidence suggests that higher tolerance for uncertainty is associated with medical students' leadership ability[202] and their willingness to practice in rural areas[203]. Conversely, there is a strong relationship between students' low tolerance for uncertainty and their fears of making mistakes[187], their negative attitudes towards the underserved[204], and bias against those who abuse alcohol[185].

2.5.2 Tolerance of uncertainty and behavioural impact

Several studies have identified associations between tolerance of uncertainty and medical decision-making. A provider's ability to deal with uncertainty at a cognitive, emotional, and ethical level has been shown to influence the diagnostic process with potential for diagnostic

error and impact on patient outcomes[205]. Suppression of uncertainty and lack of consideration of alternative diagnoses can result in premature closure—the tendency to stop considering other possibilities after reaching an initial diagnosis—the single most common phenomenon in misdiagnosis[206]. The hyperactive pattern recognition skills which may have served our ancestors well, now risk us seeing patterns where none really exist, closing our curiosity too soon as we strive for certainty, with consequent risk of error. We risk putting information that does not fit into our metaphorical blindspot, succumbing to our biases and focusing on signals that tell a story about the world as we would like it to be or as it would conveniently fit our explanation. There is growing recognition of the importance of diagnostic error with regard to patient safety. Our quest for certainty may well be driving many of the cognitive errors contributing to this crisis, and similar crises in other industries.

Radiologists with lower tolerance of uncertainty demonstrate higher diagnostic sensitivity and lower specificity, as well as an overall higher rate of abnormal mammogram interpretations[207]. Low tolerance for uncertainty has been associated with a biomedical rather than a biopsychosocial worldview[205], as well as increased test-ordering tendencies[208,209] and failure to comply with evidence-based guidelines[210], additional empiric treatment regimens[211,212], withholding negative genetic test results[173], fear of malpractice litigation and defensive practice[213], and discomfort in the context of death and grief[214,215]. It is estimated that 17% of excessive costs in medical care result from physicians' anxiety related to how they manage uncertainty[216]. These extraneous interventions not only increase healthcare costs but also place patients at risk of experiencing adverse events from unnecessary tests and treatments[191,207].

2.6 TOLERANCE OF UNCERTAINTY AND PATIENT-CENTRED IMPACT

Just as doctors often struggle in the face of uncertainty, patients are known to have complex cognitive, emotional and behavioural responses to uncertainty[190,217]—not knowing what the future will bring is psychologically difficult and can cause anxiety to increase. Their comprehension of uncertainty varies by the way it is communicated, and thus is inherently linked to the provider's tolerance of uncertainty as discussed above. Studies have reported undesirable effects of providers' uncertainty communication, including heightened perceptions and feelings of vulnerability and avoidance of decision-making[152,217-221] and negative patient perceptions (lack of confidence, low visit satisfaction, worry or concern)[222-228] highlighting the need for skills in this domain. Patients may also not desire or have sufficient psychological capacity to tolerate information about uncertainty[167].

Patients with higher tolerance of uncertainty have been shown to perceive greater benefits, lower harms, and lower ambivalence regarding common cancer screening tests such as colonoscopy, mammography, and prostate-specific antigen testing[229]. Just as with physicians, studies have shown a consistent association between tolerance of uncertainty and emotional wellbeing among patients with a higher tolerance of uncertainty generating greater wellbeing[230]. Cancer patients with higher tolerance of uncertainty have been shown to have lower perceived stress, lower non-somatic depressive symptoms, and higher general emotional wellbeing. This association was found to be mediated by avoidance and deliberate efforts not to think about or talk about one's cancer diagnosis, treatment, and recovery[231]. Epilepsy patients with higher tolerance of uncertainty were also found to worry less, be less irritable, and experience a higher quality of life[232].

2.6.1 Impact of providers' tolerance of uncertainty on patients

Physicians who are intolerant to uncertainty are reluctant to disclose their uncertainties to their patients when making decisions, which can impede open, honest and respectful communication with patients[233]. Inadequate management of uncertainty may cause unnecessary concern and distress to patients, and risks undercutting the patient-provider relationship and decreasing trust[234]. The inability to communicate uncertainty creates a false sense of certainty in patients, which can lead to substantial distrust when that certainty proves to be overstated.

Findings on the association between tolerance of uncertainty and health services utilisation have been mixed and focused on screening tests, with many showing that higher tolerance of uncertainty results in greater utilisation of screen tests[229,235]. A number of studies have explored the relationship between tolerance of uncertainty and health outcomes and have generally shown tolerance of uncertainty to be associated with positive outcomes[230].

2.7 TOLERANCE OF UNCERTAINTY AND ITS ROLE IN BURNOUT

We are programmed to want to reduce irreducible uncertainty. As we have seen in the examples above, this reality in a world where we are surrounded by uncertainty can have a negative impact on our wellbeing contributing to burnout and depression[9,113,147,236,237]. Burnout has been described as "the index of the dislocation between what people are and what they have to do"[14], and it makes intuitive sense, therefore, that stress could follow from consistently having to make decisions in the face of uncertainty especially as few strategies or training opportunities exist in medical education to help physicians embrace uncertainty.

An intolerance of uncertainty has been shown to be a characteristic involved in excessive worry[238-240], to be strongly associated with generalised anxiety disorder, as well as depression and obsessive compulsive disorder[241]. The psychological distress which is associated with an intolerance of uncertainty has consequences not only for the physical and mental wellbeing of physicians but also has a detrimental impact on their ability to perform well academically[242]. A study of medical students showed that intolerance of uncertainty can cause significant anxiety, frustration, self-doubt, disillusionment, feelings of inadequacy (not being "good enough"), and insecurity regarding professional skill level[243]. Several studies have shown an association between lower tolerance of uncertainty and increased risk or presence of provider burnout[9,113,147,244] (Figure 2.2) and work-related stress[10-12,245]. Indeed, stress from uncertainty has been shown to be the strongest predictor of work-related stress[245]. When confronted with a clinical situation whose consequences are not easy to predict—and this concerns most medical decision-making—uncertainty intolerant physicians may feel particularly worried and anxious about the implications of their decisions, thus resulting in a feeling of being 'stuck' in the uncertainty and unable to move forward[242].

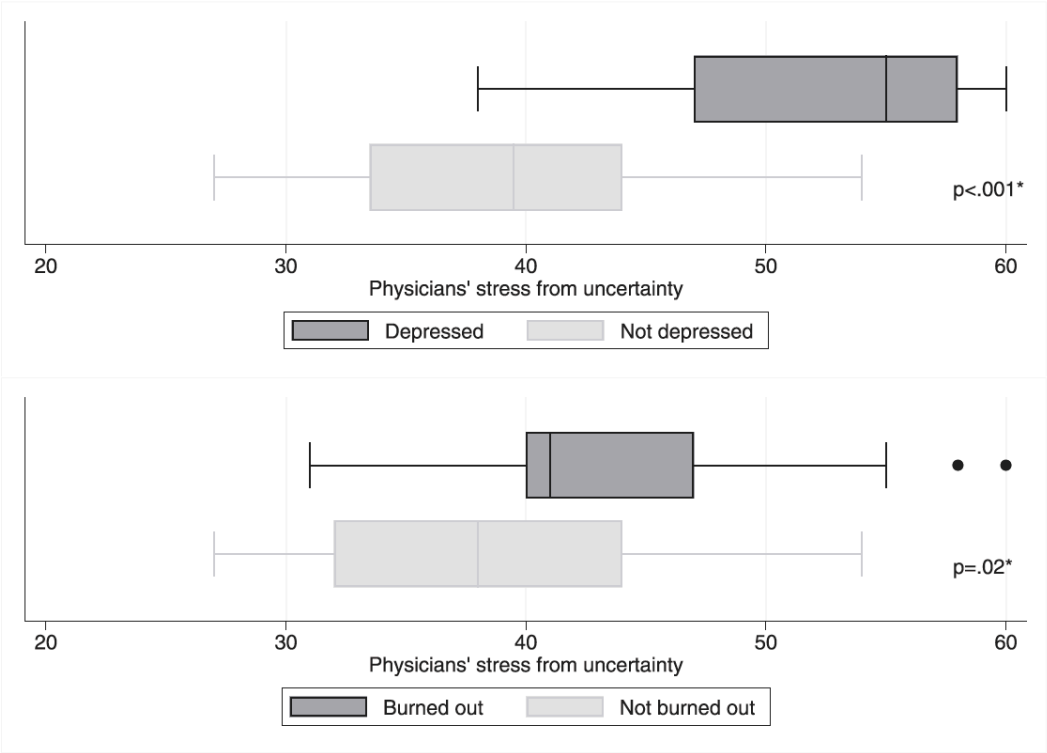

Figure 2.2: Physicians' stress from uncertainty scores for depressed and non-depressed residents and burned out and non-burned out residents adapted from "Stress from Uncertainty and Resilience among Depressed and Burned Out Residents: A Cross-Sectional Study" by Simpkin AL, Khan A, West DC, et al. In Academic Pediatrics, 2018; 18(6): 698-704[9] *(Full paper in Appendix 2.1)*.

In addition, a strong negative correlation has been shown between stress from uncertainty and resilience (r=-.60; p<.001), (Figure 2.3). Resilience is described as an adaptive capability that is born from the interplay between internal disposition and external experience and provides the ability to rebound from adverse events[246]. The role of resilience has been shown to be positively associated with wellbeing, protecting against burnout[9,113,179,247-256].

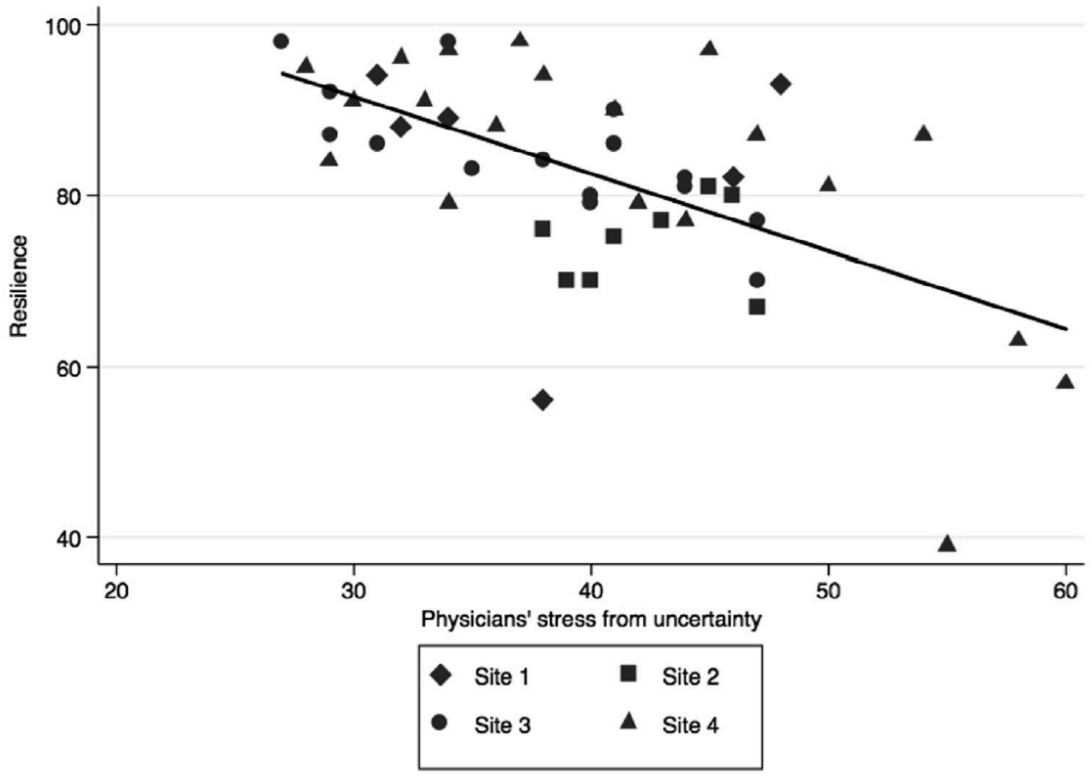

Figure 2.3: Correlation between physicians' stress from uncertainty and resilience adapted from ""Stress from Uncertainty and Resilience among Depressed and Burned Out Residents: A Cross-Sectional Study" by Simpkin AL, Khan A, West DC, et al. In Academic Pediatrics, 2018; 18(6): 698-704[9]
***(Full paper in Appendix 2.1)*.**

As we explored in Chapter 1, burnout is an accelerating phenomenon within healthcare with many proposed theories and a multitude of factors put forward to explain the crisis that has unfolded. Understanding factors associated with burnout is an important step to enhancing physician wellbeing, with downstream consequences for high-quality patient care[1,67,75,80]. We have seen how prevalent uncertainty in healthcare is, and the negative impact that it can have on provider's cognitive, emotional and behavioural outcomes. Stress from uncertainty is increasingly recognised to be a likely catalyst of burnout in healthcare, but unfortunately it is an attribute that has been missing from most studies on burnout. Further work is needed to ascertain the impact tolerance of uncertainty may be having on burnout and to see whether efforts to alleviate stress from uncertainty correlates to improved wellbeing. Future

physicians will undoubtedly need to tolerate, learn, and practice in a new frontier of ever-expanding uncertainty.

2.8 CONCLUSIONS

Research to develop and evaluate interventions to improve tolerance of uncertainty in healthcare is a critically important need given the increasing exposure of both healthcare providers and patients to uncertain situations and information[257]. This chapter has provided an overview of the presence of uncertainty in the healthcare environment and has explored what impacts an individual's tolerance of uncertainty—individual characteristics, cultural influences, and situational/social factors—and how reaction to uncertainty affects provider- and patient-centred outcomes. The prevalence of uncertainty in the healthcare environment has been emphasised, and the correlation between stress from uncertainty and burnout has been highlighted, building on Chapter 1 which provided a synopsis of the broad context of burnout in healthcare. Chapter 1 also explored the challenges that pertain to burnout research, particularly relating to challenges in measurement. A detailed overview of how human reaction to uncertainty affects both wellbeing and medical decision-making has been described, laying the foundation to understand the recent calls to prioritise understanding and embracing uncertainty as a core clinical competency in medical institutions and educational bodies internationally and the hope that by learning to embrace uncertainty we might mitigate burnout.

2.8.1 Aims of thesis

The aims of this thesis are to provide:

- An exploration of concepts:
    - An exploration of burnout in physicians and the role that tolerance of uncertainty plays as a driver of this phenomenon (Chapters 1, 2, and 4)
    - Greater understanding of what affects satisfaction at work, particularly with regard to how perceptions of value and respect impact job satisfaction for faculty in an academic medical centre (Chapter 3)
    - Improved awareness of the effect language used in the healthcare setting may have on medical students' tolerance of uncertainty (Chapter 5)
- An exploration of biology:
    - Greater clarity and pilot data in the use of biomarkers (specifically cortisol and oxytocin) as potential objective measures with clinical meaning for burnout and wellbeing (Chapters 6 and 7)
- An exploration of intervention and proposed strategies:
    - Greater understanding of the effects of an interprofessional group intervention on faculty wellbeing, engagement, and uncertainty (Chapter 8)
    - Enhanced knowledge of the strategies to help healthcare professionals thrive in clinical uncertainty (Chapter 9)

CHAPTER 3: DOCTORS SATISFACTION WITH THEIR WORK: A STUDY IN AN ACADEMIC MEDICAL CENTRE

"To each one of you the practice of medicine will be very much as you make it—to one a worry, a care, a perpetual annoyance; to another, a daily joy and a life of as much happiness and usefulness as can well fall to the lot of man."
Sir William Osler[258]

3.1 INTRODUCTION

As has been explored in the preceding introductory chapters, the academic health care environment has changed in unprecedented ways over several decades, with mounting evidence that faculty are becoming increasingly more unhappy, dissatisfied, and burnt out in their work[21,98,103,259,260]. This international crisis has serious implications for wellbeing, productivity, retention, and consequent quality of care. Although a faculty job can be incredibly fulfilling, it is a role fraught with tremendous responsibility alongside stress arising from accountability and concern for patient outcomes, changes in healthcare delivery and financing, increased competition for declining pools of funding for research and scholarly work, and expectations for innovative learning opportunities to be adopted into practice[85]. Unfortunately, the actual understanding of the origins, consequences, and effective approaches to prevent and treat burnout remain an enigma[95,128]. Comprehending what affects satisfaction at work in academic healthcare centres is critically important to stem this epidemic of discontent. For physicians, satisfaction has been reported to be associated with quality of care delivered, particularly as measured by patient satisfaction[6,261]; faculty retention and job satisfaction are intricately linked, with dissatisfied physicians more likely to leave the profession and to discourage others from entering[69,262-264].

Academic medical centres have a tripartite mission to provide high quality clinical care, to advance knowledge through research, and to train the next generation of healthcare providers. As the introductory chapter laid out, a multitude of factors have been put forward to try to explain what is causing the burnout crisis, with external factors and competing pressures from these domains often blamed for the rising discontent[84]. Physicians commonly attribute their discontent to managed care and changes in the practice environment with technological reform that has seen increased time spent in front of computer screens rather than in personal patient encounters[121,122]. Studies also cite increasing bureaucracy, loss of autonomy, diminished prestige, and a rising tide of medical-malpractice litigation as further reasons for burnout[259,265]. For researchers, National Institutes of Health (NIH) funding rates have decreased from 30% to now less than 20%[266] and the median age of the first independent federal grant has increased from 36 years old in the 1980s to nearly 45 today[267]. Given today's economic realities, academic faculty face the dual pressures of decreased support for teaching and increased demands for clinical and research productivity[260].

But, perhaps what underpins it all, driving the discontent and dissatisfaction, is a lack of feeling respected, valued and supported, with the current healthcare environment at risk of taking for granted the human capital which forms the foundation of the system and, unintentionally, cultivating loneliness and isolation[268]. In an age of increasing isolation and lack of continuity with shift systems breaking up team structure, shorter hospital stays, work-hour demands and fragmentation of patient care, and technology promoting physical disconnection (with collaborative research often occurring via conference call rather than in-person meetings), intentional efforts to establish and nurture social and supportive environments are more important than ever.

In a recent survey of nearly 20,000 employees worldwide, respondents ranked respect as the most important leadership behaviour, yet employees report increasing levels of disrespectful and uncivil behaviour each year[269]. Employees who say they feel respected are more satisfied with their jobs and more grateful for—and loyal to—their companies. Academic medicine should be no exception. It has been suggested that those in high-status roles, such as institutional leaders, feel respected regularly and can therefore be blinded to the disconnect with their employees yearning to also feel that respect[269]. Recognising this desire and understanding what constitutes respect and a sense of feeling valued for all faculty are early steps to ensure it is woven into the workplace culture.

To our knowledge the impact of sense of respect, value, and social community on satisfaction has not been looked at in academic faculty members. The questions asked in the study described in this chapter were designed to address this gap:

- Primary outcome: What are the key variables influencing satisfaction at work for faculty in large academic medical centres?
- Secondary outcome: What are the key variables influencing a sense of feeling valued for faculty in large academic medical centres?

3.2 METHODS

3.2.1 Study Design

We conducted a cross-sectional survey of faculty in the Department of Medicine (DOM) at the Massachusetts General Hospital (MGH), a large teaching hospital in the United States (US) affiliated with Harvard Medical School (HMS) to examine the culture of workplace respect, value, collegiality, satisfaction, and mentoring[270]. Data were collected in June 2016.

3.2.2 Participants and recruitment

All faculty in the DOM holding full-time appointments at MGH and HMS were invited to participate. The DOM faculty affairs database provided contact details for eligible MGH faculty to allow dissemination of the survey through email. Of the faculty identified in the databases, we identified 988 holding full-time faculty appointments in the MGH DOM and HMS. Precautions were taken to secure confidentiality. We received Partners Healthcare Human Subjects Committee Exemption (Protocol Number 2016P000935).

3.2.3 Survey Instrument and Variables

Participants completed a 12-page, 15-minute online survey (full survey included as Appendix 3.1). Survey items were developed in one of three ways: some were taken from previously administered faculty surveys; some were modified from existing items; and some were developed *de novo*. Survey domains included: personal and professional characteristics (e.g. gender, race, academic rank, and degrees); overall professional satisfaction (with regard to position, workplace, and division leadership); sense of feeling valued; collegiality and collaboration; together with other domains relating to mentoring reported elsewhere[270]. The

race variable was grouped into two categories—under-represented minority in medicine or non-under-represented minority in medicine (white/Asian). Gender was also collapsed into two categories—male or female. Questions of gradation were rated on a 5-point Likert scale. While we inquired about many aspects of job satisfaction, we measured job satisfaction with the single global survey item, "Overall how satisfied are you with your current position at MGH?". Responses from the 5-point Likert scale (very unsatisfied, unsatisfied, neither, satisfied, very satisfied) were collapsed to three categories for analysis: strongly satisfied, somewhat satisfied, and not satisfied (inclusive of all other answers). The extent to which participants agreed with the statement "the leadership values what I do" was reduced from strongly agree, somewhat agree, neither agree nor disagree, somewhat disagree, strongly disagree to 3 categories: strongly agree, somewhat agree, disagree.

3.2.4 Data Collection

The secure, web-based application, Research Electronic Data Capture (REDCap), was used to manage survey distribution and collect responses[271]. Each participant received an individualised link to the survey; no incentives were offered. The initial email was sent on June 1, 2016, with weekly reminders sent to non-respondents until the survey closed on June 30, 2016. Identifying information linking faculty to their individual survey data was destroyed, ensuring it is impossible to identify respondents or to link them to their survey answers.

3.2.5 Outcome Measures

For analysis, we first considered the variables associated with the single question about satisfaction with current position (primary outcome). We considered variables that might

have potential associations with this outcome including, but not limited to personal and professional characteristics; sense of feeling valued; and collegiality and collaboration. Next, given the strong association we found with satisfaction and "feeling valued", we sought the association of feeling valued with personal and professional characteristics; and feelings towards availability of resources, compensation, and personal discrimination, among others.

3.2.6 Statistical Analysis

Standard descriptive statistics were used to characterise the sample. We assessed for relationships between outcome variables and other variables using Chi-square tests in bivariate analyses. In multivariable analyses, we dichotomised the two outcomes using logistic regression models to predict the likelihood of strongly satisfied or strongly agree. We included only those with a bivariate $p<0.1$ in the model and tested the independent effects of each variable. A two-sided p value <0.05 was considered as statistically significant. Analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC).

3.3 RESULTS

3.3.1 Characteristics of the participants

The overall response rate was 56% (553 faculty among 988 eligible participants). Of the respondents 55.7% were male, corresponding to the proportion of male faculty in the MGH DOM (57.8%); 44.6% were instructors, 30.4% assistant professors, 14.4% associate professors, and 10.6% professors, in line with departmental rank distribution. Three quarters of the respondents reported being satisfied or very satisfied with their current position, 76.3% of faculty felt treated with respect, and 71.6% of faculty felt valued (Table 3.1).

	RESPONDENTS (N=553)		MGH DOM* (N=988)
	N	% †	%*
DEMOGRAPHIC CHARACTERISTICS:			
Gender*			
Male	308	55.7	57.8
Female	245	44.3	42.2
Race			
Non-minority‡	514	94.0	-
Minority	33	6.0	-
PROFESSIONAL CHARACTERISTICS:			
Rank*			
Instructor	245	44.6	50.3
Assistant Professor	167	30.4	26.1
Associate Professor	79	14.4	13.9
Professor	58	10.6	9.7
Degree			
MD/PhD	46	8.3	-
MD+	427	77.4	-
PhD+	71	12.9	-
Other	8	1.4	-
SATISFACTION:			
With current position			
Strongly satisfied	158	31.5	-
Somewhat satisfied	218	43.5	-
Not satisfied or neutral	125	25.0	-
RESPECT AND VALUE:			
Feel treated with respect			
Strongly agree	231	46.5	-
Somewhat agree	148	29.8	-
Disagree or neutral	118	23.7	-
Feel valued			
Strongly agree	181	36.2	-
Somewhat agree	177	35.4	-
Disagree or neutral	142	28.4	-

Table 3.1: Characteristics of the participants

MGH: Massachusetts General Hospital, DOM: Department of Medicine
* For the DOM population, gender and rank were from the faculty affairs tracking database; race and degree were not available from this database. For the survey respondents, gender and rank were from survey responses, supplemented (i.e. missing data) by tracking database. † Percentages among respondents to each characteristic question ‡ Non-minority includes Whites and Asians

3.3.2 Satisfaction with Current Position

In bivariate analyses, many parameters were significantly associated with faculty satisfaction with current position; these include: gender, rank, feeling valued by leadership, feeling treated with respect by the DOM, feeling cared about as a person by division leadership, working in a social and supportive environment, feeling comfortable raising personal and/or family responsibilities, and socially interacting with colleagues after work. Rates of satisfaction did not vary significantly by minority status or by degrees obtained (Table 3.2, Left).

In multivariable analyses, faculty who strongly felt valued for what they do had a nearly 5-fold increased odds (odds ratio[OR], 4.73; 95% CI, 2.35-9.51) of being very satisfied with their current position. Faculty who strongly agreed with the statement that they are treated with respect by the DOM had a 3.5-fold increased association (OR, 3.45; 95% CI, 2.07-5.75) with being very satisfied in their role. Feeling a strong sense of working in a social and supportive environment was associated with almost a 2-fold increased association (OR, 1.80; 95% CI, 1.05-3.09) with strong satisfaction. Importantly, there was no significant difference in satisfaction relative to gender or rank after controlling for other variables (Table 3.2, Right).

	BIVARIATE ANALYSIS				MULTIVARIATE ANALYSIS#		
	Not satisfied,* N (%)	Somewhat satisfied, N (%)	Strongly satisfied, N (%)	p-value	OR	95% CI	p-value
Gender							
Female	63 (29.0)	101 (46.5)	53 (24.4)	0.009	Ref		
Male	62 (21.8)	117 (41.2)	105 (37.0)		1.53	0.93-2.52	0.094
Race							
Non-minority	115 (24.6)	204 (43.6)	149 (31.8)	0.96	-	-	-
Minority	8 (26.7)	13 (43.3)	9 (30.0)		-	-	-
Rank							
Instructor	63 (28.3)	93 (41.7)	67 (30.0)	0.002	Ref		
Assistant Professor	45 (29.6)	69 (45.4)	38 (25.0)		0.76	0.43-1.35	0.34
Associate Professor	10 (14.5)	35 (50.7)	24 (34.8)		0.94	0.46-1.95	0.88
Professor	7 (12.5)	20 (35.7)	29 (51.8)		1.63	0.74-3.56	0.22
Degree							
MD/PhD	11 (24.4)	19 (42.2)	15 (33.3)	0.79	-	-	-
MD+	93 (24.5)	167 (43.9)	120 (31.6)		-	-	-
PhD+	20 (29.4)	28 (41.2)	20 (29.4)		-	-	-
Other	0 (0.0)	4 (57.1)	3 (42.9)		-	-	-
Feel valued by leadership							
Disagree / neutral	118 (37.5)	151 (47.9)	46 (14.6)	<0.0001	Ref		
Strongly agree	7 (3.9)	64 (35.4)	110 (60.8)		4.73	2.35-9.51	<0.0001
Feel treated with respect by the DOM							
Disagree / neutral / somewhat agree	102 (38.9)	124 (47.3)	36 (13.7)	<0.0001	Ref		
Strongly agree	18 (8.0)	88 (39.1)	119 (52.9)		3.45	2.07-5.75	<0.0001
Feel cared about as a person by division leadership							
Disagree / neutral / somewhat agree	113 (36.2)	142 (45.5)	57 (18.3)	<0.0001	Ref		
Strongly agree	12 (6.4)	76 (40.6)	99 (52.9)		0.85	0.42-1.70	0.64
Work in social and supportive environment							
Disagree / neutral / somewhat agree	107 (35.0)	141 (46.1)	58 (19.0)	<0.0001	Ref		
Strongly agree	16 (8.8)	70 (38.5)	96 (52.7)		1.80	1.05-3.09	0.034
Feel comfortable raising personal and/or family responsibilities							
Disagree / neutral / somewhat agree	109 (31.2)	162 (46.4)	78 (22.3)	<0.0001	Ref		
Strongly agree	15 (10.6)	50 (35.2)	77 (54.2)		1.59	0.92-2.77	0.099
Socially interact with colleagues after work hours							
Disagree / neutral / somewhat agree	118 (26.7)	192 (43.4)	132 (29.9)	0.005	Ref		
Strongly agree	5 (11.4)	16 (36.4)	23 (52.3)		1.16	0.50-2.65	0.73

Table 3.2: Satisfaction with current position

*Included all responses of very unsatisfied, unsatisfied, or neither satisfied nor unsatisfied; #Dichotomized outcome predicting strongly satisfied

3.3.3 Feeling Valued at Work

In bivariate analyses, several parameters were significantly associated with feeling valued at work: feeling cared about as a person by division leadership, not feeling taken for granted on a regular basis, not feeling career had been hampered by discrimination related to race or gender, feeling resources were provided for professional growth, feeling fairly compensated, and feeling able to easily schedule meetings with a supervisor (Table 3, Left).

In the multivariable model, feeling strongly cared about as a person was associated with a 28-fold increased likelihood of feeling valued (OR, 28.0; 95% CI, 15.3-51.3), while not feeling being taken for granted on a regular basis was associated with a 4.5-fold increased rate of feeling valued (OR, 4.52; 95% CI, 2.28–8.97). Faculty who felt their leadership provided resources for professional growth were more than twice as likely to feel valued (OR, 2.38; 95% CI, 1.16-4.89). Faculty who did not feel their career had been hampered by discrimination related to gender were twice as likely to feel valued for their work (OR, 2.29; 95% CI, 1.02-5.16). There was no significant association in feeling valued relative to feeling compensated fairly, or to ability to schedule meetings with a supervisor after controlling for other variables (Table 3, Right).

	BIVARIATE ANALYSIS				MULTIVARIATE ANALYSIS#		
	Disagree,* N (%)	Somewhat agree, N (%)	Strongly agree, N (%)	p-value	OR	95% CI	p-value
Gender							
Female	61 (27.9)	85 (38.8)	73 (33.3)	0.33	-	-	-
Male	81 (28.8)	92 (32.7)	108 (38.4)		-	-	-
Race							
Non-minority	129 (27.8)	164 (35.3)	171 (36.9)	0.70	-	-	-
Minority	11 (34.4)	11 (34.4)	10 (31.3)		-	-	-
Rank							
Instructor	58 (25.7)	90 (39.8)	78 (34.5)	0.14	-	-	-
Assistant Professor	50 (33.6)	49 (32.9)	50 (33.6)		-	-	-
Associate Professor	18 (26.1)	26 (37.7)	25 (36.2)		-	-	-
Professor	16 (29.1)	12 (21.8)	27 (49.1)		-	-	-
Degree							
MD/PhD	11 (24.4)	14 (31.1)	20 (44.4)	0.93	-	-	-
MD+	110 (29.0)	136 (35.9)	133 (35.1)		-	-	-
PhD+	18 (26.5)	24 (35.3)	26 (38.2)		-	-	-
Other	2 (28.6)	3 (42.9)	2 (28.6)		-	-	-
Feel cared about as a person by division leadership							
Disagree / neutral / somewhat agree	137 (43.4)	149 (47.2)	30 (9.5)	<0.0001	Ref		
Strongly agree	5 (2.7)	28 (15.2)	151 (82.1)		28.0	15.3-51.3	<0.0001
Leadership takes me for granted on a regular basis							
Disagree / neutral / agree	129 (34.9)	159 (43.0)	82 (22.2)	<0.0001	Ref		
Strongly disagree	12 (9.5)	17 (13.5)	97 (77.0)		4.52	2.28-8.97	<0.0001
Career hampered by discrimination related to gender							
To a great/some extent	51 (51.0)	32 (32.0)	17 (17.0)	<0.0001	Ref		
Very little/not at all	90 (22.6)	144 (36.2)	164 (41.2)		2.29	1.02-5.16	0.046
Career hampered by discrimination related to race							
To a great/some extent	17 (68.0)	5 (20.0)	3 (12.0)	<0.0001	Ref		
Very little/not at all	123 (26.1)	171 (36.2)	178 (37.7)		0.73	0.16-3.28	0.68
Leadership provides resources for professional growth							
Disagree / neutral / somewhat agree	133 (34.5)	156 (40.4)	97 (25.1)	<0.0001	Ref		
Strongly agree	8 (7.1)	21 (18.8)	83 (74.1)		2.38	1.16-4.89	0.018
Leadership compensates me fairly							
Disagree / neutral / somewhat agree	127 (32.2)	150 (38.0)	118 (29.9)	<0.0001	Ref		
Strongly agree	14 (13.6)	27 (26.2)	62 (60.2)		1.38	0.65-2.92	0.40
Scheduling meeting with supervisor							
Not at all / not very difficult	74 (22.6)	123 (37.6)	130 (39.8)	0.001	1.24	0.48-3.16	0.66
Somewhat/very/extremely difficult	24 (36.4)	25 (37.9)	17 (25.8)		Ref		
No supervisor	38 (42.2)	23 (25.6)	29 (32.2)		1.49	0.52-4.29	0.46

Table 3.3: Feel valued at work

*Included all responses of strongly disagree, somewhat disagree, or neither disagree nor agree; #Dichotomized outcome predicting strongly agree

3.4 DISCUSSION

In this cross-sectional study that included 988 faculty in the department of medicine at a large academic medical centre, job satisfaction was significantly associated with feeling valued, feeling treated with respect, and working in a social and supportive environment. It was not associated with gender, race, rank, or feeling fairly compensated financially. At a time when much attention is being directed at understanding what impacts faculty wellbeing, this study identifies some clear targets, amenable to change, for leadership and healthcare administrators to boost satisfaction at work. This is critical for the wellbeing of faculty, and for academic medical centres to thrive in all stated missions—clinical care, research, and education.

Human connection and the development of meaningful, genuine relationships are undoubtedly deeply rooted in our evolution and perhaps unsurprisingly, therefore, a sense of feeling valued, feeling cared about, feeling a sense of working in a social and supportive environment, and interacting socially with colleagues after work hours appears to be associated with a sense of satisfaction at work. Linked to this was a substantial, though not significant, correlation with satisfaction and feeling comfortable raising personal or family issues at work. In a high-stress, high-responsibility profession, the ability to share concerns and vulnerabilities is essential in nurturing wellbeing and mitigating against burnout. A challenge of the fast-paced, technology-driven environment that is rapidly growing around us, is the imperative to stay connected personally (and not electronically) and reduce isolation. This will be ever-more critical in the years ahead.

Studies have shown the beneficial effect of building community through, for example, faculty dinners; these activities result in an enhanced work engagement, enhanced satisfaction, and

decreased burnout[272]. Social capital is key. A sense of feeling valued was very strongly associated with feeling cared about by leadership, not feeling taken for granted, not feeling discriminated against, and having a supervisor to meet with—modifiable factors for all organisations that require relational, rather than financial, investment. In a rapidly changing world, dissatisfaction is not isolated to the healthcare profession. Other industries that have suffered similar rises in employee discontent have also found that demonstration of respect is the most important leadership behaviour in improving employees satisfaction[269].

Although much attention has been paid to gender gaps in medicine—in salary[273,274], in career advancement[275], and in leadership positions[276]—with the assumption that this drives much dissatisfaction and lack of retention among women, we did not see a significant association between gender or rank and satisfaction at work in the multivariate analysis. Similarly, there was no association between gender or rank and sense of feeling valued. This, of course, does not suggest that we should ignore the urgent call to close these gaps and promote equity in the workplace. But it highlights that if we believe that fixing these gaps alone will improve job satisfaction, we may be disappointed. Feelings of gender discrimination were associated with not feeling valued, and there is no doubt that it is imperative that leaders take measures to align and embed the values of diversity, inclusion, and respect into institutional policies[277]—recognising that discrimination, often considered an individual problem, is also an organisational one[278]. Research shows that employees who experience discrimination are more likely to depart their institutions, or leave their fields altogether, driving talented individuals out of organisations[279]. Leaders should stress that unacceptable discrimination includes not just overt expressions of misogyny and bigotry but also subtle acts of disrespect—broadening employee's conceptualisations of what it means to be unbiased and professional[280].

While value typically has an economic connotation, we did not see an association between feeling valued and feeling financially compensated fairly. This important negative finding suggests that, contrary to popular belief, financial incentives may not be effective alone in boosting satisfaction in the workplace. Compensation has previously been reported to be an important factor in faculty satisfaction[281,282], yet our results suggest wiser investments would be in social, not financial, capital.

3.4.1 Limitations

This study has several limitations. First, our results are subject to the inherent selection and reporting biases that often occur in survey studies. To minimise any social desirability biases, results were collected in a de-identified and confidential manner. In addition, participants were unaware of the specific hypothesis of this study, and we have no information to suggest that they would have chosen to participate or not on the basis of their degree of job satisfaction. Our response rate of 56% is similar to other studies of physicians[283], and the rate of male and female and academic rank respondents mirrored the Department of Medicine faculty demographics. Second, our results may not be generalisable beyond the Department of Medicine at MGH, although there is no reason to postulate that similar predictors of satisfaction would be unique to this specialty or this academic health centre. Nevertheless, further studies are needed to confirm our findings in other specialties and other hospital and academic settings. Due to the design of our study, we are careful to only test for associations and do not draw conclusions about causality from our findings alone.

3.5 CONCLUSIONS

The results from this study resonate with the challenges faced in healthcare environments described in the introductory chapter that may be driving burnout. To promote a high-performing academic faculty workforce in a rapidly changing healthcare system, medical practices and hospital systems need to pay more attention to relational connection and sense of community, which have implications for the wellbeing of faculty and patients. Critical to enhancing satisfaction at work is assessing and promoting a sense of value and respect in the work environment, identifying and eliminating sources of discrimination, and intentionally boosting collegiality. As we think about the urgent call to alleviate burnout, efforts focused in the domain of social capital seem vital. The good news is that there is much that is amenable to change, and large sums of money may not be required to begin the fix.

In this study we have looked at the association between job satisfaction, personal and professional characteristics, and perceptions of leadership, diversity, collegiality and collaboration in faculty at a large academic medical centre. As we explored in the introductory chapter on burnout, physicians across the educational continuum—undergraduate, graduate, and continuing medical education—appear to be at risk from this devastating phenomenon, with a worrying increase being seen in medical students and trainees[21-23]. As Chapter 2 highlighted, the ability to manage uncertainty has been identified as a potentially important determinant of burnout in physicians[9,113,147,244], and doctors' maladaptive responses to uncertainty are known to contribute to work-related stress[10-12]. Unfortunately, reaction to uncertainty is an attribute that has been missing from most studies on burnout. The next chapter will examine the impact stress from uncertainty may have on burnout in physicians across specialties, examining factors associated with physician tolerance of uncertainty to attempt to expand our understanding in this important area.

CHAPTER 4: ANALYSIS TO UNDERSTAND FACTORS ASSOCIATED WITH PHYSICIAN TOLERANCE OF UNCERTAINTY

"A distressing feature in the life of which you are about to enter … is the uncertainty which pertains not alone to our science and art, but also to the very hopes and fears which make us men. In seeking out the absolute Truth we aim at the unattainable, and must be content with finding broken portions"
Sir William Osler[258]

4.1 INTRODUCTION

While the previous chapter focused on identifying key variables influencing satisfaction at work for faculty in an academic medical centre, with a particular focus on the impact of sense of respect, value, and social community, this chapter will explore the impact stress from uncertainty may have on burnout in physicians. Examining factors associated with burnout is an important step to enhancing physician wellbeing, with downstream consequences for high-quality patient care[1,67,75,80]. Understanding and acknowledging uncertainty and acquiring proper coping strategies is now regarded as one of the core clinical competencies for medical graduates and trainees in the UK, US, Australia, and much of Europe[284-290], but there is still much about tolerance of uncertainty that is not understood. In particular, findings related to associations between tolerance of uncertainty and sociodemographic characteristics have been inconsistent, with discrepancies in studies looking at tolerance of uncertainty in relationship to age, gender, and other personal and professional characteristics[182-185,187-189]. Additional work to ascertain how sociodemographic characteristics may be associated with varying levels of tolerance of uncertainty is needed. To address the research gap, this chapter examines the factors associated with physician tolerance of uncertainty, including wellbeing metrics such as burnout, in a large multispecialty academic physician practice organisation.

The research presented builds on a small pilot study (presented in full in Appendix 4.1) that explored the impact stress from uncertainty may have on burnout in sub-specialty medicine fellows.

4.1.1 Challenge of studies to date

As we explored in the opening two chapters, the ability to manage uncertainty has been identified as a potentially important determinant of burnout in physicians[9,113,147,244], but unfortunately it is an attribute that has been missing from most studies on burnout, with further research required to ascertain the impact stress from uncertainty may be having on burnout. Understanding individual differences in people's responses to—or tolerance of—uncertainty is an increasingly important focus of research, but studies to date have been mainly small-scale and single specialty, limiting the generalisability of the findings to the wider population of healthcare professionals. As with any survey study there have also been challenges with response rates, with the potential for selection bias in those who participate. To get the detailed and complete information about burnout and its association with tolerance of uncertainty, a study is required that can balance granular survey data with near-complete response and minimal missing data together with a large, diverse physician population to support external validity of the results.

4.1.2 Pilot study in sub-specialty medicine fellows

In prelude to the larger multispecialty physician study described in this chapter, we carried out a small, pilot study exploring the impact stress from uncertainty may have on burnout in sub-specialty medicine fellows. A fellow is a fully credentialled physician who has completed their residency and elects to complete further subspecialty training. No prior

studies have evaluated the association of fellows' reaction to uncertainty with burnout metrics, despite fellows being a vulnerable population at high risk of burnout due to unique challenges pertinent to this final stage of training (such as increased responsibility, pressure to enter the job market, and loss of the team structure that can define residency programmes) which add to the intrinsic challenge of handling uncertainty in the clinical learning environment[8]. In 2017 the Accreditation Council for Graduate Medical Education (ACGME) changed their common programme requirements to include provisions for wellbeing and burnout prevention in accredited fellowship training programmes, reflecting the urgent need for this to be brought to the top of hospital priority lists[284].

All sub-specialty fellows in the Department of Medicine (DOM) at the Massachusetts General Hospital (MGH), a large academic medical centre, were invited to participate in a cross-sectional online survey examining reaction to uncertainty together with several validated wellbeing scales (resilience, engagement, empowerment, and burnout). As Table 4.1 demonstrates, female fellows, those less than 30 years of age, and graduates of US medical schools were found to have significantly higher stress from uncertainty. As suggested in prior literature, stress from uncertainty was positively associated with burnout and inversely associated with resilience, work engagement, and work empowerment (Table 4.2). Full details of this study can be found in Appendix 4.1.

SAMPLE CHARACTERISTICS	REACTION TO UNCERTAINTY MEAN (SD)	P VALUE
PERSONAL CHARACTERISTICS:		
Sex		
Male	38.1 (11.2)	0.002
Female	44.9 (9.7)	
Age		
<= 30 years	47.0 (6.3)	0.006
> 30 years	39.6 (11.5)	
Marital status		
Single / Separated	41.6(10.0)	0.68
Married/Live with partner	40.6(11.7)	
PROFESSIONAL CHARACTERISTICS:		
Medical school		
US med school	42.3 (10.9)	0.03
International med school	36.1 (10.6)	
Residency		
US residency	41.5(11.0)	0.22
International residency	35.2(10.8)	
Year of fellowship		
Year 1	40.2 (10.0)	0.29
Year 2	42.3 (11.3)	
Year 3	42.3 (11.5)	
Year 4	45.0 (27.1)	
WELLBEING METRICS:		
Resilience		
High	37.0 (9.4)	0.001
Low	46.1 (12.4)	
Burn Out		
High	43.8 (10.8)	0.036
Low	39.2 (10.4)	

Table 4.1: Stress from uncertainty and personal and professional characteristics

PRIMARY VARIABLE	OUTCOME VARIABLE	CORRELATION (R)	P VALUE
Stress from uncertainty	**Burnout**	+ 0.29	0.004
	Resilience	- 0.38	< 0.0001
	Work engagement	- 0.26	0.009
	Work empowerment	- 0.37	0.003

Table 4.2: Associations between stress from uncertainty and wellbeing metrics

Of the 317 eligible participants, 102 (32%) completed the reaction to uncertainty scale, resulting in a large amount of missing data. In addition, all participants were fellows from the DOM preventing analysis across level of experience and across specialty. The results from this small-scale pilot study do, however, support further robust research in this space, and allowed me to apply to add a question on tolerance of uncertainty to a large, multispecialty physician survey with a near-complete response rate, that was being conducted to understand physician perceptions of the functioning of the clinical enterprise within and across departments. The large, diverse physician population with minimal missing data counters the limitations of both the study described above and previous published research studies in this space allowing for a robust analysis of the factors associated with physician tolerance of uncertainty.

4.1.3 Chapter aims

The study presented in this chapter aims to:

- Examine the sociodemographic factors (personal and professional) associated with physician tolerance of uncertainty;
- Examine the association of tolerance of uncertainty with wellbeing metrics such as burnout.

4.2 METHODS

4.2.1 Study design

We conducted a cross-sectional survey of 2,172 faculty in the Massachusetts General Physicians Organisation (MGPO), the largest multi-specialty medical group in New England and one of the largest in the US, to examine the factors associated with physician tolerance of uncertainty, particularly with respect to wellbeing metrics. Data were collected in May and June 2019 as part of the biennial MGPO Physicians Survey to understand physician perceptions of the functioning of the clinical enterprise within and across departments, reflecting progress made on organisational priorities, and evaluating hospital leadership[291-293].

4.2.2 Participants and recruitment

All clinically active physician members of the MGPO who generate more than 50 relative value units over six months were invited to participate[294]. To protect physician confidentiality, only one analyst had access to unblinded data behind a firewall and analyses were reported without individual identifiers. All data were thus strictly anonymised so physician leaders and other administrators cannot identify respondents or link them to their survey answers. The Mass General Brigham Institutional Review Board approved this study (protocol number: 2014P002779).

4.2.3 Survey instrument and variables

Participants completed a 30-minute online survey (full survey available in Appendix 4.3). Survey items were developed in one of three ways: some were taken from previously administered faculty surveys; some domains used validated scales; and some were developed

de novo using literature review and expert interviews to develop questions. Survey domains included: personal and professional characteristics (e.g. gender, race, ethnicity, years of experience, specialty, and having a trusted advisor); and physician wellbeing metrics (e.g. overall career satisfaction, burnout, tolerance of uncertainty, work engagement, professional fulfilment, and peer support); together with other domains pertaining to compensation, administrative workload on physicians, and leadership and diversity content[291-293]. All methods for the survey are in compliance with the American Association for Public Opinion Research (AAPOR) reporting guideline for survey studies[295].

4.2.3.1 Tolerance of uncertainty

Tolerance of uncertainty was measured using the single-item, "I find the uncertainty involved in patient care disconcerting", adapted from the 15-item Physicians' Reaction to Uncertainty Scale, originally developed by Gerrity et al[175]. This single item has been shown to stratify tolerance of uncertainty in physicians[296-298], and is often used in surveys addressing multiple content areas within space constraints where use of the full scale is limited by its length. It ranges from 1–5, with 5 signifying the greatest discomfort from uncertainty (or lowest tolerance of uncertainty). For our analysis, we constructed a binary outcome where strongly agree, moderately agree, or neither agree or disagree are defined as low tolerance of uncertainty and moderately disagree and strongly disagree are defined as high tolerance of uncertainty. As a sensitivity analysis, we also constructed three categories of tolerance of uncertainty: high (strongly disagree or moderately disagree to uncertainty); medium (neither agree or disagree to uncertainty); and low (strongly agree or moderately agree to uncertainty) (Appendix 4.4 – 4.6).

4.2.3.2 Burnout

Burnout was measured using the 16-item Maslach Burnout Inventory-General Survey (MBI-GS), a validated instrument widely used to assess physician burnout[14]. Per the MBI manual, respondents with scores of greater than or equal to 3.2 on the exhaustion subscale, greater than or equal to 2.6 on the cynicism subscale, or less than or equal to 3.8 on the professional efficacy subscale were defined as having high levels of burnout in that particular scale[14]. For our analysis, we used a binary overall burnout measure defined as scoring high in two of the three scales of the MBI-GS. To understand potential implications of this analytic method on our results, as a sensitivity analysis, we examined a continuous measure (average score) for individual burnout scales separately (Appendix 4.5 and 4.6).

4.2.3.3 Work engagement

Work engagement was measured using the Utrecht Work Engagement Scale to measure work engagement—a positive work-related state of fulfilment that is characterised by vigour, dedication, and absorption[299] (a total of 9 items on a 6-item Likert scale ranging from "never" to "daily"; range 0-54). This scale has been extensively validated in various occupational groups, including physicians[300]. As recommended for this tool, we calculated mean scores for total work engagement.

4.2.3.4 Overall career satisfaction

Overall career satisfaction was measured using a 5-point Likert scale (very satisfied, satisfied, neutral, dissatisfied, or very dissatisfied) to the question "How satisfied are you with your career as a physician?" that has been used in several surveys with physicians[292,293]. For this analysis we constructed a binary outcome with satisfied and very satisfied defined as

satisfied. Having a trusted advisor is a five-point Likert scale question assessing whether they have a trusted advisor with whom they can discuss career goals and career satisfaction. For easier interpretation, we regrouped the responses into three categories: agree (strongly agree and agree), neutral, and disagree (strongly disagree and disagree).

4.2.4 Data collection

The MGPO Quality Incentive Program database provided emails for eligible faculty. A secure, web-based application, Qualtrics (Provo, Utah), was used to manage survey distribution and collect responses through email. Each participant received an individualised link to the survey. The initial email was sent on May 13, 2019, with four reminders sent to non-responders until the survey closed on July 3, 2019. Eligibility for the incentive programme is based on percentage of time physicians spend on clinical activity. Physicians earned a financial incentive for completion of the survey[291,292]. Incentive amount for completing the survey ranges from $166.67 to $833.34 depending on the physician's amount of clinical activity. This substantial financial incentive has been associated with greater than 90% of physicians answering the survey[293] and aims to assure high response rate, minimising potential threats to validity of survey data from differential missing data to help guide the organisation's work moving forward. Physicians are asked to consent to survey participation on the cover letter inviting them to participate.

4.2.5 Statistical analysis

Standard descriptive statistics were first used to characterise the sample. We used Chi-square test, t-test, and one-way ANOVA to compare outcomes across categories, as appropriate. Multivariable regressions were used to examine the association of demographic and

professional factors with outcome measures. Tolerance of uncertainty was specified as a function of gender, race, ethnicity, experience (years since training), medical specialty, and having a trusted advisor. Physician wellbeing models were specified as a function of gender, race, ethnicity, experience, medical specialty, and tolerance of uncertainty. For binary outcomes logistic regression was used, for ordinal outcomes ordered logistic regression was used, and for continuous outcomes generalised linear models were used. A significance level of 0.05 was used to establish statistical significance and regression results are reported as odds ratio (OR) or rate ratio (RR) depending on the nature of outcome measure. All statistical analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, North Carolina).

4.3 RESULTS

4.3.1 Characteristics of the participants

The overall response rate was 93% (2,020 faculty among 2,172 eligible participants). Five responses were excluded due to missing data. Of the respondents, 993 (49.3%) were male; 1379 (68.4%) were white; 1919 (95.2%) were non-Hispanic; 1186 (58.9%) practiced a medical sub-specialty; 868 (43.1%) had 10 or fewer years of experience since training; and 998 (49.5%) had a trusted advisor (Table 4.3).

SAMPLE CHARACTERISTICS	RESPONDENTS (N=2,015) N (%) *
PERSONAL CHARACTERISTICS:	
Gender	
Female	905 (44.9)
Male	993 (49.3)
Prefer not to say	117 (5.81)
Race	
Asian	316 (15.7)
Black	44 (2.2)
White	1379 (68.4)
Others	95 (4.7)
Prefer not to say	181 (9.0)
Ethnicity	
Non-Hispanic	1919 (95.2)
Hispanic	96 (4.8)
PROFESSIONAL CHARACTERISTICS:	
Experience (years since training)	
<=10	868 (43.1)
11-20	563 (27.9)
21-20	357 (17.7)
>30	227 (11.3)
Specialty	
Emergency medicine, radiology, anaesthesia, and pathology	346 (17.2)
Medical subspecialties	1186 (58.9)
Primary care	294 (14.6)
Surgical specialties	189 (9.4)
Having a trusted advisor	
Disagree	617 (30.6)
Neutral	400 (19.9)
Agree	998 (49.5)

Table 4.3: Characteristics of the participants

* These percentages represent distribution of respondents within each characteristic question

4.3.2 Tolerance of uncertainty and sociodemographic characteristics

In bivariate analyses, we found significant difference in the distribution of low tolerance of uncertainty by gender (χ^2=16.9, p<0.001), race (χ^2=29.0, p<0.001), experience (χ^2=12.5, p=0.006), and specialty (χ^2=11.4, p=0.01). Females; Asian race; those with less than ten years' experience; and those in primary care had lower tolerance of uncertainty. Tolerance of uncertainty was not associated with ethnicity (χ^2=0.06, p=0.800) or with whether the physician had a trusted advisor (χ^2=1.9, p=0.379) (Table 4.4). The same trends were seen in the sensitivity analysis (Appendix 4.4).

SAMPLE CHARACTERISTICS	LOW TOLERANCE OF UNCERTAINTY	
	N (%) *	Test of association, χ^2(P-Value)
PERSONAL CHARACTERISTICS:		
Gender		16.9 (<0.001)
Female	471 (52.0)	
Male	433 (43.6)	
Prefer not to say	66 (56.4)	
Race		29.0 (<0.001)
Asian	189 (59.8)	
Black	22 (50.0)	
White	611 (44.3)	
Others	53 (55.8)	
Prefer not to say	95 (52.5)	
Ethnicity		0.06 (0.800)
Non-Hispanic	925 (48.2)	
Hispanic	45 (46.9)	
PROFESSIONAL CHARACTERISTICS:		
Experience (years since training)		12.5 (0.006)
<=10	453 (52.2)	
11-20	267 (47.4)	
21-20	153 (42.9)	
>30	97 (42.7)	
Specialty		11.4 (0.01)
Emergency medicine, radiology, anaesthesia, and pathology	177 (51.2)	
Medical subspecialties	545 (46.0)	
Primary care	164 (55.8)	
Surgical specialties	84 (44.4)	
Having a trusted advisor		1.94 (0.379)
Disagree	308 (49.9)	
Neutral	197 (49.3)	
Agree	465 (46.6)	

Table 4.4: Tolerance of uncertainty and personal and professional characteristics
* These percentages represent distribution of low tolerance of uncertainty within a given category of a characteristic (row percentages).

In multivariable analyses, low tolerance of uncertainty was associated with female gender (OR, 1.29; 95% CI, 1.07–1.57); those who prefer not to state their gender (OR, 1.66; 95% CI, 1.34–2.25); Asian race (OR, 1.74; 95% CI, 1.34–2.25); and primary care practice (PCP) (OR, 1.54; 95% CI, 1.18-2.01). More experience is associated with lower odds of low tolerance of uncertainty (OR, 0.99; 95% CI, 0.98–0.995) (Table 4.5).

COVARIATES	ODDS RATIO	
	ESTIMATE	[95% CI]
Gender		
Male	Ref	
Female	1.29	[1.07 – 1.57]
Prefer not to say	1.66	[1.02 – 2.71]
Race		
White	Ref	
Asian	1.74	[1.34 – 2.25]
Black	1.13	[0.61 – 2.07]
Prefer not to say	1.09	[0.73 – 1.62]
Others	1.57	[1.01 – 2.45]
Ethnicity		
Non-Hispanic	Ref	
Hispanic	0.86	[0.55 – 1.34]
Experience (in years)	0.99	[0.98 – 0.995]
Specialty		
Medical sub-specialties	Ref	
Emergency medicine, radiology, anaesthesia, and pathology	1.22	[0.95 – 1.56]
Primary care	1.54	[1.18 – 2.01]
Surgical specialties	1.05	[0.76 – 1.44]
Trusted Advisor		
Disagree	Ref	
Neutral	0.95	[0.73 – 1.23]
Agree	0.82	[0.73 – 1.01]

Table 4.5: Ordered Logistic Regression Model Predicting Association of Physicians Covariates and Tolerance of Uncertainty

4.3.3 Tolerance of uncertainty and physician wellbeing

In bivariate analyses, physicians with low tolerance of uncertainty were more likely to be burned-out than those with high tolerance of uncertainty (43.4% vs 23.5%; $p < 0.0001$), less likely to be engaged at work (average total engagement score of 4.2 vs. 4.7; $p < 0.0001$), and less likely to be satisfied with their career (82.4% vs 92.7%; $p < 0.001$). Similarly, physicians with low tolerance of uncertainty were more likely to have higher rates of exhaustion (3.3 vs 2.5; $p < 0.001$); cynicism (2.4 vs 1.7; $p < 0.0001$); and reduced personal efficacy (1.5 vs 1.1; $p < 0.001$).

In multivariable model, adjusting for demographic and professional characteristics, physicians with low levels of tolerance of uncertainty were more likely to be burned-out (OR, 2.38; 95% CI, 1.96–2.90), less likely to be satisfied with their career (OR, 0.38; 95% CI, 0.28–0.51), and less likely to be engaged at work (OR, 0.89; 95% CI, 0.87-0.92) than physicians with high tolerance of uncertainty (Table 4.6). Compared to physicians with higher levels of tolerance of uncertainty, physicians with low levels of tolerance have higher rates of exhaustion (RR, 1.30; 95% CI, 1.23-1.37), higher rates of cynicism (RR, 1.46; 95% CI, 1.34-1.60), and higher rates of personal inefficacy (RR, 1.36; 95% CI, 1.27-1.46) (Table 4.6). The same trends were seen in the sensitivity analysis (Appendix 4.5 and 4.6).

PHYSICIAN WELLBEING MODEL	EFFECT OF LOW TOLERANCE OF UNCERTAINTY†	
	ESTIMATE	95% CI
Overall Burnout*	2.38	1.96 – 2.90
Career Satisfaction*	0.38	0.28 – 0.51
Total Work Engagement **	0.89	0.87 – 0.92
Burnout Subscales (in rate ratio) **		
Exhaustion	1.30	1.23 - 1.37
Cynicism	1.46	1.34 – 1.60
Reduced Personal Efficacy	1.36	1.27 – 1.46

Table 4.6: Multivariable Regression Results Predicting Association of Low Tolerance of Uncertainty with Physician Wellbeing Measures

* Burnout and career satisfaction are specified as binary outcome measures and modelled using logistic regression. Results for these models are reported as odds ratio. **Total work engagement and individual burnout subscales are specified as continuous measures and modelled using generalised linear model with log link and gamma distribution. Results for these models are reported as rate ratio.
† In addition to tolerance to uncertainty, all models also controlled for differences in gender, race, ethnicity, years of experience, and specialty.

4.4 DISCUSSION

This study supports the concept that stress from uncertainty appears to be strongly associated with burnout in healthcare professionals. It adds new knowledge to existing literature by comprehensively examining the factors associated with physician tolerance of uncertainty in a large sample of multispecialty physicians, with a range of experience. Given this research question requires detailed and complete information about burnout, this research question is likely unanswerable from large national datasets. As such, the work here provides an ideal balance between granular survey data with minimal missing data and a large, diverse physician population to support external validity of the results. At a time when concern about faculty wellbeing is high, with much speculation about causes of burnout[95], we found a strong relationship between tolerance of uncertainty and physician wellbeing, regardless of how physician wellbeing is measured.

This study builds on earlier research outlined in Chapter 2 evaluating tolerance of uncertainty and burnout in healthcare providers, with several studies showing an association between lower tolerance of uncertainty and increased risk or presence of provider burnout[9,113,147,244] and work-related stress[10-12,245]. This association has been shown to be present early in training, with a study of medical students showing that intolerance of uncertainty can cause significant anxiety, frustration, self-doubt, disillusionment, feelings of inadequacy (not being "good enough"), and insecurity regarding professional skill level[243]. Previous studies have been inconsistent in reporting higher levels of tolerance of uncertainty in men or women, with some reporting higher levels in women[10], some reporting higher levels in men[301], and others remaining inconclusive[173]. There has also been previous inconsistency with tolerance of uncertainty and age, with some reporting increased tolerance with older age[182-184], some demonstrating tolerance is higher with younger age[185], and some showing no association[186]. Our study showed that female sex, Asian race, primary care specialty, and lack of experience were associated with lower tolerance of uncertainty.

Our findings generate the hypothesis that reducing tolerance of uncertainty might improve physician wellbeing. As healthcare organisations look to improve tolerance of uncertainty among their physicians, it may be helpful to focus on potentially modifiable factors associated with lower tolerance of uncertainty. Particular attention likely needs to be paid to those with less experience, and perhaps those in specialties with high rates of undifferentiated illness and uncertainty, such as primary care. It is important to recognise that talking openly about uncertainty in the clinical environment helps normalise the experience of uncertainty, especially for those colleagues with less experience[302]. Enabling individuals to express anxieties and concerns with a colleague in a safe space may help those with less experience[302].

4.4.1 Limitations

This study has several limitations. First, our results are subject to the inherent reporting biases that often occur in survey studies. To minimise any social desirability biases, respondents were informed about extensive efforts to collect and analyse data in a de-identified and confidential manner. In addition, survey participants were unaware of the specific hypothesis of this study, and we have no information to suggest that they would have chosen to participate or not on the basis of their tolerance of uncertainty or degree of burnout. Our response rate of 93% is a robust response across a large multispecialty group which increases the accuracy of the data and minimises any selection bias. Second, our results may not be generalisable beyond the academic faculty practice of physicians at the MGPO. However, we are reassured that the external validity of these results is strong, since this is the largest physician organisation in New England and includes physicians from a diverse range of practice settings and specialties. Nevertheless, further studies are needed to confirm our findings in other hospital and academic settings. Finally, due to the observational design of our study, we are careful to only test for associations and do not draw conclusions about causality from our findings alone.

4.5 CONCLUSIONS

Identifying and effectively managing physician burnout has proven to be extremely difficult, with high rates persisting in numerous studies over time, despite increased attention to this issue. The results from this study build on the introductory chapters that frame stress from uncertainty as a potential driving force behind the burnout pandemic. As we outlined in Chapter 2, reducing stress from uncertainty may positively impact physician wellbeing, patient safety, and healthcare delivery.

This study supports the hypothesis that efforts to improve management of uncertainty may be useful for addressing burnout among physicians, across specialties, and gives insight into the sociodemographic characteristics of those who may be at highest risk of stress from uncertainty. The ability to deal with uncertainty is increasingly recognised as a major goal of medical education and growing evidence suggests it may be possible to decrease stress from uncertainty. Later in the thesis, we will explore suggested strategies to help students, trainees, and faculty in healthcare embrace uncertainty and thrive in its presence in the clinical learning environment.

CHAPTER 5: A RANDOMISED EXPERIMENTAL STUDY TO ASSESS THE EFFECT OF LANGUAGE ON MEDICAL STUDENTS' ANXIETY DUE TO UNCERTAINTY

"When people believe a conclusion is true, they are also very likely to believe arguments that appear to support it, even when these arguments are unsound."
Daniel Kahneman[303]

5.1 INTRODUCTION

In the last chapter we explored associations between personal and professional characteristics and tolerance of uncertainty in physicians and confirmed the strong correlation between stress from uncertainty and burnout. Understanding what factors and processes affect anxiety due to uncertainty in healthcare professionals is an important and urgent goal as we seek to develop strategies to help trainees and faculty embrace uncertainty constructively, minimising the risk of burnout and the downstream negative consequences to themselves, their patients, and healthcare institutions.

Chapter 1 provided a general overview of the broad context of burnout in healthcare, highlighting its global and accelerating prevalence in healthcare professionals and giving an overview of the interventions that exist to reduce burnout. To date it is not clear which interventions may be considered effective. Many interventions have been physician-directed, targeting the individual which risks ignoring the sources of chronic stressors in the workplace (such as uncertainty), and implies that burnout is a wholly personal issue. Organisational-directed interventions have tended to focus on logistical changes such as scheduling and reductions in intensity of workload and efforts to cultivate a sense of teamwork and job

control. While these latter interventions have been the most effective in reducing burnout[142], there is limited robust research to assess their true value, with very few reported in the literature[143]. Efforts have therefore mainly been focused on attempting to help physicians cope with the inevitable stress associated with the tremendous responsibility and concern for patient outcomes, but with little attention paid to one of the likely driving forces behind the burnout pandemic—the uncertainty that is a ubiquitous problem in healthcare.

In light of any set clinical context (which of course carries its own uncertainty), it is important to understand whether there are aspects of the work environment, such as elements of communication, that increase or decrease anxiety due to uncertainty. There is likely a "sweet spot" of uncertainty acknowledgment that drives curiosity, preventing premature closure and enhancing performance and decision-making, but does not result in unhealthy anxiety that drives stress, poor decision-making, and burnout. This chapter aims to assess the effect of language used in healthcare settings on medical students' anxiety due to uncertainty to understand how our choice of words may affect perception of certainty.

5.1.1 The influence of medical language on uncertainty

The presentation of uncertainty has been highlighted as one of the most difficult elements of risk communication[190], and studies have shown that human response to a given message can depend on how the message is tailored and subsequently encoded by the recipient[304]. Although many studies have demonstrated that decisions are affected by the way in which situations are described, for example with regard to the influence of medical versus lay language on diagnostic choice in medical students[305], there has been little research on how language choice in the healthcare setting affects anxiety due to uncertainty in physicians, particularly in settings tied to clinical decision-making[306]. Increasingly, hospital and

healthcare system protocols are standardising guidelines, including language used, and it is therefore important that we understand how our choice of words may affect our reaction to uncertainty.

As we saw in Chapter 2, our intolerance of uncertainty seems likely to be a potential driver of burnout and all the negative downstream consequences that come from this debilitating phenomenon. A secondary effect of tolerating uncertainty may be a reduction in premature closure by reducing the need to go into early decision-making to get out of the uncertain space. An estimated 40,000 to 80,000 US hospital deaths result from misdiagnosis annually[307], and diagnostic errors are the number one cause of medical malpractice claims[308], representing a major source of preventable mortality, morbidity and cost. The single most common phenomenon in misdiagnosis is premature closure—the tendency to stop considering other possibilities after reaching an initial diagnosis[206,309]. Thus, by helping people to tolerate uncertainty there may be a two-fold benefit: reduction in burnout and reduction in premature closure.

This phenomenon of misdiagnosis may be particularly prevalent in settings like the accident and emergency department (A&E) where pressures on time drive the need to rapidly reduce the uncertainty in a clinical presentation to form a working diagnosis. The practice of emergency medicine involves dealing with multiple sources of uncertainty, combined with a very stressful environment with high volume, high acuity, and high complexity of disease together with a need for rapid decision-making in a highly ambiguous environment[147]. Thirty-eight percent of patients report experiencing concern about a potential medical error during their encounter in the A&E, with the most common (22%) being misdiagnosis[310]. Studies have shown A&Es to have the highest proportion (70% to 82%) of preventable errors, most

commonly diagnostic errors, with data indicating that cognitive errors associated with clinical decision-making are critically important in the A&E[311]. The downstream impact of such diagnostic errors is particularly great if this initial diagnosis is accepted when the patient is admitted, with anchoring and confirmation biases taking hold in interpretations of the illness narrative—subconsciously seeking signs that confirm the 'diagnosis' and refuting those that do not fit.

Many factors contribute to premature closure, including systems issues[312], but it has been shown that cognitive errors are an important source of diagnostic error in almost 75% of cases[206]. Because of imperfections of human perception and decision, changes of perspective which can be induced through framing effects preferentially highlighting gains or losses, can dramatically affect decision-making behaviour[313]. In particular, as we explored in Chapter 2, the quest for certainty that is central to human psychology can drive cognitive errors as we struggle to sit comfortably with uncertainty and undifferentiated signs and symptoms, craving closure on a 'diagnosis'[8]. Disclosing and discussing uncertainty has been recognised to be one of the most challenging elements of risk communication[190]. Following the work of Kahneman and Tversky in the 1970s and 1980s[313-315], studies have shown that human response to a given message can depend on how that message is framed consequently how the recipient encodes and perceives the tailored information[304]. Thus, it is possible that language used may influence the likelihood of cognitive errors, particularly if it exacerbates a sense of certainty—increasing the chance of anchoring and confirmation biases and premature closure. Importantly, decision-makers are not normally aware of the potential effects of different decision frames (such as variance in language) on the influence and relative attractiveness of options[313].

5.1.2 The clinical hand-over

Handing over responsibility for patients has always been a critical part of medical practice, aiming to ensure effective continuity of care and patient safety and allowing the opportunity to communicate pertinent information in a succinct, easily digestible, manner. Hand-over happens predictably as a routine part of the clinical day when teams of healthcare professionals change over and unpredictably when patients are transferred between teams, units, or parts of the healthcare system for further investigations, treatment, or care. Communication and hand-over failures are both common and potentially hazardous and have been identified as a contributing cause in approximately two out of every three sentinel events—serious, often fatal, preventable adverse events in hospitals[316,317]. Any transition of care represents a critical juncture in the patient's journey and transfer of accurate information, free from biases, is essential. Recognising the role of hand-over failures in medical errors, the medical education bodies in the US and UK now require all training programmes to teach trainees hand-over skills and to monitor the quality of hand-overs. Consequently, the ability to give or receive a patient hand-over to transition care responsibility has been identified as a core professional competency that all medical students should be able to perform upon entering a training programme. To meet these needs, hand-overs have increasingly become standardised, with mnemonics and set language used to ensure all elements are remembered and included. The clinical hand-over, therefore, represents an excellent example of a common pattern of communication between healthcare professionals which offers a good opportunity to explore the impact that language used in the hand-over has to the receiver, particularly with regard to their stress from uncertainty.

5.1.3 Chapter aims

This study was designed to allow us to understand whether changes in the language used in a clinical hand-over from the A&E to the inpatient medical team would affect medical students' sense of uncertainty, reflected in their uncertainty about the specific clinical diagnosis and their level of anxiety due to uncertainty. We used a randomised experimental study design to allow us to test different language constructs used in the hand-over setting when medical professionals are handing patients' over from one unit to another and conveying the presumptive 'diagnosis' and current plan.

Our primary aims were:

- to determine whether using the word 'hypothesis' in a clinical hand-over scenario would lead to greater uncertainty about the clinical diagnosis in comparison to using the word 'diagnosis';
- to determine whether using the word 'hypothesis' in a clinical hand-over scenario would lead to higher levels of anxiety due to uncertainty in comparison to using the word 'diagnosis'.

Our secondary aims were:

- to test the impact of two alternative formats for conveying diagnostic uncertainty in the hand-over, specifically with the word choices: 'working diagnosis'; and 'probability'.

5.2 METHODS

5.2.1 Study Design

We conducted an online experiment comparing the impact of four hypothetical hand-over scripts on sense of uncertainty among clinical medical students from Harvard Medical School (HMS), a large medical school in the US. Participants were randomised to one of four language conditions to describe the presumed diagnosis. Due to the nature of the study with clinical cases of varying uncertainty, we used a between-subject design to prevent confounding effects of seeing the same case with varying language conditions.

5.2.2 Participants and recruitment

All HMS students with direct clinical experience within the hospital setting were eligible for participation. As the study was conducted in the Spring, second year students and above had been on clinical rotations for at least six months, while first year students had not yet been on any clinical rotations. As participation required knowledge of common clinical presentations, only second year students and above were included. We recruited participants through email (class list provided by the medical school) and distributed the survey through an individualised online link embedded in the email, leaving the survey active for four weeks in April 2017. Two reminder emails were sent to non-responders. Participation was elective and responses were anonymous. As an incentive to participate, we offered the chance to win one of two $50 Amazon vouchers for completion of the survey. Subjects were randomised to one of the four language conditions according to a pre-determined allocation list based on the order in which they assented to participate. The HMS Institutional Review Board considered this study to be exempt from review.

5.2.3 Survey instrument and variables

The survey collected demographic information (age and gender); medical school information (training year); and intended specialty choice, if known. The survey consisted of four clinical scenarios—cardiac; respiratory; infectious diseases; and psychiatry—written in the form of a hand-over report for a patient transferring from the A&E to the inpatient ward. Each subject was presented with all four scenarios in a random order, randomised to receive one of the four language arms. After each clinical scenario, participants were asked to complete five items to assess their certainty about the A&E provider's presumed diagnosis and also to complete the Anxiety due to Uncertainty subscale from the Physicians' Reaction to Uncertainty Scale[236].

5.2.3.1 Development of the clinical scenarios

The four scenarios—cardiac; respiratory; infectious diseases; and psychiatry—were developed based on the following steps.

1. We reviewed all medicine service admissions from the A&E at one of the affiliated teaching hospitals between April 2016 and January 2017 to identify the top ICD10 primary diagnoses and clinical admissions by volume.
2. We then created clinical scenarios to reflect these common presentations.
3. These cases were refined by an expert panel of experienced senior physicians, and four were chosen by consensus agreement, to reflect realistic scenarios with a range of clinical uncertainty. The cases operated independently of each other.

5.2.3.2 Development of the language arms

We identified expert physicians interested in how uncertainty affects medical decision-making to develop variations in the language used to describe the A&E provider's presumed diagnosis, which constitutes the independent variable for this study. Phrases used in clinical hand-overs on the medical services to describe the presumed diagnosis were identified, and four variations were chosen by the expert panel to be included as the four language arms. Subjects were randomised to one of these four language conditions:

- Control language arm described the presumed diagnosis as "Our **diagnosis** is..."
- Experimental language arms varied this language to:
    1. replace the word 'diagnosis' with '**hypothesis**'
    2. replace the word 'diagnosis' with '**working diagnosis**' and include a short differential
    3. include a statement that the A&E provider was **60% sure of the diagnosis**

Table 5.1 shows the scenarios presented and text appended for each language condition.

SCENARIO	DIAGNOSIS	HYPOTHESIS	WORKING DIAGNOSIS	PROBABILITY
You are sitting in the call room when you receive a page from the emergency room resident: Hey, we have a 50-year-old guy who's come in with a three-day history of worsening cough and shortness of breath. He's got known COPD and a 30-pack year history of smoking. He's on amlodipine. He has crackles at the right base and a CXR shows bilateral hazy opacification, worse on the right.	Our diagnosis is right lower lobe pneumonia and we've started him on antibiotics.	Our hypothesis is right lower lobe pneumonia and we've started him on antibiotics.	Our working diagnosis is a right lower lobe pneumonia, but we are also considering a non-infective exacerbation of his COPD, or decompensation of heart failure.	We've started him on antibiotics for a right lower lobe pneumonia. We think there is a 60% chance that he has pneumonia.
You are sitting in the call room when you receive a page from the emergency room resident: Hey, we have a 55-year-old male who's presented with central chest pain which is worse on breathing in. He was at a party last night and vomited a few times. He's had some flu-like symptoms over the past week and has taken quite a lot of Tylenol and Advil. He has no past medical history and a normal examination. His EKG shows normal sinus rhythm, with non-specific ST changes in some of the leads. His troponin is normal.	Our diagnosis is pericarditis and we've started him on high dose NSAIDs and colchicine for the pain.	Our hypothesis is pericarditis and we've started him on high dose NSAIDs and colchicine for the pain.	Our working diagnosis is pericarditis and we've started high dose NSAIDs and colchicine for the pain. We are also considering whether something else could be going on, such as unstable angina, esophagitis, or coronary spasm due to cocaine taken at the party.	Our diagnosis is pericarditis and we've started high dose NSAIDs and colchicine for the pain. We think there is a 60% chance that he has pericarditis.
You are sitting in the call room when you receive a page from the emergency room resident: Hey, we have a 60-year-old female who has presented with flank pain. She reports feeling ill for a couple of days. She is tachycardic with a heart rate of 100 and has leukocyte positive urine. She looks a little dehydrated with reduced skin turgor.	Our diagnosis is pyelonephritis and we've started her on iv antibiotics.	Our hypothesis is pyelonephritis and we've started her on iv antibiotics.	Our working diagnosis is pyelonephritis and we've started her on iv antibiotics. We are also considering if something else could be going on, such as gastroenteritis, diverticulitis or inflammatory bowel disease.	Our diagnosis is pyelonephritis and we've started her on iv antibiotics. We think there is a 60% chance she has pyelonephritis.
You are sitting in the call room when you receive a page from the emergency room resident: Hey, we have a 35-year-old male who's been brought into ED in an agitated and aggressive state. His mother is with him and says he has a history of amphetamine misuse. She says he has flu-like symptoms for a week and woke this morning feeling unwell with generalised body pain. He has a GCS of 11 (M5, E4, V2). We haven't been able to perform a full physical examination due to his agitation. We've sent routine bloods and toxicology screen. CT head was negative.	Our diagnosis is amphetamine overdose and we've started him on iv diazepam.	Our hypothesis is amphetamine overdose and we've started him on iv diazepam.	Our working diagnosis is amphetamine overdose and we've started him on iv diazepam. We are also considering whether something else could be going on, and whether he might have an infection, perhaps infective endocarditis.	Our diagnosis is amphetamine overdose and we've started him on iv diazepam. We think there is a 60% chance that it's an amphetamine overdose.

Table 5.1: Clinical scenarios with varying language conditions

5.2.3.3 Items to assess clinical uncertainty

After each clinical scenario, participants were asked to complete five items to assess their level of uncertainty about the A&E provider's presumed diagnosis:

1. *I am confident that I know what is going on with this patient*
2. *I think the admitting diagnosis for this patient is incorrect*
3. *The patient should be told that we are not sure what is going on*
4. *More tests are needed to understand what is going on with this patient*
5. *Getting the input of a specialist will be important to care for this patient*

Each statement was answered on a 6-point Likert scale with response options ranging from "strongly disagree" to "strongly agree". Scale scores range from 5 to 30, with higher values indicating increased clinical uncertainty. These items were developed by consensus agreement from an expert panel of practicing physicians to reflect statements of uncertainty relating to the presumed diagnosis and next steps with regard to clinical management and discussion with the patient (Cronbach's alpha = 0.7).

5.2.3.4 Anxiety due to uncertainty

At the end of all the scenarios, subjects completed the 5-item Anxiety due to Uncertainty subscale from the Physicians' Reaction to Uncertainty Scale, a validated and reliable instrument, that measures affective reactions to uncertainty in clinical situations (Cronbach's alpha = 0.85):

1. *I usually feel anxious when I am not sure of a diagnosis*
2. *I find the uncertainty involved in patient care disconcerting*
3. *Uncertainty in patient care makes me uneasy*
4. *I am quite comfortable with the uncertainty in patient care**
5. *The uncertainty of patient care often troubles me*

The items are rated on a 6-point Likert scale with response options ranging from “strongly disagree” to “strongly agree”. Item 4(*) is reverse-scored. The ability to measure relevant differences in reaction to uncertainty with this scale has been demonstrated in several studies[9,175,236,318]. Scale scores range from 5 to 30, with higher values indicating more anxiety due to uncertainty.

5.2.3.5 Pilot testing

The scenarios and outcome measures were piloted with first year preclinical medical students. As the focus of this study is on the clinical students, this pilot data was not included in the analyses.

5.2.4 Data collection

A secure, web-based online survey platform, Qualtrics, was used to manage survey distribution and collect responses. Each participant received an individualised link to the survey via an online email. The initial email was sent at the start of April 2017, with two reminder emails sent to non-respondents. The survey was left active for four weeks. Completion of the survey was considered implied consent of participation. All data used was strictly anonymised; only a research coordinator, who was not involved in this study, had access to the file linking responses with identifiers.

5.2.5 Outcome measures

The primary outcome of this study was anxiety due to uncertainty immediately after the presentation of all four scenarios. In addition, we assessed their level of uncertainty about the clinical diagnosis in each individual scenario. The independent variable for this study was the variations in the language used to describe the A&E provider's presumed diagnosis:

- 'diagnosis'
- 'hypothesis'
- 'working diagnosis' with differential
- '60% chance'

5.2.6 Statistical analysis

Standard descriptive statistics were used to characterise the study population, and baseline demographics were tabulated for each language condition. Chi-square and t-tests were carried out as appropriate to ensure balance between groups. The responses to the 5-items in the Anxiety due to Uncertainty scale were summed (Cronbach alpha = 0.89 in our study population). We performed t-tests on the Anxiety due to Uncertainty scores and the items assessing clinical uncertainty after each scenario by language condition comparing the 'diagnosis' language control arm against each of the three experimental language arms. Analyses were performed using commercially available statistical software (STATA version 15.0; StataCorp LP, TX). Tests with $p < 0.05$ were considered statistically significant.

5.3 RESULTS

5.3.1 Characteristics of the participants

Of the 114 participants who started the survey, 88 completed all items and were included in the analyses. Differences in rate of partial completion across language arms were present but were not statistically significant. The mean age of the sample was 26.7 years ± 2.3 SD years. The sample was predominantly female (71.6%). Respondents were distributed across 4 medical school years with the majority being from the 4th year (19.3% year 2, 15.9% year 3, 53.4% year 4, 11.4% year 5+). Table 5.2 shows participant characteristics tabulated by language condition and educational phase.

		DIAGNOSIS	HYPOTHESIS	PROBABILITY	WORKING DIAGNOSIS	TOTAL
n		18	23	26	21	88
Female (%)		11 (17.5)	17 (27)	20 (31.7)	15 (23.8)	63 (71.6)
Age, mean (SD)		26.22 (1.77)	26.61 (2.92)	26.69 (1.95)	27.48 (2.42)	26.7 (2.3)
Year (%)	**2nd year**	4 (22.2)	4 (17.4)	5 (19.2)	4 (19.0)	17 (19.3)
	3rd year	4 (22.2)	4 (17.4)	4 (15.4)	2 (9.5)	14 (15.9)
	4th year	9 (50.0)	13 (56.5)	12 (46.2)	13 (61.9)	47 (53.4)
	5+ year	1 (5.6)	2 (8.7)	5 (19.2)	2 (9.5)	10 (11.4)

Table 5.2: Demographic characteristics by language condition and educational phase

5.3.2 Clinical uncertainty

There were no statistically significant differences in the items assessing clinical uncertainty after each of the scenarios, regardless of language used to describe the presumed 'diagnosis' (Table 5.3).

ITEM	ARM 1	MEAN(SD)	ARM 2	MEAN(SD)	P VALUE
I am confident that I know what is going on with this patient.	Diagnosis	3.6(0.8)	Hypothesis	3.5(1.0)	.76
			Probability	3.2(1.0)	.26
			Working Diagnosis	3.6(1.1)	.90
I think the admitting diagnosis for this patient is incorrect.	Diagnosis	3.6(0.9)	Hypothesis	3.5(0.7)	.75
			Probability	3.4(0.6)	.58
			Working Diagnosis	3.2(0.6)	.18
The patient should be told that we are not sure what is going on.	Diagnosis	5.0(0.6)	Hypothesis	3.7(1.1)	.75
			Probability	3.9(1.0)	.28
			Working Diagnosis	4.0(1.1)	.23
More tests are needed to understand what is going on with this patient.	Diagnosis	3.5(0.7)	Hypothesis	5.0(0.7)	.94
			Probability	4.6(0.9)	.09
			Working Diagnosis	5.0(0.7)	.80
Getting the input of a specialist will be important to care for this patient.	Diagnosis	3.2(0.7)	Hypothesis	3.2(1.0)	.99
			Probability	3.1(0.7)	.56
			Working Diagnosis	3.0(0.6)	.50

Table 5.3: Clinical uncertainty following each scenario

5.3.3 Anxiety due to uncertainty

Anxiety due to uncertainty was significantly higher in subjects receiving the 'hypothesis' language arm than those receiving the control 'diagnosis' language (19.2(4.6) vs 15.5(3.4), $p < 0.008$). There was no difference in anxiety due to uncertainty in subjects who received the probability language (17.2(5.8) vs 15.5(3.4), $p = 0.26$) and the 'working diagnosis' language (16(5) vs 15.5(3.4), $p = 0.69$). Figure 5.1 shows the results of Mann-Whitney U testing on the Anxiety due to Uncertainty scale by language condition (control vs experimental arms).

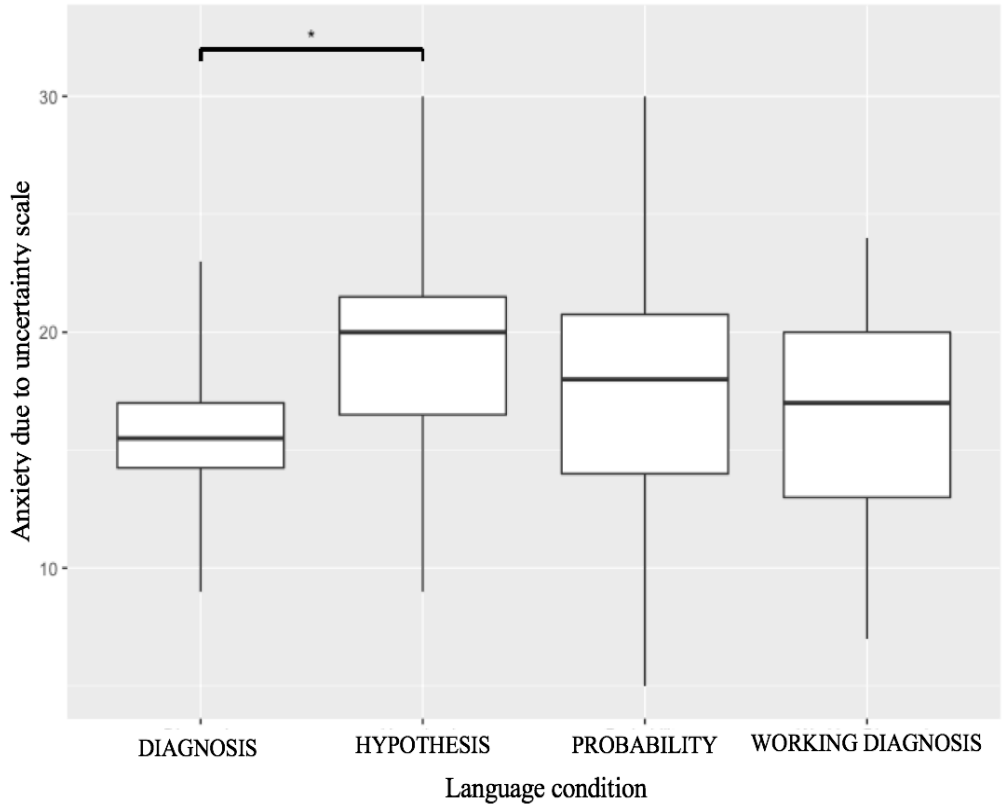

Figure 5.1: Boxplot to show student's anxiety due to uncertainty scale by language condition
* significant ($p < 0.008$)

5.4 DISCUSSION

This is the first study to examine how language used in clinical hand-overs affects sense of uncertainty among the receiving clinician. Interestingly, while there was no difference in the perception of uncertainty about the specific clinical diagnosis for each scenario, the medical students who received a hand-over using the language variation 'hypothesis' had significantly higher anxiety due to uncertainty than those who received the language variation 'diagnosis'. Although the content of the clinical scenarios was identical, difference in language used had a significant effect on students' anxiety due to uncertainty, though it did not affect their level of clinical uncertainty. There was no difference in students who received the language variation 'probability' or 'working diagnosis'. Our findings suggest that, in addition to perceptions of clinical uncertainty, anxiety due to

uncertainty may be an important measure to assess in research examining interventions addressing tolerance of uncertainty in medicine given its responsiveness in this study.

These results suggest that the word 'hypothesis' increased anxiety related to uncertainty in comparison to the use of the word 'diagnosis' in clinical hand-over scenarios demonstrating how language variation can influence emotional perception. Interestingly, we did not find a difference in the items assessing clinical uncertainty about the diagnosis in the specific scenarios, which may suggest that language can affect emotional reaction to uncertainty without affecting their perception of the level of clinical uncertainty. It may also, however, reflect the lack of validation of the items or the limited experience of medical students with many of the actions described (e.g. getting the input of a specialist) which resulted in the same level of uncertainty regarding the presumed diagnosis regardless of language used. Uncertainty is a critical phenomenon in healthcare because of its ubiquitous presence and its many potential psychological effects, both negative and positive[149]. Internationally, the medical profession has begun to recognise the need to identify, address, and tolerate clinical uncertainty as a core professional competency, acknowledging its impact on patient safety and wellness among practicing physicians and trainees[285,319].

It is important to consider that the word 'diagnosis' (often used whilst still in the clinical reasoning process) may have unintended correlations with certainty, risking the diagnostic reasoning process being closed too soon, with an increased chance of diagnostic error and downstream negative ramifications for the patient and healthcare system[206]. The less concrete 'hypothesis', which perhaps emphasises uncertainty, may be useful to use (especially early in the diagnostic reasoning process) to help physicians avoid premature

closure and unintentional cognitive errors. To date available research has suggested that the responses to uncertainty depends very much on the clinician's and patient's personal characteristics and values[320]. Our findings suggest that the language used to frame clinical scenarios may impact response to uncertainty, regardless of personal characteristics. More work is needed to define the circumstances and communication strategies for this critically important arena, with studies needed to explore the fundamental questions about how people process, interpret, and respond to various types of uncertainty inherent in clinical decisions[190].

In parallel with these efforts, it will be important to ensure that we develop interventions to help physicians manage stress or anxiety due to uncertainty in clinical environments[8]. A physicians' ability to deal with uncertainty at a cognitive, emotional, and ethical level has been shown to influence the eventual diagnostic decision with potential impact on the patient and their outcomes[205]. Physicians' maladaptive responses to uncertainty are known to contribute to work-related stress[257], and we have shown in the last chapter that low tolerance of uncertainty appears to be strongly associated with burnout. There is much evidence to suggest that tolerance of uncertainty and resilience are states, not traits, and therefore amenable to change through an educational and experiential process[179,321,322]. Cultivating an optimal tolerance of uncertainty, and identifying the language that allows individuals to practice in this sweet spot, will likely be an important step in improving communication, patient safety, and physician wellbeing[8,323].

5.4.1 Limitations

There are several limitations to this study. Data were collected in a single centre with a small sample size of medical students. These data reflect students who chose to participate in the study and may be influenced by selection bias. Furthermore, the items assessing clinical certainty after each scenario were not validated as noted above. However, students were not aware of the hypotheses of this study and we deliberately provided little information about our aims. Although the differences in dropout rates across conditions raise concern about potential differences between groups, these differences were not significant and the between-participants experimental design greatly increases the confidence in the findings. Although an experimental design provides the highest level of evidence in support of the hypothesis that hand-over language affects the uncertainty measure, it is possible that randomisation did not fully balance potential confounders across groups. Further research with larger samples is needed to validate these results.

5.5 CONCLUSIONS

As we have established in the introductory chapters, despite the remarkable trajectory of biomedical research over recent decades, uncertainty will always be part of clinical medicine[116], and indeed is likely to grow in the years ahead. Understanding and acknowledging uncertainty and acquiring proper coping strategies is now regarded as one of the core clinical competencies for medical graduates and trainees in the UK, US, Australia, and much of Europe[284-290], but there is still much about tolerance of uncertainty that is not understood. In particular, there has been little research on how language choice in the healthcare setting affects anxiety due to uncertainty in physicians, particularly in settings tied to clinical decision-making[306]. In this study, we found that the use of the word

'hypothesis' significantly increased anxiety due to uncertainty compared to the word 'diagnosis', although this had no impact on level of uncertainty about the specific clinical diagnosis. It may be that the word 'diagnosis' connotes a level of certainty that is misguided, under-representing the complexity of clinical reasoning, and resulting in a risk of premature closure and consequent error. This lends support to careful consideration of the language used in healthcare settings, especially in hand-over scenarios as standardised protocols are developed, to prevent unintended (and unwanted) consequences. Errors in the hand-over process may occur not just due to what information is conveyed, but also how it is conveyed in terms of language choice. We know very little about the optimal approaches and outcomes of communicating different types of uncertainty[190]. Future research is needed to understand more fully what factors and processes affect anxiety due to uncertainty in healthcare professionals, how maladaptive stress can be avoided, and how language choice may affect medical decision-making and diagnostic error.

PART II

EXPLORATION OF BIOLOGY: EXPLORATION INTO POTENTIAL USE OF BIOMARKERS TO MEASURE BURNOUT

CHAPTER 6: BIOMARKER MEASUREMENT OF WELLBEING

"We are, by nature, a highly affiliative species craving social contact."
Thomas R. Insel[324]

6.1 INTRODUCTION

In the opening chapters we explored burnout in physicians and the role that tolerance of uncertainty may play as a driver of this phenomenon, through a review of the literature together with observational research studies. We highlighted the concerns in the field regarding challenges that pertain to burnout research, particularly in regard to how best to measure burnout. This second part of the thesis aims to explore the novel use of cortisol and oxytocin levels as potential biomarkers of wellbeing.

6.1.1 Cortisol as a biomarker of wellbeing

The detrimental effects of stress on human health, and the correlations with burnout, are increasingly recognised. Due to its crucial role for the human stress response, the hypothalamic-pituitary-adrenal (HPA) axis and its regulation by glucocorticoids (such as cortisol) have been the main focus for systematic research on biomarkers in burnout so far[325-328]. By widespread central receptors, glucocorticoids can influence cognitive processes like learning and memory[329] or exert effects on mood[330]. Both aspects, cognition and mood regulation, seem to be pivotal for burnout development and progression[331]. While biomarkers exist to measure acute changes at a single point in time, there is critical need for the establishment of a biomarker that accurately measures its intensity and course

over time. Such a biomarker would allow monitoring of stress, perhaps a proxy for burnout, and may enable appropriate and successful wellness interventions to be identified.

6.1.2 Oxytocin as a biomarker of wellbeing

Over the past 30 years oxytocin—a neuropeptide synthesised in the paraventricular nucleus and supraoptic nucleus of the hypothalamus and released to both central and peripheral circulation—has received increased attention for its role in social functioning. Evidence from preclinical, clinical, and human laboratory studies indicate that oxytocin is involved in social behavioural and cognitive domains, including attachment and pair bonding in laboratory animals, as well as social affiliation, parental care behaviours, socio-emotional processing, social reward, and generosity and interpersonal trust in humans[332-340]. This work has generated considerable excitement about identifying the neurochemical underpinnings of sociality in humans.

At the same time, the power of social environments to promote satisfaction at work is increasingly recognised[272]. Trust is commonly defined as "a psychological state comprising the intention to accept vulnerability based upon positive expectations of the intentions or behaviour of another"[341]. It is an adaptive mechanism essential to building social relationships. As shown in Chapter 3, job satisfaction is significantly associated with feeling valued, feeling treated with respect, and working in a social and supportive environment[124]. Social ties are known to reduce morbidity and mortality[342,343], and those who engage in more social interactions are less stressed physiologically[344]. Unlike other mammals, humans tend to spend a great deal of time around others who are unfamiliar. This is especially true in the healthcare environment, which is full of dynamic teams with changing membership and shift-pattern structures with rotating trainees and students.

Mutual respect and trust have been shown to be fundamental for effective teams—essential to ensure effective and safe patient care. Oxytocin's operations within the body are, of course, quite dynamic; the peptide interacts with other hormones and neurotransmitters whose levels vary minute by minute and over one's life span. Residing in a safe, nurturing environment may stimulate us to release more oxytocin when someone trusts us—and to reciprocate that trust. Stress, uncertainty, and isolation all work against the development of a trusting disposition.

6.1.3 Chapter aims

In this chapter we will explore the role of stress in health and the neurobiology underpinning cortisol, a hormone whose release is triggered by physical or psychological stress. We will also explore the physiology of the oxytocin system, reviewing studies that examine the effects of oxytocin—both anxiolytic properties and social-cognitive effects—to introduce the idea that oxytocin may be a useful biomarker by which to measure the physiological basis of pro-social behaviour, known to have a positive effect on faculty wellbeing (as demonstrated in Chapter 3). We will look in detail at the different measurements of cortisol and oxytocin that are available to capture physiological change that may represent a proxy measure of burnout. A concluding section summarises limitations in human cortisol and oxytocin research and discusses potential applications of these biomarkers, setting the stage for the exploratory biomarker study in Chapter 7. As we look to understand whether the multitude of wellbeing interventions that are being explored have the desired effects and outcomes, the ability to understand objectively physiological change seems increasingly relevant.

6.2 THE NEUROBIOLOGY OF CORTISOL

Cortisol is a glucocorticoid hormone which is synthesised from cholesterol and released by the adrenal cortex through stimulation of the HPA axis. Systemic cortisol levels are highly variable, due to the diurnal rhythm, acute stress and pulsatile secretion[345]. In general, cortisol levels in the blood peak during the early morning and gradually decrease thereafter[346]. Due to its low molecular weight and lipophilic nature, unbound cortisol enters the cells through passive diffusion, which makes it feasible to measure the free cortisol in many body fluids[347]. During times when an organism undergoes physiological duress, cortisol acts to mobilise energy stores and modulate the immune system.

6.2.1 The role of stress in health

Stress is an unavoidable component of life, and the stress response is a crucial survival mechanism. The term "stress" refers to the body's nonspecific adaptive response to try to adapt to a perturbation. The source of the stress, the stressor, can be actual or perceived, and can be physiological or psychological[348]. The sum of physiological effort to compensate for the perturbations caused by a stressor is defined as the allostatic load[130]. Allostatic load can be quantified through measurement of physical changes such as blood pressure, heart rate, waist-hip-ratio, and body fat percentage, or though biochemical concentrations of various substances, including cortisol, catecholamines, high-density lipoprotein (HDL), total cholesterol:HDL ratio, triglycerides, glycosylated haemoglobin, glucose levels, C-reactive protein (CRP), fibrinogen, D-dimer, and tumour-necrosis-factor-alpha[349]. Initially, the physiologic changes induced by the stress response serve an adaptive role as the body attempts to maintain homeostasis in spite of the stressor, but a sustained increase in allostatic load is associated with a host of deleterious consequences, adversely

affecting the immune, cardiovascular, neuroendocrine, and central nervous systems[350]. A crucial neuroendocrine axis involved in mediating these effects is the HPA axis leading to the secretion of two classes of hormones; catecholamines and glucocorticoids.

6.2.2 Time frame of hormone exposure

An important aspect to consider regarding glucocorticoid-mediated effects on health relates to the time frame of hormone exposure. Whilst the occasional occurrence of acute cortisol reactions may not be particularly problematic for an organism, the cumulative burden of frequent HPA axis activation and/or long-term changes to basal cortisol secretion is associated with a range of maladaptive effects[351]. It would seem likely that this chronic exposure to cortisol secretion may be linked to propensity of burnout in individuals. Whilst it may be that this would result in abnormally high cortisol levels, it has also been hypothesised that in burnout the autonomic nervous system (ANS) and HPA axis have become exhausted due to prolonged or recurrent stress, and therefore blood levels of adrenaline and cortisol and their metabolites may be abnormally low.

6.3 THE NEUROBIOLOGY OF OXYTOCIN

Oxytocin is an evolutionarily highly preserved nonapeptide (Cys-Tyr-Ile-Gln-Asn-Cys-Pro-Leu-GlyNH_2) with a sulphur bridge between the two cysteines (Figure 6.1). It is structurally similar to the closely related peptide arginine vasopressin, an antidiuretic hormone, which differs from oxytocin in two of the nine amino acid residues.

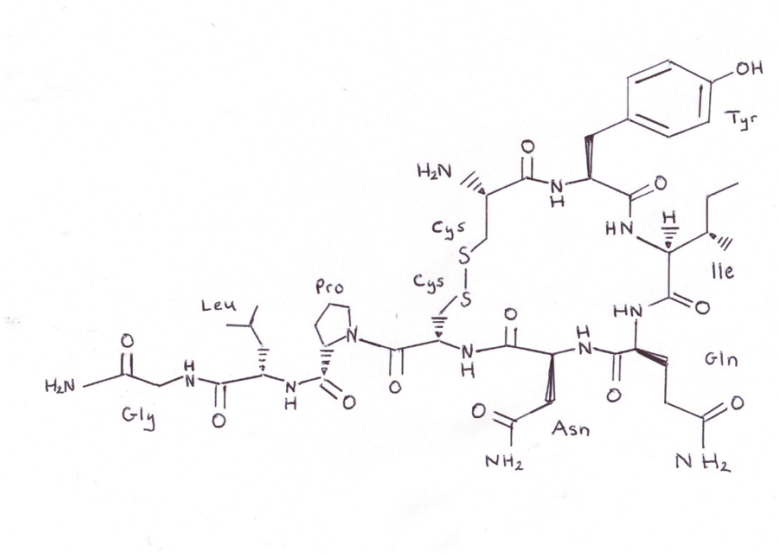

Figure 6.1: Oxytocin

Oxytocin is an abundant neuropeptide exerting a wide spectrum of central and peripheral effects as neurohormone, neurotransmitter, or neuromodulator. In the central nervous system (CNS), the oxytocin gene (located on chromosome 20) is predominantly expressed in magnocellular neurons in the hypothalamic paraventricular (PVN) and supraoptic nuclei (SON). The magnocellular oxytocin neurons release their products into the general circulation in the neurohypophysis where it enters the peripheral bloodstream for its hormonal actions, while the mediocellular oxytocin neurons secrete elsewhere in the CNS (Figure 6.2).

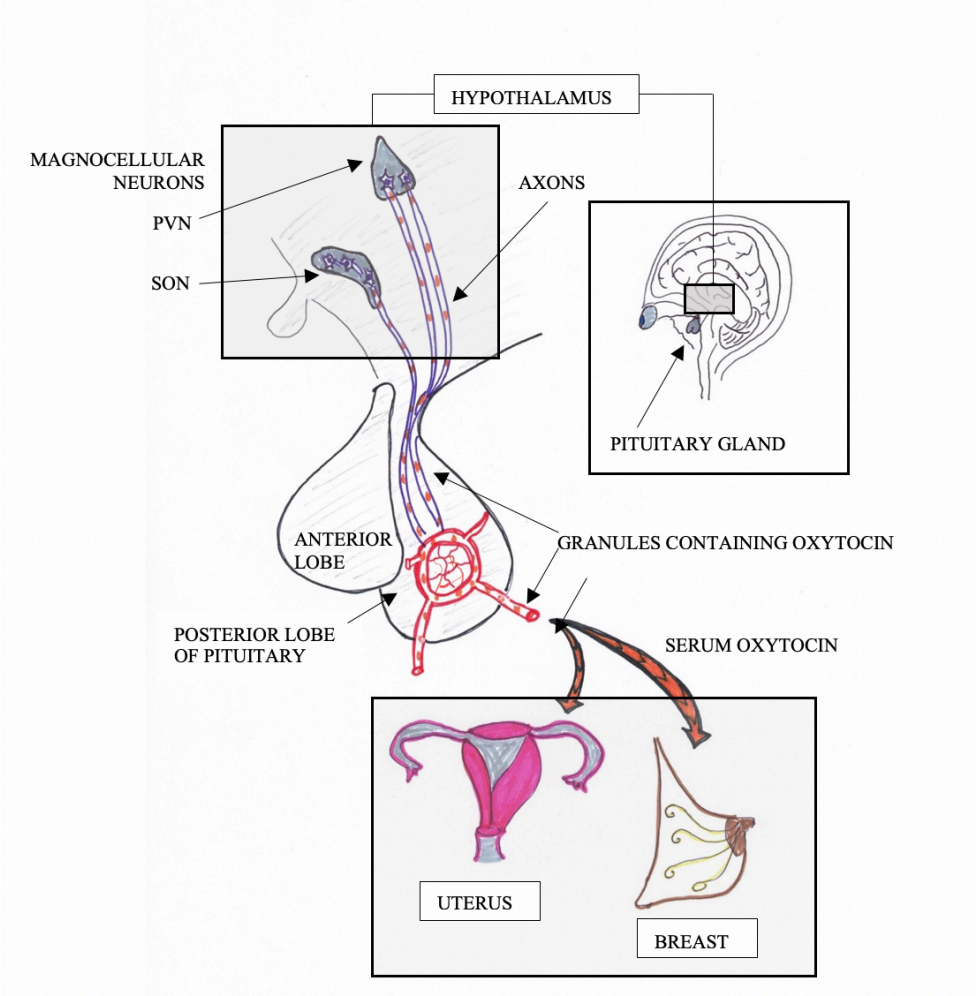

Figure 6.2: Central synthesis and peripheral effects of oxytocin adapted from "The peptide that binds: a systematic review of oxytocin and its prosocial effects in humans. In Harvard Review Psychiatry, 2010; 18(1): 1-21[336]

Under normal physiological conditions oxytocin is present within the cerebrospinal fluid (CSF) in concentrations slightly higher than those in plasma. The pituitary oxytocin content (estimated by bioassay) is ~14IU (28µg)[352]. Circulating concentrations are ~1-10 pg/mL with ~1% excreted in urine[353]. Oxytocin is also produced in peripheral tissues, e.g. uterus, placenta, amnion, corpus luteum, testis, and heart. The oxytocin receptor is a 389-amino-acid polypeptide with seven transmembrane domains belonging to the rhodopsin-type (class I) G protein-coupled receptor (GPCR) family[354]. Its gene is located on chromosome 3p25[355]. With central and peripheral branches of the oxytocin system, some of its effects appear to be mediated via both dynamic (i.e., hormone-driven) and more

static (i.e., genetically determined) alterations in receptor density and location. These receptor variations likely occur over multiple time frames, as the result of both static and mutable influences. Importantly, the central and peripheral release of oxytocin can be unyoked, and peripheral oxytocin levels may not mirror central activity or release[356,357]. There is still much research to be done in exploring the genetically mediated differences in oxytocin receptors and the epigenetics (experience-dependent) of oxytocin genes. It is undoubtedly a complex and plastic system.

6.3.1 Evolving interest in oxytocin's properties

In 1895, Oliver and Schäfer revealed the first physiological effects of the pituitary gland and its extracts—specifically demonstrating the vasopressor properties. In 1906, the English researcher Sir Henry H. Dale found—rather incidentally and reported as a side note—that a posterior pituitary gland extract applied to an early pregnant uterus of a cat has uterine-contracting properties[358]. This led to the name, oxytocin, derived from the Greek words *"oxys"* and *"tokos"*, meaning "quick birth", and later its therapeutic use in obstetrics with Bell conducting the first clinical trial of this extract in 1909, reporting that it powerfully contracted the uterus of women in labour[359]. Within four years, the Professor of Obstetrics and Gynaecology at the University of Toronto declared "it has been employed in practically every obstetrical clinic throughout this continent and in Britain and Europe"[360]. The third major hormonal function of pituitary extracts was discovered by Ott and Scott in 1909 and by Schäfer and Mackenzie in 1911, who described its ability to trigger milk ejection from the mammary gland[361]. It is only recently that interest in oxytocin outside its role in female reproduction has begun to gather steam. The broader scope of oxytocin's role in social behaviour was triggered by the ground-breaking discovery that injection of oxytocin into the brain of female rats brought on full maternal

behaviour towards foster pups[362], followed by the discovery of the role of oxytocin in mate attachment in prairie voles[363,364], and social recognition in mice.[365]

True neuropeptide chemistry started in 1953 with the first successful sequencing of oxytocin, a nine amino acid peptide, after its isolation from lyophilised posterior lobes of cow pituitary glands by Vincent du Vigneaud[366]. The structure of the oxytocin gene was elucidated in 1984[367], and the sequence of the sole known oxytocin receptor was reported in 1992[368]. Despite its relatively recent discovery, it is well established that an evolutionary precursor of oxytocin, the peptide vasotocin, existed at least 700 million years ago. Vasotocin controls courting sounds, sexual behaviour, and birthing in reptiles[369]. It is thought that this more ancient peptide evolved in mammals into two different, but related, social neuropeptide systems: the oxytocin and arginine vasopressin systems[333,370,371]. The highly conserved biochemical structure of oxytocin homologs suggests a strong selective pressure. Their receptors also show a remarkable structural and functional stability throughout evolution[368]. Studies in neuroendocrinology and social neuroscience provide mounting evidence for an intimate link between pro-sociality and the evolutionary ancient and highly preserved neuropeptide oxytocin[333,372]. Critical to the normal operation of human societies, the neurobiology of trust is increasingly attracting attention. In parallel, the potential clinical utility of oxytocin for treating conditions such as autism, schizophrenia, and other social disorders is being explored[333,373].

6.3.2 Oxytocin-mediated regulation of behaviour in humans

We are an intensely social species. Indeed, it has been argued that our social nature defines what makes us human. Humans form long-term attachments to close others, empathise with others, and sacrifice their immediate self-interests to promote the overarching

interests of the groups and communities they belong to[374]. Together, these and related observations fit Darwin's insight that, throughout evolution, pro-social behaviour served individual survival and prosperity: through self-sacrifice and cooperation humans promote the functioning of their in-group that provides for levels of security and prosperity well beyond what individuals could possibly achieve alone[375]. For altricial species (i.e., those species born needing parental care), the immediate initiation and maintenance of social bonds is a survival necessity on a par with food and other basic elements[376]. As such, natural selection has privileged the development of a variety of socially oriented neural circuits that underlie selective attention, perception-action programmes, and social memory[377]. Functionally, these circuits bias mammals to reflexively and actively orient themselves toward seeking, remembering, protecting, and maintaining specific social bonds: these are the neural ties that bind[369]. Functioning as both a neurotransmitter and hormone, oxytocin's targets are widespread and include the hypothalamus, amygdala, hippocampus, brainstem, heart, uterus, and regions of the spinal cord that regulate the autonomic nervous system, especially the parasympathetic branch[356,378]. Long recognised for its role in reproductive functions, oxytocin also appears to modulate broad profiles of social and emotional behaviours in both males and females[333,379], construed to be an integral part of the neurochemical milieu that creates a reflexive sense of safety in the context of social bonds[336].

*6.3.2.1 **Anxiolytic properties of oxytocin***

Social, stress-related, and anxiety-related behaviours have been evolutionarily manifested as critical factors for the survival and biological success of mammals. Social interactions affect every aspect of our lives—both at home and at work. All kinds of social attachment provide a feeling of safety, reduce predator risk, reduce anxiety and stress levels, and thus

promote general fitness and reproduction. The various members of the oxytocin and vasopressin families are strongly involved in the regulation of stress- and anxiety-related responses, and in the regulation of these highly species-specific social behaviours, which is undoubtedly more nuanced and complex in humans as opposed to other animals. Their roles in facilitating social behaviours have been as evolutionarily conserved as the molecular structure of the nonapeptides, their receptors, as well as the neuronal expression patterns within the brain[333].

Insights into the neural mechanisms by which oxytocin modulates social cognition have come from imaging studies which have consistently found that oxytocin decreases amygdala activity, regardless of the experimental scenario. The amygdala has been implicated in social information processing in both humans and animals, and bilateral amygdala lesions in humans impair their ability to judge the trustworthiness of others. As amygdala activation is also indicative of threatening or fearful stimuli, oxytocin mediated attenuation of amygdala activation may facilitate social interactions by decreasing potentially negative, anxiety-provoking associations[380]. In addition, oxytocin has been found to suppress the "classic" stress hormones of the HPA axis[381], reducing cortisol levels after exposure to stressors[382,383], and inhibiting cardiovascular stress responses[383,384]. Hypothalamic release of oxytocin dampens neural circuitries involved in fear-signalling and the regulation of distress[385,386]. Attenuated peripheral levels of oxytocin have been found in patients with depression[387]. A reduction of physiological and psychological reactivity to stressors is a common consequence of oxytocin, with many pathways leading to this outcome. Chronic exposure to oxytocin has been described as a "physiological metaphor for safety"—it appears to activate the "calm, vegetative" parasympathetic

nervous system[388], biasing sensory hormonal, autonomic, emotional, and motor systems toward calm, receptive social connection[336].

6.3.2.2 ***Social-cognitive effects of oxytocin***

Recent human studies have directly manipulated oxytocin systems by using intranasal administration to investigate the potential role for this peptide in modulating human social interactions. Human social inferences are derived largely from viewing facial expression, especially in the eye region. Intranasal infusion of oxytocin increases gaze to the eye region of human faces[389], and participants given oxytocin have been shown to be better at classifying emotions displayed on faces[390], perhaps due to this relatively simple mechanism for increasing the accuracy of mental state inference through increased information availability. Complementary studies also support a role for oxytocin in modulating trust, thereby influencing cooperative interactions. Intranasal oxytocin significantly increases the amount of money that an "investor" is willing to offer to a "trustee" who, after the amount is amplified by the experimenter, can then choose to return a smaller or larger sum back to the initial investor: in one study, 45% of oxytocin-treated subjects demonstrated the maximal trust level, versus 21% in the placebo group[339]. Oxytocin does not, however, increase monetary allocations when the return on an investment is determined by impersonal random lottery. This important control indicates that the effects of administration of this peptide are specific to the social interaction between the investor and trustee, not a generalised effect on risk-taking or optimism, and therefore represents a quantifiable indication of interpersonal trust. Interestingly, oxytocin did not have an impact on any of the subjective states (e.g. reported mood, calmness, beliefs about the trustworthiness of others or about the likelihood of a good outcome) tested at several points during the experiment. These findings are replicated in most extant

human studies of oxytocin in normal subjects and highlight that although oxytocin biases socially sensitive decision circuits and behaviour, it typically does so without affecting conscious awareness[391].

The role of oxytocin in facilitating bonding between parent and child, and between couples, is well established. In addition, it has been shown that when a dog and its owner interact, oxytocin is secreted[392]. Indeed, the more time spent gazing at each other, the bigger the rise. Studies have demonstrated that oxytocin is released when we experience prosocial behaviour (being trusted in a game, receiving a warm touch, and so on) and that a positive feedback loop is established as levels rise[339]. Assessments of plasma oxytocin in humans find that oxytocin levels relate to parental-child bonding behaviours[393], feelings of romantic love and trust[394], and empathy and subsequent generosity towards strangers[395]. What is not known, however, is the role oxytocin may play in facilitating collegiality and familiarity among work colleagues. As the findings in Chapter 3 demonstrated, it has been shown that satisfaction at work is significantly associated with feeling valued, respected, and a sense of social support and community at work.[124] It may be that, at a neurobiological level, oxytocin has a critical role to play in the formation and maintenance of social groups, underpinning the biology of positive social interactions.

In general, people have stronger trust in, and concern for, others they like and feel close to[396], with whom they share common goals and values[397], with whom they anticipate future interaction, or with whom they share group membership[374]. Thus, cooperation is parochial—people more readily cooperate with members of their in-group than with members of more or less rivalling out-groups[398,399]. The development of trust, and the reduction of fear and vigilance, is mediated by amygdala activity[386,400], and in humans,

amygdala activity is lower when exposed to in-group rather than out-group targets[401]. Hypothalamic release of oxytocin promotes the development of trust in in-group others.

6.4 MEASUREMENT

6.4.1 Acute measurement of cortisol—saliva, serum, urine

Biomarkers of acute stress, commonly using glucocorticoids, have been well established, designed to reflect acutely circulating levels or cortisol. Both saliva and serum samples provide a measurement of cortisol concentration at a single point in time, subject therefore, to major physiological daily fluctuations and making long-term systemic cortisol exposure difficult. In general, acute cortisol levels fluctuate markedly depending on many physiological factors including circadian rhythmicity, and it likely provides a rather poor reflection of normal, chronic cortisol secretion[402,403].

6.4.1.1 Salivary cortisol

There is a high correlation between salivary cortisol levels and free (unbound) cortisol in serum. Since free cortisol represents the biologically active hormone fraction, salivary cortisol measures have been considered a better method than serum cortisol for the evaluation of adrenocortical function[404]. Previous studies measuring diurnal salivary cortisol levels have reported no difference in diurnal cortisol between burnout cases and healthy controls[325,349,405] or decreased daytime and/or evening cortisol[406,407], whereas elevated daytime cortisol levels has been related to burnout in other studies[408-410]. Patients reporting higher burnout scores had lower salivary cortisol responses than controls, indicating that patients with more severe burnout symptoms may be hypocortisolaemic in

their response to acute stress[411]. The time point of measurements matters due to the circadian variations[137].

6.4.1.2 Serum cortisol

Measuring cortisol in serum samples assesses total serum cortisol that includes both protein-bound and bioactive (free) cortisol. Consequently, total serum cortisol is affected by changes in levels of cortisol-binding globulin that can result in increases in total cortisol concentration measured, even though there is no increase in stress or free cortisol concentrations. In addition, the act of obtaining a sample via venepuncture can by itself be a source of stress and increase cortisol in the acute phase[412].

6.4.1.3 Urinary cortisol

24-hour urine collections provide an integral of the free cortisol concentrations through the day, thus overcoming the issue of its diurnal rhythm[413]. However, the collection is labour intensive for participants, and still only reflects a single day in time. It is especially prone to measurement error and sloppiness as the samples are usually collected by the participants themselves, without supervision.

6.4.2 Chronic measurement of cortisol—hair

Finding a "gold standard" biomarker for chronic stress has proven to be challenging, given its complex aetiology and highly individual manifestations.

6.4.2.1 ***Development of cortisol detection in hair***

Hair analysis has been used for decades to monitor exposure to exogenous compounds in forensic science and toxicology, with particular emphasis on detecting drugs of abuse[414]. In these situations hair is valued for it unique characteristics of reflecting extended periods of time (months to years) and for providing retrospective information on the time course of substance exposure[415]. More recently there has been a growing interest in quantifying endogenously produced compounds such as cortisol in hair[416].

Hair is produced in hair follicles which are small skin organs embedded in the epidermal epithelium, reaching ~3-4mm below the surface of the skin[417]. The precise mechanisms by which substances are incorporated into hair are still incompletely understood, but it is thought that cortisol enters primarily at the level of the medulla of the hair shaft via passive diffusion from blood capillaries, reflecting the integrated free cortisol fraction rather than the total cortisol concentration in serum[418] (Figure 6.3).

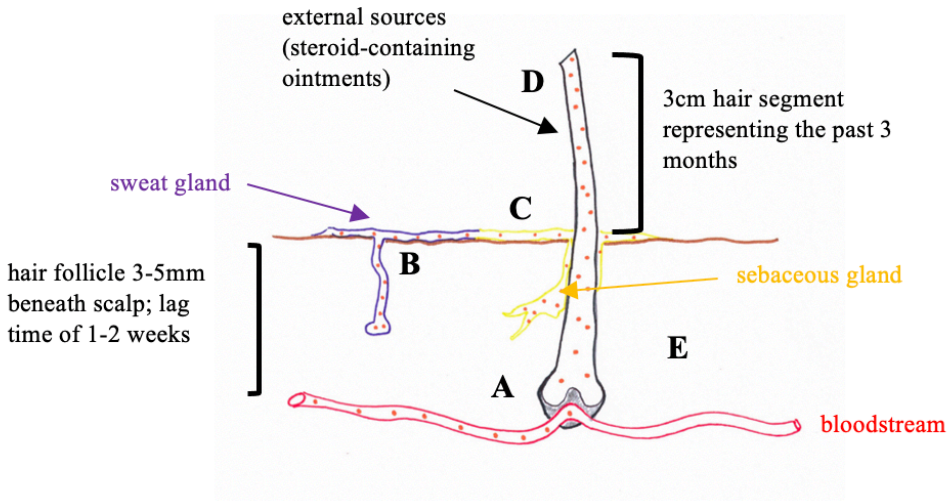

Figure 6.3: Assumed mechanisms of cortisol incorporation into hair and retrospective reflection of long-term cortisol secretion adapted from "Analysis of cortisol in hair—state of the art and future directions" by Stalder T and Kirschbaum C. In Brain, Behaviour, and Immunity, 2012; 26: 1019-1029[402].

Cortisol may be incorporated into hair via passive diffusion from blood (A), sweat (B) and/or sebum (C) as well as from external sources (D). In addition, it has been proposed that locally produced cortisol may also contribute to hair cortisol concentrations (E).

In contrast to the biological fluids, hair can provide biological information of long-term cortisol exposure because its growth rate is fairly predictable at about 1cm/month. Therefore, the most proximal 1cm segment to the scalp approximates the last month's cortisol production, the second most proximal 1cm segment approximates the production during the month before that and so on[419]. Due to the cumulative nature of the sample, the issue of intra- and inter-day cortisol fluctuations is mitigated. The sample can be collected non-invasively by simply cutting a sample of hair at the base of the vertex posterior of the head (Figure 6.4). This eliminates the risk that the sampling may have an impact upon cortisol production.

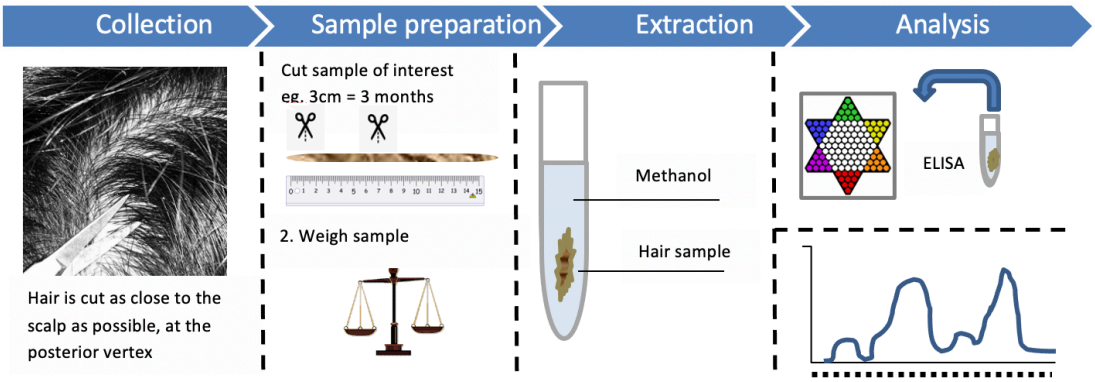

Figure 6.4: Overview of the hair sample collection, work-up and analysis adapted from "Clinical applications of cortisol measurements in hair" by Wester VL and van Rossum EFC. In European Journal of Endocrinology, 2015; 173: M1-M10[420].

Unlike the bodily fluids that require special storage conditions prior to analysis, hair samples are easily transported and stored in envelopes at room temperature[416]. Table 6.1 summarises the specific features of the storage medium scalp hair with regard to the analysis of endogenous cortisol concentrations.

Covering an extended secretion period	The analysis of a 3cm hair segment reflects integrated cortisol secretion over a 3-month period—a window of time virtually impossible to cover adequately using previous methods
"Window into the past"—retrospective assessment	Hair cortisol concentration for the first time provides an opportunity to examine past cortisol status after an event has already occurred
Small amount of hair and non-invasive sampling	As only 10mg of hair/segment are required for analyses, hair sampling normally does not leave any visible marks and is mostly well tolerated by participants
Easy storage	Samples can be stored at room temperatures over long periods of time, making this method ideally suited for field research
Lack of situational confounding	Due to the retrospective nature of hair sampling and the extended detection window, hair cortisol concentrations should not be affected by situational characteristics
Avoiding problems of non-adherence	As hair samples are mostly obtained by the researcher, problems of non-adherence can largely be excluded

Table 6.1: Unique characteristics of the analysis of cortisol in scalp hair adapted from "Analysis of cortisol in hair—state of the art and future directions" by Stalder T and Kirschbaum C. In Brain, Behaviour, and Immunity, 2012; 26: 1019-1029[402].

6.4.2.2 Hair cortisol analysis in clinical practice

Hair cortisol concentrations have been associated with a wide range of clinical outcomes, the results of which are summarized in Table 6.2.

	INCREASED HAIR CORTISOL	DECREASED HAIR CORTISOL
Somatic health factors	Cushing's syndrome Hydrocortisone use Obesity Metabolic syndrome Diabetes mellitus Cardiovascular disease Heart failure severity Recent myocardial infarction	Childhood asthma with inhalation glucocorticoids
Chronic and acute stressors	Intensive aerobic exercise Trauma Life events Unemployment Shift work Severe chronic pain	Traumatic experience
Psychopathology	PTSD Major depressive disorder Bipolar disorder, late onset	PTSD Generalised anxiety disorder Panic disorder

Table 6.2: Clinical and situational factors associated with higher or lower hair cortisol levels adapted from "Clinical applications of cortisol measurements in hair" by Wester VL and van Rossum EFC. In European Journal of Endocrinology, 2015; 173: M1-M10[420].

6.4.2.3 Confounding influences on hair cortisol measurement

The identification of potential confounding influences is an important step in establishing hair cortisol analysis. No influence of natural hair colour on hair cortisol concentration has been reported by human studies[421-424], and research suggests that hair cortisol concentration is unaffected by hair characteristics, such as waves or curls, or by self-reported frequency of hair washing[424,425]. Studies are inconclusive as to whether use of chemical hair treatments (dyeing, bleaching, straightening or permanent waves) affects hair cortisol concentration with some showing no effect[422,424] while others suggest treatments to be associated with reduced hair cortisol concentrations[426]. Age has not been found to be associated with hair cortisol concentrations in most research[421,424,426,427], although many of the studies are small samples with relatively restricted age ranges. Body fat has been suggested as a potential influence on hair cortisol concentrations[426], more sensitively captured by waist-to-hip ratio (WHR) than body mass index (BMI), a finding

concurring with evidence that glucocorticoids are specifically associated with abdominal obesity[424]. No influences of smoking status, use of oral contraceptives, or general medical intake on hair cortisol concentration have been reported[425].

6.4.2.4 Comparison of the various matrices for cortisol measurement

In Table 6.3 properties of the various matrices for cortisol measurement are compared.

PROPERTY	SERUM	SALIVA	URINE	HAIR
Subjective level of invasiveness associated with sample collection	High	Low	Moderate	Low
Cortisol affected by stress of sampling procedure?	Possibly	Possibly	Possibly	No
Storage requirements	Spinning and refrigeration followed by freezing	Refrigeration or freezing	Refrigeration or freezing	Room temperature; stable for years
Time periods of cortisol production represented	Single point measure	Single point measure	12-24 hours; integral of exposure	Months to years; integral of exposure
Affected by changes in cortisol binding globulin	Yes; total cortisol measured	No; only free cortisol measured	No; only free cortisol measured	No; only free cortisol measured
Clinically relevant reference ranges established?	Yes	Yes	Yes	No

Table 6.3: A comparison of properties of the various matrices for cortisol measurement adapted from "Hair cortisol as a biological marker of chronic stress: current status, future directions and unanswered questions" by Russell E, Koren G, Rieder M, and Van Uum S. In Psychoneuroendocrinology, 2012; 37: 589-601[403].

6.4.3 Measurement of oxytocin

The role of oxytocin in human social behaviour has been investigated mainly using two approaches:

- examining the difference in social cognition or behaviour between or within subjects as a result of exogenous oxytocin administration (usually using an intranasal method);
- measuring participants' level of exogenous oxytocin to determine whether those levels change as a function of experimental manipulation (e.g., experimental exposure to a particular type of social interaction, such as expressions of trust) or whether individual differences in either basal levels of task-related reactivity are associated with individual difference variables[334,428].

Endogenous oxytocin is typically released in a context-specific, pulsatile pattern, and is involved with many short-duration effects (e.g., parturition, milk let-down, orgasm, the initial phase of attachment)[356]. There are a variety of confounding factors, in particular the release of other hormones, that are difficult to control for in endogenous stimulation paradigms. Thus, the specific effects of central oxytocin as an underlying biological mechanism for the reduction of stress and anxiety and for positive social interactions in humans are yet to be determined.

6.4.3.1 CSF and plasma oxytocin measurement

The most straightforward approach would likely seem to be measurement from CSF, which might better reflect availability in the brain[429], though central half-life is only about 30 minutes[356]. Realistically, however, this invasive route is not really feasible for routine

use in humans. Oxytocin has a short plasma half-life (1-2 minutes), limiting feasibility of plasma sampling. In addition, whether peripherally measured oxytocin is indicative of central release patterns and activities within the brain and therefore associated with social and emotional behaviours remains up for debate. Some studies suggest that certain stimuli lead to coordinated release of central and peripheral oxytocin, whereas other studies indicate that certain stimuli change central levels while leaving peripheral levels unchanged[430]—it appears that the relationship between central and peripheral oxytocin levels is complex. Perhaps unsurprisingly, therefore, studies comparing basal CSF-oxytocin and plasma-oxytocin levels have yielded mixed results: i.e., both positive correlations[431] and no correlation[432]. Nevertheless, plasma oxytocin levels have been found to be positively associated with several behavioural outcomes, including less anxiety in children[431], and parents' positive communication and social engagement with their children[433], suggesting that this peripheral measure may be an indicator of oxytocin functioning in the brain.

*6.4.3.2 **Urinary oxytocin measurement***

Another method to determine peripheral levels of oxytocin is to measure urinary oxytocin, with the rationale that all the oxytocin in excreted in a pooled manner in urine, without the pulsatile variability. This is a simple method and can be calibrated for fluid intake/excretion variability. Urinary oxytocin may not replace measuring oxytocin levels in CSF or plasma, but it is a non-invasive approach for studying oxytocin and its relationships with behaviours. Researchers have reported associations between social outcomes and urinary oxytocin[433-435], although there remains limited data comparing plasma oxytocin with urinary oxytocin levels. Some correlational evidence suggests correspondence between plasma and urinary oxytocin levels[436,437], while other studies have

reported a lack of correspondence between the two measures[433]. Some of these discrepancies may be related to differences in time course and steady-state in different body fluids, which have varying volume distribution and clearance processes.

6.4.3.3 ***Salivary oxytocin measurement***

Efforts to measure oxytocin in saliva sadly remain in development. Salivary assays typically yield estimates of ~10pg/ml of saliva, and correlate only weakly with enzyme immunoassay-based estimates of oxytocin in unextracted plasma (with r values ranging from .41 to .59)[334,438]. To those unfamiliar with validation standards for new assays, correlations on this order might look like reasonably flattering evidence for the validity of salivary oxytocin assays, but correlations of 0.41 and 0.59 imply coefficients of determination (i.e., percentages of shared variance between the salivary and plasma measures) of 0.17 and 0.35 (i.e., 17% and 35% shared variance), respectively—low magnitude[439]. Moreover, a rigorous evaluation of whether bioavailable oxytocin can be measured in saliva led Horvat-Gordon et al to conclude that "measurement of oxytocin in saliva does not yield meaningful indices of individual differences or intra-individual change"[440].

6.4.3.4 ***Chronic measurement of oxytocin exposure***

Although there is great interest in developing measures of cumulative oxytocin exposure, there is to-date no such validated measure.

6.5 IMPLICATIONS FOR THE STUDY OF BURNOUT

6.5.1 Hair cortisol analysis as a marker of chronic stress

Both physical and psychological stress can induce a biological stress response in the human body, including hyperactivation of the HPA axis. As hair cortisol can measure cortisol levels over extended periods of time and is not affected by the influence of acute stress or time-of-day at the moment of sampling, it is a highly attractive method to investigate the association between chronic stress and long-term cortisol exposure. Disruption of the circadian rhythm is known to be both a physical and psychological stressor[441], and an increase in hair cortisol concentration has been reported in shift workers, compared to day workers[442]. This is an important finding, because shift work is associated with metabolic syndrome components, and cortisol may be in part responsible for this association[420].

The relationship between experienced psychological stress and the HPA axis is complex. Conflicting results have been reported in the association between perceived stress and hair cortisol concentration. Both increased[443] and decreased[444] hair cortisol levels have been associated with higher perceived stress, while other studies have failed to find a relationship altogether[445,446]. This heterogeneity could be a consequence of the diverse composition of study samples, many of whom are patient populations with underlying morbidity[446].

Kalra et al[443] were the first to correlate cortisol levels in hair with self-reported stress using the Perceived Stress Scale (PSS), a validated self-report questionnaire of an individual's stress level over the past month[447]. The concordance between cortisol as a measure of

stress and a self-report measure indicated that hair cortisol analysis might provide a good assessment of an individual's chronic stress level. Dettenborn et al used hair cortisol analysis to rate levels of psychological stress comparing individuals who had been unemployed for at least 1 year with currently employed control subjects. All participants provided a hair sample and rated their level of chronic stress with the Trier Inventory for the Assessment of Chronic Stress (TICS) and a PSS. Cortisol concentrations in hair segments representing the most recent three months were significantly higher in the unemployed group, who also had significantly higher levels of worry on the TICS subscale and higher scores on the PSS, further indicating its effectiveness as a biomarker of chronic stress[427]. Several cross-sectional studies have shown elevated hair cortisol in stressed populations[132,441]. Unfortunately, prospective studies that assess within-person changes in hair cortisol accumulation in the context of long-term stress exposure are lacking.

As outlined above, hair is an exciting new matrix able to provide unique long-term retrospective measures of cumulative cortisol secretion. It offers high potential as a biomarker of long-term stress, known to be associated with a range of negative effects on health. It may be able to be utilised as an objective marker of cortisol exposure and could provide an important mechanism by which to measure physiological change following wellbeing interventions and initiatives due to the ability to assess stress-induced changes in cortisol exposure longitudinally. It will be a crucial goal and intriguing prospect for future enquiries to further exploit the unique characteristics of hair cortisol in relevant burnout research contexts. It certainly holds great promise to significantly enhance our current research efforts.

6.5.2 Oxytocin as a biomarker of wellbeing

In humans, the evolutionary ancient and highly preserved neuropeptide oxytocin modulates a range of cognitive and behavioural functions related to affiliation and bonding. Studies demonstrate that the oxytocin system is an important component in the suite of neural systems that operate, often unconsciously, to bias humans toward prosocial ends, and that it demonstrates prominent effects on the amygdala, a central nexus of the social brain[448]. Oxytocin has been shown to inhibit the stress-induced activity of the HPA axis responsiveness, suggesting an inhibitory influence of oxytocin on stress-responsive neurohormonal systems. It is known that teams function at their best when trust is high and that this feeling of working in a social and supportive environment significantly correlates to increased job satisfaction[124] (as demonstrated in Chapter 3). This stress-protective effect of social support might be mediated through increased oxytocin concentrations, impacting on the brain and human behaviour. It is feasible, therefore, that oxytocin assays could potentially be utilised as an objective biomarker of wellbeing.

6.6 CONCLUSIONS

This chapter has explored the rationale for the use of cortisol and oxytocin as potential biomarkers of wellbeing, outlining the different measurements available to capture physiological change that may represent a proxy measure of burnout. We have considered the limitations in research to-date and discussed potential applications of these biomarkers. To-date no studies have explored the use of these biomarkers as proxy measures of wellbeing in healthcare professionals. The ability to objectively understand physiological change seems increasingly necessary in light of the increasing need to understand whether wellbeing interventions are effective, and the time is ripe for further research in this space.

The next chapter presents an exploratory early-stage study among clinical faculty in an academic medical centre to assess feasibility of biomarker collection, together with correlations of salivary and hair cortisol with burnout, and correlation of urinary oxytocin with connection, engagement, and trust among colleagues.

CHAPTER 7: BIOMARKERS OF PHYSICIAN BURNOUT

"The beginning is the most important part of the work."
Plato

7.1 INTRODUCTION

The last chapter examined important background information on the neurobiology of oxytocin and cortisol, exploring mechanisms of measurement of both these biomarkers and examining the role they both may play in being utilised as proxy measures of human wellbeing. As the opening part of the thesis outlined, burnout is a critical issue impacting the healthcare environment with numerous adverse consequences to healthcare quality and safety, staff wellbeing, and patient satisfaction[20,33,34,67,74,75,98,293,449]. As such, many international organisations have called for healthcare systems to take both programmatic and institutional responsibility for prioritising healthcare professionals wellbeing[126,127,450]. As has been described, these efforts to address burnout are hampered by challenges in conceptualising and measuring burnout, in part because of inadequate understanding of its pathophysiology[95]. Although the Maslach Burnout Inventory (MBI) is widely used and regarded as the gold standard of measurement[14], concerns exist about heterogeneity in results and applicability of the underlying conceptual framework[15,128], including the integration of domains of emotional exhaustion (EE) and depersonalisation (DP) into a composite burnout score. Multiple experts have emphasised the importance of advancing the current approach to conceptualising and measuring burnout[128].

7.1.1 Cortisol

As burnout and stress are conceptually linked, neuro-hormonal changes in response to stress, such as cortisol levels, may provide a novel avenue for understanding the pathophysiology of emotional exhaustion and depersonalisation and for improving measurement using biomarkers. Physiological stress responses, mainly triggered through the sympatho-adrenal medullary system and the hypothalamic-pituitary-adrenal (HPA) axis result in the release of glucocorticoids, specifically cortisol.[130] Given that physician burnout may represent a stress response to an adverse work environment, high burnout may result in high levels of cortisol. High levels of cortisol have been associated with mental health and coronary heart diseases[451]. Thus, as outlined in Chapter 6, cortisol may be a candidate measure to capture physiological burnout. In addition to measuring cortisol in saliva, which reflects acutely circulating hormone concentration with diurnal variation that may limit usability, measuring cortisol in hair for cumulative long-term stress exposure has recently started[131]. Capitalising on the continuous incorporation of lipophilic substances, such as steroid hormones, into the growing hair, hair cortisol concentrations are assumed to provide an easily obtainable index of cortisol levels integrated over the extended period of hair growth, i.e. several months[132]. There is strong evidence to suggest that hair cortisol concentration is a valid and solid index of long-term glucocorticoid secretion, with high intraindividual stability and test-retest reliability[132]. Despite a myriad of studies on stress and cortisol published in the past decades, surprisingly few studies have examined alterations of glucocorticoid levels in relation to burnout. Published data are inconsistent with reports of both high and low cortisol levels[452], though these studies mainly employ spot measurements with single blood or saliva samples which are sensitive to transient fluctuations of HPA axis activity and likely do not reflect glucocorticoid output over prolonged periods of time.

7.1.2 Oxytocin

Another hormone that may be implicated in burnout is oxytocin, which is known to increase in situations with high trust or bonding[133]. Stress, uncertainty, and isolation all work against the development of a trusting disposition. As discussed in Chapter 3, workplaces where there is a sense of supportive connection and community have higher rates of satisfaction at work. As discussed in Chapter 6, oxytocin may be a useful biomarker for protection against workplace stress. Trust is known to be an adaptive mechanism essential to building social relationships and trust and respect have been shown to be fundamental for effective teams. Inspection of the literature reveals that the effects of oxytocin in the social domain are weak and inconsistent, with no studies to-date in healthcare professionals. Although there is great interest in developing measures of cumulative oxytocin exposure, currently oxytocin is measured in plasma or urine, as salivary measurements have not been well-validated, and measurement in hair is not currently an option. Peripheral levels of the hormone are used as a proxy for central hypothalamic release given the challenges, risk, and invasiveness of measuring oxytocin centrally in cerebrospinal fluid.

7.1.3 Chapter aims

This chapter describes an early-stage study among clinical faculty in an academic medical centre to assess feasibility of biomarker collection, together with correlations of salivary and hair cortisol with burnout, and correlation of urinary oxytocin with connection, engagement, and trust among colleagues. We hypothesised that emotional exhaustion and depersonalisation would both be associated with higher cortisol levels, and that increased connection, engagement, and trust would correlate with higher oxytocin levels.

7.2 METHODS

7.2.1 Study Design

As part of an early-stage study of inter-disciplinary support groups (reported in Chapter 8), we collected data on perceived burnout, salivary and hair cortisol, and urinary oxytocin on 26 clinical faculty members in the Department of Obstetrics and Gynaecology at the Massachusetts General Hospital (MGH), a large teaching hospital in the US affiliated with Harvard Medical School (HMS).

7.2.2 Participants and recruitment

All full-time clinical faculty in the Department of Obstetrics and Gynaecology were invited to participate. Exclusion criteria were a current pregnancy or current breast-feeding. Participants were recruited through electronic departmental communications, and announcements at departmental meetings. Participants provided written informed consent and precautions were taken to secure confidentiality. Data were collected in May 2018 at the start of a series of monthly support groups designed as part of an ongoing study of strategies to reduce burnout (described in Chapter 8). All data used were strictly anonymised; only a research coordinator, who was not involved in this study, had access to the file linking responses with identifiers. Due to sex differences in expression of oxytocin and its receptor[370,453], and insufficient hair length, the single male participant was excluded from the data analysis. The study was approved by the Partners Institutional Review Board (Protocol Number 2018P000415).

7.2.3 Survey instrument and variables

7.2.3.1 Survey instrument

Participants completed a 5-minute online survey in May before the support groups had commenced. Survey items were developed in one of three ways: some were taken from previously administered faculty surveys; some domains used validated scales; and some were developed *de novo* using literature review and expert interviews to develop questions. The survey included personal and professional characteristics (e.g. gender, years in practice, years at MGH, and discipline); a 2-item validated burnout scale; engagement at work; sense of connection and trust; together with other domains reported in Chapter 8. The secure, web-based application, Research Electronic Data Capture (REDCap), was used to manage survey distribution and collect responses[271]. Each participant received an individualised link to the survey. The initial email was sent at the beginning of May 2018, before the first support group. Reminders were sent to non-responders.

Perceived burnout was assessed using the single-item measures of emotional exhaustion and depersonalisation from the MBI[14,129], "I feel burned out from my work" and "I've become more callous towards people since starting this job", each answered on a 7-point Likert-type scale with response options ranging from never to daily. These two items have been shown to stratify risk of burnout in healthcare professionals[129,454]. Consistent with previous literature, participants indicating that they experienced symptoms at least weekly were considered to meet the criteria for high burnout in that domain. We used the Utrecht Work Engagement Scale to measure work engagement—a positive work-related state of fulfilment that is characterised by vigour, dedication, and absorption[299] (a total of 9 items on a 6-item Likert scale ranging from *never* to *daily*; range 0-54). Higher scores reflect

increased engagement. Sense of connection was measured using a 6-item Likert scale (ranging from *strongly disagree* to *strongly agree*) to the statement "I feel a sense of connection and community at work". Sense of trust was measured using a 6-item Likert scale (ranging from *strongly disagree* to *strongly agree*) to the statement "I trust my ob-gyn colleagues and feel safe discussing concerns with them". Responses for connection were reduced to strongly/moderately agree against everything else; responses for trust were reduced to strongly agree against everything else. These category classifications were chosen to ensure even spread in distribution across participants.

7.2.4 Biomarker collection

All samples were collected at 5pm before support groups started. Due to the short half-life and fluctuating nature of salivary cortisol and urinary oxytocin, these biomarkers were also collected between 6-7pm when the support groups finished. The mean of these two samples was used for analysis to increase reliability of assessment.

7.2.4.1 Salivary cortisol

Salivary cortisol is considered a reliable and valid measure of unbound ("free") cortisol concentrations in plasma[455]. Salivary samples were obtained by giving participants a cotton swab to chew for about one minute. The cotton swabs were then placed in a commercially available saliva-collecting device (Salivette; Sarstedt, Rommelsdorf, Germany) and frozen at -80ºC. Before assaying for free cortisol, samples were thawed and spun at 3000 rpm for 15 minutes to obtain 0.4-1.0mL clear saliva with low viscosity. The free cortisol concentrations were determined using an enzyme linked immunosorbent assay (ELISA) kit (Salimetrics; State College, Pennsylvania). The detection limit was

0.007ug/dL, and the intra- and inter-assay coefficient of variations (CVs) were 3-7% and 3-11%, respectively.

7.2.4.2 Hair cortisol

Hair cortisol concentrations were provided from the 3cm most proximal to the scalp. Samples were taken from the vertex posterior region of the scalp as this has been shown to have the lowest intra-individual coefficient of variation for cortisol concentration[422]. As the sample is collected non-invasively, it eliminates the risk that the sampling may have an impact upon cortisol production. Due to the average hair growth of 1cm per month[419], a 3cm sample reflects a measure of cumulative cortisol secretion for the period of 3 months prior to the sampling[402], with issues of intra- and inter-day cortisol fluctuations mitigated. Because of this lag, an additional hair sample was collected in August 2018, three months after the initial collection in May 2018. There are no requirements for special storage conditions prior to analysis, and hair samples were stored in aluminium foil at room temperature[416]. Washing procedure and cortisol extraction were conducted in accordance with the laboratory protocol by Gao et al[456]. All samples were analysed by liquid chromatography coupled with tandem mass spectrometry at the Biopsychology Laboratory, Dresden University. Intra and inter-assay CVs for cortisol analysis by this method are reported to range between 3.7% and 8.8%.

7.2.4.3 Urinary oxytocin

Urinary oxytocin assays were chosen as they offer a simple, easy, and non-invasive method to measure peripheral hormone levels. Sampling of urine has the added benefit of being stress-free, which is of importance for stress-sensitive experimental designs.

Participants were asked to urinate into a urine cup; the sample was then immediately stirred with a disposable pipette. The same plastic pipette was used to measure two 2ml aliquots. The aliquots were snap frozen by placing the vials immediately on dry ice. The samples were moved to long-term storage in a -80ºC freezer until shipment on dry ice to the University of Wisconsin-Madison National Primate Research Centre for assay of oxytocin and creatinine to adjust for sample volume. Urine samples were thawed while remaining below room temperature, vortexed, centrifuged and aliquoted as 1ml for solid-phase extraction (SPE, 100mg, C-18, Oasis SepPak, Waters WAT 023590), which purified the urine and removed possible contaminates[435]. The samples were assayed with oxytocin ELISA kits (Oxytocin ELISA kit, ADI-901-153A, Enzo Life Sciences). Pre-treatment of each column was done with 1ml methanol and 1ml water. The sample was then loaded and vacuum applied. The solid-phase extraction was washed with 10% acetonitrile (ACN) plus 0.1% trifluoracetic acid (TFA) and eluted with 80% acetonitrile. Samples were evaporated in a SpeedVac at 45ºC for 1 hour. After drying, samples were stored at 2-8 º in 300µl ethanol until day of assay. Samples were dried and resuspended in 250µl of assay buffer using 100µl of sample into duplicated wells, using one third of the sample per well. Following an overnight incubation, substrate was added to the wells, and the plate was read using a Molecular Devices Spectramax 340PC 384 at 405nm. The sensitivity of the assay was 15pg/ml. The intra-assay CV was 13%. To compensate for participant's potential daily variable fluid intake, creatinine levels were measured in each urine sample and divided into the hormonal concentration ([oxytocin]/[creatinine]), expressed as the oxytocin to creatinine ratio (pg/mg creatinine) with 1ml SepPak C18 cartridges.

7.2.5 Statistical Analysis

Linear regression was used to assess the relationship between hormone levels and measures of wellbeing, focusing on the association between cortisol and burnout (high vs. low emotional exhaustion and depersonalisation) and oxytocin and engagement, connection and trust. For analyses of repeated cortisol measures, we adjusted the standard errors for correlation within subjects. Analyses were conducted retaining all samples and after excluding outlier values more than 2SD beyond the mean. All p values were from 2-sided tests and results were deemed to be statistically significant at $p<0.05$. All statistical analyses were performed with the use of commercially available statistical software (Stata version 14.0; College Station, TX: StataCorp LP).

7.3 RESULTS

7.3.1 Characteristics of the participants

Study population characteristics, including rates of completion of biomarker assessment, are reported in Table 7.1.

	RESPONDENTS (N=25)			
	N	%	Mean	SD
Years in practice				
<5	0	0	-	-
5-10	4	16	-	-
11-15	5	20	-	-
16-20	7	28	-	-
>20	9	36	-	-
Burnout				
Low emotional exhaustion	10	40	-	-
High emotional exhaustion	14	56	-	-
Low depersonalization	19	76	-	-
High depersonalisation	5	20	-	-
Engagement				
Utrecht work engagement scale	24	96	38.9	6.5
Trust among colleagues				
Low trust	14	56	-	-
High trust	10	40	-	-
Connection				
Low sense of connection/community	12	48	-	-
High sense of connection/community	12	48	-	-
Biomarkers				
Salivary cortisol (ug/dL)	21	84	0.056	0.027
Hair cortisol (Time 1) (pg/mg)	16	64	8.14	13.35
Hair cortisol (Time 2) (pg/mg)	20	80	24.8	30.14
Urinary oxytocin (pg/mg/creatinine)	20	80	22.7	12.4

Table 7.1: Characteristics of the participants

7.3.2 Feasibility

All of the faculty members enrolled in the study of interdisciplinary support groups consented to the collection of biomarker data including saliva, urine, and hair. However, collecting biosamples from faculty was challenging because of conflicting time pressures, unpredicted clinical demands at the collection timepoints, and inadequate samples.

7.3.3 Burnout

Emotional exhaustion was associated with significantly higher salivary cortisol levels (0.03ug/dL increase with high vs low emotional exhaustion; p = 0.036) whereas depersonalisation was associated with significantly lower salivary cortisol levels (0.04ug/dL decrease with high vs low depersonalisation; p = 0.018). When hair cortisol was analysed as a repeated measure, it was positively correlated with emotional exhaustion (coefficient 20.21, SE 8.77; p = 0.026) and inversely correlated with depersonalisation (coefficient -20.18, SE 10.42; p = 0.06). These associations were not significant when adjusting standard errors for clustering within subject (p = 0.19 for both).

7.3.4 Connection, engagement, and trust

Urinary oxytocin was significantly higher among participants reporting higher sense of connection and community (29.2(16.2) vs 17.3(3.8); p = 0.028) and there was a strong positive correlation among participants with higher engagement (r = 0.45; p = 0.048). Urinary oxytocin was higher among participants reporting higher trust in colleagues (29.4(19.2) vs 19.1(4.5)) but this did not reach statistical significance (p = 0.076).

7.4 DISCUSSION

To our knowledge, this is the first study to examine the feasibility and potential associations between burnout symptoms and the physiological markers of stress and connection and trust in clinical faculty at an academic medical centre. At a time of limited understanding of the pathophysiology of physician burnout[95,128], these results suggest that the two commonly identified burnout domains, emotional exhaustion and depersonalisation, may have opposing effects on endogenous cortisol levels, suggesting

that emotional exhaustion may increase the physiologic stress response while depersonalisation may result in a dampened stress response, perhaps because of its connection to apathy and emotional disconnection. As hypothesized, urinary oxytocin levels were associated with higher levels of connection and engagement and this biomarker may be a useful objective measure of workplace culture and relatedness, known to be critical for the functioning of healthcare[116]. We found a potential signal between oxytocin and trust. Future studies will be important to confirm these novel findings in larger samples.

This study demonstrates the feasibility of collecting and evaluating biomarkers in working academic medical faculty, suggesting that future studies can be done to continue to examine potential associations between burnout symptoms and the physiological response to stress in faculty at an academic medical centre. Although statistical significance was strongest for the association with salivary cortisol, hair cortisol levels may be easier to assess in most settings as they are not sensitive to transient fluctuations of HPA axis activity, do not require collection at the same time of day, and are a measure of chronic cortisol exposure. Biomarkers are extensively used in occupational health practice, but their use to measure markers of stress and burnout in faculty is not common practice. With calls from national organisations to prioritise health professionals' wellbeing, there is a critical need for objective, easy-to-obtain, noninvasive biomarkers that reflect wellbeing. In particular, there is a need for the establishment of a biomarker that accurately measures intensity and course of stress over time. This study demonstrates a potential signal indicating that hair cortisol concentrations may be an effective and objective chronic measure correlating with burnout symptomatology. Evidence from an increasing number of studies across a range of paradigms now supports the general validity and reliability of

hair cortisol concentrations. This novel use of hair cortisol, an easy-to-collect and store medium, could prove to be a meaningful measure of physiological stress representing harmful burnout and could provide a measure by which interventions to improve wellbeing could be assessed.

The study also demonstrated a positive correlation between engagement and oxytocin, and sense of connection and community and oxytocin. As the findings in Chapter 3 demonstrated, it has been shown that satisfaction at work is significantly associated with a sense of social support and community at work[124], suggesting that oxytocin may be a novel way of evaluating workplace culture and relatedness, particularly with regard to familiarity among colleagues, known to be important in the promotion of wellbeing. At a neurobiological level, oxytocin may have a critical role to play in the formation and maintenance of social groups, underpinning the biology of positive social interactions.

As with previous studies, we looked at perception of burnout, measured using the single items from the MBI to capture emotional exhaustion and depersonalisation and dichotomised burnout to be high or low, as opposed to continuous scores. Previous research has shown associations between hair cortisol concentrations and burnout dichotomised in this way[131]. This has been hypothesised to be due to a nonlinear relationship between burnout and glucocorticoid exposure—burnout symptoms may not affect basal glucocorticoid levels until a certain level of severity is transcended, whereas burnout symptoms in the upper severity range would hardly unfold any additional impact on glucocorticoids. To understand the time-course of biological alterations in burnout, prospective longitudinal studies are needed. Future research should compile detailed intra-individual information about severity and duration associated with burnout symptoms.

Based on that information it should be tested if there is a change point, where symptom severity and duration start to significantly alter basal glucocorticoid secretion and further immune competence.

7.4.1 Limitations

The study has several limitations. It included a small number of volunteer faculty within a single department. Missing information on some biomarkers further limited statistical power. However, to our knowledge, it is the first study to demonstrate that biomarkers may provide valuable information in both measuring and understanding professional burnout. Research exploring the role of biomarkers such as cortisol and oxytocin in humans is difficult owing to the release in both body and brain, together with the interaction effects with other hormones and neuromodulators. With oxytocin, specifically, there are additional difficulties due to the intricacies of the blood-brain barrier and oxytocin's instability, which creates measurement issues. Measurement through urine is, however, accepted as a valid medium with benefits owing to the non-invasive, easy nature of collection. With regards to hair cortisol measurement, we did not collect information regarding hair colour, frequency of hair washing, or any cosmetic treatments to hair. However, previous studies have not detected significant differences in cortisol levels due to hair colour[422]. In addition, though the mean hair growth rate averages about 1cm/month, variations in hair growth profile do exist which were not accounted for in our study. To limit intra-scalp differences, all samples were taken from the vertex posterior of the scalp. The speculative nature of our interpretation underscores the need for additional research to determine if these results hold in larger samples and to understand how best to incorporate biomarkers into ongoing efforts to understand and address clinician burnout.

7.5 CONCLUSIONS

Medical education programmes are now required to monitor burnout, with mandatory wellness promotion programmes. To measure efficacy and success, we need to work towards consensus on how to accurately and reliably measure and define burnout. Perceptions of acute stress and burnout, as captured by survey instruments, may not correlate with physiological changes. The addition of objective measures of chronic stress exposure that capture physiological variance may be particularly important in helping to design interventions that mitigate harmful stress exposure. Our findings call attention to the potential novel use of biomarkers to measure burnout and connection and trust in healthcare professionals which may be a valuable starting point for the ongoing search for objective measures that have clinical meaning.

PART III

EXPLORATION OF INTERVENTIONS TO REDUCE BURNOUT AND STRATEGIES TO EMBRACE UNCERTAINTY

CHAPTER 8: EFFECTS OF AN INTERPROFESSIONAL GROUP INTERVENTION ON FACULTY WELLBEING, ENGAGEMENT, AND UNCERTAINTY

"Groups with a greater number of courageous, sympathetic and faithful members, who were always ready to warn each other of danger, to aid and defend each other … would spread and be victorious over other tribes."
Darwin[398]

8.1 INTRODUCTION

As has been emphasised throughout this thesis, professional burnout is a critical issue impacting the healthcare environment with numerous adverse consequences to quality and safety, faculty wellbeing, and patient satisfaction[20,33,34,67,74,75,98,293,449]. As we have seen, many research studies have explored the drivers of burnout, drawing attention to the consequences of reduced relational connection with colleagues and a lack of feeling valued and respected (as we saw in Chapter 3)[124], and the distress caused by uncertainty[9,113,242] (as we saw in Chapter 4). To date, most wellbeing initiatives have focused on faculty who share the same professional role, e.g., physicians, rather than studying the inclusive interprofessional groups that make up most academic departments[8,124,144]. Even among those there is still much debate regarding interventions that are sustainable, scalable, effective, and evidence-based within single departments let alone applicable to the interprofessional environment. This chapter presents a novel study evaluating an interprofessional wellbeing intervention designed to increase relational connection between clinical faculty and enhance faculty engagement in an obstetrics and gynaecology (ob-gyn) department at a large academic medical centre.

8.1.1 Burnout risk for obstetrics and gynaecology faculty

National surveys indicate that faculty and trainees in ob-gyn are at particular risk of burnout[24,457,458], due to the physical and temporal demands of practicing a specialty that spans both surgical skills and primary care responsibilities, and which involves a high degree of emotional intensity[459]. As was explored in Chapter 1, the consequences of burnout in healthcare professionals are wide-reaching: from increased rates of depression and suicide[37-41], and decreased patient safety[58,59,61,63,64,66,67], to increased healthcare costs through loss in productivity and turnover of staff, with recent estimates of the organisational cost to replace a physician in the realm of $500,000 to. $1,000,000[1,74,76,79].

8.1.2 Limitations of wellbeing strategies shown to be effective

The wellbeing strategies that have been shown to be effective are limited in three key ways, as outlined below.

8.1.2.1 Efforts focus on behaviour of individual faculty

Many of the practices that have emerged as evidence-based solutions, such as stress management training, self-care behaviours, and mindfulness techniques[143,179,460-463] may be limited in efficacy by focusing on the behaviour of individual faculty. Many have expressed concern that framing burnout as an individual problem, with solutions to be implemented by individual faculty, may unintentionally exacerbate burnout by absolving institutions from the responsibility to change the systemic factors that contribute to burnout[57,464].

8.1.2.2 Challenges with regard to feasibility, cost, and sustainability

Studies show that feeling valued and respected is significantly associated with job satisfaction[124] (as demonstrated in Chapter 3) and that promoting a culture that encourages vulnerability and sharing of uncertainty and concerns is important[32], but there are significant barriers to this in healthcare[33]. While a culture of psychological safety, defined as "being able to show and employ one's self without fear of negative consequences of self-image, status or career"[465], is at the core of successful team functioning, shown to play a vital role in helping people thrive in challenging and high-stakes work environments[466], it is unfortunately too often elusive in the healthcare setting where a salient hierarchical structure and powerful professional norms may threaten an ability to speak up or ask for help. An additional challenge to the creation of camaraderie and community on healthcare teams relates to the fluid nature of human capital as trainees rotate through healthcare environments, with shift-pattern work structures and reduced duty hours. This dynamic team structure, with constantly changing membership, adds complexity to the creation of psychological safety and openness in work groups.

One promising study in internal medicine physicians demonstrated that strengthening connections between colleagues increased empowerment and a sense of meaning at work, while reducing emotional exhaustion and depersonalization[272]. In that intervention, physicians met fortnightly for nine months in small groups with a trained facilitator to discuss topics related to wellbeing. Although interventions like this go beyond individual practices of mindfulness or yoga and invest in a broader sense of community among faculty, the need for trained facilitators, written guides, and long-time commitments may pose challenges with regard to cost and sustainability.

8.1.2.3 Lack of focus on interprofessional interventions

Most studies of wellbeing interventions in healthcare have tended to focus on faculty who share the same professional role, such as physicians-only or nurses-only, rather than studying the inclusive interprofessional groups that make up most academic departments, in which physicians, nurse practitioners and other allied health professionals work collegially together[8,124,144]. Whilst there is little doubt in the benefits of interprofessional education and team-based collaborative practice[467,468], the literature is lacking in evidence-based interprofessional interventions that might enhance workplace engagement and reduce burnout for these faculty.

8.1.3 Developing a wellbeing intervention to address these challenges

In light of the concerning impact of faculty burnout, and the limitations of current interventions, proactive strategies are needed that transform institutional culture, have realistic time and cost footprints, and include the full community of healthcare providers. This chapter presents the results of a pilot randomised clinical trial evaluating a departmental intervention to increase relational connection between interprofessional faculty and enhance faculty engagement. In an effort to expand upon previous studies, and explicitly address some of the limitations outlined above, this intervention consisted of self-facilitated, interprofessional groups meeting regularly for three months. Table 8.1 outlines the rationale for the design of the intervention, building on issues explored here and in Chapter 1.

STRATEGY	RATIONALE
Self-facilitated	Prevents need for trained facilitators, which can be both costly and hard to find, limiting scalability and sustainability[272].
	Interventions that engage faculty in their process might heighten their sense of control and engagement, which might be expected to effectively reduce burnout[145].
Interprofessional	Most studies to date have focused on faculty who share the same professional role, rather than studying the inclusive interprofessional groups that make up most academic departments[8,124,144]. As we move towards more collaborative practice and interprofessional education, efforts in the wellbeing space to match this format.
Three-month time period	Long-time commitments can pose challenges with regard to feasibility, sustainability, and cost[143].
Group meetings at work	Moves away from concept of burnout as an individual problem to be addressed in faculty's own time at home to a team-based and organisationally embedded strategy which is more likely to have longevity and sustainability[57,71,464].
Dinner provided	Creating a social culture where faculty feel supported and cared about by the department has been shown to be significantly associated with increased satisfaction at work[124].
Structured discussion guide	Unclear whether any benefit that results is from simply bringing people together, or whether a structured discussion guide that addresses themes relevant to challenges in the healthcare environment enhances group bonding. Strategies that foster communication between members of the healthcare team, cultivating a sense of team tend to be most effective in reducing burnout[142], and as loss of meaning from work is a common driver of burnout, explicit discussion around this may be an effective solution.
	We designed this aspect of the study as a randomised controlled trial, which is a rigorous study design rarely reported in the literature in this space[143]. The control group had no guide; the intervention group had a structured discussion guide

Table 8.1: Rationale for features of the interprofessional intervention designed for this study.

8.1.4 Chapter aims

As highlighted above, there is a paucity of research focused on wellbeing interventions that target the inclusive interprofessional groups that make up most academic departments. The study presented in this chapter was designed to address the research question: Do self-facilitated, interprofessional groups meeting regularly for three months enhance faculty wellbeing, engagement, and tolerance of uncertainty?

- Primary aim: To determine whether burnout is reduced; and engagement, empowerment, trust, satisfaction, and tolerance of uncertainty are increased, in a setting of self-facilitated, interprofessional groups meeting regularly for three months.
- Secondary aim: To determine whether a series of structured written discussion guides for use during the group meeting is necessary to achieve the outcomes listed above.

We hypothesise that increased relational connections between faculty would build engagement, trust, and community at work and result in measurable reductions in burnout, with an increased sense of professional satisfaction and support from the department. This study is novel in two key ways: it is the first to examine the benefit of self-facilitated faculty small groups and is the first to test a burnout intervention in an interprofessional group of physicians, certified nurse midwives and nurse practitioners.

8.2 METHODS

8.2.1 Study design

We conducted a single centre randomised trial of 26 practicing obstetrics and gynaecology faculty at a large US academic medical centre to test the hypothesis that an intervention involving self-facilitated interprofessional group meetings would result in improvement in wellbeing and to determine whether use of a structured written discussion guide provided increased benefit. Data were collected between May and August 2018.

8.2.2 Participants and recruitment

All faculty in the obstetrics and gynaecology department at the Massachusetts General Hospital (MGH) in Boston, US, were invited to participate. Participants were recruited through electronic departmental communications, and announcements at departmental meetings. Participants provided written informed consent and precautions were taken to ensure confidentiality. The study was approved by the Partners Institutional Review Board (Protocol Number 2018P000415); clinicaltrials.gov identifier: NCT04305886.

8.2.2.1 Randomisation, allocation concealment, and evaluation

Participants were randomised in a concealed fashion into either control or intervention group via a computer-generated algorithm that factored in their schedule availability. Participants were surveyed at baseline and at the end of the 3-month study period. Participants were aware that the groups were part of a departmental wellness initiative but were not informed as to the hypotheses of the study and were deliberately provided with little information about the aims.

8.2.2.2 Study arms

Volunteers in both arms of the trial were invited to three dinners, each spaced approximately one month apart. Participants randomised to the intervention group were given a one-page discussion guide and self-facilitated the discussion over dinner. There was no pre-work required and groups were free to use the guide as much or as little as they wished. The 14 intervention arm participants were divided into two small groups (6-8 interprofessional participants in each) with similar compositions by sex and professional group. The one-page discussion guides addressed themes chosen through expert consensus and literature review with topics relevant to the work experiences of practicing faculty and included 'Reframing Challenging Patient Interactions'; 'Embracing Uncertainty in Our Work'; and 'Coping with Errors, Near Misses, and Bad Outcomes' (see Appendix 8.1 – 8.3). Each guide followed the same general structure:

(1) Introductory check-in and welcome;

(2) Brief explanation of the topic;

(3) Discussion prompts to guide conversation;

(4) Closing words and time for reflection;

(5) Resources for further reading if interested.

The 12 participants randomised to the control group were also divided into two small groups (5-6 interprofessional participants in each) but were not given a discussion guide or any other instructions about what to discuss during the dinner session.

All groups conducted their first and third dinner in a conference room at the hospital, with catered food, with their second dinner held in a local restaurant. Groups were not given a time limit for the duration of their dinner, and sessions ranged between one to two hours. The cost per faculty member per dinner was $29.40 (approximately £23).

8.2.3 Survey instrument and variables

Participants in both arms of the study completed a short 5-minute online baseline survey in May 2018 before the groups began that consisted of several validated instruments, including burnout, stress from uncertainty, work engagement and work empowerment, together with questions relating to their perception and experience of wellbeing initiatives in the ob-gyn department. Demographic characteristics were also collected, together with information on length of practice and years at the institution. Participants completed a 3-month survey in August 2018 after the dinner meetings had finished which included some additional questions about satisfaction with the groups and likelihood of future participation or recommending the groups to others. Questions of gradation were rated on a 5-point Likert scale. Participants were included in the data analysis if they attended at least two dinners.

8.2.3.1 Stress from uncertainty

To determine stress from uncertainty, we used the Physicians' Reaction to Uncertainty Scale, developed by Gerrity et al[236], which measures affective reactions to uncertainty in clinical situations. Subscales included: anxiety caused by uncertainty (Cronbach alpha, 0.85), concern about bad outcomes (Cronbach alpha, 0.74), reluctance to disclose uncertainty to colleagues (Cronbach alpha, 0.72), and reluctance to disclose uncertainty to patients (Cronbach alpha, 0.76). The items are rated on a 6-point Likert-type scale. Its ability to measure relevant differences in reaction to uncertainty has been demonstrated in several studies[216,236], and it is distinguished by its well documented psychometric properties and its relevance to medical situations. The subscales are scored so that higher values indicate more stress from uncertainty.

8.2.3.2 Burnout

We used single item measures of emotional exhaustion and depersonalization from the Maslach Burnout Inventory (MBI) to assess the prevalence of burnout. Although the 22-item MBI is the criterion standard in medical research literature for the assessment of burnout[14], its length limits feasibility for use in surveys addressing multiple content areas within space constraints and we therefore chose to use the 2 single-item measures. Emotional exhaustion was assessed by the statement "I feel burned out from my work" and depersonalization by the statement "I've become more callous toward people since I took this job". Each question was answered on a 7-point Likert-type scale with response options ranging from never to daily. These two items have been shown to stratify risk of burnout in physicians and medical students[129,454]. Consistent with previous literature[14,23,129], participants indicating that they experienced symptoms in either domain at least weekly were considered to meet the criteria for high burnout. In light of the debate of how to quantify burnout with several authors emphasising that the burnout score should be seen as a continuous measure of increasing levels of professional stress as opposed to a dichotomous measure[15,128], we also report the continuous burnout score.

8.2.3.3 Engagement and empowerment

We used the Utrecht Work Engagement Scale to measure work engagement—a positive work-related state of fulfilment that is characterised by vigour, dedication, and absorption[299] (a total of 9 items on a 6-item Likert scale ranging from never to daily; range 0-54). The Empowerment at Work Scale (a total of 12 items on a 7-item Likert scale ranging from very strongly disagree to very strongly agree; range, 12-84) was used to measure empowerment and meaning at work[469].

8.2.4 Data collection

The secure, web-based application, Research Electronic Data Capture (REDcap), was used to manage survey distribution and collect responses[271]. Each participant received an individualised link to the survey. The initial email was sent a few days before the first dinner, with reminders to non-respondents. The 3-month survey was sent a few days after the final dinner, approximately 8-10 weeks from the baseline survey. Again, reminders were sent to non-respondents.

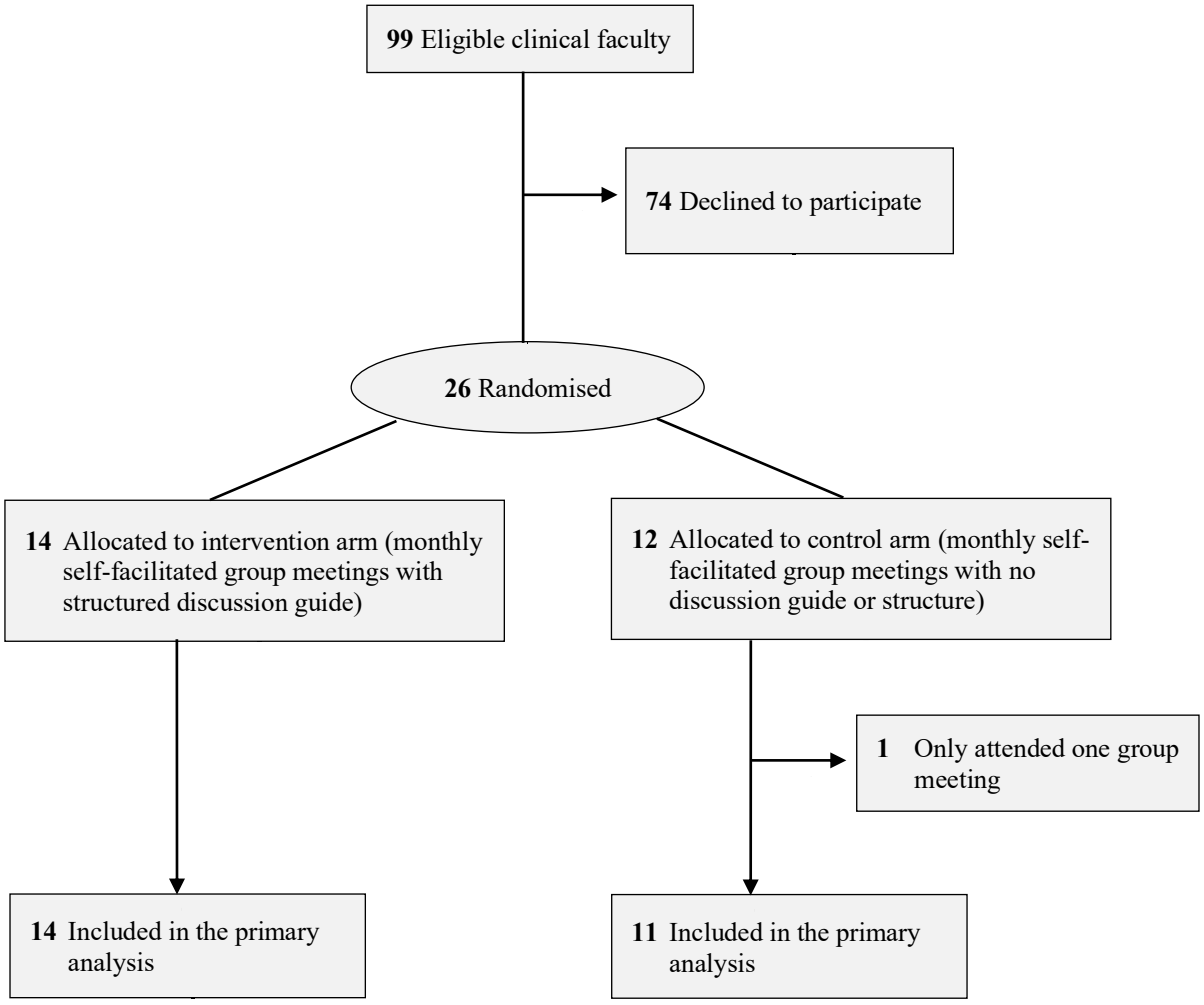

Figure 8.1: Consolidated Standards of Reporting Trials diagram for participant flow through the trial.

8.2.5 Statistical analysis

Standard descriptive statistics were used to characterise the sample. To evaluate changes in burnout, work engagement, work empowerment, and stress from uncertainty, scores were compared between the baseline and 3-month surveys using paired t-tests for continuous variables and Pearson chi-square tests for categoric variables; additional stratification by discussion guide randomization group was also performed. To evaluate associations between burnout, work engagement, work empowerment, and stress from uncertainty, we conducted a series of bivariate analyses assessing for confounders with the dependent variable by means of t-tests or one-way analysis of variance (ANOVA) for continuous variables and Pearson's chi-square tests for categoric variables. All tests were 2 sided, with a type 1 error level of .05. All statistical analyses were performed with the use of commercially available statistical software (Stata version 14.0; College Station, TX: StataCorp LP).

8.3 RESULTS

8.3.1 Characteristics of the participants

Twenty-six of 99 eligible faculty members (26% participation rate) volunteered to take part in the trial and were randomised equally to the two arms of the intervention study (Figure 8.1). Baseline characteristics and composition of study participants were similar to the characteristics and composition of the department with no statistically significant differences observed (Table 8.2). The majority were female (96%) and had been in practice for more than 20 years (32%). Of the study participants, 19 were physicians (76%), 6 were certified nurse midwives or nurse practitioners (24%). This is in line with the composition of the department which is composed of 65 physicians (66%), and 32

certified nurse midwives or nurse practitioners (32%). The baseline burnout rate of our study participants (56%) was similar to the rate of burnout (59%) found in an internal survey of all physicians in this department in 2017 (Table 8.2).

VARIABLE	METRIC (SCALE)	CONTROL ARM *no curriculum* (N = 11)	INTERVENTION ARM *curriculum* (N = 14)	MGH DOG
Sex, No. (%)	Female	10 (91)	14 (100)	86 (87)
Years in Practice, No. (%)	<5	0 (0)	0 (0)	-
	5-10	2 (18)	2 (14)	-
	11-15	3 (27)	2 (14)	-
	16-20	2 (18)	5 (36)	-
	>20	4 (36)	5 (36)	-
Years at MGH, No. (%)	<5	2 (18)	0 (0)	-
	5-10	4 (36)	3 (21)	-
	11-15	2 (18)	3 (21)	-
	16-20	1 (9)	4 (29)	-
	>20	2 (18)	4 (29)	-
Discipline, No. (%)	In-patient obstetrics	8 (73)	11 (79)	73 (74)
	Certified nurse midwife or practitioner	3 (27)	3 (21)	26 (26)
Burnout, No. (%)	High depersonalization	2 (18)	3 (21)	-
	High emotional exhaustion	7 (64)	7 (50)	-
	Overall high burnout	7 (64)	7 (50)	58 (59)
Burnout, mean (SD)	Continuous burnout	8.1 (0.8)	8.7 (0.6)	-
Engagement at work, No. (%)	High engagement	9 (82)	11 (79)	-
Engagement and empowerment at work, mean (SD)	Engagement at work	39.4 (6.7)	38.8 (6.3)	-
	Empowerment at work	70.3 (8.1)	62.7 (8.5)	-
Reaction to uncertainty, mean (SD)	Stress from uncertainty	43.3 (9.9)	42.2 (12.2)	-

Table 8.2: Baseline demographic characteristics of randomised arms of the study

DOG, Department of Obstetrics and Gynaecology; MGH, Massachusetts General Hospital

8.3.2 Impact of burnout intervention

Percentage of faculty with high emotional exhaustion and depersonalization significantly decreased over the course of the 3-month study (56% to 36%; $p < 0.001$; and 20% to 15%; $p = 0.006$) and overall burnout decreased from 14 faculty (56%) at baseline to 9 faculty (41%) at the end of the study ($p = 0.002$), with a significant decrease in mean score from 8.4(2.4) to 6.9(0.7) ($p = 0.017$). The number of faculty who felt engaged in their work increased from 20 (80%) to 22 (96%) ($p = 0.03$) over the course of the 3-month dinner meetings. There was a significant increase in number of faculty who felt that the department was committed to their wellbeing and who felt a sense of connection and community at work from baseline to end of study ($p = <0.001$ for both). There was no significant change in faculty members feeling empowered at work or in reaction to uncertainty (Table 8.3). Nineteen (83%) faculty strongly or moderately agreed that they felt satisfied with the group meetings; 20 faculty (87%) said they would be interested in attending the group meetings if they continued; and 21 faculty (91%) said they would recommend these meetings to other departments and institutions.

VARIABLE	BASELINE	3-MONTH	P VALUE
High depersonalization, No. (%)	5 (20)	4 (15)	0.006
High emotional exhaustion, No. (%)	14 (56)	8 (36)	< 0.001
Overall high burnout, No. (%)	14 (56)	9 (41)	0.002
High engagement, No. (%)	20 (80)	22 (96)	0.03
Continuous burnout, mean (SD)	8.4 (2.4)	6.9 (0.7)	0.017
Empowerment at work, mean (SD)	66.0 (9.0)	67.6 (9.9)	0.33
Reaction to Uncertainty, mean (SD)	42.7 (11)	43.6 (13.5)	0.48
Feel that department is committed to faculty wellbeing, No. (%)	7 (28)	10 (43)	< 0.001
Feel sense of connection and community at work, No. (%)	12 (48)	13 (57)	< 0.001

Table 8.3: Changes from baseline for all study participants

8.2.2.1 Randomised arms: guide versus no guide

There was no significant difference in outcomes between the randomised arms of the study at the end of the 3-month intervention period.

8.4 DISCUSSION

To our knowledge, this study is the first known trial of an interprofessional intervention to reduce burnout and enhance professional engagement in physicians, certified nurse midwives, and nurse practitioners participating together. Clinical faculty meeting together monthly for a three-month period demonstrated a significant reduction in burnout, and a significant increase in engagement (Table 8.3). In addition, at the end of the study, participants had a significant increase in sense of departmental commitment to their wellbeing and sense of connection and community at work. As a secondary aim, faculty were randomised to either participate in dinner groups with a structured self-facilitated discussion guide addressing themes relevant to challenges in the healthcare environment (intervention arm) or dinner groups with no rubric (control arm) to evaluate whether a discussion guide would provide increased benefit. The outcomes for the groups with the written discussion guide did not significantly differ from the control groups that met without the discussion guide. The positive findings in both groups suggest that self-facilitation may be an effective strategy and that the therapeutic benefit of the intervention was related to the relationships strengthened with colleagues through time and conversation, rather than any specific curricular content directed by a written discussion guide, making this a cost-effective and sustainable strategy for departments. The study also demonstrated benefit in a relatively short period of time (three dinners in three months), with an average total cost per participant of approximately $90 (approximately £70),

showing that as outlined in our rationale in Table 8.1 prolonged interventions may not be necessary and that perhaps short wellbeing initiatives are a more feasible strategy for healthcare institutions. This study demonstrates a low-cost, low-time commitment intervention that can significantly decrease burnout and increase sense of engagement and connection.

As we have seen earlier in the thesis, studies have shown that faculty have higher job satisfaction when they feel valued, feel that their workplace provides resources for their professional growth, and feel that their work environment is social and supportive[124]. An effective intervention such as the one shown in this chapter which invests in social capital, has, therefore, the potential to have a transformative positive effect on the culture of a department, especially when coupled with other institutional commitments to increase faculty quality of life. The results from this study suggest that, as hypothesised in the rationale outlined in Table 8.1, developing groups that provide a sense of support and community can help faculty feel more engaged in their work. A challenge of the fast-paced, technology-driven environment that is growing around us is the imperative to stay connected personally and reduce isolation[124]. At a time when national organisations require institutions to mandate wellness programmes[284], effective strategies to help reduce burnout are desperately needed. Intentional efforts to establish and nurture social and supportive environments that promote interprofessional connections are critical.

As faculty were randomised into groups, many did not know each other despite often having worked in the department for many years. The concept of psychological safety, defined as "being able to show and employ one's self without fear of negative consequences of self-image, status or career"[3] is at the core of successful team functioning

and has been shown to play a vital role in helping people thrive in challenging and high-stakes work environments[5]. Unfortunately, it is often elusive in the healthcare setting where a salient hierarchical structure and powerful professional norms may threaten an ability to speak up or ask for help. As demonstrated in this study, bringing interprofessional faculty together in small groups resulted in a significant increase in sense of connection and community at work. This may be, therefore, a critical strategy in creating psychological safety and openness in healthcare workgroups, which often have changing membership. Aside from improving sense of comradery and community, likely to positively impact wellbeing, psychological safety has been shown to be a crucial element in organisational efforts to detect and prevent patient harm by errors and process failures[144].

The results of this study are novel in revealing the benefit and feasibility of wellbeing interventions that include the full interprofessional complement of faculty within an obstetrics and gynaecology department, mirroring the team structure that occurs in the clinical environment. Faculty of differing professional backgrounds work collegially together in teams at academic medical centres worldwide and are impacted by the same systemic factors that drive professional burnout. Too often, wellbeing initiatives focus only on faculty who share the same professional role. It is powerful to set a precedent that wellbeing interventions can be equally effective (and perhaps even more effective) when they are inclusive of all professional roles. Several studies have demonstrated a relationship between burnout and profession satisfaction with reduction of clinical work hours, increased sickness absence, and early retirement[1,2,72]. At a time when healthcare institutions are projecting shortages of clinical faculty, efforts to ensure interventions are put in place that decrease burnout and the consequent negative impacts are essential. We

saw no difference in empowerment at work or stress from uncertainty and it may be that longer interventions are required to affect these domains.

8.4.1 Limitations

This study has several limitations. First, our results are subject to the inherent selection and reporting biases that often occur in survey studies. To minimise any social desirability biases, results were collected in a de-identified and confidential manner. In addition, participants were unaware of the specific hypothesis of this study, and we have no information to suggest that they would have chosen to participate or not on the basis of their degree of burnout. Indeed, an internal survey of faculty in this obstetrics and gynaecology department showed an overall burnout rate that was not significantly different to the baseline results, suggesting our participants are a representative sample. Second, the sample size is small, and the participants were all self-selected volunteers from one department at a single institution. Our results, therefore, may not be generalizable beyond the Department of Obstetrics and Gynaecology at MGH, although there is no reason to postulate that these results would be unique to this academic health centre. We did not evaluate the long-term effect of the intervention. Further studies are needed to expand the array of known interprofessional interventions that impact burnout in sustainable ways for groups of faculty.

8.5 CONCLUSIONS

This study shows that a short series of self-facilitated dinner meetings for an interprofessional group of obstetrics and gynaecology faculty is a low-cost intervention to reduce burnout, increase engagement, and increase faculty sense of connection to colleagues. Importantly, benefits were seen in both groups, with the randomised group who received the structured written discussion guide showing no significant difference from the control groups that met without the discussion guide. This suggests that the therapeutic benefit of the intervention may be related to the relationships strengthened with colleagues through time and conversation, rather than any specific curricular content directed by a guide, making this a practical and sustainable strategy for departments. At a time when concern about faculty wellbeing is high, and effective interprofessional collaborative teamwork is a goal, this study broadens the possibilities for transforming institutional culture and effectively enhancing faculty wellbeing and is an important addition to the healthcare profession's urgent call to reduce burnout and increase engagement.

CHAPTER 9: NARRATIVE REVIEW IDENTIFYING STRATEGIES TO HELP PHYSICIANS THRIVE IN CLINICAL UNCERTAINTY

"Doubt is not a pleasant condition, but certainty is an absurd one."
Voltaire

9.1 INTRODUCTION

As the opening introductory chapters outlined, stress from uncertainty is increasingly recognized as a likely driver of burnout in healthcare[8,9,113,147]. Chapter 4 supported this concept and added new knowledge to existing literature by comprehensively examining the factors associated with physician tolerance of uncertainty in a large sample of multispecialty physicians, with a range of experience. Efforts focused in understanding and managing uncertainty seem promising for reducing burnout and there is an urgent need for strategies and interventions to help the 21st century healthcare professional embrace uncertainty. We saw in Chapter 5 that anxiety due to uncertainty can be influenced by language choice, highlighting the need for explicit strategies that recognise the challenges in communication and the importance of thought in how a message is framed as this is critical to how the recipient encodes and perceives the tailored information. This fits with previous research suggesting that tolerance of uncertainty is a state determined by situational or contextual factors[166,178], and therefore amenable to change through an educational and experiential process[179]. It has been shown to improve over time and with experience[181]. Whilst not deliberately designed to enhance tolerance of uncertainty, our group intervention outlined in Chapter 8 did include a discussion guide specifically created to open conversation about the impact of uncertainty in healthcare; mechanisms to cope with uncertainty; and methods to communicate uncertainty (Appendix

8.2). However, we saw no change in tolerance of uncertainty in the participants who used this guide and it is clear that it is a complex domain that is likely not easily shifted.

Recently the medical profession has begun to recognize the need to identify and address clinical uncertainty, acknowledging its impact on patient safety and wellness among working physicians and trainees. Understanding and acknowledging uncertainty and acquiring proper coping strategies is now regarded as one of the core clinical competencies for medical graduates and trainees in the UK, US, Australia, and much of Europe[284-290]. Unfortunately, medical education at both undergraduate and graduate levels is struggling to keep pace with these recommendations, with few strategies existing to embrace uncertainty in clinical practice.

9.1.1 Chapter aims

In this chapter, current literature on tolerance of uncertainty, cognitive biases, decision-making, and distress tolerance is synthesised alongside the findings of this thesis, self-experience, and experience of colleagues and students in a narrative review to identify strategies to help healthcare professionals thrive in the face of clinical uncertainty. In line with the scope of the thesis, the strategies are aimed primarily at physicians (from medical student through to experienced practitioner) though it is likely that many would translate across to allied healthcare professionals who undoubtedly also need to thrive in the space of uncertainty. The strategies are divided into three sections:

- strategies to enable the physician to help themselves;
- strategies to help physicians work with patients;
- strategies to help physicians guide students, trainees, and less experienced colleagues.

This chapter concludes by looking at potential challenges and barriers in the quest to change a deeply embedded culture.

9.2 STRATEGIES TO ENABLE THE PHYSICIAN TO HELP THEMSELVES

Recognising that uncertainty is rife in the healthcare environment, there is much that the individual physician can do on a day-to-day basis to help embrace uncertainty in their clinical practice. This is the first step towards the acknowledgment and acceptance of uncertainty—an essential shift in the revolution to embrace uncertainty in clinical practice. Empowering individual physicians to help themselves sit comfortably with uncertainty begins the process of reframing uncertainty as a surmountable challenge rather than as a threat. Below I describe five strategies that the individual physician can use to recognise and modify their individual reaction to uncertainty:

1. Understand gut reaction to uncertainty;
2. "Diagnose" the type of uncertainty;
3. Learn to hold uncertainty;
4. Plan for uncertainty: use safety-netting and follow-up;
5. "Don't worry alone"—lean on colleagues.

9.2.1 Understand gut reaction to uncertainty

Our own reaction to uncertainty is important to be aware of and is highly variable[470]—though often unpleasant. It depends, in part, on nuances of the present clinical situation, previous experiences, knowledge, culture of practice, and societal pressures[230]. The human brain is hardwired to perceive reward from certainty and discomfort from increasing levels of uncertainty[114,115]. Unfortunately, the healthcare environment is a breeding ground for

uncertainty, arising from hard-to-predict disease processes, ambiguous laboratory and imaging findings, and from healthcare outcomes that are far from binary[8]. Intentionally acknowledging one's own implicit response to uncertainty enables each individual physician to gain insight into their reactions—both emotional and behavioural. Table 9.1 outlines some example exercises that can be helpful to enable individuals to identify their own gut reaction to uncertainty. By reflecting on the emotions and thoughts uncertainty triggers within us, we can begin to gain more control over our automatic behaviours and actions. This allows us to respond mindfully and choose more functional rather than dysfunctional ways to deal with uncertainty[471]. Indeed, evidence suggests modifying one's reaction to uncertainty is possible with practice[180]. By identifying areas where physicians can anticipate feeling uncertain, the individual can prepare themselves to face these situations, rather than being blindsided by them[472]. For example, one colleague reported feeling uncertain when caring for immunosuppressed post-transplant patients. She developed a practice of involving infectious disease colleagues sooner rather than later for such cases. In this way, she set up a deliberate practice of managing her reaction and dealing with the anticipated uncertainty.

ACTIVITY	QUESTIONS TO POSE TO SELF
Recall an instance where you were uncertain.	• How did you feel? • What emotions arose? • What thoughts came to mind?

Identify a priori areas where you anticipate feeling uncertain	• Are there diagnoses or situations that make you feel uncomfortable?
	  • A particular type of patient?
	  • A challenging procedure?
	  • When a colleague asks you a question?

Table 9.1: Example exercises to enable individuals to identify their own gut reaction to uncertainty

9.2.2 "Diagnose" the type of uncertainty

Distinguishing and acknowledging the multiple meanings and varieties of uncertainty in healthcare is likely an important step, as each is likely to have unique effects or warrant different courses of action[152]. "Diagnosing" the type and sources of uncertainty that a physician is facing can be helpful in clarifying the path forward and suggesting appropriate management strategies[473]. A classification scheme may also identify skills physicians in training and practice need to develop, guiding educational interventions to help manage uncertainty[471].

What may be most relevant and practical for the everyday practitioner is making the distinction between "knowable" and "unknowable" forms of knowledge underlying uncertainty. Identifying, articulating, and prioritising the minimisation of such "unnecessary uncertainties" (that is, the knowable unknowns) is a first step and specific action physicians can take to manage clinical uncertainty better. Each type of uncertainty demands a different response: for instance, a knowledge gap can be addressed through reference materials while a situation of conceptual or personal uncertainty may require a more individualised and nuanced approach.

9.2.3 Learn to hold uncertainty

Our desire for certainty leaves us open to the influence of cognitive biases. To prosper in the face of increasing knowledge and a busy workplace, well-versed experts learn to recognize patterns that allow them to think and act quickly. Such quick-thinking heuristics, first identified by Tversky and Kahneman[474], serve a useful purpose—recognizing the cardinal signs of an acute stroke or myocardial infarction and initiating appropriate therapy

and organising the appropriate personnel—yet they leave physicians vulnerable to cognitive bias, and in turn, false assumptions, misdiagnosis, and errors[475]. Physicians would do well to pause when making medical decisions and ask themselves if there is any uncertainty that they are avoiding: Do they feel confident in their reasoning? What else have they left out? "Holding uncertainty" can allow more possibilities to remain "in play"[476].

An awareness of the common cognitive pitfalls and biases can allow physicians to recognise scenarios when they are at particular risk of curtailing the diagnostic process too soon and when they would do well to hold the uncertainty and avoid premature decision making:

- **Availability heuristic:** when physicians make a diagnosis based on what is easily accessible in their minds, rather than what is actually most probable.
- **Anchoring heuristic:** when physicians settle on a diagnosis early in the diagnostic process and subsequently become 'anchored' to that diagnosis, despite evidence to the contrary.
- **Confirmation bias:** as a result of anchoring, physicians may discount clinical information discordant with the original provisional diagnosis and accept only that which supports their original diagnosis.
- **Representativeness heuristic:** physicians depend greatly on this cognitive short-cut in which a patient's presentation is compared to a 'typical' case of specific diagnoses but leaves off the 'atypical' presentations.

9.2.4 Plan for uncertainty: use safety-netting and follow-up

While we have a strong desire to reduce uncertainty in clinical decision-making, to find the correct diagnosis and initiate treatment in a timely fashion, sometimes uncertainty lingers beyond the immediate clinic visit or hospital stay—and we can plan for it. It is wise to proactively include a role for uncertainty in management plans. By creating safety-nets and following-up, physicians can reduce the potential harms of uncertainty and catch outcomes that run the risk of veering off course sooner.

Safety-netting is well described in the primary care practice literature[477]. It provides contingency planning in the face of diagnostic or management uncertainty and is particularly useful in high-risk clinical populations. Safety netting can provide relief for providers facing uncertainty and a path forward. Physicians can specifically ask themselves: If I'm right what do I expect to happen? How will I know if I'm wrong? What would I do then?

With changing patterns of medical practice to include more shift work, shorter encounters, and more episodic care, trainees and physicians alike are often challenged to follow the full course of a patients' care. This undermines the feedback loop critical for improving diagnostic reasoning and learning about the expected clinical course of common conditions[478]. Clinicians can make a practice of following-up with patients, whether by phoning a patient following discharge, following them as an outpatient, communicating with continuity providers (e.g. phoning or messaging primary care doctors), or tracking a patient's course virtually through the electronic medical record. Additionally, communicating the level of patient "instability" or uncertainty onto the next team of healthcare providers can promote safety in care transitions (e.g. see IPASS system[479]).

Building a default mechanism of "follow-up" into clinical practice gives the clinician an opportunity to course correct as the illness evolves if a "wrong decision" was made when only limited information was available; it is also essential to building a broader repertoire of "illness scripts"[480].

9.2.5 "Don't worry alone"—lean on colleagues

Early stages of medical training—with a predominance of multiple-choice questions with "right" answers—inculcate a notion that there is one absolute truth or single best answer in medicine. This suggests an element of certainty that often does not translate from the textbook and classroom to the real-world bedside. An unintended consequence of this educational approach is that not knowing the best answer becomes a fear-inducing mark of incompetence for physicians-in-training and even experienced practitioners. With clinical experience and over time, physicians evolve to recognize that clinical problems most often have poorly defined borders, evolving characteristics, and multiple legitimate treatment approaches rather than a single correct one[481]. In this way, dealing with uncertainty in a mature manner requires accepting one's own fallibility. This is challenging however, and we must do what we can to support each other in this process. It can be very reassuring to hear from peers and senior colleagues that uncertainty is not only appropriate, but also an expected component of medical practice, and nothing to be ashamed about. By talking about it, asking for help, and leaning on colleagues when overwhelmed we can help build a culture that accepts and embraces uncertainty.

Further, increasing sub-specialization has led to disparate groups within medicine—we should break down traditional silos to embrace uncertainty together. Sticking to subspecialty 'tribes' has the risk of narrowing one's diagnostic vision, fostering belief in

the superior effectiveness of treatment in one's own sub-specialty over others, camouflaging and avoiding uncertainty, and missing opportunities for sharing learning and the perceived burden of uncertainty among clinicians. Fragmented healthcare is a leading cause of medical errors, while effective teamwork and open communication can promote improved outcomes in the face of clinical complexity, acuity, and uncertainty[482].

9.2.6 Summary of strategies to enable the physician to help themselves

Figure 9.1: Strategies to enable the physician to help themselves

9.3 STRATEGIES TO HELP PHYSICIANS WORK WITH PATIENTS

How a physician reacts to uncertainty has direct impact to patient care. The ability to acknowledge and discuss uncertainty with patients is particularly important, and indeed morally and ethically obligated[160]. Authentic disclosures and communication of uncertainty in meaningful ways has been shown to enhance trust in the patient-provider relationship and improve decision-making and healthcare outcomes. It is important that as physicians work to enhance their own tolerance of uncertainty as highlighted above, they also intentionally develop strategies that can be used in their patient interactions. It is likely that by openly discussing uncertainty and promoting shared decision-making with the patient, physicians may find a consequent reduction in their stress and anxiety.

9.3.1 Discuss uncertainty openly with patients

Thriving in the face of uncertainty requires an ability to communicate uncertainty to patients. The recent National Academy of Medicine report "Improving Diagnosis in Health Care" recommends that physicians share their working diagnosis with patients including the degree of uncertainty associated with each diagnosis[483]. As we strive for an era of patient-centred care and shared decision-making, we must authentically discuss all elements of clinical uncertainty—from diagnostic decisions, to therapeutic decisions, to conversations about prognosis. This is often challenging for physicians, trained in a culture that prioritises certainty and can mistake uncertainty for ignorance or failure. Below I discuss some strategies physicians can use to enable more open discussion of uncertainty with patients—of benefit to both themselves and their patients:

- Normalise uncertainty;
- Use appropriate and direct expressions of uncertainty.

9.3.1.1 Normalise uncertainty

Normalising uncertainty is important as it seeks to reset expectations. Patients are bombarded in the lay media with the notion that high-tech advances in imaging and genomics have resulted in definitive answers to clinical questions, such as prognosis. Clinicians should be honest with patients about the boundaries of knowledge, saying, for example, "I understand that you want more accurate information about the future. The reality is that it's like predicting the weather—we can never be absolutely certain about the future. I wish I could be more certain."[234]

9.3.1.2 Use appropriate and direct expressions of uncertainty

Although physicians often worry that admitting uncertainty will lead to a loss of patient confidence, it has been suggested that appropriate expressions of uncertainty can lead to stronger physician-patient relationships[116]. One study found that when primary care providers used direct expressions of uncertainty, such as "I don't know" or "It's not clear," there were higher levels of positive talk, patient engagement, and patient satisfaction[484]. This must certainly be done carefully: in a study with paediatric cases, Bhise et al. discovered parents react more favourably—in terms of perceived competence, physician confidence and trust, and intention to adhere to recommendations—when diagnostic uncertainty is communicated with implicit rather than explicit strategies (e.g. broad differential diagnoses)[485].

"The question is not whether to share uncertainty with our patients, but how best to share it to create trust instead of unnecessary anxiety," Armstrong concludes[116]. Such conversations require empathy and are more effective in the context of a partnering

relationship. Physicians must ensure the patient that regardless of one's uncertainty, they will be there to support them through the process[486]. Saying "I don't know exactly what is going on, but I will be with you and will support you" goes a long way in reassuring the patient even if the clinical "answer" is unclear. Open discussion, including admitting vulnerability and acknowledging our limitations, builds trust and shared responsibility when it is grounded in mutual recognition of the inevitable uncertainty of clinical medicine[487].

Clinicians can invite patients to discuss the emotional reactions that often occur in the face of uncertainty, saying for example, "It's tough not knowing what the future is going to bring." To help a patient refocus on the here and now, clinicians might ask, "What can we do to help you now, given that we are unsure of exactly what the future will bring?". This can help ground both doctor and patient in the present and prevent rumination about a future that cannot be predicted with complete accuracy or control.

Although the empirical evidence about the optimal approaches for communicating uncertainty to patients is limited, current recommendations can be grouped under four primary domains:

1. Assessing patient preferences for communication;
2. Risk and ambiguity communication strategies;
3. Providing emotional support;
4. Clarification of contingency plans[190,217,224,488].

Further strategies that physicians can use to help communicate uncertainty with patients are outlined in Table 9.2.

BROAD DOMAIN	INDIVIDUAL STRATEGIES
Explicitly assess patients desire for information and method of delivery for that information	Assess individual's informational preferences and capacity for understanding uncertainty[489].
	Tailor conversation for individual, altering specific type/amount of information according to various characteristics (gender, culture, education, psychological factors, behaviours of interest) that relate to patients' capacity to use/respond to such information[490-492].
Strategies to communicate risk and ambiguity	Bracket estimates with ranges to convey realistic uncertainty, being sure to allow for exceptions in both optimistic and pessimistic directions[493]
	Round off numbers to avoid false illusions of precision[494].
	Use qualitative descriptions, but beware that many have no generally accepted anchoring at specific quantitative levels of frequency[494,495]; may work to relate medical risks to nonmedical risks so they can be placed in larger perspective of persons' life.
	Visual aids to communicate probabilistic information improves cognitive outcomes[190,496].
	Be aware of framing effects in conveying information on uncertainty which may impact uncertainty aversion: for example, gains versus losses; qualitative versus quantitative[494,496,497].
	Consider presenting risk information in several formats (qualitative, graphical displays, positive frame, negative frame, frequency, proportions, absolute, relative) to avoid framing biases in perception of message[493].
Ensure support is fostered	Education/communication approach: CBT to improve patients' resilience and ability to cope with uncertainty[498,499].
	Clarify the type of uncertainty that is most distressing to patient and explain complexities of each[500]: uncertainty about probabilities; uncertainty about sources of information; uncertainty about evidence.
	See uncertainty as opportunity rather than danger[501].
	Provide emotional support: "With you on the journey"; "I don't know, but I will be there no matter what happens" takes humility and a commitment to a meaningful engagement—that commitment is often what patients want most[502].
	Assure will answer all questions, provide resources, inform of own biases and values, inform of alternative treatments[503,504].
Clarify plan	Safety-netting is often used especially if diagnosis is uncertain and differential includes serious illness: say precisely what to look for; say precisely how to seek further care; be precise about time course[477].

Table 9.2: Current strategies to communicate uncertainty, adapted from "Communicating uncertainty: a narrative review and framework for future research" by Simpkin AL and Armstrong KA. In Journal of General Internal Medicine, 2019; 34: 2586-2591[160]

9.3.2 *Use patients as allies in shared decision-making*

Increased tolerance of uncertainty correlates with increased engagement in patient-centred care[191]. The more ambiguous, complex, and uncertain a situation, the more likely an experienced physician is to engage in patient-centred decision-making[505]. Partnering with patients in shared decision-making has positive benefits for care received, satisfaction, and outcomes[506]. By discussing uncertainty with patients, whether about diagnosis, prognosis, or treatment and management options, providers may find a reduction in their stress and anxiety through sharing decision-making responsibility. A patient's values and preferences can often guide treatment choices where otherwise the best means of proceeding would be uncertain.

9.3.3 *Summary of strategies to help physicians work with patients*

Figure 9.2: Strategies to help physicians work with patients

9.4 STRATEGIES TO HELP PHYSICIANS GUIDE STUDENTS, TRAINEES, AND LESS EXPERIENCED COLLEAGUES

Most physicians find themselves in teaching roles—whether formal or informal—throughout their careers. They are well poised, therefore, to help students, trainees, and less experienced colleagues embrace uncertainty and this is a critical step in seeking to shift the culture in medicine from one which suppresses and denies uncertainty. Published calls for, and descriptions of, formal educational initiatives to address uncertainty have ranged from including questions with multiple correct answers through the medical curriculum to using fine art as an educational tool. Teaching philosophical understanding and approaches to uncertainty should occupy multiple levels of medical education and practice. The strategies below are to help all physicians in their role as teachers and mentors:

1. Teach students about the fundamental nature of medicine;
2. Set the culture: role-model embracing the inherent uncertainty of clinical medicine;
3. Promote curiosity over certainty;
4. Be explicit about the level of uncertainty.

9.4.1 Teach students about the fundamental nature of medicine.

Schön, in *Educating the Reflective Practitioner*, describes professional practice as "high, hard ground overlooking a swamp." For medicine, the high, hard ground is the scientific zone, which is fact-based, predictable, and consists of solvable problems, whereas the swamp is characterised by uniqueness, conflict, and ambiguity[507]. Physicians often practice in the swamp, and medical education curricula should acknowledge that some degree of anxiety is natural and predictable when operating in this zone of uncertainty. We

should strive to equip students with knowledge on how to act wisely in states of ambiguity and uncertainty.

Professionalism courses that include faculty-facilitated small-group discussions provide good venues for reminding students of their own humanity and help them learn to connect with the humanity we all share. These small-group courses easily lend themselves to discussions on the anxiety, frustration, and disillusionment that can result from ambiguity and uncertainty. It is essential to carry forward these professionalism ideals into the clinical years, when students face ambiguity and uncertainty in "real time," so they can learn to incorporate coping and communication strategies into their daily practice. Frequent dialogues between students, trainees, and faculty members to examine what students perceive as ambiguous situations will be valuable and should be a formal part of the clinical curriculum. Nevalainen and colleagues found that reflective writing exercises were an effective method for medical students in their first clinical year to express and deal with clinical uncertainty[243]. Development programmes to address the perceived needs of the faculty, to ensure that they are prepared to facilitate these discussions, will be beneficial as well[150].

9.4.2 Set the culture: role model embracing inherent uncertainty of clinical medicine

Talking openly about uncertainty in the clinical environment helps normalise the experience of uncertainty not only for colleagues but also for learners, modelling that it is "safe" and necessary to express uncertainty and setting a new culture that embraces uncertainty.

Role modelling uncertainty includes thinking out loud and being explicit about probabilistic (or Bayesian) thinking; it may also include searching for answers in real-time. Rencic writes: "Doing quick, highly focused literature searches with internet-based resources or compiled evidence reviews while seeing a patient in clinic demonstrates to learners that rapidly accessing relevant medical literature is both feasible and valuable"[508]. Likewise, asking consulting teams or colleagues for help or to educate you and your team is an effective means of recognising the limits of one's knowledge and practising life-long learning.

Never be afraid to say, "I don't know." These simple words welcome input and curiosity, helping learners gain confidence in recognizing where clinical uncertainty exists, and understand that communicating and sharing uncertainty is what the healthcare culture ought to expect.

9.4.3 Promote curiosity over certainty

Curiosity is a basic element of our cognition and a fundamental motivator for learning. Appreciate when trainees express curiosity and make time for discussion to answer their questions[509]. This is pivotal to the development of sound clinical reasoning. According to Wenzel, "whereas throughout their previous schooling [medical students] were judged by their answers, in their medical education and their careers they will often be judged predominantly by their questions. We should applaud students for curiosity…"[510].

One way to prioritise learners' open-ended thinking is by asking questions that begin with "How" or "Why" rather than "What" or "When"[8,511]. Questions that start with "What" or "When" suggest a specific answer is expected which is either known or not—further

inculcating the notion that there is a right answer and rewarding certainty. Questions that start "How" or "Why" promote higher-order skills, such as synthesis and evaluation[508,512-514], and allow for answers that can more easily acknowledge and embrace uncertainty. To improve teaching skills, faculty may choose to adapt an evidence-based teaching tool such as One-Minute Preceptor[515,516]. On the other hand, teaching learners presentation models like SNAPPs[517], which explicitly calls on students to ask questions and identify areas of uncertainty, can equip trainees with a tool to infuse curiosity, questioning, and discussion of uncertainty among their clinical teams even if this is not brought up by the supervising physician[518].

Finally, as we explored in Chapter 5, physicians should be aware of how language choices can influence perceptions and reinforce values. For example, using the word 'hypothesis' instead of 'diagnosis' conjures a very different expectation of certainty[8].

9.4.4 Be explicit about the level of uncertainty

Clinical educators should be explicit about their thought processes and their level of uncertainty in a clinical situation, engaging the team in navigating uncertainty in real-time. They can do this by describing the ambiguity, asking questions, and offering contingencies as outlined in Table 9.3. Physicians can increase trainee's mastery of probability-based logic by explicitly discussing thresholds to test and treat and how such thresholds may change from patient to patient (i.e. Bayesian reasoning)—this strategy brings discussion of the individualised nature of uncertainty to the clinical learning environment. To help shift the culture, physicians should consider adding an explicit discussion about the level of uncertainty during clinical hand-overs and transitions in care. By embedding these discussions into clinical practice and the healthcare environment, physicians help reinforce

that what matters is not the absence of uncertainty, but rather the processes and thinking patterns one uses to manage it.

TEACHING TOOL	WHAT TO ASK TRAINEES
Discuss how much and what types of uncertainty are being faced in a particular scenario	"How does xxxx make everyone feel?"
Consider which biases the team is at risk for	"Name a cognitive bias and how it might apply in the relevant situation."
Perform a "prospective hindsight" analysis with the team[519] and temporarily assume the working diagnosis or decision is wrong	"What if we are wrong?" "What might we have missed?" "What else could it be?"
Explicitly identify the evidence, or absence of evidence, for the clinical management that is being pursued	"Can you see the synergy of evidence-based medicine and clinical intuition?"
Articulate level of uncertainty that you are willing to tolerate in the particular case and why.	"How would this test or a patient's response change your uncertainty?"

Table 9.3: Teaching tools to help physicians be explicit about level of uncertainty

9.4.5 Summary of strategies to help physicians guide students, trainees, and less experienced colleagues

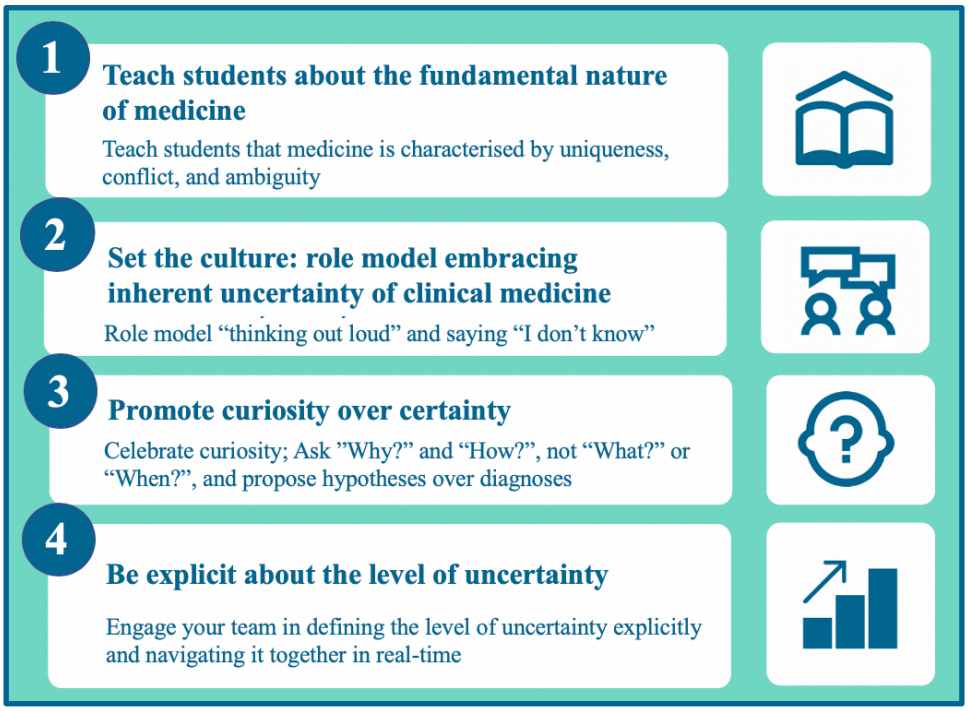

Figure 9.3: Strategies to help physicians guide students, trainees, and less experienced colleagues

9.5 POTENTIAL CHALLENGES AND BARRIERS

It is important to highlight a few of the challenges and barriers that need to be considered as strategies are developed. As has been discussed widely through this thesis, there are major cultural challenges to successfully embracing uncertainty, in part due to the false narrative that has been created in medicine that uncertainty equates to ignorance or failure[8]. In striving for certainty, the healthcare field widens a gap between expectation and reality. This must be challenged to enable open and authentic expressions of uncertainty for physicians at all stages of their training. As we have outlined above, it is particularly important for more experienced practitioners to role-model to trainees the safe and desired discussion of uncertainty. There is often disagreement within teams about level of disclosure of uncertainty, and this must be carefully navigated by the clinical leader. Changing communication behaviour is challenging, and it will be important that medical education begins to address important factors in this domain, such as motivation, confidence, barriers, and skills.

One important area that undoubtedly needs attention and change is the healthcare system's infrastructure that is not currently set up to embrace uncertainty easily. In particular, there are few incentives to encourage embracing clinical uncertainty. Certainty is valued implicitly and explicitly in healthcare institutions, policies, and in the learning environment. In many hospitals, admission from the accident and emergency department (A&E) to the in-patient ward requires a formal diagnosis to be entered in the patient's chart; electronic health record (EHR) systems require laboratory testing, imaging, and prescriptions to be associated with specific diagnoses in the record[520]; and billing for an encounter is often stratified according to the final diagnosis or the treatments offered without crediting, recognizing, or valuing the work and time required for clinical

reasoning, patient education and shared decision-making, as well as the consideration and communication of uncertainty. Amidst the 87,000 ICD codes, there is none for "I don't know." Many physicians eschew tasks they feel are time-consuming, including discussions of goals of care, patient education, evaluating health literacy, or discussing uncertainty. Yet these are the components of a clinical encounter that patients and providers both find valuable[521], and such conversations may serve to reduce readmissions, improve adherence, and improve the quality of patient's health and wellness over time[522].

Changes to support uncertainty could include more flexible diagnostic codes and treatment algorithms that build in uncertainty and room for modification over time; clinical decision support tools and electronic medical record systems that offer provisional diagnoses or better, and more flexibly, capture how diagnostic knowledge and certainty evolves over time, enabling tolerance of uncertainty rather than undermining it[523]. We do not reimburse physicians for their 'thinking time', nor for the important but nuanced work of carefully and compassionately communicating uncertainty. But perhaps we should. We must advocate for better ways to measure, assess, and train the management of uncertainty.

A final means to thrive in the face of uncertainty is to see it as a natural starting point for system quality improvement in healthcare. Clinical uncertainty may unveil unnecessary variation, inconsistent practices, safety errors or near misses, or areas in which new knowledge or new processes are necessary. This is a natural precursor for improvement—health systems would do well to draw on the observations, questions, and ideas of trainees and physicians in practice to identify areas for future research, clinical practice or guideline development, or organizational process improvement[524].

9.6 CONCLUSIONS

The practice of medicine involves innate uncertainty due to inherent variability in outcomes and unpredictability of patient response (aleatoric uncertainty) and due to the limitations and imperfection of our knowledge and complexity of risk information reliability, accuracy, and generalizability (epistemic uncertainty). Although the ideal of informed or shared decision-making implies a need for communicating this uncertainty to patients, there is currently wide variability in the degree to which providers actually engage in communicating conditions of scientific uncertainty, with few evidence-based recommendations for such communication.

Embracing uncertainty is critical for ourselves, our trainees, our patients, and our healthcare systems[8]. The strategies described in this chapter will help to provide healthcare educators and professionals across the educational continuum (undergraduate, graduate, and continuing medical education) with a framework of strategies to thrive in the face of clinical uncertainty.

CHAPTER 10: DISCUSSION AND CONCLUSIONS

"At once it struck me what quality went to form a Man of Achievement … when a man is capable of being in uncertainties, mysteries, doubts, without any irritable reaching after fact and reason"
John Keats, December 1817[525]

10.1 INTRODUCTION

This final chapter draws together the findings within the thesis and reflects on them, in the context of both the research itself, with its methodological strengths and weaknesses, and the wider clinical and educational environment in which they apply. Whilst this thesis has attempted to fill some of the gaps in the literature and provide greater clarity and new insight into aspects of burnout—drivers, measurements, and solutions—there remain many unanswered questions which I will highlight in this final chapter as they provide opportunities for exciting research in the future.

10.2 SUMMARY OF KEY FINDINGS

The first two introductory chapters of the thesis laid out the rationale for undertaking this research, and provided a selective overview of the broad context of burnout in healthcare presenting existing literature on the impact of burnout—to physicians, to patients, and to healthcare organisations—and considering the challenges that pertain to burnout research, particularly relating to challenges in measurement. The concept that reaction to uncertainty may be a critical, and much overlooked, driving force to burnout, was introduced and I explored the presence of uncertainty in the healthcare environment looking at what

impacts an individual's tolerance of uncertainty and how the reaction affects provider- and patient-centred outcomes. These chapters sought to lay the foundation to understand the basis for the series of empirical, experimental, and narrative review studies that followed, divided into three parts:

- Part I: an exploration of concepts;
- Part II: an exploration of biology;
- Part III: an exploration of intervention and proposed strategies.

10.2.1 Part I: Exploration of concepts

At a time when much attention is being directed at understanding what impacts faculty wellbeing, the opening observational survey study identified key variables that might influence faculty satisfaction in large academic medical centres:

- feeling valued;
- feeling treated with respect;
- and working in a social and supportive environment.

Although much attention has been paid to gender gaps in medicine—in salary[273,274], in career advancement[275], and in leadership positions[276]—with the assumption that this drives much dissatisfaction and lack of retention among women, we did not see a significant association between gender or rank and satisfaction at work in the multivariate analysis.

The current healthcare environment has been criticised for undervaluing faculty, risking taking for granted the human capital which forms the foundation of the system and, unintentionally, cultivating loneliness and isolation[268]. Understanding what constitutes a sense of feeling valued is an essential step to ensure it is woven into the workplace culture and we identified the following factors to be significantly associated with feeling valued:

- feeling cared about as a person;
- not feeling taken for granted;
- feeling resources were provided for professional growth;
- and not feeling discriminated against by sex.

Despite value typically having an economic connotation, we did not see an association between feeling valued and feeling financially compensated fairly. While compensation has previously been reported to be an important factor in faculty satisfaction[281,282], our results suggest wiser investments would be in social, not financial, capital.

As we explored in the opening two chapters, the ability to manage uncertainty has been identified as a potentially important determinant of burnout in physicians[9,113,147,244], but unfortunately it is an attribute that has been missing from most wellbeing studies, with further research required to ascertain the impact stress from uncertainty may be having on burnout. Building on a pilot study evaluating the association of fellows' stress from uncertainty with wellbeing metrics, we conducted a cross-sectional survey in a large multispecialty academic physician practice organisation and found a strong relationship between tolerance of uncertainty and physician wellbeing, across specialties, regardless of how physician wellbeing was measured. While there has been previous inconsistency with sociodemographic associations, we found lower tolerance of uncertainty was significantly associated with female gender, Asian race, primary care practice, and lack of experience. These results support stress from uncertainty as a potential driving force behind the burnout pandemic suggesting efforts to improve the management of uncertainty may be useful for addressing burnout and giving insight into the demographic characteristics of those who may be at highest risk of stress from uncertainty.

In light of the significant association of physician reaction to uncertainty to burnout, it is important that we better understand what factors and processes affect anxiety due to uncertainty, particularly whether aspects of the work environment such as elements of communication increase or decrease the anxiety. In Chapter 5, we explored the effect of language used in healthcare settings on medical students' anxiety due to uncertainty to understand how the choice of words used to describe a presumed 'diagnosis' may affect perception of certainty—both with regard to the uncertainty about the specific clinical diagnosis and the individual level of anxiety due to uncertainty. While discussion of uncertainty has been highlighted as one of the most difficult elements of communication[190], there has been little research on how language choice affects sense of uncertainty in healthcare professionals, particularly in settings tied to clinical decision-making[306].

A randomised experimental study design was used to test different language constructs used in the hand-over setting when medical professionals are handing patients' over from one unit to another and conveying the presumptive 'diagnosis' and current plan. Interestingly, while there was no difference in the perception of uncertainty about the specific clinical diagnosis for each scenario, the medical students who received a hand-over using the language variation 'hypothesis' had significantly higher anxiety due to uncertainty than those who received the language variation 'diagnosis', demonstrating how language variation can influence emotional perception. The implications of these findings will be discussed later in this chapter.

10.2.2 Part II: Exploration of biology

Recognising challenges that pertain to burnout research, particularly in regard to how best to measure burnout, the second part of this thesis explored the novel use of cortisol and oxytocin levels as potential biomarkers of wellbeing. In Chapter 6 we outlined the reasons behind the choice of these two biomarkers exploring the different mediums available for measurement to capture physiological change that may represent a proxy measure of burnout, setting the stage for the exploratory biomarker study in Chapter 7.

Chapter 7 described a small early-stage study among clinical faculty in an academic medical centre to assess feasibility of biomarker collection, together with associations of salivary and hair cortisol with burnout, and association of urinary oxytocin with connection, engagement, and trust among colleagues. While all of the faculty members enrolled in the study of interdisciplinary support groups consented to the collection of biomarker data including saliva, urine, and hair, collecting biosamples from faculty proved challenging because of conflicting time pressures, unpredicted clinical demands at the collection timepoints, and inadequate samples. The dynamic nature of salivary cortisol and urinary oxytocin measurements necessitated the need for collection at a specific time of day to counter confounding effects of the diurnal variation and short half-life.

Although we had hypothesised that both aspects of burnout—emotional exhaustion and depersonalisation—would be associated with increased cortisol levels, we found that while emotional exhaustion was associated with significantly higher salivary cortisol levels, depersonalization was associated with significantly lower salivary cortisol levels. Similarly, hair cortisol was positively correlated with emotional exhaustion and inversely correlated with depersonalization, although these correlations did not reach statistical

significance. Urinary oxytocin was significantly higher among participants reporting higher sense of connection and community and there was a strong positive correlation among participants with higher engagement. Urinary oxytocin was also higher among participants reporting higher trust in colleagues, but this did not reach statistical significance. The implications will be considered later in the chapter.

10.2.3 Part III: Exploration of intervention and proposed strategies

The final part of the thesis examined an interprofessional wellbeing intervention designed to address challenges with existing interventions that tend to focus on faculty who share the same professional role, often with unrealistic time and cost footprints. Explicitly addressing some of the limitations in current interventions, our intervention consisted of self-facilitated, interprofessional groups meeting monthly for dinner for three months. As it is unclear whether any benefit that results is from simply bringing people together or whether a structured discussion guide that addresses themes relevant to challenges in the healthcare environment enhances group bonding, we randomised participants to either have no guide or to be given a structured discussion guide.

Faculty in both arms of the study demonstrated a significant reduction in burnout, and a significant increase in engagement. There was no significant difference in outcomes between the randomised arms of the study with both groups showing a significant increase in sense of departmental commitment to their wellbeing and sense of connection and community at work. The study demonstrated benefit in a relatively short period of time, with a low budget, suggesting that perhaps short wellbeing initiatives are a feasible strategy for healthcare institutions. This study builds on the empirical findings from Chapter 3 to suggest that institutions may see benefit from investment in social capital.

Our social nature defines what makes us human, and those who engage in more social interactions are less stressed physiologically[344], perhaps mediated by oxytocin as Part II explored.

Part III concluded with a narrative review that synthesised current literature on tolerance of uncertainty, cognitive biases, decision-making, and distress tolerance alongside findings from this thesis, self-experience, and experience of colleagues and students to identify strategies to help healthcare professionals thrive in the face of clinical uncertainty. Strategies were suggested to enable the physician to help themselves, for example highlighting ways to understand their own reaction to uncertainty with tips on how to plan for, and manage, this uncertainty; and strategies were outlined to help physicians work with patients, using patients as allies in shared decision-making, with specific discussion of strategies to communicate uncertainty with patients, known to be a particularly challenging domain for healthcare professionals. Strategies were also suggested to help physicians guide students, trainees, and less experienced colleagues, such as role-modelling embracing the inherent uncertainty of clinical medicine and tips to explicitly open conversations about the management of uncertainty in the clinical learning environment. The narrative review concluded with potential challenges and barriers to the implementation of these strategies, with particular focus on the healthcare system's infrastructure that is not currently set up to support the embracing of uncertainty at the institutional and operational level.

The implications of the interprofessional group intervention and the strategies suggested to embrace uncertainty will be discussed later in this chapter.

10.3 METHODOLOGICAL STRENGTHS AND LIMITATIONS OF STUDIES

The above findings should be interpreted in the context of certain methodological limitations of the work presented in this thesis. While detailed limitations for each study are outlined in the relevant chapters, below I discuss generic strengths and limitations that span several studies.

10.3.1 Study design

The majority of the studies described in this thesis were observational, cross-sectional studies and due to this design, we are careful to only test for associations and do not draw conclusions about causality or potential direction of effect from our findings alone. In the two studies that utilised randomisation of participants (Chapter 5 and Chapter 8) it is possible that randomisation did not fully balance potential confounders across groups, although we were careful to ensure the groups had similar compositions by sex and professional group. Randomisation for the group intervention study was limited to some extent by clinician schedule, although there were no significant differences between groups at baseline to suggest that randomisation had not occurred.

It is important to note that as these studies were conducted in real clinical settings, other wellbeing interventions may have been underway that potentially could have confounded results, although I am not aware of any other such interventions or initiatives taking place at the time of these studies. As, however, we are looking to effect change in the real clinical working environment, studying students, trainees, and faculty within this true-to-life context seems appropriate, despite the limitations with ability to control the

environment. Undoubtedly, therefore, a strength of these research studies is that they took place within the context of the participants daily lives and realities.

10.3.2 Sample size

For many of the studies the sample size was small, which may affect reliability of results due to higher variability, leading to bias. This can also risk the study being underpowered to detect significant differences that may be present, with an increased margin of error. This may be particularly true for the exploratory early-stage biomarker study, which had the additional challenge of missing information on some biomarkers further limiting statistical power. This may have been responsible for the lack of significant associations seen between hair cortisol and burnout, and oxytocin and trust. Therefore, the findings of this study should be interpreted with caution. It is important, of course, to recognise that despite the small numbers there were many significant findings and associations which might suggest a large effect size due to the ability to see a difference even with a small sample. These differences and findings may, therefore, be even more pronounced in the larger studies that are needed.

Small samples sizes can be a particular challenge in real-world medical student and faculty research that is conducted in the clinical learning environment, but as with many of these studies small sample sizes do allow for new research hypotheses to be tested in short periods of time without utilising too many resources. The early-stage data can then be used to design larger, multi-site, prospective, confirmatory studies.

10.3.3 Generalisability

All studies were single-site, which may limit the generalisability of the findings to the wider population of healthcare professionals. The sites chosen were large academic medical centres in busy urban areas. It may be that healthcare professionals working for district general hospitals or hospitals and community centres in rural areas have different experiences of burnout and uncertainty, and this may also be true for other parts of the world. In addition, organisational issues specific to the institutions studied in this thesis may have had an impact on student, fellow, and faculty experiences. However, there is no reason to postulate that similar predictors of satisfaction, tolerance of uncertainty, and burnout would be unique to this geographical location given the plethora of research indicating this is a global crisis in healthcare throughout the world, across specialties and training levels. And, conducting these research studies within the context of real-life clinical work is a strength as we look to better understand burnout in this context and the impact that uncertainty might have.

10.3.4 Sensitivity of the topics under investigation

A final overarching strength and limitation of the presented work is pertinent to the sensitive and challenging nature of the topic under investigation and the implications of this. As we explored in the opening introductory chapters physicians are slow to seek help[50,51] owing to fears of judgment, stigma[52], and punitive actions[43]. They are less likely than the general population to receive appropriate treatment despite seemingly better access to care[53-55] and, despite their training, often fail to recognise that depression is a significant illness that requires treatment[53]. Similar denial of, and strong defences against, uncertainties in the healthcare environments are consistent observations made by

sociologists studying the process of medical training—embodied in healthcare teaching, case-based learning curricula, and medical research is the notion that physicians must unify a constellation of signs, symptoms, and test results into a solution[8]. These factors of course make this a research area of utmost importance, but the sensitivity of the topics may have affected the validity of the findings. For instance, participants who completed the surveys may have felt more comfortable talking about these oft-taboo topics or may have been more or less likely to be burned out, and thus the data may have been influenced by selection bias. Furthermore, although we used measurement scales that have strong validity evidence, many of the studies were self-reported survey designs and potentially susceptible to social desirability bias. To minimise these biases results were collected in a de-identified and confidential manner, and participants were unaware of the specific hypotheses of the studies. We have no information to suggest that they would have chosen to participate or not on the basis of their degree of burnout or tolerance of uncertainty, and our response rates were similar to other studies of physicians.

Trainees are considered a vulnerable group by ethics review committees as there is a fear they may feel pressurised into taking part in research studies worried they will be penalised by programme leadership if they do not. In the studies undertaken in this thesis involving trainees (fellows in the pilot study described in Chapter 4 and Appendix 4.1, and medical students in Chapter 5) participation was not shared with any programme leadership and responses were de-identified before analysis.

10.4 DIRECTIONS FOR FUTURE RESEARCH

A thesis such as this raises more questions than it provides answers, and there are undoubtedly many avenues in the burnout and uncertainty domains that still need to be explored. In particular it will be important to develop additional evidence of causal relationships with the use of prospective longitudinal studies.

10.4.1 Burnout

Further research is undoubtedly needed into what triggers and drives the development of burnout. As has been explored in this thesis, we need to work towards a consensus on how to accurately and reliably measure and define burnout, particularly with regard to the addition of objective measures with clinical meaning. Large, prospective, longitudinal studies that attempt to capture how burnout and stress change throughout the academic year for healthcare professionals across specialties and across training grades together with the impact on individual wellbeing, patient satisfaction and healthcare outcomes, and institutional goals, will be important in helping to define and create this consensus. As the interprofessional intervention explored, research and conceptual development that includes multidisciplinary participation is needed for definitive progress. This thesis has strengthened intriguing hypotheses about the relationship between distress in the physician workforce and tolerance for uncertainty. Again, longitudinal prospective trials are needed to test the conceptual model that educational efforts to encourage tolerance of uncertainty could reduce important endpoints like burnout.

10.4.2 Uncertainty

Our findings give impetus to further psychometric and conceptual research on tolerance of uncertainty scales. Understanding how tolerance of uncertainty can be recognised, developed, and supported during and after clinical training, could be enhanced by research with larger samples of physicians at all levels across specialties and healthcare environments. Further studies are undoubtedly needed that concentrate on links between reactions to uncertainty and patient outcomes to establish to what extent it affects quality of care. As discussed above, research to develop and evaluate interventions to improve tolerance of uncertainty in healthcare is a critically important need given the increasing exposure of both healthcare providers and patients to uncertain situations and information[257].

More work is needed to define the circumstances and communication strategies for uncertainty, with studies needed to explore the fundamental questions about how people process, interpret, and respond to various types of uncertainty inherent in clinical decisions. Although the ideal of informed or shared decision-making implies a need for communicating this uncertainty to patients, there is currently wide variability in the degree to which providers actually engage in communicating conditions of scientific uncertainty, with few evidence-based recommendations for such communication. The development of such recommendations will require empirical research in multiple domains including: the neurobiology underpinning how people process, interpret, and respond to various types of uncertainty[526,527]; defining the circumstances and communication strategies to discuss uncertainty[152,190]; understanding how individuals vary in their reaction to uncertainty[9,149]; the impact of uncertainty discussions on health-related decisions and outcomes[190]; and in

the development and validation of measures of component and composite uncertainty[149] (Table 10.1).

BROAD DOMAIN	RESEARCH AREAS
Neuroscience	How do people process, interpret, and respond to various types of uncertainty inherent in clinical decisions?
Communication techniques	What are the mechanisms of framing effects in different patient populations that may affect how information is perceived and responded to, impacting uncertainty aversion?
	Is information about uncertainty best presented verbally, numerically, graphically, or using multiple formats?
	What is the effect of non-verbal communication to emphasize and embrace uncertainty (changes in tone, phonetics, and body-language)?
Communication content	Under what circumstances is the communication of both aleatoric and epistemic uncertainty appropriate, and why? What degree of precision in communicating both types of uncertainty is necessary and optimal?
Assessing individual preference	How can an individual's tolerance of uncertainty be assessed? Do patient factors, including cultural background, influence attitudes about uncertainty?
	Do physicians perceptions represent accurate assessments of their patients' preferences about uncertainty?
	What are the most effective ways to reduce an individual's intolerance of uncertainty?
	What patient characteristics influence effective communication of uncertainty?
Creating and assessing impact of communication	What are the trade-offs in different approaches to communicating uncertainty?
	What strategies enhance the likelihood that the discussion of uncertainty is viewed as a sign of honesty rather than incompetence and how does this impact vary by patient characteristics?
	In what ways, and under what circumstances, does communication of uncertainty improve outcomes for patients? What is the longer-term impact of protective uncertainty on patient outcomes?
Measurement tools	How do we accurately measure and quantify uncertainty?

Table 10.1. Areas for future research focus, adapted from "Communicating uncertainty: a narrative review and framework for future research" by Simpkin AL and Armstrong KA. In Journal of General Internal Medicine, 2019; 34: 2586-2591[160]

10.4.3 Biomarker measurement of burnout

Further research is needed in the search to identify objective measures of wellbeing that have clinical meaning. It will be a crucial goal and intriguing prospect for future enquiries to further exploit the unique characteristics of hair cortisol in relevant burnout research contexts. It certainly holds great promise to significantly enhance current research efforts in this area, and unlike so many biomarkers it is an easy-to-collect and store matrix with no diurnal variation or short-term pulsatile variability making collection windows broader and more feasible for busy healthcare professionals. Future research should compile detailed intra-individual information about severity and duration associated with burnout symptoms. Based on that information it should be tested if there is a change point where symptom severity and duration start to significantly alter basal glucocorticoid secretion and further immune competence.

The specific effects of oxytocin as an underlying biological mechanism for the reduction of stress and anxiety and for positive social interactions in humans are yet to be determined, and further research is needed in this field. It will be important to continue work to develop measurements of oxytocin that correlate to central concentrations, and to develop measures of cumulative oxytocin exposure.

10.5 IMPLICATIONS OF FINDINGS

The work described in this thesis hold wider implications for the training of junior doctors and the wellbeing of faculty.

10.5.1 Implications for clinical training

10.5.1.1 Need to formally integrate uncertainty into medical education curricula

As we have seen, the presence of uncertainty in the medical environment is not a new revelation; yet its absence in medical curricula is conspicuous[150]. There is a need to refine how we define, measure, and teach clinical uncertainty in the pre-medical, pre-clinical, and clinical experiences of future physicians. In a longitudinal study over the course of medical school, Han et al. found that rather than growing comfort with clinical uncertainty, between the first and final year, there was a significant decrease in tolerance of ambiguity among students[528]. Counterproductively, we currently train students for certainty, rather than preparing them for uncertainty.

One promising direction is that the ability to deal with uncertainty is increasingly recognized as a major goal of medical education. It is now listed by the UK's GMC as among the core professional competencies for physicians[285] as well as one of the 21 competencies defined by the US's ACGME as important to foster, measure, and track in physicians over time. Specifically, trainees must demonstrate "the capacity to accept that ambiguity is part of clinical medicine and to recognize the need for, and to utilize appropriate resources in, dealing with uncertainty"[319]. Likewise, standardized tests in medicine (including the Medical College Admission Test (MCAT)) are shifting away from pure basic science topics to include questions of psychology, social sciences, and system

level issues[529], while Geller has argued for assessing prospective students' tolerance for ambiguity in the selection process.[180]

Medical schools are broadening admissions criteria to include students with diverse backgrounds and experiences and incorporating more 'true to life' clinical learning, case-based approaches and training in health systems sciences[530]. Formal training methods for uncertainty must be developed, disseminated, and evaluated for their effectiveness[531]. We must advocate for and support such changes in policy and pedagogy in medical schools and healthcare systems, such that lessons learned in this generation are sustained and institutionalised for the future.

10.5.1.2 Understanding stress from uncertainty

The culture of medicine has, for too long, demonstrated a deep-rooted unwillingness to acknowledge and embrace uncertainty[8], driven in part by the scientific communities quest to eliminate uncertainty in clinical decision-making which has propagated the emergence of evidence-based medicine, precision medicine, and biomedical artificial intelligence[116]. The lived reality for students, trainees, and faculty is, however, one in which uncertainty is rife. Part of the reason for the discrepancy in culture and reality is an unwillingness to openly discuss uncertainty and a failure in the way we train our healthcare professionals to explicitly manage, communicate, and embrace uncertainty. Specifically, we have an education system that prioritises and rewards certainty and assessments that too often focus on the notion of a black-and-white, "right" answer. In Chapter 4, I explored the demographic characteristics of those who may be at highest risk from uncertainty. An intolerance of uncertainty has been shown to be a characteristic involved in excessive worry[238-240]. The psychological distress which is associated with an intolerance of

uncertainty has consequences not only for the physical and mental wellbeing of physicians but also has a detrimental impact on their ability to perform well academically[242]. Our findings suggest that females and those with less experience are at increased risk of detrimental stress from uncertainty. This could allow medical educators to develop focused efforts to target the most vulnerable, recognising the need for all physicians to understand, acknowledge, and acquire proper coping strategies for uncertainty as a core clinical competency. As the narrative review study outlined, talking openly about uncertainty in the clinical environment and role-modelling the inherent uncertainty in clinical medicine, can help normalise the experience of uncertainty, especially for more junior colleagues. Educators should ask questions that focus on "how" and "why", not "what" and "when", stimulating discussion that embraces the uncertainty rife in all aspects of human health and illness and moving away from answers that can be neatly categorised. In parallel, assessments should prioritise uncertainty, shifting away from the black-and-white multiple-choice questions that are all too common due to their apparent objectivity, to emphasise that certainty is not always the end goal. Training programmes should explicitly ensure mentorship is in place to discuss uncertainty and create guidelines to help clinical leaders discuss uncertainty and role-model the management of uncertainty. The narrative review presented in Chapter 9 of this thesis provides a framework of strategies to help physicians thrive in the face of clinical uncertainty. It is time to change the long-held culture in medicine that ignores, denies, and suppresses uncertainty[8].

10.5.1.3 Acknowledging the importance of language used in clinical settings

Building on the above, understanding what factors and processes affect anxiety due to uncertainty in healthcare professionals is an important and urgent goal. Our findings from Chapter 5 suggest that the language used to frame clinical scenarios may impact physician

response to uncertainty, regardless of personal characteristics, lending support to careful consideration of the language used in healthcare settings, especially in hand-over scenarios as standardised protocols are developed, to prevent unintended (and unwanted) consequences. In particular, when uncertainty is still present in diagnostic discussions, the use of the word "hypothesis" as opposed to "diagnosis" may help individuals recognise the uncertainty, preventing premature closure and unwanted biases to creep in. Speaking about "hypotheses" rather than "diagnoses" may change the expectations of both patients and physicians, facilitating a shift in culture. In parallel with these efforts, as highlighted throughout the thesis, it will be important to ensure that we develop interventions to help physicians manage stress or anxiety due to uncertainty in clinical environments[8]. Cultivating an optimal tolerance of uncertainty, and identifying the language that allows individuals to practice in this sweet spot without being paralysed by anxiety associated with uncertainty, will likely be an important step in improving communication, patient safety, and physician wellbeing[8,323].

10.5.1.4 Increased understanding of effective wellbeing interventions

Burnout interventions that are effective, feasible, scalable, and cost-effective continue to evade healthcare organisations. The positive findings from the interprofessional group intervention study reported in this thesis suggest that self-facilitation may be an effective strategy and that the therapeutic benefit is related to the relationships that get strengthened through time and conversation, regardless of specific content or structured discussion. This intervention is low-cost and low-time commitment and would be easy to implement across institutions without huge financial burden. While there has been much recent focus on interprofessional collaborative teamwork and education, interprofessional wellbeing initiatives are yet to become commonplace. Faculty of differing professional backgrounds

work collegially together in teams at academic medical centres worldwide and are impacted by the same systemic factors that drive professional burnout. Too often, wellbeing initiatives focus only on faculty who share the same professional role. It is powerful to set a precedent that wellbeing interventions can be equally effective (and perhaps even more effective) when they are inclusive of all professional roles. Several studies have demonstrated a relationship between burnout and professional satisfaction with reduction of clinical work hours, increased sickness absence, and early retirement[1,2,72]. At a time when shortages of clinical faculty are projected, efforts to ensure interventions are put in place that decrease burnout and the consequent negative impacts are essential. The study described in Chapter 8 broadens the possibilities for transforming institutional culture and effectively enhancing wellbeing.

10.5.2 Implications for measurement of wellbeing initiatives

The exploratory work presented in Part II of this thesis has attempted to address current measurement limitations in self-reported surveys, particularly those attempting to capture burnout metrics. We demonstrated the feasibility and acceptability of collecting biomarker samples from clinical faculty and as discussed in the summary of key findings above, saw significant correlations between cortisol measurements and burnout, and between oxytocin measurements and engagement and sense of connection and community. These findings suggest that cortisol concentrations may be an effective and objective measure correlating with burnout symptomatology. Hair is an exciting new matrix able to provide unique long-term retrospective measures of cumulative cortisol secretion, offering high potential as a biomarker of long-term stress. Our findings suggest that it could provide an important mechanism by which to measure physiological change following wellbeing interventions

and initiatives due to the ability to assess stress-induced changes in cortisol exposure longitudinally.

The findings demonstrating an association between oxytocin and engagement and sense of connection and community suggest that oxytocin may be a novel way of evaluating workplace culture and relatedness, particularly with regard to familiarity among colleagues, known to be important in the promotion of wellbeing. With increased pressure to promote effective team functioning with diverse members, objective clinical markers that might correlate with a sense of connection and trust could be of vital importance to training programmes and healthcare organisations moving forwards.

Overall, the findings from Part II of the thesis call attention to the potential novel use of biomarkers to measure burnout and connection and trust in healthcare professionals which may be a valuable starting point for the ongoing search for objective measures that have clinical meaning. Medical education programmes are under increasing pressure to monitor and report burnout, with mandatory wellness promotion programmes. The ability to accurately and reliably measure wellbeing has never been more urgent.

10.5.3 Implications for patient care

The ultimate goal of any medical research is to provide patient care of the highest quality and safety. As was discussed in the opening chapters, burnout is an accelerating global public health crisis that threatens patient care through both direct and indirect consequences. The impact to the healthcare service of mitigating burnout is huge with the potential to reduce patient safety incidents, enhance quality of care, improve patient satisfaction, and promote better healthcare outcomes. Enhancing a tolerance of uncertainty

not only has the potential to positively affect patient care through the reduction of burnout, but it also promises to reduce medical error due to premature closure and early decision-making as physicians learn to sit more comfortably in the uncertainties of clinical practice without needing certainty too soon. This comfort with uncertainty increases the ability to consider other possibilities after reaching an initial diagnosis, reducing the likelihood of diagnostic error due to blindspots as a result of cognitive biases. These errors currently represent a major source of preventable mortality, morbidity, and cost. Embracing uncertainty may be one step to tackling this devastating phenomenon, enhancing patient safety and ultimately saving lives.

A provider's ability to deal with uncertainty at a cognitive, emotional, and ethical level has been shown to influence the diagnostic process with potential for diagnostic error and impact on patient outcomes[205]. When confronted with a clinical situation whose consequences are not easy to predict—and this concerns most medical decision-making—physicians who are intolerant of uncertainty may feel particularly worried and anxious about the implications of their decisions, thus resulting in a feeling of being 'stuck' in the uncertainty and unable to move forward[242]. It is estimated that 17% of excessive costs in medical care result from physicians' anxiety related to how they manage uncertainty[216], with increased test-ordering tendencies[208,209], failure to comply with evidence-based guidelines[210], and fear of malpractice litigation and defensive practice[213]. These extraneous interventions not only increase healthcare costs but also place patients at risk for experiencing adverse events from unnecessary tests and treatments[191,207], causing unnecessary concern and distress to patients.

Hiding uncertainty from patients is a betrayal and risks the destruction of interpersonal trust, detrimental to high quality patient-centred care. Perhaps a part of the patients' history and examination should include explicit acknowledgment of the uncertainties present, ensuring this important domain is visibly part of the dialogue. By shifting the culture of medicine to acknowledge and openly discuss uncertainty—both between colleagues and with patients—empathetic, positive, and partnering relationships can be established which may bolster trust and increase patient engagement and satisfaction.

10.6 CONCLUDING REMARKS

"Now this is not the end. It is not even the beginning of the end.
But it is, perhaps, the end of the beginning"
Sir Winston Churchill

The work presented in this thesis sets out to explore burnout in healthcare professionals, with a focus on the impact that uncertainty has on this domain, by using various methodological designs across pharmacology and experimental psychology and a multiple stakeholder approach, with medical students, fellows, and interprofessional faculty all included. Through a series of cross-sectional survey studies and randomised experimental intervention studies, together with an in-depth review of the literature and experiences of healthcare professionals, advances have been made in understanding what affects satisfaction at work, the sociodemographic characteristics of those who may be most at risk of stress from uncertainty and consequent burnout, together with an understanding of how language variation may influence emotional perception of uncertainty. Through an early-stage study exploring the use of biomarkers as proxy measures of stress, burnout, and trust, progress has been made in the attempt to identify objective clinical measures by

which to measure wellbeing—a critically important goal as we seek to better understand and evaluate mechanisms through which to mitigate burnout. And finally, as suggested by the initial study in this thesis, the potential therapeutic gain that may come from bringing people together to build a supportive and social community was demonstrated in the interprofessional intervention study.

The findings and focus of this thesis feel particularly pertinent in the context of the current global climate and the Covid-19 pandemic that has swept the world without pause. There is much uncertainty ahead in regards to the future evolution of the virus, particularly with regard to development of immunity and while the research community works at breakneck and unparalleled speed to devise a vaccine, antibody tests, and an array of effective treatments, we remain in the unknown period of discovery[146]. One of the biggest challenges facing the coming era is the authentic disclosure and communication of uncertainty in a meaningful way that enhances trust in the patient-provider relationship and improves decision-making and healthcare outcomes. The current pandemic will undoubtedly leave in its wake a raft of economic and social costs and repercussions that will likely extend Covid-19-associated uncertainties well into the next decade. The burden of responsibility and strain on an already stretched healthcare service risks causing an increase in burnout. Never has the need been greater for focused efforts that build on the results of this thesis to enhance our knowledge and understanding of drivers and effective measures of burnout allowing interventions to be developed that can be rigorously evaluated and assessed.

I opened this chapter with a quote from John Keats, a fellow Briton and fellow doctor, that poignantly reminds us of our human struggle to embrace uncertainty: *"At once it struck me what quality went to form a Man of Achievement … when a man is capable of being in uncertainties, mysteries, doubts, without any irritable reaching after fact and reason"*. Uncertainty has long been an unwelcome guest. Perhaps this next era will see us eliminate the toxic fear and anxiety that has for too long been fuelled by our unhealthy reaction to uncertainty. I hope to continue to build on the results of this thesis to participate in the quest to embrace uncertainty, mitigate burnout, and ultimately enhance provider wellbeing and patient care.

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