SECTION 1 Patients and their treatment

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ESSENTIALS Those who practise medicine should remember that we are all pa- tients at some time, most likely at the beginning and end of our lives. We therefore begin this textbook with an account of encounters with the medical and nursing professions, written by an outstanding doctor, medical historian, and leading clinical scientist. After a highly distinguished and eventful career which spanned the introduction of the British National Health Service in 1948, Christopher Booth died in 2012, aged 87 years. Latterly, he experi- enced the protracted misery of illness punctuated by repeated sur- gery; but to the end he retained his intellect and penetrating wit. His piquant observations are a challenge to us all as we try to provide care for our patients, as is his parting shot: 'If you are a physician, no matter how important you may think that you are, you should, so far as your own illnesses are concerned, consider yourself a layman.' Introduction We are all patients sooner or later, but particularly at the beginning and end of our lives. A general practitioner brought me into the world, a second twin, by manual removal when my mother was suffering from uterine inertia. Later, as a four-year-old, I can recall being in- jected against some form of infectious disease and passing out cold on the floor. There were then many infections to which my gener- ation was susceptible. Chickenpox, mumps, and measles were fre- quent. During the misery of measles I remember seeing the flag on our nearby church flying at half-mast for the death of King George V. Our doctor, the one who had delivered me, was a tall, distinguished man, smelling, as they all did in those far-off days, of ether. Later I con- tracted scarlet fever, a streptococcal illness of importance in those days before antibiotics. I was kept in strict isolation at home, with a resident nurse to care for me and daily visits from our general practitioner. Between those childhood days and the years of maturity, I was but rarely a patient. There was a hazardous episode during training as a naval diver when I had an alarming allergic reaction to the sting of a jellyfish (Portuguese man-of-war). The main symptoms were caused by severe oedema of the throat, and breathing became difficult. I had no idea then, long before I became a physician myself, that the large dose of morphine given by the naval doctor might well have exacer- bated the respiratory distress. Beyond that, as a young man I was only a patient for a brief period with glandular fever. I have been fortunate to escape those chronic conditions such as multiple sclerosis, Crohn's disease, or rheumatoid arthritis that blight young lives so terribly. It was not until I was in my fifties that I developed any significant illnesses. I had intermittent atrial fibrillation, which usually subsided with antiarrhythmic drugs. My blood pressure was normal and has re- mained so. There were repeated electrocardiograms, but no attempts at cardioversion by DC electric shock. For the first time I began to make visits to hospital outpatient clinics or enter the sumptuous rooms of those who undertook private practice. It was this experi- ence that made me realize that the particular feature of being a pa- tient means having patience. One came to accept that so much time is spent waiting—for an appointment, for a blood test, or an X-ray, for a consultation, or for drugs from the hospital pharmacy. As the years go by, you should realize that,

like your patients, you are more liable to afflictions which may be truly frightening and threaten your life over prolonged periods. My next encounter with medicine in practice came about entirely by chance. I had been retired for some years when my partner encouraged me to have a ‘check-up’. The excel- lent lady general practitioner was not one of those many who spend more time staring at a computer screen than they do looking at you. She examined me carefully, found nothing amiss but despatched some blood tests. These too were normal with one exception, a test with which I was then unfamiliar. The blood concentration of prostate-specific antigen (PSA) was 15 µg/litre and thus above the healthy range. I was informed that this suggested the presence of a symptomless cancer of the prostate and although I was reassured that the significance of the finding was uncertain, a subsequent prostate biopsy revealed that there was indeed cancer of the prostate, apparently localized to the gland. The question therefore arose as to what should be done. Much today is made about choice; perhaps this has value when there can be truly an informed discussion, as subsequent events in my case show. So far as I was concerned, I had no interest in where I should be referred for treatment. My doctor could advise me about that. Nor had I much interest in choosing between the options available—surgery, radio- therapy, or hormonal treatment. It was for my advisers to recommend what they thought was best. It was only in later years that I realized that 1.1 On being a patient Christopher Booth† † It is with great regret that we report that Christopher Booth died on 13 July, 2012.

4 SECTION 1 Patients and their treatment the choice of radiotherapy was unfortunate. At the time, daily treatment as an outpatient for more than six weeks was a tormenting experience since the resulting radiation cystitis caused excruciating pain. I was constantly reminded during those days of the urologist who prayed nightly to his maker: ‘Lord, when thou takest me, take me not through my bladder.’ In the end the symptoms subsided. The PSA level returned to normal and has remained so. Mercifully, the cancer had been eradicated. I soon devel- oped severe muscle pain—diagnosed by a rheumatologist as polymyalgia rheumatica and which required treatment with steroids. Nothing will ever convince me that these symptoms were not the result of the radiotherapy. These events took place during my 70th year. A few years later, while in manifest good health, illness suddenly struck again. One evening, out of the blue, I developed severe upper abdominal pain. In the ab- sence of an out-of-hours service from the local general practice, at midnight we attempted to obtain medical advice from NHS Direct on the telephone—this was a fruitless task made very trying by ‘language difficulties’. I finished up in the accident and emergency department of our local hospital. There, a very competent Asian doctor treated me with pethidine: and there too I first experienced lying on a trolley for the rest of the night. Lying on a trolley is no great problem for a patient blissfully enjoying the delight of repeated injections of pethidine but it is extremely dispiriting for one’s partner. Deeply troubled by my illness, seated in a small and uncomfortable plastic chair, my wife had nothing to do but watch and wait hopefully for the dawn. A week in hospital taught me how to manage my life while attached to an intravenous drip, which had to accompany me at all times. It turned out that I had acute pancreatitis, possibly associated with a gallstone. The pain soon subsided and, apart from one other minor event, has not recurred. All remained well for four or five months. Then, attending a clinic for a follow-up appointment, I found out why, for a little while my wife had noticed that I was thirsty and polyuric. She, of course, had made the right diagnosis, which my medical adviser at once recog- nized when he smelt the acetone on my breath and found my blood sugar to be in excess of 30 mM. I was immediately admitted and the diabetes was brought under control by intravenous therapy. On this occasion I was admitted to a geriatric ward where the noises at night generally made sleep no

more than an aspiration. One particularly un- fortunate man, suffering from expressive dysphasia caused by a stroke, kept shouting in frustrated attempts to make himself understood. Becoming a diabetic at once changes your lifestyle. You find out how to control your blood sugar, initially on oral medication. But soon, as is so often the case, you require subcutaneous insulin and you now have to learn how to inject yourself as well as keeping to a strict diet. You also have to ensure that you avoid the unpleasantness and fear of hypoglycaemic attacks. In addition, you may require visits to the foot clinic to ensure you neither develop ulcers nor infected toe-nails. If, in the case of that illness, it was a matter of one thing following another, my next and most serious medical encounter was even more Odyssean. By my 82nd year, I had thought that the prostate cancer, 12 years after radiotherapy, could safely be forgotten. The PSA con- centrations had remained within the normal range and I seemed in good health. But then haematuria developed. Cystoscopy as an out- patient failed to identify a source for the bleeding and while waiting for an appointment for an inpatient cystoscopy, I suddenly developed clot retention. It is no pleasant experience driving through metro- politan rush-hour traffic during an attack of acute retention. Nor was attention at once forthcoming in an accident and emergency department, dealing as usual with the overwhelming evening intake of drunks and dropouts. Finally installed once more on a trolley, a junior house officer attempted the necessary catheterization. Only after repeated and painful efforts is a more experienced registrar sent for; he at last blissfully relieved the obstruction. Then again, the long wait—and finally, admission to a high-dependency ward. I remained in hospital for treatment over the next three and a half months. The events of that first week in a high-dependency ward set the scene for what was to happen during the next months. A regime of constant bladder washouts was instituted in the hope that the haematuria would subside. Several drugs were tried, all to no avail. There was obvious re- luctance to undertake surgery in an elderly patient for a condition which showed no sign of being malignant. So in due course I was transferred to a single room in a urological ward where the haematuria persisted des- pite continuous bladder washouts. Maintaining the flow of fluid from two large containers hanging on a drip stand became one’s constant concern, nurses not always leaving enough fluid supplies, particularly at night. If the flow ceased, clot retention would recur. For a brief period I was sent home in the hope that the symptoms would subside. But it was to no avail—as was the search for the cause of the bleeding. Two careful cyst- oscopies under general anaesthesia failed to identify a bleeding point, an- other reason why there was reluctance to consider surgery at that time. One soon became used to a ward routine that scarcely varied from day to day, with the exception that at weekends nothing ever seemed to happen. You might be gently woken by a kind nurse from the Philippines wanting to give you something but whose command of English might not be fully up to the task. You would be increasingly less surprised to see the unfamiliar blank wall that had been there when you drifted off to sleep. You would at once be aware of noise, trolleys being pushed along corridors, the clatter of metal containers, and sometimes the cries of the afflicted. You have breakfast, the same cereal most days, sometimes por- ridge. You are given the morning’s drugs. A venesector takes your blood every day, the veins becoming progressively less easy to find. Your blood pressure, oxygen saturation, and pulse rate are measured on a machine every four hours or so and it may be necessary for a drip to be inserted, a task undertaken better by some than others. Your insulin dosage has to be adjusted, depending on the results of your blood sugar obtained by pinprick. Your bed is made, your body washed. You sometimes see the intern who has the care of you, but they change frequently. Then there is the consultants’ ward round. Instead of a single individual taking care of you, you find that up to five consultants, and their acolytes, visit to- gether. Invariably courteous and considerate, you learn to hang on every word. There are those who find the

recumbent position of the patient in bed, in the presence of massed ranks of consultants, to be demeaning. I have preferred not to acknowledge my obvious inferiority but to im- agine myself a mediaeval potentate receiving his courtiers. Then, at last, another surgeon is brought to see me. The waiting is now over. Briskly and unhesitatingly, he decides to operate within three days. I am lucky—he is one of the best in the country. The operation is to be a total cystectomy and prostatectomy, the creation of an intestinal pouch to replace the bladder and transplantation of the ureters into this pouch. One can easily understand why my advisers had been so hesitant to inflict such a procedure on an individual in his 82nd year, irrespective of my status as a former Professor of Medicine. Fortunately the surgery is brilliantly successful and we now have a diagnosis. The pathologist reports that there are no specific bleeding points in the bladder but that there are signs of widespread radiation damage. As with my diabetes, one thing has again led to another: the diffuse pathological bleeding was caused by that course of radiotherapy given so long ago. Surgical success depends on the support you receive before and after the operation. Languishing in hospital, I had lost a considerable amount

1.1 On being a patient 5 of weight and nutritional advice from a gastroenterologist was needed for recovery. There were other complications. My thumbs became septic because of a faulty technique in obtaining blood for sugar estimations and both were later shown to be infected with the near-ubiquitous methicillin-resistant Staphylococcus aureus (MRSA)—as was a small unhealed focus in my abdominal scar. More drugs—this time, anti- biotics to control the MRSA. Still feeling weak and scarcely able to walk the distance from the kerb to my front door, I was sent home. I felt terrible that day and by evening had developed severe dys- phagia. Back in hospital I was soon drifting dreamingly in and out of consciousness; little did I know that my wife had been told by my ad-visers to expect the worst. By the next morning, however, the gastro- enterologists had done an oesophagoscopy and identified oesophageal candidiasis. I was treated with nystatin and soon recovered. Although the appetite took time to recover, I was able to eat again and returned home to convalesce. But it was to be a year or more before my strength fully recovered and for some months my voice was weak and husky. Certain memories of life as a hospital patient persist.
I encountered so many consultants during that time: seven urologists, a gastroenterolo- gist, a cardiologist to check whether my heart would stand up to surgery, a diabetologist, a rheumatologist to check my steroid dosage and the status of my polymyalgia rheumatica, as well as a dermatologist when a presumed drug eruption occurred. There was also the infectious diseases expert who treated the MRSA infection. Throughout, the international nature of the team who contributed to my care was impressive. Among doctors, nurses, porters, radiographers, and other staff, I counted mem- bers of 38 nationalities, including many nurses from sub-Saharan Africa and the Philippines—clearly countries favoured for recruitment to the United Kingdom and one wonders about their loss of national skills. Despite laudable attempts to make it tempting, hospital food was generally unappetizing and I depended largely on my wife for susten- ance: she brought in dinner with a small bottle of red wine most even- ings, and on this I survived. Yet above all, a patient depends on the support of friends and family, upon whom a greater burden lies than is often realized: my wife visited on every day of my incarceration—a task that she undertook despite her commitment to our household and her own affairs, when travel was not always easy and when, having arrived at the hospital, parking might be difficult. It is the doctors and nurses whom you meet every day who can do most to sustain your spirits. As a medical student in Scotland I was taught to treat a duchess or a dustman just the same. The patient should, of course, always be treated with respect: I am convinced that this starts with their being addressed naturally using

their surname (given name) rather than the all-too-prevalent belief that use of their first name would be preferred from the outset. Clearly this familiarity may come later—by invitation- and when desired by the name-holder. It is astonishing to see how frequently patients are offended by the pre- sumption of first-name familiarity, at least in hospitals in the United Kingdom; it is a behaviour perceived as institutionally controlling by adults of all ages and status—and not only by elderly professionals. But if the staff genuinely sympathize with your lot, spending time an- swering your questions and those of your family, you are greatly en- couraged. It is so often the little things which count. I recall being much moved and heartened by a young Zimbabwean nurse, who had cared for me during one of my hospital admissions and who later took the trouble to visit me in a far-off part of the hospital to see how I fared. Continuity of care is also important. Being under the care of an in- tern or nurse whom you get to know and who understands your illness is essential for morale. Having to explain your problems to a stranger who drops in for a brief uncomprehending visit after hours or at a weekend does nothing for confidence. There are also practical matters which may be overlooked. Whereas major interventions involving surgery, for example, may be explained scrupulously, staff doing ap- parently simple procedures such as venesection, cannula insertion, arterial puncture for blood gas determination or catheterization and the like, often forget that these activities also require explanation since they may distress anxious or confused patients—to whom the slightest invasion of their person rapidly becomes anathema. Anxious des- pondency also mounts when there is unaccountable delay in carrying out procedures that have been arranged: timely explanation can often mollify this distress but when it comes to the relief of pain, there is no excuse for delay—diagnostic or otherwise. The failure immediately to catheterize a patient with acute retention of urine is clearly unforgiv- able but as I learnt, is still regrettably common. Practical and important though many procedures are, requiring both skill and experience—for the patient, nothing can replace the compassion and sympathy that the caring professions owe the af- flicted. So many aspects of excellent practice stem from these simple human qualities, which thankfully survive despite the strong busi- ness ethic that pervades medicine in many countries today. Of the lessons that I have learnt, however, perhaps the most im- portant is that to be a patient entails, as the Oxford English Dictionary puts it, ‘enduring pain, affliction, inconvenience, etc, calmly, without discontent or complaint’. It is equally necessary to be ‘able to wait calmly’. In our later years, it easier to agree with this advice. After all, as a man reaches his eighties, he has little choice but to accept with equanimity the world of Shakespeare’s sixth age, when he shifts Into the lean v and slipper’d pantaloon, With spectacles on nose and pouch on side His youthful hose, well sav’d, a world too wide For his shrunk shank; and his big manly voice, Turning again towards childish treble . . . That passage accurately describes me in the immediate postoperative period, even to the urostomy pouch—but my voice has now recovered. I do not, however, wish to survive into the last of Shakespeare’s seven ages when we are doomed to ‘mere oblivion; sans teeth, sans eyes, sans taste, sans everything’. While I have so far benefited from the cour- ageous decisions of those who did not give up when the end looked inevitable but who saw that there was a ‘quality of life’ worth striving for, I only hope that common sense, compassion, and proper confer- ence with my nearest and dearest will be brought to bear when the seventh age draws nigh. One does wonder if such a perspective truly holds today—especially in wards for older people in modern Western hospitals. One other lesson remains. If you are a physician, no matter how important you may think that you are, you should, so far as your own illnesses are concerned, consider yourself a layman. FURTHER READING Booth CC (1987). Doctors in Science and Society. Essays of a Clinical Scientist. Cambridge University Press, Cambridge. Cox TM, Tansley EM (2012). Sir Christopher Charles (Sir) Booth. Royal College of

Physicians of London, Munk’s Roll, Volume XII (2005-) http://munksroll.rcplondon.ac.uk/Biography/VolumeXII. Lock SP (2012). Christopher Booth. BMJ, 345, e5768.

1.2 A young person’s experience of chronic disease

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ESSENTIALS For as long as I can remember, my life has involved hospital care, both as an inpatient and as an outpatient. I’ve never really thought of myself as having a chronic condition, but I have three of them— haemophilia A, hepatitis C and HIV—and have had innumer- able medical interactions. Over the years there have been many changes in my treatments, and although these have been to my benefit I have found that they can be unsettling, as are changes in the medical team looking after me, and some changes in the ways that doctors have tried to communicate with me, a notable example being reluctance to give clear recommendation about the best course of action. What remains constant is the trust and communication you can share with the medical team. The Collins dictionary defines chronic as something continuing for a long time; constantly recurring or (of a disease) developing slowly, or of long duration. I’ve never really thought of myself as having a chronic condition. I recently turned 39 but it never really struck me. I was diagnosed with severe haemophilia A at the age of about 14 months. Later, I re- member having hepatitis (when I was older this was confirmed as hepatitis C) and later still, I remember being told I was HIV positive. It wasn’t until recently that these infections have been referred to as chronic conditions and it feels strange writing the words as they seem to add a sense of permanence to my illnesses. For as long as I can remember, my life has involved hospital care, both as an inpatient and as an outpatient, under the care of many dif- ferent departments of the National Health Service. There have been numerous medical interactions, too many to recount here. However, as time has progressed there have been underlying broader themes that affect the level of care I have received and I think are very rele- vant to anyone who is receiving ongoing medical care. These themes are Trust and Communication, the cornerstones of relationships. ‘Learning to trust is one of life’s most difficult tasks’—Isaac Watts A trip to the hospital or to see the doctor for a single issue doesn’t

require an advanced level of trust. A chronic condition requires the patient to develop a bond of trust with their care provider to make decisions that will maintain or, ideally, improve the condition. Vice versa, the care provider, be it doctor or nurse, needs to be able to trust the patient to take on board their advice and be sure any medical plan will be followed, whether it is a set of exercises or a rigid treatment regime. This is a process that occurs over time and, with a chronic condition, time is something that can be afforded. I was diagnosed with haemophilia A as an infant. This was when my family and I were introduced to my first doctors. These were the doctors who explained what haemophilia was, how to treat the con- dition, and how best to manage the condition and its consequences. They taught my mother, and then me, how to infuse factor VIII. These were the doctors who I grew up with. I learnt their manner- isms, I grew accustomed to their tones of voice, and how these would change depending on what they needed to tell me. The trust was solidified by their consistent approach to treatment and, for want of a better word, the safety and assurance they provided. When they re- tired in my early teens, this process had to begin again with new doctors and a change in treatment procedures (something I will touch on later). Not only is trust important, but familiarity also plays a part in the feeling of safety within healthcare. My haemophilia clinic has been in the same place for 39 years. It has had a facelift and been made slightly bigger, but it is still the same place. My HIV clinic was built alongside it. For all my check-ups and appointments I have been going to the same place. For years there were the same staff, med- ical, nursing, clerical; everyone knew my name and who I was. It is like a home from home (I even refer to it as mine without conscious thought). But this familiarity and trust can cause problems for both the patient and medical staff. I have never really liked change. It could be argued that my con- ditions are always there and, to a point, are stable now anyway. Previously they were changeable, be it the development of anti- bodies to factor VIII, a reduction in my CD4 count, or the need to change my HIV medication. There is always the anxiety when I go to the hospital that something might have changed for the worse. Changing doctors and locations immediately makes me uneasy. A prime example would be going to university. I went away to university to study when I was 18. While most freshers were finding their feet with new friends, housemates, and experiences I was also having to meet new doctors, which for me 1.2 A young person’s experience of chronic disease Anonymous

1.2 A young person’s experience of chronic disease 7 was one of the most uneasy experiences of my life. During the three years at university I can count on one hand how many times I visited the local haemophilia clinic in the university city. It was hard to de- velop trust, especially as I knew my time there would be temporary. This is not to say I was unsure of the care I would receive, it was more that I couldn’t get used to their systems of working. I didn’t have any shared experiences with the staff and no one knew my name, knew my foibles, or knew my family. I never felt at ease, to the point I made sure all my haemophilia check-ups were at a time when I was home from university so I could have them close to home in my usual clinic. Even during times of bleeding (unless it was an emer- gency) my parents would pick me up and take me to my regular haemophilia centre. My HIV experiences were very similar. I tried to make my check- up appointments at my usual clinic when I was home, but sometimes this was not always feasible. Also, in my second year it was decided that that I needed to start taking HIV medication. The decision was made by my regular clinic doctor but, due to the regularity of check- ups to monitor me on the new regime, these had to be conducted while at university. I never felt at ease there. I had spent years with my regular doctor and, again, a relationship of trust had been built up. I knew when he was going to tell me good news and bad. This wasn’t the case when I was at

university. Every dip in CD4, or rise in viral load, or the need to change my regime was a shock. I couldn't pre-empt how my appointment would go. I no longer had that split second of preparation because I couldn't read the tone of voice or body language easily. This was not an ideal situation for the doctor, and I believe I came across as defensive or cagey. I didn't feel I could be open with him, which can only have made his job harder. This affected my care to the point I left it probably longer than I should have done to notify my doctor when I noticed I was having side ef- fects to a new triple therapy regime (one of several during my time at university). Trust is vital for both sides when dealing with chronic conditions. Linked to this is the topic of communication. I've already touched on this; my failure to communicate a change in condition and the ability, once a relationship has been established, to communicate without speaking. Over the years, I have noticed the change in the way patients are spoken to. As an inpatient, as a child, I was spoken to softly with a high degree of empathy, everything was explained clearly in plain language. As I got older and moved to an adult ward, I noticed that the language became more clinical. The empathy is not lessened but it is different, almost as if there is an assumption that now you are older you have more ability to cope. But any change in condition, any increase in pain will always be scary, no matter how old you are. As time goes by, medical practices change. I imagine as a healthcare professional this is all part of the ongoing professional development, be it training courses or conferences. New practices, new treatments are taught. As a patient who only sees a doctor/ nurse once in a while, these changes can go unnoticed. However, I generally see one of my doctors/nurses/physiotherapists every 4 months, and I notice differences in protocols, which can be un- settling. Over time one gets used to a certain way of doing things and suddenly things change, with little or no time to adjust to the changes. A prime example is during consultations. It used to be that you were told the treatment options and the clinician would see what you thought about each option and then it would be made clear which option the clinician believed to be best. In some cases, they would decide for you on the best course of action. However, during a consultation for a surgical procedure, protocols seemed to change. All options were outlined and then I was asked 'What do you want to do?'. It took a lot of questioning to get a suggestion from the doctor about what the best option was likely to be. There is a lot of pressure on the individual, as the patient, to make this deci- sion. I felt once the options were outlined, communication stopped. While one knows how the condition feels and affects your day to day being, the decision for ongoing treatment/surgery cannot be made without medical knowledge and input. The communication of this knowledge, not just what the options are, but what each one means and which would be the most viable option, remains a vital part of the consultation. With a chronic condition the patient stays with the care team for a long time; longer than some of their own personal relationships. I've seen young house officers develop into renowned surgeons. I've seen doctors and nurses come and go. I've seen changes to buildings and to treatments. The only real constant in the life of a patient with a chronic condition is the patient themselves. Everything seems to change around you but you stay, perhaps a little older, a little greyer and, hopefully, with little fluctuation in your condition(s). What re- mains constant is the trust and communication you can share with the medical team.

1.3 What patients wish you understood 8

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ESSENTIALS If I have an acute curable condition, it is likely that your aims as a doctor and mine as a patient are aligned: we both want the problem to go away. But more people are now like me, living with disease rather than dying of it, and that change means that your role becomes less healer and curer, and more an advisor and supporter. A good model of care would be for you to see me, a patient with a long-term condition, as a full-time colleague on a job where you are only working part-time. Please understand that I am the
primary caregiver, part of the healthcare team, in fact I am leading that team most of the time. I am very likely to access patient- sourced information (support groups, online forums, crowd-sourced information) and find this valuable, and you should not feel threatened by this. If you see me as a full-time worker with local practical knowledge, and yourself as an advisor to our project rather than leader, that may help us work together. Where we can, let's learn from each other. Introduction I'm a patient. I have lived with a demanding long-term condition for more than
25 years. I also teach medical students with the help of other patient tutors and carers, and I am the BMJ's Patient Editor. This means, first of all, that I have had to change the way I interact with the world, because my condition makes me different from healthy people. It means I have to spend a lot more time with doc- tors and other healthcare staff than most people of my age. But it also means that I have been given the chance to work with patients and carers from all kinds of backgrounds to ensure their experience and expertise is shared with readers of the BMJ, working with them to create educational articles that doctors can use to improve their practice. At the University of Oxford, I collaborate with medical educators to incorporate different patients' and carers' priorities in course design and lesson plans. I have also been lucky enough to be asked, as a patient, to intro- duce this book. I can't represent every patient, carer, parent, or lay- person you will meet; but I can offer some insights into our world. Before I share what patients say they want you to know, here is some context. Healthcare is changing Learning medicine has traditionally meant a strong focus on acute medicine—diagnosing, treating, curing, and concentrating on one part of the body at a time. Traditionally, the doctor has always been the expert, the person we come to when something is wrong, so you can help make our bodies healthy again. Those skills are still vital, but things are changing in several key ways. What happens after diagnosis We have done so well in treating and managing communicable dis- eases that acute care does not dominate

medicine in the way it used to (Fig. 1.3.1). Helping patients manage chronic conditions requires a different set of skills from those used in acute medicine. Diagnosis becomes only a tiny part of the story, because people can live with a long-term condition for a lifetime, and restoring people to full health is often impossible. Dividing the body up into textbook chapters be- comes less and less relevant because chronic illnesses can impact on many body parts at once. What happens after the patient leaves the clinic The other major change is the way laypeople can now interact with each other about their illness experience, and learn for themselves about their bodies. Patients themselves have changed the way they communi- cate, their willingness and ability to seek out and share information, and the opportunity to connect online in ways that the traditional medical model has never had to address before. We look things up, we ask each others' advice, we help each other when doctors cannot be there. 1.3 What patients wish you understood Rosamund Snow† † It is with great regret that we report that Rosamund Snow died on 2 February, 2017.

1.3 What patients wish you understood 9 There are more and more people living with conditions that stay with them for life, that demand their attention and management at varying levels. Some of us have illnesses that require daily work, some may be reminded of our ill health only when our chronic con- dition flares up, but we cannot be simply treated and cured as in the acute model of care. For many of us this means a different kind of re- lationship with our doctors than our parents and grandparents had. What patients want to teach When I ask people to identify the things we wish our doctors were taught, what do they say? What do they ask to be included on the medical curriculum? Rethink what you mean by listening to the patient Among people who submit patient-authored articles to the BMJ, one of the most common things they want to teach is listening: 'Read my notes. Take what I am saying seriously. Take my time and emotions seriously. Find out what matters to me, and address that.' All of this more or less adds up to: 'Listen to me.' Many authors say exactly that, in their suggested key messages, in the proposed title of their article, or both.
I have to ask them to change the titles, or so many of them would be the same: Listen to me. Listen to the patient. Listen to the patient's family. Yet when I talk to doctors and medical students outside the clin- ical setting, they say they feel as if they are already listening. They know they ought to take patients' concerns and ideas seriously, even probe us for what we are feeling if we haven't volunteered it. In short, many doctors are trying hard to listen, but many patients still don't feel listened to. Why is there such a communication mis- match? I don't know the answer, but here are some thoughts for discussion by both sides. The clash of worlds A lot of medical training focuses on deciding which elements of the patient's story are key to diagnosis and treatment. Determining which elements have priority is usually left to the clinician. This can lead to problems, as can be seen by comparing the columns in Fig. 1.3.2. On the left, the priorities one might expect a doctor to choose when writing medical notes on a miscarriage. On the right, answers from women who had personally experienced miscarriage, when we asked 'what would you most like us to prioritize when teaching stu- dent doctors about pregnancy loss?'. Most of what is important to the women, and what they remember for the rest of their lives, is left out in the clinical record: it is unre- corded in the medical notes, not prioritized in service delivery, and not counted as part of patient safety. The medical notes are vital, but they are not the only things that need recording. The clash of agendas In teaching doctors I've found that one of the hardest things for them to take on board is the way patients feel when offered information they didn't ask for. Some patients who talk about communication 100% 90% 80% 70% 60% 50% 40% 30% 20% 10% 0% 1990 1995 Global deaths, both sexes, all ages 2000 2005 2010 2013 Noncommunicable diseases Communicable, maternal, neonatal, and nutritional disease Fig. 1.3.1 Global deaths due to

communicable and noncommunicable diseases. Data from Institute of Health Metrics and Evaluation (http://www.healthdata.org/results/data-visualizations).

10 SECTION 1 Patients and their treatment problems have asked their doctor for help on one topic, but were given information on something else entirely, because the healthcare professional felt the patient ought to have it. Often it is something the patient is told by every doctor, whether it is useful or not. If you have a patient who you consider to be overweight, but they are coming to see you about something else, giving them information about the benefits of losing weight can feel as if you are not listening to what they are saying. If you have a patient who has a long-term condition with risks of complications, and you insist on reminding them of these complications at every encounter, it feels as if you are seeing them as a disease rather than a person. Ask yourself: What is this person already likely to know? What did they come in for? Have I understood and answered that? 'That can't be true' Sometimes patients don't feel listened to because the doctor just doesn't seem to believe them. If a patient tells you about something that has happened in their body—the interaction of one disease with another, the unusual reaction of their body to a particular drug, the fact that they feel ill even when a blood test says they ought to feel well—be very careful not to dismiss what they have to say. Evidence- based medicine has improved many aspects of care, but there are still a great many areas where evidence has not yet been collected, where patients themselves are collecting that evidence, or where your pa- tient may be in a minority that responds in a way that a large-scale trial cannot pick up. In short, it may not be what you are expecting to hear, it may not be in this book, but that doesn't mean it isn't true. You as a doctor can ignore a symptom that you think can't be real, but we as patients have to go home and continue to manage it. You have enormous power over many of us, because you control access to the drugs and equipment that keep us alive and well. We need you to keep on working with us to find a solution. What does this mean for the way you communicate with patients? In general, when I have talked to doctors and patients who feel they have got this relationship right, the doctor is not asking him or her- self 'what is wrong with this patient?' or 'what can I do for this pa- tient?', but 'what is this patient asking me for?' and 'what does this problem mean to this patient?' These seem simple changes to the way you listen and the nature of your questions, but if done correctly could transform the way you hear and act. What medicine records: Parity-0+0 Gestation-?12/40 Symptoms—bleeding, pain Scan result: 11 weeks, No Fetal heart Otherwise fit and well Diagnosis: missed miscarriage. Treatment options discussed —medical, surgical, conservative. Risks explained. What patients said they wanted doctors to know: The antenatal unit is not the right place for care: 'My god that screwed me up seeing mums with little newborn and knowing full well my situation would end so badly' Remember the rest of the family : 'My partner had asked if he should stay in the room during the examination but no one bothered to answer him; I was left trying to talk him through what was happening whilst I was very frightened and upset' Remember what miscarriage can mean: '[My GP] was amazing. She let me cry and then told me the two most important things—that this is a bereavement and I must allow myself time to grieve and that it was nothing I had done and there was nothing I could have done to prevent it. I will never be able to thank her enough for this as it was far more important than anything medical she could have told me' Fig. 1.3.2 A woman has had a miscarriage: what medicine records, and what patients said they wanted doctors to know.

1.3 What patients wish you understood 11 We don't all share your interests or agree with your priorities When I was diagnosed with a serious illness, I had to become an expert in

biomedicine, drug interactions, nutrition, and healthcare systems: I had to become ‘health literate’. The difference is that, un- like you, I was not interested in finding out more about it, I did not choose this life path, and nor am I paid to develop my skills in it; it’s something that was forced on me. Imagine the situation the other way around. You have a full day ahead of you doing your job as a doctor. In your spare time, if you can get any, you would also like to see family or friends. Now think of the thing you’d hate the most to have to spend your life learning about—stamp collecting, a children’s TV programme, fashion, cars, whatever you find tedious. Imagine that you have to expend a lot of effort working on this in order to function. You have to do it in addition to your job, even if it gets in the way and your colleagues get frustrated with the amount of time it takes up. You can’t even leave the subject alone at the end of the day, you have to work on it even when you’d rather be talking to your children. You have to take time off from your job or in your own time to go to clinics where experts in your hated topic test you on your skills (just as people like me have blood tests that show whether we’ve been ‘compliant’ with treatment). And this will never go away, as long as you live. Managing a long-term condition, particularly one where the healthcare system demands many interactions, is like having a second unpaid job on top of the one you do to pay the bills. What does this mean for the way you deliver care, particularly for people who are living with long-term illness? Firstly, the more doctors can do to understand and relieve those pressures, practising ‘minimally disruptive medicine’ where possible, the better (see ‘Further reading’). Are there ways for us to get the things we need—results, advice—at times and in ways that don’t disrupt the things we love or need to do? Secondly, if we don’t share your priorities when it comes to treatment and self-management, can you find a way to respect that? Ultimately, we are responsible for our own bodies. For example, if I choose a behav- iour you believe to be noncompliant, risky, or that you simply disagree with, it is me, not you, who lives with that choice every day. I cannot walk away from it, my illness comes with me. In fact, perfect compli- ance with a recommended treatment is sometimes impossible in the real world, especially if you are asking someone to do it for the rest of his or her life. When you talk about doctors and patients reaching ‘con- cordance’ over treatment or practising ‘shared decision-making’, there is still an underlying assumption that at the end of our discussion, we will agree with each other—perhaps most likely, that you as a doctor will get us as patients to agree with you. But not all your patients will agree with you, though, and that is not a terrible thing. We may even prefer to hand some of the decision-making back to you, and that is not a terrible thing either. It’s not your job to make us think like you, or even to make us share your decisions and your enthusiasm for medicine, but we need you to help us live the lives we choose. We are still doing healthcare when you’ve gone home In the traditional patient/doctor model, the doctor is seen as doing the ‘work’, deciding what is wrong and what should be done about it, and the patient is the passive recipient of care. But once that patient is diagnosed with type 1 diabetes, or Crohn’s disease, or Parkinson’s, or thyroid disease, or has chronic pelvic pain, or another condition that changes life on a permanent basis, that model stops being ef- fective. As patients we are having to do our own healthcare work, not just while we wait to get well, not just during working hours, but all the time. In many situations, a carer may also be doing a lot of that work, and their life choices are affected too. My condition is a particularly good example of this. In the last year I had to make over 2000 decisions about the dosage and timing of the dangerous drug I need to keep alive, and then followed up those de- cisions with action. I have also made at least another 2000 decisions about monitoring the effects of that drug, as well as monitoring other related aspects of my health. Some of those actions have been in the middle of the night, in the middle of important workplace meetings, on planes and trains and buses; doctors were not present for any one of those. On

2 days out of 365, doctors helped me discuss a few of my de- cisions and supported me to get further tests that I needed. I am very glad of their help, but however good my doctors are, their work is only a part of the story of my illness. People like me are making healthcare decisions when you are not there, because we have to (Fig. 1.3.3). What does that mean for the way you work with patients? Well, a good model might be to see us, particularly those with long-term condi- tions, as full-time colleagues on a job where you are only working part- time. Please understand that we are in fact the primary caregivers, part of the healthcare team, in fact we are leading that team most of the time. We will know less than you about particular topics and may need your help in new or difficult situations, but that is true of your coworkers too. We will certainly know more than you about the way our disease affects Discussion with doctors Decisions made alone (99.8% of time) Ad-hoc adjustments Healthcare access work Decisions about dose/timing Medication delivery Self-monitoring Nutrition management Fig. 1.3.3 Hours of healthcare work done in a year. Data approximated from the author's personal experience, diaries, and medical data in a typical year of living with a complex chronic condition.

 us and how feasible it is to incorporate your suggestions into our lives. After years with a chronic illness, we may well know a great deal more of the biomedical facts about our condition than you do. Just as you would take advice and gain knowledge from a colleague on something you aren't an expert in, you can take our advice too. If you see us as a full-time worker with local practical knowledge, and yourself as an advisor to our project rather than leader, that may help us work together. And just as you would ensure a good handover of care to the healthcare professional taking over from you at the end of a shift, you also need to ensure good handover of any changes to our care to us. This means explaining what has changed and why, what needs to happen next, and where we can look for support and training in areas we are not yet familiar with. If you don't, we can't do our work safely. We look for information just like you do If you are ill, what do you do? You probably do one or more of the following: 1. Think about what you already know about the possible causes and management of your illness 2. Ask colleagues or friends who might have more information 3. Look information up 4. Make a decision about whether you need to get more formal ad- vice and tests Everyone does a version of this, although how far each of us takes it depends on how scared we are or how difficult it is for us to gather the information. In the past, patients had to be particularly educated or motivated to access medical facts and penetrate doctors' jargon. Now it is becoming far easier for all of us, if we want to find out how to cope with an illness, to go online to find what we need. For some doctors, that has in the past been seen as a source of annoyance or a threat. When I teach medical students, I often show them social media and online forum discussions between patients, with no doctor moder- ating the information. It is interesting to watch the students' unease shift, after spending time on those forums, as they realize that crowd- sourced patient advice is transforming people's lives for the better. Peer support is particularly valuable for those of us with conditions that need constant work. Often we encourage each other online, share the rationale for our decisions, offer advice and help in the middle of the night, when you cannot be there to advise us. Sometimes, we correct inaccurate advice given by well-meaning health professionals whose knowledge is too general to be helpful. In an era when people can connect so easily with others in similar situations, patient-sourced information (support groups, online forums, crowd-sourced info) is at least as valuable as the informa- tion in your textbooks, if not more so (Fig. 1.3.4). Don't be afraid of it. Learn from it. Don't be worried if your patient has gone to the internet for more information—isn't that what you do, if you can't Fig. 1.3.4 Many patient communities have been set

up by and for those living with a particular condition, such as #GBDOC. They are not moderated by the medical profession. Regular tweetchats share information about treatment and technology, as well as offering emotional support.

1.3 What patients wish you understood 13 get it from colleagues and the books around you? And if patients are seeking out more information about their condition, it means they are interested and engaged. What does this mean for the doctor's role? Again, this means a change in medical thinking: if we know things you don't know, if patients help each other and seek information in other places than your clinic or surgery, then work with us, add your expertise to ours rather than being threatened by it. Where we can, let's learn from each other. The future of good care In my work in medical education I have met many clinicians who are already practising these different working relationships with their patients and finding it rewarding. There is no need to be afraid of patients who know more than you, who think differently from you, or who challenge the traditional doctor/patient relationship. For doctors who have learnt to focus purely on diagnosis and treatment, perhaps it is a question of using your knowledge and skills in a slightly different way. Thanks to modern medicine, more people are living with disease rather than dying of it, but that change means that the doctors' role becomes less healer and curer, and more an advisor and supporter. If I have an acute curable condition, it's likely that your aims and mine are aligned. We both want the problem to go away. If I have a more complex issue, or a lifetime of living with a condition, I may challenge your ideas of the best outcome: I may need to define my- self as something other than just my disease. I may need to com- promise on your medical goals in order to live the life I want to live. I may disagree with the outcomes you have set for me. I may be doing nearly all the healthcare work my condition demands, and I appreciate it when you notice and respect that, but I do still need you. Let's work together. Acknowledgements My sincere thanks go to the authors in the BMJ's What Your Patient Is Thinking series, and to those patients, carers, and doctors who have advised me while writing this chapter. In particular I would like to acknowledge the help of Ruth Bender-Atik, Mary Cheetham, Jo Crocker, Sally Crowe, David Griffiths, Abi McNiven, Rajiv Mehta, Jane Moore, Tessa Richards, Sara Riggare, and Michael Seres for their input and support. FURTHER READING DeBronkart D, Sands D (2013). Let patients help. Create Space Independent Publishing, New Hampshire. Entwistle VA, et al. (2011). How information about other people's personal experiences can help with healthcare decision-making: a qualitative study. Patient Education and Counseling, 85, e291–8. Greenhalgh T, et al. (2015). Six 'biases' against patients and carers in evidence-based medicine. BMC Med, 13, 200. May C, Montori VM, Mair FS (2009). We need minimally disruptive medicine. BMJ, 339, b2803. Miscarriage Association. What women and their partners think student doctors should learn about pregnancy loss. https://www.miscarriageassociation.org.uk/information/for-health-professionals/. Patients Like Me. https://www.patientslikeme.com/ What Your Patient Is Thinking, a monthly BMJ series written by patients and carers, with learning outcomes for healthcare professionals. http://www.bmj.com/specialties/what-your-patient-thinking

1.4 Why do patients attend and what do they want f

1.4 Why do patients attend and what do they want from the consultation? 14

ESSENTIALS It is the job of doctors to know about disease and how to diagnose and treat it, and textbooks such as this are part of that endeavour. However, proportionally little actual physical disease remains in resource-rich countries of today, yet the demand is for more and more medicine. This prompts the conclusion that other forces de- termine the demand for contemporary healthcare. A counterculture view of the traditional medical model is offered here in which the reasons why patients consult their doctors is explored. In countries with developed healthcare, the traditional medical model of illness is dead or at least dying. A simplistic and reductionist approach to medicine is insufficient and signally fails to recognize or integrate the complexities of illness behaviour, and why it is that patients seek medical advice today. Contrary to traditional thinking and teaching, it is not illness that dictates the health-seeking be- haviour of a population but the healthcare system itself, and—most importantly—our actions as healthcare professionals.
A scourge af- fecting clinical practice in the developed world today is the med- icalization of all interactions, accompanied by overinvestigation, overdiagnosis, and overtreatment. Our profession retains its traditional duty, wherever possible, to diagnose disease and treat or cure illness appropriately, also to com- fort the sick, irrespective of the ability to cure. At the same time, a long-held principle of medicine at all levels is to do no harm, while at the same time supporting the maintenance of health and pro- tecting those who are well. Maintaining the balance between these apparent conflicting precepts is a scarce skill that needs to be taught by example during the education and training of the modern doctor. Introduction In the traditional ‘medical model’ we assume that the reason for the consultation is self-evident: patients have symptoms, a his- tory is taken, an examination is conducted, and the diagnosis is made—treatment is then offered. It is a process perfected by countless generations of doctors through the ages: concrete, fa- miliar, and certain. Knowledge of clinical signs and symptoms is the foundation of our professional status and the basis of the pro- fessional fees charged. But the concrete is beginning to crumble. Clinical knowledge is no longer the preserve of the profession; anyone with a smart (mo- bile) phone can

access global medical knowledge in a matter of sec- onds. In a lifetime, illness has changed out of recognition. In the developed world there is no rheumatic fever or diphtheria and finally with the introduction of new vaccines, even bacterial meningitis is being eradicated. Infectious disease as we know it, the great scourge of humanity a century ago, has gone. Tuberculosis is still present but occurs principally in recent immigrants. Similarly, we are witnessing the end of smoking-related conditions with pre- mature ischaemic heart disease and stroke rapidly disappearing, and lung cancer in decline. For other common cancers we offer screening programmes that detect cancers long before they become symp- tomatic and drive the traditional medical consultation (screening is discussed later). In resource-rich countries of today, proportion- ally little actual physical disease remains. Predicted health spending should fall but in reality health costs are burgeoning: figures from the World Bank show that in the United States almost one in every five dollars is consumed by healthcare and figures published by the US Center for Disease Control in 2014 provide compelling evidence for this trend. This prompts the conclusion that other forces determine the costs of contemporary healthcare as it is provided as well as util- ized. A counterculture view of the traditional medical model is offered here in which the reasons why patients consult their doctors is explored. Importance of clinical communication Communication skills are often maligned as ‘soft skills’; indeed, the old idea of ‘bedside manner’ is a pejorative term representing a mode of practise seen as increasingly irrelevant to the gleaming scientific new world of medicine. But the art and craft of commu- nicating with patients in the new world of disappearing diseases is far more powerful than any machine or investigation. If we truly seek to establish ‘why’ the patient has consulted us, we need to listen and converse. 1.4 Why do patients attend and what do they want from the consultation? Des Spence

1.4 Why do patients attend and what do they want from the consultation? 15 Every time a person, or a parent or guardian calls, and takes time out of their day to do so—often after an unconscionable wait and an even more punishing internal debate—they always have a specific reason. This reason—the so-called ‘patient agenda’—is frequently overlooked, even though its crucial importance is a fundamental principle which applies across all healthcare settings. The traditional mechanistic approach, a tick list of questions, frequently fails since the ‘agenda’, either through fear or simple embarrassment, is so often ‘hidden’. It is worth reflecting on own experiences as a patient: Did the doctor really discover what our concerns were? A simplistic guide which helps us to elicit this agenda is not a ‘tick box’ exercise, rather it is a more general and analytical way to understand the person who has become a patient by exploring their ideas, concerns, and expectations. Ask the patient if they have any ‘idea’ what might be causing their symptoms, what ‘con- cerns’ they might have about the symptoms, and what ‘expect- ations’ they have of the consultation. This may appear obvious, but doctors constantly and spectacularly fail to explore these aspects of their patients’ motivation. Among many other disadvantages, this failure leads to overinvestigation, unnecessary referral and, ultimately, dissatisfaction. If we were to supplement the clin- ical approach with improved nonverbal communication which notes eye contact, posture, and facial expression, the chances of establishing why the patient has attended and of addressing what they seek from the consultation would be greatly enhanced. Development of skilful communication is important in life gen- erally, but it is a crucial part of clinical education and clearly best reinforced by instruction and self-critical evaluation throughout one’s entire professional career. Health beliefs We all have health beliefs. These may not be based on commonly accepted scientific precepts, but often defy scientific reasoning des- pite being held with absolute conviction. Many patients (and some doctors) for example, passionately believe in

homeopathy—this, despite the counterintuitive nature of the science (in homeopathy the more dilute a treatment, the stronger it is alleged to become). We may berate these ideas, but for the patient the effectiveness of homeopathy is a fixed ‘health belief’ held in the face of accepted scientific concepts and evidence. Strong health beliefs concern the benefit of other alternative medicines and medical interventions such as chiropractice, osteopathy, acupuncture, Reiki, and many others—despite little or no obvious scientific basis for their clinical use. As with many believers in matters requiring a large element of faith and trust, a challenge to these beliefs is frequently met by anger and defensiveness. However, it is not just those who pursue alternative treatment who have unscientific health beliefs. Does removing tonsils reduce the rates of sore throat? Do annual physician examinations offer any value to health? Do screening programmes cause more harm than good? Indeed, individual doctors strongly disagree over much of the foundation of what may be termed medical science. A fascinating aspect of health beliefs is that they seem to be in- herited, passed down through the family. If your parents have cer- tain health beliefs, you are likely to share them. For example, patients who attend doctors frequently often belong to family clusters. In one study conducted by the author, members of families classified as frequent attenders constituted about 10% of the population but ac- counted for 50% of consultations. Health culture Consider what shapes and influences health beliefs that differ radic- ally between people and populations. Why should otherwise appar- ently similar populations have wide variation in consultation rates across the world? How can health costs vary about twofold between countries such as the United Kingdom and the United States? In the United Kingdom most doctors are salaried and are not gen- erally paid according to their activity. In most systems, however, ‘fee for service’ is payable. This remunerates doctors for activity and en- courages more testing, more prescribing, and more consumption of healthcare. The simple truth is that many doctors consciously or subconsciously have vested financial interests in ensuring that pa- tients return for care, even for minor illness. A cynical view would be that many have a vested financial interest in rendering patients doctor-dependent and health-anxious. Making those who are well, worried, can certainly be a great business model. Doctors often blame patients for needless health-seeking behav- iour, but in truth, doctors and their medical health systems forge this health culture. The wide variation in health-seeking behaviour between different nationalities owes much to the health system that operates in the countries of origin. Changing health beliefs An important principle to reduce health-seeking behaviour is based on the concept of Numbers Needed Not to Treat—the number of patients we need not to treat, to prevent one patient returning with the next episode of illness. Intervene more, and more patients will return: intervene less and less patients return. So health systems should seek to intervene less. A simple illustration is the use of antibiotics for sore throat. Declining to prescribe antibiotics might lead initially to conflict with patients. In time, however, as shown by Little and colleagues in a study involving nearly 800 patients from 11 primary care centres of general practice in the United Kingdom, the patients will realize that they will not be prescribed an antibiotic, and will appreciate the natural course of many types of sore throat, which improve without this treatment. Their health belief changes and gratuitous attendance decreases. This is better clinical practice and frees up access, thus reducing pressure on the medical system. While the complications of sore throat may not be rare and can be severe (with some requiring intravenous antibiotic treatment, management of fluid balance, and sometimes surgical intervention due to lack of treatment or inadequate antimicrobial therapy), correctly applied, the principle offers a way to reduce de- mand in all healthcare services. Changing the clinical practice of doctors, changes the behaviour of patients. This facile idea is one that is beyond the comprehension of many with responsibility for healthcare. We must not conflate more

medicine as better medi- cine: generally less medicine is better medicine.

16 SECTION 1 Patients and their treatment The i-patient effect Two doctors working in the same healthcare system, same area, and serving patients with similar demographic characteristics can vary their referral rates—in a recent study by the author—by as much as 10-fold, with highly divergent investigations and prescribing pat- terns. How can this be explained? Like all of us, doctors are hostage to their own health beliefs: those who take antibiotics for coughs and colds will duly dispense anti- biotics to patients for similar indications. Doctors anxious about their own cardiovascular health will prescribe more statins and antihypertensive drugs. Doctors worried about their own pigmented lesions will refer patients with skin lesions more frequently. Simply put: doctors' personal beliefs affect their clinical practice. This is what I and others have termed the 'i-patient' effect. Doctors who are anxious and who struggle with uncertainty and risk, practise very differently from the those who do not. We cannot prevent doctors bringing their individual health bias into the consulting room, but understanding and acknowledging our own health beliefs allows us to control its influence. While this may appear to be an obvious concept, it is one that is scarcely acknowledged and little studied. One might ask whether there is an argument that universities should select medical students who have low personal anxiety about their own health anxiety. Medical reviews—the problem of 'bring backs' How often do patients need to be invited to return for review? Every week, every month, every year, or perhaps never. Intervals recommended for medical 'check-ups' have a limited scientific basis and are frequently found to be a mere thoughtless habit. It is appropriate to reflect on how much time is dedicated to reviewing appointments for raised cholesterol, hypertension, routine blood tests and the remaining justifications for such 'bring backs'. In most systems of healthcare, these review appointments are highly lucra- tive activities driven simply by financial interest. But in systems with limited budgets, access for the sick is restricted because of this factor. Many medical systems are busy, often with numerous pointless, unscientific but easy recall appointments, rather than busy serving the sick. The so-called 'inverse care law' dictates that most healthcare is consumed by those least at risk, rather than those with the most medical need. In financial terms, 'contact time' with medical professionals represents the greatest expenditure, yet many healthcare systems appear to be devoid of any reflection on how this costly resource is used. Simply changing the interval be- tween reviews would free up numerous appointments, but this important aspect of healthcare practice has attracted very little at- tention for research. Particular difficult issues Medically unexplained symptoms The medical model has a familiar simplicity that is accessible to doc- tors, but the classic description of disease is unravelling in developed countries because many diseases are themselves in terminal decline. The patterns and frequency of vascular or infectious diseases are changing rapidly, some cancers are in decline, and there is even an end in sight for smoking-related disease. Patients now more frequently present with nebulous symp- toms such as tiredness, weakness, numbness, dizziness, headaches, bladder symptoms and, most commonly, unexplained or bizarre forms of pain. Such patients are often the majority of those attending primary care and in several hospital settings. Clearly, because such symptoms could represent a more serious condition, those who complain of them generate a whirlwind of uncertainty in doctors weaned on the traditional medical model. This uncertainty precipi- tates testing and the prescription of medications. These patients are the frequent attenders: they accumulate thick medical files and report persistent, and ever-changing patterns of symptoms which constitute a chronic illness. Despite endless in- vestigations these symptoms remain 'medically unexplained': this term is not used here to dismiss these patients, because their symp- toms are real to them, but there is no

underlying pathological process. Estimates indicate that a quarter of consultations are for unexplained symptoms, but experience suggests that in reality the proportion might be even higher. So, medically unexplained symp- toms should hold a priority position in every medical textbook (see Chapter 26.3.3), and this author contends that every medical school should have an academic group devoted to their study, although clearly this is not the case. Current medical teaching usually suggests that symptoms equate to the presence pathology, and accordingly many doctors are simply unable to recognize patients with symptoms that will defy under- standing in straightforward pathological terms. Doctors should reassure these patients, and their failure to do so is the cause of ever-increasing use of investigations, polypharmacy (most notably analgesics and psychoactive agents), interventions, and hospital ad- missions, thereby employing vast resources. In the United States, the epidemic of deaths from the use of prescription drugs is in part caused by the fact that pain has been treated as a simple symptom, and not a subjective, complex, and often medically unexplained pro- cess. Moreover, in a private healthcare system, patients presenting with medically unexplained symptoms are at a particular risk of being exploited cynically for profit. As our insights into many medically unexplained symptoms are not likely to be rapidly enhanced by innovative research, we would do well to consider the views of a few wise physicians, often with experience in primary care, that while this may not be the science of medicine, it more accurately reflects the art of medicine. Some of these views are epitomized in the following cautionary statements, some of which may appear cynical or might prove to be inappro- priate in individual cases: ‘If the symptoms don’t make any sense then there is nothing wrong with them.’ ‘Remember, frequency of attendance is inversely proportional to likelihood of pathology.’ ‘Referring the anxious only makes them more anxious.’ ‘Medicine is just magic and misdirection.’ ‘Everything you were taught in medical school is wrong.’ ‘Look for normality, not pathology.’ ‘Do nothing, but with style.’

1.4 Why do patients attend and what do they want from the consultation? 17 The sick role and conversion syndromes Many forces encourage patients to attend a doctor, but sometimes we should remember that there may be a personal gain from being ‘sick’. There is a range of illness behaviours: at its most basic, it can generate a spontaneous day off work, the ‘sickie’; but more destruc- tive behaviour can be seen in which the patient appears completely wheel-chair bound. The sick role affords attention, sympathy, and even status within family and society. The role can excuse us from work and responsibility, and may be rewarded with financial bene- fits. Such patients typically complain of medically unexplained symptoms and often have no insight into their illness behaviour. It not as simple as ‘just pretending’ but much more complex: family members, either consciously or subconsciously, often collude in maintaining this sick role by acting as advocates. In addition, ex- treme sickness behaviour can be expressed through a proxy, such as a child or older person, who is offered up as having an illness which is fabricated: ‘Munchhausen disease by proxy’. Tackling ex- treme sickness behaviour is very challenging, if not impossible, for doctors: patients and families alike can become very hostile and angry at any suggestion that symptoms might be psychologically based. Doctors need to be taught and made aware of the extremes of sickness behaviour. Drug-seeking and manipulative behaviours Doctors have replaced the gruff paternalism of the past with ‘patient- centredness’: we are encouraged to use expressions like ‘choice’, ‘patient power’, and to adopt a ‘nonjudgemental’ stance. This is a seismic shift in the doctor-patient relationship. Today, it is hard to say ‘no’ to the patient; indeed, even challenging patients’ views or requests for particular treatment is difficult in our complaint-driven culture, hence a form of consumerism is the new norm of medicine. However, giving patients what

they ‘want’ can lead to very bad medi- cine, which is harmful to the recipient. Sometimes patients wilfully seek to deceive doctors—a state- ment that is not cynicism but realism, and perhaps best illus- trated by those seeking psychoactive medications, such as opioids, benzodiazepines, and the antiemetic, cyclizine; more recently gabapentin and related drugs are implicated. Patients can either sell these medications or personally abuse them (often both) in what is overt deception. Often pain or anxiety symptoms are re- ported at the time of presentation. Doctors accept this history in good faith and prescribe psychoactive medication. Soon there are stories of mislaid or lost medications and dose escalation. In coun- tries where healthcare is poorly integrated, patients may go ‘doctor shopping’, attending multiple doctors from each of whom they are independently prescribed medication. Active deceit of this kind is signalled by inconsistent accounts and aggressive or tearful reac- tions to any form of challenge. Lack of ability to address or recognize manipulative behaviour is in part responsible for the epidemic of drug-related deaths in North America. The Centers for Disease control report data from the National Vital Statistics System 2013 that in the United States, 44 people die every day from overdose of prescription opioid pain- killers, and many more become addicted. More than twice as many residents die annually from unintended prescription drug overdoses than the total number of US soldiers killed in Iraq. Drug-seeking places a huge pressure on practising doctors. Trust in medicine has great power to heal; but mistrust and manipulation of medicine exerts a huge power and harm. Welfare benefits In many countries, doctors act as gatekeepers to welfare benefits. If you could receive more income would there not be a strong incen- tive to overplay and invent symptoms? Many people cheat on claims for expenses or seek to minimize or avoid income tax, and so there are well-known parallel behaviours. Some would ask, if you were injured in a road traffic accident, where is the harm in overstating your neck pain to improve your pay out? There are huge variations in reported sickness rates across countries and regions that simply cannot be accounted for by illness prevalence, and it is a statement of fact that patients will attend doctors seeking to manipulate insur- ance and benefit systems. External forces There are, of course, the individual reasons why patients attend doc- tors. However, other major environmental forces are in play, which constantly effect health-seeking behaviour and health beliefs. These are not always predictable and are often beyond intervention and thus largely outside the remit of medical control. Medical charities and advocacy groups Patient advocacy groups and charities are considered to be im- portant and legitimate to healthcare. Charities also offer important photo opportunities for politicians and are a constant source of human-interest stories for the media; they have real grass roots sup- port. So charities sponsor campaigns advertising disease awareness that encourage patients to seek medical advice. But we should ask the question: Is the role of charities always positive? Advocacy pressure groups can dominate agendas, potentially distorting resource allocation. Health messages promulgated by charities are often in effect simplistic sound bites that are factually flawed and couched in emotionally charged language. Often, despite there being a lack of evidence of benefit, they call for more screening, testing, and treatment. There are nefarious interests at work, too. Charities are sometimes exploited by the corporate medicine and pharmaceutical companies in an activity colloquially known as, ‘astroturfing’. In this activity, companies provide large sums of money to charities, who unwit- tingly act as proxy advocates of these companies. For a charity, pro- moting a disease is also promoting the treatment, and this might be one of several competing medications. Not cynicism, but again merely good business sense. It is always worth exploring the re- ported sources of funding of medical charities, for the distorting ef- fect of corporate money is widespread. Direct-to-consumer advertising There has been an explosion of prescribing in the last few dec- ades, such that today lifelong polypharmacy is the norm and not the exception.

Coprescription of several drug classes is frequent, including statins, antihypertensives, bisphosphonates, antidiabetic agents, nonsteroidal analgesics, opioids, proton-pump inhibitors, and ever-mushrooming mental health medication. For ‘chronic dis- ease’ is the golden goose that provides most of the revenue for Big

 Pharma. So how better to promote your medication (sometimes for dubious conditions, especially in relation to sexual ‘performance’ in women and men) than directly to patients? In the United States (one of only two countries to allow public ad- vertising), flashing logos, tear-jerking stories, and smiling celebrities paid to offer personal endorsements (e.g. a famous sportsman in the promotion of sildenafil) fill the airways. For example, in 2011 it was reported that one company (Pfizer) had spent $220 million on ad- vertising its top-selling cholesterol drug in the previous year, which was almost 25% of its overall $900 million in direct-to-consumer (DTC) spending. And as the internet is poorly regulated, companies are advertising the world over: after all, who knows who is behind online blogs and medical forums. There seems to be little we can do to resist the power of marketing and advertising. The patient is reduced to the status of a health ‘consumer’ (where the customer is always right), thus disturbing the equilibrium in the doctor–patient relationship forever. Money shapes the reason and outcome of our consultations, and it is a telling fact that despite competition in the free market of the United States, not only the charges for branded drugs are up to twice those in other countries, but the expenditure per capita is the highest of any country.

Internal forces

Paid experts and ‘disease creep’

Despite the essentially egalitarian nature of science and scientific en- quiry, medicine remains a deeply hierarchical and deferential pro- fession. The professional medical agenda is set by a few international specialists and opinion leaders, often cultivated by companies and referred to as KOLs, or key opinion leaders. Small groups of special- ists define conditions, control guidelines, and sit on national govern- mental advisory boards. An example of the influence is provided by national recommendations which change the boundaries of treat- ment for raised serum cholesterol concentrations, thus encircling ever more people who become patients receiving lifelong treatment. It has been suggested that 25% of people in the United States have a ‘mental illness’, a simply incredible figure which reflects a pervasive ‘disease creep’ observed in numerous definitions and conditions. This softening and blurring of boundaries has the effect of ensnaring people into the world of unmet medical needs. Defining the ‘unmet medical need’ is a critical point for meaningful interactions. Despite a strong backlash and the recent Sunshine Act in the United States, with tight controls in Europe, some medical opinion leaders are still found to be on the take, and over past years, some have been paid very large sums of money by pharmaceutical com- panies to work as their paid advisers and advocates. It is an uncom- fortable truth that everywhere in the world there are undisclosed payments to practising doctors. Indeed, in relation to the generous figures for mental illness cited earlier, the author noted in 2012 that about three-quarters of the contributors to the 5th edition of the Diagnostic and Statistical Manual of Mental Disorders published by the American Psychiatric Association report conflicts of interest and links to pharmaceutical corporations. Other countries are belatedly introducing Sunshine legislation which forces companies and doc- tors to disclose payments and links, but in many ways this has been too little and too late.

Evidence-based medicine

In the mid-1990s, evidence-based medicine arrived to save medi- cine from the vagaries of opinion and bring ‘best clinical evidence’ to the care of the individual patient. Naturally, the explicit articulation of the previously arcane process of therapeutic decision-making was a source of wide-ranging reflection and has undoubtedly rid medi- cine of much poor practice. But

evidence-based medicine has itself become a shackle, a vehicle of judgement, a new source of defer- ence, and spurious virtue. Where rigorous evidence is unobtainable or simply lacking, the approach has replaced the deferential behav- iour and unquestioned practices of the past with another parody of the Emperor with no clothes. Emperors were tyrants and so doc- tors mutter: ‘better not go against the evidence’. Thus, clinical care is increasing proscriptive, and ‘clinical guidelines’ have become an instrument of pervasive political control. The problem is much of the evidence is not what it seems. There is an inherent commissioning bias, for pharmaceutical companies own and commission most of the available ‘evidence’. Thus the evidence-based agenda is dominated by a commercial therapeutic mindset. Also the available research is riven with surrogate end points which are required by regulatory authorities for licensing and approval of drugs for reimbursement. Often these have been arrived at and agreed in the absence of a true clinical perspective of the dis- ease as experienced by patients and seen by their doctors: achieving the predetermined outcomes with endpoints that maybe statistic- ally significant is of little use if the outcomes are clinically irrelevant. Moreover, research data from high-risk populations often recruited into clinical trials are usually wide off the mark but sometimes cyn- ically extrapolated to patients with low risk present in unselected general populations. Unfortunately, the temptation to cheat, and opportunities for cheating in research are legion. In research involving clinical trials, there are incentives to err because there are literally billions of dol- lars to be made. One US researcher faked research leading to billion- dollar sales. Research fraud related to pharmaceutical activity and clinical trials remains even now an important matter. Corrupt re- searchers affiliated to the pharmaceutical industry face little by way of punishment other than the indirect reputational damage cast onto their employing organization. The importance of good clinical prac- tice and rigorous monitoring of clinical trial results should not be overemphasized. Evidence-based medicine has become the prin- cipal marketing tool of the pharmaceutical industry: naturally, this is a scientifically persuasive and appropriate stance, but it requires ceaseless vigilance to ensure that those who engage in evidence- laundering to sell their medication are in a tiny minority and that they are punished rigorously for misdemeanours. Screening Medical screening consumes increasing amounts of professional ef- fort, especially in primary care. The intuitive principle is extremely attractive at first glance: catch a condition early and the better the outcome—or so it appears. Thus, even questioning the value of screening generates angry defensiveness. But the issues at stake are not simple. Detecting a condition earlier may merely mean you know about a cancer earlier, rather than live longer. Also, detecting cancer early might give an artificial appearance of better outcome, if the outcome is determined by the ‘5-year survival ’. This is known as

 ‘lead time bias’ and confounds attempts to compare survival statis- tics between countries. However, the major issue for all screening is the effect of ‘overdiagnosis’. Cancer screening programmes provide illustrative examples. They may often identify tiny nonprogressive tumours, as a result of which we witness a rapid increase in cancer prevalence, such as has been noted in melanoma, breast, and bowel cancers. Since the detection by screening includes nonprogressive cancers, screening tends to produce a better relative overall survival rate but, depending on the type of tumour screened for, the change in abso- lute death rate is often very limited. There is then an epidemiologic pattern of overdiagnosis generated by screening. Screening is often hailed as the equivalent of Mao’s Great Leap Forward for Medicine, and while it may lead to absolute benefit in terms of health, such benefits tend to be less than expected. Moreover, they must be balanced against the certain costs

of real harm: it is highly disin- genuous to trumpet clinical success if millions of people are ‘diag-nosed’ with a cancer that is not progressive but who then undergo unnecessary chemotherapy and surgery with consequential loss of well-being and independence. How not to harm the healthy is a sophisticated challenge for the authentic success of many contem- porary, and superficially attractive, screening programmes. The need for change Given that the traditional medical model of illness is moribund, the scope, as well as style of medical education must adapt at all levels. The current reductionist approach to medicine classically fails to recognize or integrate the complexities of illness behaviour and often ignores the factors which drive patients to seek medical advice. It is now clear that it is not illness that dictates the health- seeking behaviour of a population but the healthcare system itself, and importantly the actions of healthcare professionals. A key prin- ciple of medicine, that the most important intervention is non-intervention, is linked strongly to the notion that our most potent medicine is reassurance. If, through enlightened teaching and re- search, we were able to enhance understanding of why patients at- tend health services, then we might be able to at least contain the burgeoning scourge of contemporary medicine: medicalization. Medicalization of all clinical interactions leads to overinvestiga tion, overdiagnosis, and overtreatment. Our profession retains its traditional duty, wherever possible, to diagnose disease and treat or cure illness appropriately, also to comfort the sick, irrespective of the ability to cure. At the same time, a long-held principle of medicine at all levels is to do no harm, while at the same time sup- porting the maintenance of health and protecting those who are well. Maintaining the balance between these apparent conflicting precepts is a scarce skill that needs to be taught by example during the education and training of the modern doctor. FURTHER READING Centers for Disease Control and Prevention (2014). Health, United States http://www.cdc.gov/nchs/data/hus/hus14.pdf#103 Centers for Disease Control and Prevention (2015). National Vital Statistics System Mortality Data. http://www.cdc.gov/nchs/deaths.htm Hatcher S, Arroll B (2008). Assessment and management of medically unexplained symptoms. BMJ, 336, 1124–8. Kanavos P, et al. (2013). Higher US branded drug prices and spending compared to other countries may stem partly from quick uptake of new drugs. Health Affairs, 32, 753–61. Little P, et al. (1997). Reattendance and complications in a randomised trial of prescribing strategies for sore throat: the medicalising effect of antibiotics. BMJ, 315, 350–2. Moynihan R, Doust J, Henry D (2012). Preventing overdiagnosis: how to stop harming the healthy. BMJ, 344, e3502. Spence D (2008). The i-patient. BMJ, 337, a1919. Spence D (2011). Explaining the unexplainable. BMJ, 342, d1039. Spence D (2011). The painful truth: deaths and misuse of prescribed drugs. BMJ, 343, d7403. Spence D (2012). The psychiatric oligarchs who medicalise normality. BMJ, 344, e3135. Spence D (2013). The art of deception. BMJ, 347, f5889. Spence D (2013). The cause of clinical variance. BMJ, 346, f1122. Spence D (2013). The power of doing nothing. BMJ, 347, f4409. Spence D (2013). Why I worry about large international studies. BMJ, 347, f6510. Spence D (2014). Evidence based medicine is broken. BMJ, 348, g22. Spence D (2014). Frequent attenders are getting poor care. BMJ, 348, g208. Staton T (2012). Lilly takes the lead in DTC ad spending, surpassing Pfizer. FiercePharma, 16 August 2012. http://www.fiercepharma. com/story/lilly-takes-lead-dtc-ad-spending-surpassing-pfizer/ 2012-08-16

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ESSENTIALS Medicine is both a scientific and a moral enterprise. It is as important to give reasons for the ethical aspects of clinical decisions as it is for the scientific aspects. The corollary of evidence-based medicine is reason-based ethics. Two concepts central to many ethical aspects of clinical practice are autonomy and best interests. Autonomy—Mill argued that society has no right to exercise its power over individuals against their will purely for their own good. In the medical context, a competent adult has the right to refuse any, even life-saving, treatment. Some conceptions of autonomy focus on competent choice; others emphasize the importance of reasons that relate to a person's long-term interests and goals. The requirement to respect patient autonomy can be problem- atic when it harms the patient, or others, or when a patient lacks capacity. Best interests—when patients lack capacity to make their own choices they should generally be treated in their own best inter- ests. But what does this mean? Philosophers have given three broad answers: maximizing positive states of mind, such as pleasure; maximizing the fulfilment of desires; and maximizing aspects of life that are objectively valuable. The legal concept of best inter- ests is a composite of all these. Three of the most common issues for which doctors seek ethics support are consent, end of life, and confidentiality. Consent—a crucial issue if a patient is refusing beneficial treat- ment is whether he or she is competent to do so. The assessment of competence involves three steps. First, identify the key informa- tion relevant to the decision. Second, assess the patient's cognitive ability: Can the patient understand, retain, and weigh the key infor- mation to come to a decision? Third, assess other factors that may interfere with decision-making, such as delusions. When a patient lacks capacity doctors must consider the patients' best interests, whether there is a proxy decision-maker, and whether the patient has made any relevant advance directive. End-of-life decisions—different ethical approaches disagree over the significance of two distinctions: that between acts and omissions; and that between intending and foreseeing an out- come. These distinctions are important in considerations of mercy killing; the moral difference between withholding life-extending treatment and killing; and in giving

treatments that relieve distress but might shorten life. The law varies on these issues in different countries. Confidentiality—when should doctors breach confidentiality, either for the good of the patient or to prevent harm to someone else? There are differing accounts of the most important reason for medical confidentiality: respect for patient autonomy; keeping an implied promise; and bringing about the best
consequences. These different accounts can have different im- plications for when it is right to breach confidentiality in prob- lematic situations. Introduction Evidence-based medicine emphasizes the importance of critical assessment: interventions should be evaluated on the basis of evi- dence, not tradition. Critical skills are therefore crucial to modern scientific medicine. Importantly, medicine is a moral enterprise as well as a scientific one. Many clinical decisions involve a combin- ation of factual and ethical aspects. It is as important to be able to give good reasons for the ethical aspects of clinical decisions as it is for the science. Society increas- ingly expects this from doctors as part of transparent decision- making. Doctors' reasoning about ethical aspects of care will need to stand up to scrutiny—in a court if necessary—just as much as will the scientific aspects. The corollary of evidence-based medicine is reason-based ethics. Two concepts central to many ethical aspects of clinical practice are autonomy and best interests. Two concepts: Autonomy and best interests Autonomy John Stuart Mill's essay, On Liberty, is one of the great statements of liberal thinking. Mill wrote: ' . . . the only purpose for which power can be rightfully exercised over any member of a civilised community, against his will, is to pre- vent harm to others. His own good, either physical or moral, is not 1.5 Medical ethics Mike Parker, Mehrunisha Suleman, and Tony Hope

1.5 Medical ethics 21 a sufficient warrant. He cannot rightfully be compelled to do or for- bear . . . because, in the opinion of others, to do so would not be wise, or even right'. (Mill 1859, Chapter 1) This principle imposes strict limits on the interference of the state into individual's lives. Mill articulates at its most general level a prin- ciple that in the medical setting is known as the principle of respect for (patient) autonomy. This principle has had an enormous effect in changing attitudes to the doctor–patient relationship over the last 40 years. It has been used to criticize medical paternalism, and has informed the development of 'patient-centred' medicine. It has led to an emphasis on providing patients with information, and to the development of the concept of informed consent. It is one of the main grounds for the importance of patient confidentiality. In situations where a competent adult patient refuses treatment that is, in the doctor's considered view, good for the patient, a con- flict arises between respecting the patient's wishes, and doing what is best for him or her. This is widely seen as a conflict between the principle of respect for patient autonomy and the principle of acting in patients' best interests (often called the principle of beneficence). The concept of autonomy, however, is not straightforward, and re- specting what a patient says (e.g. his refusal of treatment) and re- specting his autonomy may, on some views of autonomy, be different. Some aspects of autonomy The term autonomy has no clear single meaning. As Dworkin wrote (Dworkin, 1988, p. 6): 'It is sometimes used as an equivalent of lib- erty . . . , sometimes as equivalent to self-rule or sovereignty, some- times as identical with freedom of the will. . . . It is identified with qualities of self-assertion, with critical reflection, with freedom from obligation, with absence of external causation, with knowledge of one's own interests. . . . It is related to actions, to beliefs, to reasons for acting, to rules, to the will of other persons, to thoughts and to principles.' In the ideal of autonomy decisions should be rational, consistent with the person's life plans and based on critical reflection. If a desire, or choice, is not based on a rational evaluation then, on some views, it is not autonomous. This is one reason why

respecting a person's autonomy is not necessarily the same as respecting her choice. Respecting patient autonomy can be problematic for doctors in at least three situations: 1. when to do so harms the patient herself; 2. when to do so harms others; and 3. when the patient lacks the capacity to make choices for herself. With regard to the first situation patients sometimes refuse treat- ment that doctors believe is strongly in their best interests. This be- came a legal matter in England when an adult patient with motor neurone disease and who had capacity wanted to have her life sup- port removed. Her doctors refused because they thought this was tantamount to killing her. The court, consistently with Mill's prin- ciple and English common law, said that her wishes must be com- plied with: 'The doctors must not allow their emotional reaction to or strong disagreement with the decision of the patient to cloud their judgement in answering the primary question whether the patient has mental capacity to make the decision' (Re B, 2002). The conflict between respecting autonomy and harm to the patient or to others can also arise in the context of confidentiality (see next). In the third situation, when a patient lacks capacity to make de- cisions for himself, is it possible to respect the patient's autonomy. Consider the following case (Hope et al., 2007). Case example: Alzheimer's disease Mr D always valued academic and artistic pursuits. 'If I develop Alzheimer's disease allow me to die if given the chance,' he says. Mr D subsequently develops Alzheimer's disease. He no longer recognizes his family, but he remains physically fit. He is looked after in a nursing home and appears to enjoy a simple life: flowers, food, TV. Mr D gets a chest infection. This could be treated with antibiotics. Without cur- ative treatment he could be kept comfortable and would probably soon die. On a straightforward view it would seem that we respect Mr D's au- tonomy by withholding antibiotic treatment and allowing him to die. This is consistent with the wishes that he expressed when he had the capacity to do so. But there are at least three concerns that we might have even if our only ethical value were to respect autonomy. First, do we know that when he expressed his view about being al- lowed to die he had taken into account all the relevant facts of his current situation? For example, at what stage in Alzheimer's disease did he want to be allowed to die; was he meaning to refuse even a simple treatment like giving antibiotics; and did he take into account the possibility that he would generally be enjoying life? Second, he might have changed his mind after he had made the statement about being allowed to die and before he lost capacity, but no one knows of this change of mind. Third, is it possible for a person when healthy to imagine sufficiently the state of having Alzheimer's? When we allow a person with capacity to refuse beneficial treatment we can take care to ensure that this is what the person really wants, and that he understands all the relevant issues. Even if it is possible in this case to respect the patient's autonomy, in many (probably most) situations where a patient lacks capacity there will not be sufficient information about his previous views and values to make a decision about what to do based only, or even mainly, on this principle. The more useful principle in such situ- ations is the principle of beneficence that is treating people in their best interests. Best interests In many situations judging a patient's best interests is straightfor- ward but this is by no means always the case. Consider again Mr D. What is in his best interests? The answer may differ depending on your conception of best interests. The philosophical discussion relevant to best interests has been conducted mainly in terms of the concept of well-being. There are three main theoretical approaches to well-being. Mental state theories According to these theories, well-being is defined in terms of mental states. At its simplest (hedonism) it is the view that happiness or pleasure is the only intrinsic good, and unhappiness or pain the only intrinsic bad. If Mr D with Alzheimer's disease is generally enjoying the 'simple' pleasures then, on this view, it will be in his best interests to continue to live by treating the infection. The fact that he might

 previously have despised enjoying the TV soaps he now enjoys is irrelevant. Desire-fulfilment theories According to desire-fulfilment theories, well-being consists in having one's desires fulfilled. If desire-fulfilment theories are to provide a plausible account of well-being it is necessary to restrict the relevant set of desires. In one view, only those desires pertaining to life as a whole count as relevant in the analysis of well-being. These are desires that relate to a person's life plans. According to this view Mr D's prior intellectual values would be relevant. Withholding antibiotic treatment would be fulfilling his previous desires and these are the desires that fit with his long-term values. Desire-fulfilment theories of well-being have much in common with respecting autonomy, but they are not the same. In the case of Mr D, desire-fulfilment the- ories highlight the question of whether Mr D, at the time of deciding whether to give antibiotics, has relevant desires. From the perspec- tive of autonomy, the issue is whether he has capacity. Objective list theories According to objective list theories of well-being certain things can be good or bad for a person and can contribute to her well-being, whether or not they are desired, and whether or not they lead to pleasurable mental states. Examples of the kind of thing that have been given as intrinsically good in this way are engaging in deep per- sonal relationships, rational activity, and the development of one's abilities. Examples of things that are bad might include being be- trayed or deceived, or gaining pleasure from cruelty. An objective list theory does not give an unequivocal answer to what is in Mr D's best interests. On most lists—although not all— the pursuit of worthwhile life goals would normally take precedence over very simple pleasures. But that is not the choice that faces the carers of Mr D. The question is whether it is in Mr D's best interests to be dead, given that he can only enjoy these simple pleasures. Composite theories Each of the three theories of well-being outlined earlier identifies something of importance, but none seems adequate. Because of this, we might opt for a composite theory in which well-being is seen as requiring aspects of all the theories. A composite theory has some practical implications for medical practice. The main implication is that when considering what is in a patient's best interests, par- ticularly when these are not clear, it may be relevant to consider the aspects of well-being that are highlighted by each of the three the- ories. This does not tell us how to balance these considerations but it does suggest that in coming to a decision about Mr D's best interests it is relevant to take into account all of the following factors: his pre- vious values and wishes, his current experiences (of enjoyment, for example), and any current desires. Three issues in medical ethics Doctors who seek help with ethical issues in their clinical practice often do so with regard to three types of issue: consent, end of life, and confidentiality—each of which presents questions relating to autonomy and best interests. We will discuss each in turn. Consent The philosophical basis of informed consent rests on the principle of patient autonomy. Valid consent is widely regarded as requiring three main criteria: that the patient be informed and competent (or having capacity); and that the consent is voluntary. In the legal and ethical analysis of treating people against their will, a great deal depends on whether the patient is competent (or has capacity) to make the relevant decision. The approach to com- petence endorsed by both law and most ethical analyses is what is known as the functional approach. This focuses on the process by which the person comes to the particular decision. One implication of this approach is that competence is specific to a particular deci- sion. A person may, at one time, be competent to make one decision (e.g. whether to take a particular medication) but not a different de- cision (e.g. whether she is capable of living alone). When patients are making decisions (e.g. refusing treatment) that appear to be (signifi- cantly) contrary to their best interests, then doctors must carefully assess the capacity of that patient to make that decision. In broad terms, if patients have the capacity, then their decision must be re- spected, although the doctor must make sure that the

implications of the decision have been fully understood. The law in the United Kingdom and North America gives competent adult patients the right to refuse any, even life-saving, treatment. If, on the other hand, patients lack capacity to consent to (or refuse) treatment then they should be treated, generally, in their best interests (but see next). Assessing competence There are three main steps in assessing competence. Step 1: Identify the information relevant to the decision The critically relevant information includes the likely consequences of different decisions (e.g. different possible treatments, or treatment versus nontreatment) and including both wanted and unwanted ef- fects; and understanding in broad terms what would be involved in carrying out a decision. Step 2: Assess cognitive ability The Mental Capacity Act (2005) which is the key legislation in England and Wales states that a person is unable to make a deci- sion (i.e. lacks capacity) if he is unable to understand the information relevant to the decision; to retain that information; to use or weigh that information as part of the process of making the decision; or to communicate his decision (whether by talking, using sign language or any other means). Step 3: Assess other factors that may interfere with competence Cognitive impairment is only one factor that may interfere with the elements of information processing just outlined. It may also be im- portant to assess whether there is such interference due to a mental illness. A delusion, for example, may interfere with believing the in- formation. An affective illness (depression or mania) may interfere with the weighing-up of information and coming to a decision. Making decisions for people who lack competence There are four theoretically possible approaches to making deci- sions about the healthcare of incompetent patients (Buchanan and Brock, 1989).

 Best interests One approach for a doctor faced with an incompetent patient is to ask which plan of management serves the patient’s best interests. We have already outlined some different approaches to the ques- tion of what is in a person’s best interests (see the case example on Alzheimer’s disease earlier). Proxy An alternative approach is for a proxy to make decisions on behalf of an incompetent patient. Such an approach raises the question of why the proxy has such a right. The most obvious answer is that the patient had nominated the proxy at a time when she was compe- tent to do so. The proxy of course is left with the question of the basis on which the decision should be made. English law, under the Mental Capacity Act [2005] allows a competent person to nominate someone else (‘Lasting Power of Attorney’) as proxy in the case of loss of capacity. The proxy (rather like a parent of a young child) must act in the person’s best interests. If doctors believe a proxy is refusing highly beneficial treatment, then they may need to seek a court ruling. Substituted judgement The criterion of substituted judgement asks the hypothetical ques- tion: suppose the patient were (magically) able to become compe- tent, what treatment would he choose? In order to try and answer this question, the doctor could use a range of evidence: reports of what the patient has said about this kind of situation in the past; the kind of general values the patient held; and experience with other patients. This criterion is problematic, not only in practice, but also theoretically since it is unclear precisely what are the person’s abil- ities and beliefs in this magical state. Advance directives Advance directives (or advance decisions as they are called in the English Mental Capacity Act [2005]) are statements made by people at a time when they are competent, about how they want to be treated in the future were they to become ill and at the same time incompetent to give consent for treatment. The central justification for advance directives is that they extend patient autonomy to include situations in which a person is no longer competent. One problem with advance dir- ectives is that they need to be interpreted when applied to the specific situation and this can be difficult. More fundamen- tally is the concern that when completing the advance directive, the person may not have been able to

sufficiently imagine the situation at the time a decision needs to be made (see the earlier discussion of Mr D). End of life Killing someone is of course morally wrong. Doctors often care for patients who are near the end of life and perhaps who are suf- fering. Modern medicine can in many circumstances prolong life. Paradoxically it is the very fact that doctors care for patients that can make the general moral ban on killing ethically problematic. It is problematic in at least two ways. First killing can, to some at least, appear merciful. Second, there is some ambiguity around what counts as killing. Mercy killing Lillian Boyes was an English patient with very severe rheumatoid arthritis, so severe that she was expected to die within a few weeks. She was in so much distress that she wanted to be killed, but she re- tained full decision-making capacity. Painkillers did not overcome her distress. Her caring relatives also wanted her to be killed. If the doctor caring for Mrs Boyes were to apply the principle of autonomy and respect her competent wishes, should he not kill her? If every day of continued life was for her a burden, and there was no pro- spect of significant change until she died naturally, was it not in her best interests to be killed? The principles of autonomy and of ben- eficence point to the same action: to kill Lillian Boyes. In the United Kingdom, and North America, however, a doctor who killed such a patient would commit murder. In some counties, the Netherlands, for example, such a mercy killing (active voluntary euthanasia) can be legally carried out under carefully controlled conditions. The principle of the sanctity of life One reason why mercy killing might be wrong is because of an add- itional relevant principle: the principle of the sanctity of life. There are differing versions of this principle. The most extreme form is called vitalism: human life is of absolute value. Whenever possible, human life should be maintained; and it is always wrong to take human life. A less extreme form is one that sees life as a basic but not an abso- lute good. Preserving life on this view does not necessarily outweigh all other goods but the value of life cannot be completely accounted for in terms of a person’s experiences and beliefs. In English law, and in that of many other countries, there are two components to the act of killing. First, the death results from a pos- itive action on behalf of the killer, and second that the killer intends to cause the death. In a clinical setting this means that omitting to do something, such as withholding life-extending treatment (IV fluids, mechanical ventilation, for example) on the grounds that it is kinder to the patient to ‘let nature take its course’ is not considered to be a positive action, and is not killing. Such withholding of treatment is not only perfectly legal but might be seen as good clinical practice, and morally required. Furthermore, in English law, withdrawing treatment (taking down the IV line; switching off the ventilator) is seen as equivalent to withholding treatment. The intention too is crucial, at least legally. Sometimes a treatment for unpleasant symptoms can shorten life. This might be the case when large doses of morphine are given to very ill patients in order to control pain, because morphine can reduce respiratory drive. Giving morphine in such a situation is not killing and would nor- mally be perfectly legal because the shortening of life is not intended, but is only foreseen. If killing is wrong but these two examples are not killing and not generally wrong, a lot of ethical weight rests on two distinc- tions: that between acts and omissions and that between intending and foreseeing. Those who believe that what is of primary importance in judging the morality of an act is the foreseeable consequences will not find any significant moral difference in either of these distinctions. If we foresee, for example, that giving morphine will shorten life, then this has the same moral weight as if we intend the shortening of life. We cannot close our eyes, on this view, to the foreseen consequences of

 our actions by claiming that although we foresaw them, we did not intend them. An alternative framework sees the nature of the choices and not only the

foreseeable consequences as of moral significance. One idea within such a framework is known as the Doctrine of Double Effect. At the core of this doctrine is the claim that there is a moral distinction between foreseeing a result and intending a result. Thus, it may be forbidden on moral grounds to bring about a bad result if that re- sult is intended (even if as a means to a better overall outcome), but not forbidden to bring about the same result if the result is foreseen but not intended. Confidentiality Much of the information that a doctor gains about a patient in her professional duties is confidential. By this it is meant that there is an expectation that the doctor will not divulge that information to an- other person without the agreement (possibly implied) of the patient. What is the basis for medical confidentiality? There are at least three different grounds. On all three approaches doctors should nor- mally keep information about patients confidential. The ethically problematic situations are generally those in which breaching con- fidentiality will reduce a risk of harm either to the patient himself, or to someone else. The professional guidelines for UK doctors em- phasize the importance of confidentiality but state that: 'Disclosure of personal information about a patient without consent may be jus- tified in the public interest if failure to disclose may expose others to a risk of death or serious harm' (General Medical Council, 2009). Such guidelines need interpretation in applying to particular cir- cumstances, and the interpretation will sometimes be affected by one's views about what underpins the importance of confidentiality. Three different answers to this question are: respect for patient au- tonomy; keeping an implied promise; and bringing about the best consequences. Respect for patient autonomy This principle implies that a person has the right, by and large, to decide who should have access to personal information about him- self. If respect for patient autonomy is considered an important ethical principle, then any breach of confidentiality is potentially serious and only the prevention of serious harm would justify it. Furthermore, on this approach, it might be argued that, contra to the General Medical Council (GMC) guidelines, if a competent patient refuses to give consent for a doctor to inform a third party, where failure to inform risks serious harm to that patient only, breaching confidentiality is wrong. After all, we allow a competent patient to refuse even life-saving treatment. Can there be a serious breach of confidentiality if the patient never knows about the breach? On the view of confidentiality which con- siders that respect for patient autonomy is of key importance, the answer is yes. Keeping an implied promise Some views of the doctor–patient relationship see it as having elem- ents of an implied contract. Such a contract may include an implied promise that doctors keep information about their patients confi- dential. Patients generally expect doctors to treat information con- fidentially, and professional guidelines emphasize the importance of high standards of confidentiality. This view of confidentiality is different from that of patient au- tonomy. It does not ultimately depend on what the patient would want or believes. It depends on a concept of the doctor–patient rela- tionship that is independent of what a specific patient believes. There are, however, two problems with this view: first, there has been no explicit promise, so the issue of an implied promise is to some extent a fiction; second, it raises the whole issue of why it is important to keep promises. The reason for the importance of keeping promises is likely to be grounded either in autonomy or consequences. Bringing about the best consequences From the perspective of a consequentialist ethical perspective it is the (foreseeable) consequences of the breach of confidentiality that determine the seriousness of the breach, and indeed that underlie whether breaching confidentiality is wrong in the first place. There are several different types of consequence that could be relevant, and the analysis of the situation depends in part on how these are viewed. If respect for autonomy is the principal basis for confidentiality, then when maintaining confidentiality puts others at risk of harm there is a clash of two incommensurable values: respecting the patient's autonomy and preventing harm to others. From the con-

sequentialist perspective, the judgement is conceptually simpler. There is only one question: Which action (breaching or maintaining confidentiality) has the better overall consequences? At first sight it might seem that on this consequentialist view risk of even modest harm to others justifies a breach since we have to balance the harm to others against only the patient's emotional response to the breach. But this is too simplistic. Unless doctors are trusted to maintain high levels of confidentiality patients in general may lose trust and not seek healthcare. The issue is not just about ill health: there are other consequences of untreated illness. For example, if people with uncontrolled epilepsy drive they may kill other road users. There is a public interest in ensuring that such people receive good healthcare in order to maximize control of the epilepsy. Even where the harm to others is potentially great, as in the example of epilepsy, it could be the case that more lives will be lost if doctors do breach confi- dentiality because fewer people with fits will seek medical help. So although the consequentialist approach can deal with difficult cases in a conceptually clear way, in practice the lack of evidence and com- plexity can make such judgements difficult. From a consequentialist perspective, as opposed to the perspec- tive of respect for patient autonomy, if a patient never finds out that a doctor has breached confidentiality and no harm comes to the pa- tient as a result, that breach is trivial, even if it concerned something that the patient would strongly wish to keep confidential. Conclusion Ethics, like science, is at root a rational enterprise. For those of us who are concerned to do the right thing, and this includes most medical students and doctors, the questions arise: How can we examine our own moral standards and behaviour in specific situ- ations; how can we develop these standards; and how can we ensure that our views stand up to scrutiny? We believe that rational enquiry is central to an answer to these questions. Such enquiry involves ar- guing with others, facing counterarguments, and seeing how good our own arguments are. If the counterarguments are stronger, we

 need to change our views. If there is a contradiction between what we thought our principles were and what we think is right in a spe- cific situation, then we need to resolve that contradiction. There may be no final grounding of morality in nature but from that it does not follow that our personal moral system and our decisions in specific situations should be irrational or arbitrary. FURTHER READING Ashcroft R, Draper H, Dawson A, McMillan J (eds) (2007). Principles of health care ethics, 2nd edition. John Wiley & Sons, Chichester. Beauchamp TL, Childress JF (2008). Principles of biomedical ethics, 6th edition. Oxford University Press, New York. Buchanan AE, Brock DW (1989). Deciding for others: the ethics of surrogate decision making. Cambridge University Press, Cambridge. Dworkin G (1988). The theory and practice of autonomy. Cambridge University Press, Cambridge. General Medical Council (2009). Confidentiality: protecting and pro- viding information. GMC, London. https://www.gmc-uk.org Hope T (2004). Medical ethics: a very short introduction. Oxford University Press, Oxford. Hope T, Savulescu J, Hendrick J (2007). Medical ethics: the core curriculum, 2nd edition. Churchill Livingstone (Elsevier), Edinburgh. Mill JS (1859). On liberty. Many modern editions, including: Harmon dsworth: Penguin Books, 1982. Parker M (2012). Ethical problems and genetics practice. Cambridge University Press, Cambridge. Re B (2002). Adult: refusal of medical treatment. All England Reports 449 at 445. Shakespeare T (2006). Disability rights and wrongs. Routledge, London.

1.6 Clinical decision- making 26 Timothy E.A. Peto

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ESSENTIALS Clinicians make decisions at every stage of the patient pathway. In routine practice complex decisions are often made rapidly using ‘intuition’ or common sense, but this can lead to suboptimal man- agement plans. Clinical decision analysis is a way of formalizing the logical process behind decision-making, and when combined with evidence from medical research is described as the practice of evidence-based medicine. Clinical decision analysis consists of five discrete steps: (1) con- structing the ‘decision tree’—structuring the problem so that alter- native courses are defined; (2) estimating the probability of each possible outcome; (3) assigning a relative value or utility to each potential outcome; (4) calculating the best alternative using the decision tree model; (5) performing a set of sensitivity analyses, which provides insight into which values are the most critical to a decision. In practice, most clinicians do not have the time, intellectual en- ergy, or training to perform a formal clinical decision analysis and they tend to use short cuts and go for the ‘safe’ decision which is suitable for the ‘average patient’ and often in keeping with guidelines for local practice. However, clinicians who follow the logical process of clinical decision analysis find it easier to live with the uncertainty of an inexact science and subjective wishes of the patient. Good understanding of the decision tree and use of sensitivity analyses allow clear documentation of the reasoning behind each decision that is made. This approach provides the tools to help make the right decision for each patient, free from the artificial constraints of clinical guidelines. Introduction Clinical decision-making is an essential skill required to practice medicine, yet the process of clinical decision-making is often rushed. Complex decisions can be made rapidly using ‘intuition’ or common sense, based on a combination of information derived from theor- etical knowledge and personal experience. This intuitive approach alone, although it saves the busy clinician valuable time, may lead to suboptimal treatment plans. The discipline of ‘clinical decision analysis’ has, therefore, evolved to formalize the logical process be- hind decision-making. When combined with evidence from med- ical research to make decisions, this is described as the practice of ‘evidence-based medicine’. Clinical decision analysis is used by

national clinical and public health services. In practice, this mean that clinical decision aids are widely available as guidelines, both national and local. Government guidelines often also include cost-benefit or economic analysis to decide which treatments to fund. However, as every patient is dif- ferent, it is helpful to understand how guidelines should be adapted to tailor treatment for individual patient needs. Ideally the patient should also play an active role in decision-making. This is called ‘shared decision-making’. In this chapter we set out the principles of clinical decision-making and give guidance as to how it can be applied by the busy clinician in routine practice. Clinical context Clinicians make decisions at every stage of the patient pathway. Typical decisions made for a patient attending a hospital emergency department are summarized in Table 1.6.1. 1.6 Clinical decision-making Timothy E.A. Peto and Philippa Peto Table 1.6.1 Typical decisions made for a patient attending a hospital emergency department Decision node Choice Decision to admit to hospital Admit or send home? Medical Investigations Which tests? Diagnosis Which diagnosis? Treatment plan Which treatment? Resuscitation plan For cardio-pulmonary resuscitation? Management of incidental findings To investigate further or not? Discharge plan When and where to? Discussion with relatives How much do you tell them? These points are called ‘decision nodes’ in decision theory. The most critical decisions are made at points on the pathway where some of the consequences may be irreversible.

1.6 Clinical decision-making 27 Analysis Clinical decision analysis consists of five discrete steps which can be performed at each decision node (see Fig. 1.6.1): 1. Constructing the ‘decision tree’; structuring the problem so that alternative courses are defined The different possible management choices need to be defined and the different possible outcomes, good and bad, need to be listed for each. In decision analysis terminology, this is referred to as con- structing a ‘decision tree’. To busy clinicians, this may seem trivial but is critical because the omission of important treatment options or outcomes may lead to a suboptimal management plan. For instance, for any clinical treatment decision, failure to consider a ‘no intervention’ option could result in an unnecessary poor out- come for the patient. 2. Estimating the probability of each possible outcome For each possible outcome, the probability of that outcome needs to be estimated. While past experience and the expert opinion of colleagues may be an attractive source of information, a system- atic review of the evidence produces a more unbiased estimate of probabilities. Where little evidence is available, a range of plausible probabilities using expert opinion should be made which will allow a sensitivity analysis to be made for the final decision. These might be available in published guidelines and the uncertainty can be cap- tured by the level of evidence quoted. 3. Assigning a relative value or utility to each potential outcome The most challenging, and more subjective step, is to assign utility to each outcome. The purpose is an attempt to compare the rela- tive importance of different outcomes. A variety of different metrics have been proposed including quality adjusted life years, disability adjusted life years or monetary value of health cost. All such metrics will provide a numeric value for each outcome that are then easily compared to show the optimum outcome. For example, death is usually awarded value 0, disease free life awarded 1, and morbidity such as side effects from chemotherapy would be awarded a value between 0 to 1, depending on perceived severity. To create an individualized decision analysis requires the patient to express their personal views about different outcomes. This is ‘shared decision-making’. For guidelines which have been con- structed nationally, or for cost-effective analyses, groups of patient representatives are asked to provide the patient’s perspective. One problem with this approach is that the relative utility as- signed by doctors may be different from that assigned by a par- ticular patient. The patient’s views may also be in conflict with their own family. In addition,

personal views may change with time as the understanding of each outcome changes and anxieties are allayed or fuelled. The decision to discuss every outcome with a patient is in itself a decision. Judgement is required to decide whether the psychological distress that may be caused by such a discussion is justified by the benefit of assigning a personalized utility to each outcome. For instance, the discussion of resuscitation with a relatively well patient for whom cardiorespiratory arrest is an unlikely event might in itself cause unnecessary distress. Table 1.6.2 shows examples of common unfavourable outcomes. These outcomes may be differently valued by doctor and patient, re- sulting in differing assumptions of the relative utility of each. 4. Calculating the best alternative using the decision tree model For each management plan chosen, the probability and utilities chosen are used to produce a combined numerical value. The values can then be easily compared to determine the best possible outcome for that pa- tient. In some cases, the utilities assigned by the medical practitioner may be so different from those chosen by the patient that the practi- tioner is unwilling to proceed with the identified management plan. Sometimes a change in clinician might be required before a decision can be made which will be acceptable to the patient (see Fig 1.6.1a). 5. Performing a set of sensitivity analyses A sensitivity analysis explores how outcomes vary depending on making changes to the probability or utility values. This is par- ticularly helpful when there is uncertainty over the probabilities of different outcomes or when there are differing views on the util- ities, such as where the patient is themselves unsure as to their own views. Sensitivity analysis provides insight into which values are the most critical to a decision. Sometimes it is found that a particular decision is robust even when there are major differences of opinion on a particular probability or utility (see Fig 1.6.1b). For example, the precise probability of bleeding makes little difference to the Table 1.6.2 Examples of common unfavourable outcomes Adverse outcome to patient Examples Death Significant adverse events Stroke Amputation Unnecessary surgical intervention End stage renal failure Seizure ITU admission Readmission to hospital Prolonged hospital stay Psychological distress Fear of possible future morbidity Hypochondria Unnecessary frequent emergency department attendance Drug side effects Bleeding Anaphylaxis Immunosuppression Public health implications Spread of TB Road accident Pregnancy outcome Fetal or maternal death Fetal or maternal morbidity Social consequences Loss of job Loss of driving licence Breakdown of trust within a family Adverse outcome to doctor Guilt Complaint from angry patient Litigation or fear of litigation Loss of professional reputation Loss or fear loss of licence to practice

 decision to anticoagulate a patient following a life-threatening pul- monary embolus. Decision-making in clinical practice In practice, clinicians do not have the time, intellectual energy, or training to perform a formal clinical decision analysis and they tend to use short cuts and go for the ‘safe’ decision, which is suitable for the ‘average patient’ and often in keeping with guidelines for local practice. Clinical decisions are often made heuristically, using ‘intuition’ which is a combination of pattern recognition and personal ex- perience, to come to a rapid conclusion regarding the most likely best outcome. Unfortunately, intution is not reliable and can lead to suboptimal outcomes. Utility Expected value (Probability x utility for each outcome) Overall value for
each decision 1 0.5 x 0.8 x 1 = 0.4 0.98 0.5 x 0.2 x 0.98 = 0.098 0 0.5 x 0.1 x 0 = 0 0.6 0.5 x 0.8 x 0.6 = 0.24 0.7 0.5 x 0.1 x 0.7 = 0.035 0.7 BKA BKA AKA Death Recovery with limp Full recovery Foot saved (a) 0.5 0.5 0.8 0.2 0.1 0.1 0.8 Infection not controlled Antibiotics Infected fractured ankle 0.7 Decision node: amputate or give antibiotics BKA – Below knee amputation AKA – Above knee amputation Total for ‘give antibiotics’ 0.773 Total for ‘amputate’ 0.7 Immediate amputation

better (b) Probability of antibiotics saving leg Overall value of utilities 0 0.2 0.4 0.6 0.8 1 BKA antibiotics 1 0.9 0.8 0.7 0.6 0.5 Antibiotics better Sensitivity analysis Fig. 1.6.1 (a) Decision tree showing the possible outcomes of a case of a seriously infected compound fracture of the ankle following a decision to either amputate immediately or give antibiotics with the hope of saving the leg but with the risk of mortality from infection. Blue square represents the decision node; green circles show different possible outcomes following the decision with the assigned probability of the outcome documented on the branches. The triangles represent the final outcomes with the utility shown alongside. The calculations showing the expected values for each outcome and the overall values for each decision is also shown. (b) Sensitivity analysis showing how changes in the assigned probability of antibiotics saving the leg affects the overall values of amputation versus antibiotics. The original calculation estimated that antibiotics would prevent amputation in 50% of cases. The red line shows that amputation is the preferred option only if antibiotics prevents fewer than 33% of cases. The sensitivity analysis can also be altered to reflect changes in utility awarded to each outcome which could also impact on the decision. Adapted from Lee A, et al. for the EBM Teaching Scripts Working Group (2009). Tips for Teachers of Evidence-based Medicine: Making Sense of Decision Analysis Using a Decision Tree. J Gen Intern Med, 24, 642–8.

1.6 Clinical decision-making 29 Most clinicians informally use the ‘decision tree’ but often without being aware that they are doing so, and can easily be swayed by per- sonal bias which may distort their perception of probabilities. For example, a physician who has recently seen a patient die from an undiagnosed subarachnoid haemorrhage is much more likely to perform a diagnostic lumbar puncture even when the clinical indi- cation is negligible. To introduce a more systematic approach, ensuring use of best available evidence, guidelines are widely available. National guide- lines summarize best available evidence to clarify the probabilities for common clinical outcomes. Local guidelines are then created to ensure that local clinicians are also aware of the subjective utility value for each outcome to the department. In order to make the best possible decision for an individual pa- tient, the clinician needs to be aware that the utility to the depart- ment may be at odds with the utility to the patient. This is where shared decision-making is critical. Shared decision-making, where the doctor and patient are both involved in making the decision, is well documented to lead to the best patient outcomes and greater patient satisfaction. There are two main reasons why the departmental guideline might not be followed: 1. Objective factors which alter the assumed probabilities for each outcome: a. Diagnostic uncertainty b. Specific physical factors for a particular patient c. No relevant guideline or limited evidence base 2. Subjective factors altering the utility allocated for each outcome. a. Patient would like to be supported not to follow guideline for personal reason Clearly, if the physician has a personal reason to fear a particular outcome, this can affect their own assignment of utility, but this must be recognized as subjective and should not be allowed to influ- ence the final clinical decision. Case studies Comparison of two possible treatments A 60-year-old man presents with a badly infected compound fracture of the left ankle. The infection is not only threatening to destroy the ankle itself, but is spreading proximally and the septic complications are potentially life-threatening. The options are either to perform a below-knee amputation immediately or to perform surgical debride- ment followed by antibiotic treatment to save the leg. Although the second option offers a chance of complete recovery, it is associated with a substantial risk of infection that spreads leading to below-knee amputation or possible an above-knee amputation, or even death. Even if conservative management with debridement plus antibiotics is successful, there is still a chance of minor long- term disability. A decision tree is drawn and, after discussion with the patient, util- ities are

assigned to each of the possible outcomes (see Fig 1.6.1a). A sensitivity analysis is performed (see Fig 1.6.1b) which shows that immediate amputation is only indicated if the chance of antibiotics working is less than 33%. After discussion with colleagues it was de- cided that antibiotics had a better than 33% chance of working and therefore the patient was treated conservatively. (Case study based from A. Lee et al. for the EBM Teaching Scripts Working Group (2009). Tips for Teachers of Evidence-based Medicine: Making Sense of Decision Analysis Using a Decision Tree. J Gen Intern Med, 24(5), 642–8.) Variations in utility a. A 70-year-old man, living alone since the death of his wife 6 months ago, is admitted at 7 pm with acute onset of haema- temesis and melaena and blood pressure 160/100, pulse 140 bpm, and haemoglobin 82. He is resuscitated with IV fluids and given 4 units of blood after which his haemoglobin is 102 and his pulse rate settles to 88 bpm. ECG showed sinus tachycardia and chest X-ray and all other blood tests were normal including clotting. He is usually well with no past medical history but has recently taken nonsteroidal anti-inflammatory medication for knee pain. He regularly exercises by walking his dog. The following morning, he is haemo-dynamically stable but the medical team plan for him to stay in hospital for a repeat blood test and endoscopy to reduce the risk of further bleeding. The patient becomes very agitated and states that he feels perfectly all right now and needs to go home immedi- ately. The consultant's view is that the patient is at high risk for fur- ther bleeding with possible life-threatening complications and local hospital policy is that severe gastrointestinal bleeds require inpatient endoscopy with at least 24 h observation as an inpatient in order to reduce the hospital readmission rates. On discussion, the consultant establishes that the patient's main concern is to get home to look after his elderly dog who requires daily medication with regular painkillers and will be suffering without his owner. Finally, a compromise is reached as the patient agrees to come in to hospital daily for review and blood tests with clear understanding of the risks to his own health if he bleeds again while alone at home. The patient did not want to die but was prepared to take a mod- erate risk in order to look after his dog. The main risks and the patient's views were clearly recorded in the notes to explain the ra- tionale behind the decision. This case illustrates the different utility accorded by each party to a particular outcome, in this case rapid discharge home. Clear com- munication can help make a decision that both doctor and patient are happy with. b. A 60-year-old woman is referred with a new diagnosis of acute myeloid leukaemia. She has successfully gone into remission fol- lowing chemotherapy and is told that the median life expectancy is 5 years. She is given the option to have a bone marrow transplant from her sister which will give her a 50% chance of total cure but a 15% chance of dying immediately as a consequence of the trans- plant. Her daughter is due to give birth next month. The doctors advise immediate transplantation, with enforced 6-week hospital stay to maximize her overall chance of survival. However, the patient values short-term life as she wants to see her new grandchild and therefore decides not to go ahead with the transplant immediately but requests a six month delay, despite the risk that the leukaemia will progress. Variation in probability of clinical events A 32-year-old woman presents with rapidly deteriorating kidney function. Her estimated glomerular filtration rate is now down

 to 14, from baseline more than 60, one month before. She has a history of systemic lupus erythematosus (SLE) for which she takes regular painkillers and low-level immunosuppression. The differential diagnosis includes analgesic nephropathy or lupus nephritis requiring immediate immunosuppression. Standard procedure would be to stop the nonsteroidal anti-inflammatory drugs (NSAIDs) and perform a renal biopsy to confirm the diagnosis. However, the patient announces that she is a lifelong Jehovah's witness and would decline blood

transfusion under any circumstances. The possible adverse events following a kidney biopsy include bleeding requiring transfusion and possible death. In this case, because the patient is not willing to have the routine treatment for bleeding, the probability of more serious consequences of bleeding, such as death, is much higher. It is essential, therefore, to perform a new decision analysis reflecting the uncertainties of the diagnosis and the increased risks of performing the renal biopsy, in order to make a rational management plan. Conclusion Clinicians who follow the logical process of clinical decision analysis find it easier to live with the uncertainty of an inexact science and subjective wishes of the patient. Good understanding of the decision tree and use of sensitivity analyses allow clear documentation of the reasoning behind each decision. This approach provides the tools to help make the right decision for each patient, free from the artificial constraints of clinical guidelines. FURTHER READING Barry MJ, Edgman-Levitan S (2012). Shared decision making— pinnacle of patient-centered care. N Engl J Med, 366, 780–1. Charles C, Whelan T, Gafni A (1999). What do we mean by partner- ship in making decisions about treatment? BMJ, 319, 780–2. Cooper N, Frain J (eds) (2016). ABC of clinical reasoning. Wiley Blackwell BMJ Books, Oxford. Croskerry P (2013). From mindless to mindful practice—cognitive bias and clinical decision making. N Engl J Med, 368, 2445–8. Elstein AS, Schwartz A (2002). Clinical problem solving and diag- nostic decision making: selective review of the cognitive literature. BMJ, 324, 729–32. Elwyn G, et al. (1999). Towards a feasible model for shared decision making: focus group study with general practice registrars. BMJ, 319, 753–6. Rodriguez-Osorio CA, Dominguez-Cherit G (2008). Medical decision making: paternalism versus patient-centered (autonomous) care. Curr Opin Crit Care, 14, 708–13. Sondhi M, et al. (2005). DEALE-ing with lung cancer and heart failure. Med Decis Making, 25, 82–94. Weinstein MC, Feinberg HV (1980). Clinical decision analysis. Saunders, Philadelphia, PA.

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Foreword

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Foreword Professor Sir John Bell, Regius Professor of Medicine, University of Oxford In 1983, David Weatherall, John Ledingham, and David Warrell launched the first edition of the Oxford Textbook of Medicine. That era of medicine looked entirely different from today but the need for a scholarly repository of medical knowledge remains as important as ever. Medicine is now firmly in a digital age; sources of information abound and are readily available and the field is moving so quickly that it is harder than ever to provide up to date relevant informa- tion for the profession. Despite this, the sixth edition of the Oxford Textbook of Medicine still provides the foundation of knowledge upon which good clinical practice is based. Never before has there been such a rapid advance of medical know- ledge and practice. Since the first edition of the Oxford Textbook of Medicine, medical practice has reduced cardiovascular mortality by up to 70% in Western countries, there are now multiple new ther- apies for diseases such as rheumatoid arthritis and multiple scler- osis, disorders where the descriptions of therapeutic options in the first edition were necessarily brief. Cancer is now increasingly man- aged with immune and targeted therapies. Whole new diseases have appeared (Hepatitis C and HIV) and have been either controlled or conquered with drug therapy. The sequencing of the human genome seemed an impossible dream in 1983 while today we have sequenced more than a million genomes and have had insights into rare disease and cancer that were unimaginable then. Life expectancy has risen by nine years for men and ten for women in the United Kingdom, creating a demographic shift that will fundamentally change society and medicine forever. The pace of change has been dramatic. The Oxford Textbook of Medicine gained a reputation by moving medical practice forward from the Oslerian view of medicine ori- ginally expounded in his text book the Principles and Practice of Medicine into an era of more molecular and scientifically based understanding of disease. Constrained by the lack of tools for ex- ploring the molecular basis of pathogenesis, Osler was limited in how he could describe the world of disease, largely based on bed- side observations or those from the post-mortem room. The Oxford Textbook of Medicine shifted this focus and aligned it with the emerging field of molecular medicine which has begun to create a new taxonomy of disease but also an approach to therapy which is based on pathogenesis. There has been a wave of new information, with new insights appearing weekly into the underlying molecular events associated with disease. Diseases characterized by phenotype are now broken down into multiple subtypes and disease is being individualized. This is rapidly leading to a very significant change in our perception of pathogenesis as well as the classification and nomenclature of disease, all crucial roles for a textbook of medicine. We now are aware that many of the classic definitions of diseases such as diabetes or cancer were descriptions of phenotypic charac- teristics. Interrogation of these disorders at a molecular level has demonstrated that these terms mask disease subtypes defined by molecular pathology where natural history and response to therapy may differ. Combine this with the explosion of new diseases coming from studies of rare disease and there is a challenge to

conventional disease nomenclature. This molecular precision creates real oppor- tunities for targeted highly effective therapies, but it also creates challenges for the model of drug discovery when novel treatments can only be used in increasingly small patient populations. These are major issues for medicine, health systems, but also textbooks such as this one where, historically, the stewardship of disease nomenclature has been maintained. The therapeutic options available to practising clinicians have also advanced beyond all recognition since the first edition of the Oxford Textbook of Medicine. We have seen an era of biologic therapy which has provided important new therapeutic alternatives for many hard- to-treat diseases including cancer. We are now entering a new era where modalities such as gene therapy and interfering RNA thera- peutics have demonstrated their utility in the clinic. Similarly, an era of cell therapy has also begun which will provide important new alternatives to some diseases. These new therapeutic alterna- tives and other opportunities for improving healthcare using med- ical technology or novel diagnostics such as sequencing also bring with them the challenge of how healthcare systems can continue to be affordable, either for individuals in private healthcare settings, or in state-funded, single-payer systems. In this context, it is remark- able that the authors and editors of the Oxford Textbook of Medicine have managed to sustain both its relevance and the accuracy of its content. The pace at which our understanding of disease, our therapeutic options, and our healthcare systems are likely to change makes it nearly impossible for a textbook of medicine to be truly comprehen- sive given the speed of change, the impact of new innovations and the multiple additional sources of information available to practi- tioners. The Oxford Textbook of Medicine has provided remarkable levels of detail in this rapidly changing world but, more importantly, the textbook continues to provide a source for readers to access information on the fundamental features of disease. This founda- tional knowledge remains crucial to our ability to understand, diag- nose, and treat patients whether they are in the developing world or

Foreword vi Western healthcare systems. Having a source of such information across all major diseases accessible in a single source remains the bedrock of both teaching and practising medicine. The foundations provided by the Oxford Textbook of Medicine form a core of know- ledge which practising clinicians will continue to need. The editors of this edition have been faithful to the vision of the original three editors. Science, in all its forms, is at the heart of our understanding of disease and has enabled progress in clinical medi- cine to occur at a remarkable pace. By providing a textbook that describes the foundations of our understanding of disease and its management, the editors have successfully given us an authoritative text which practising clinicians will find invaluable to support their day-to-day decisions. David Weatherall, one of the three original editors and who died in 2018, would be gratified by this new edition.

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Abbreviations 5-FU 5-fluorouracil 5-HIAA 5-hydroxyindoleacetic acid 5-HT 5-hydroxytryptamine 5-HT 5-hydroxytryptamine AAA acquired aplastic anaemia AAFB acid- and alcohol-fast bacilli AASLD American Association for the Study of Liver Diseases AAV antineutrophil cytoplasm autoantibody-associated vasculitis (also aplastic anaemia ABC ATP-binding cassette ABCDE airway, breathing, circulation, disability, and exposure ABG arterial blood gas ABMR antibody-mediated rejection ABPA allergic bronchopulmonary aspergillosis ABPM ambulatory blood pressure measurement ACE angiotensin-converting enzyme AChE acetylcholinesterase, define at first mention ACPA anticitrullinated peptide/protein antibodies ACR American College of Rheumatology (also albumin:creatinine ratio) ACS acute coronary syndromes ACTH adrenocorticotropic hormone AD Alzheimer's disease ADEM acute disseminated encephalomyelitis ADH antidiuretic hormone ADL activities of daily living ADME absorption, distribution, metabolism, and excretion ADPKD autosomal dominant polycystic kidney disease ADR adverse drug reaction ADRT advanced decision to refuse treatment AECA antiendothelial cell antibodies AF atrial fibrillation AFP α-fetoprotein AGT alanine–glyoxylate aminotransferase aGVHD acute graft-versus-host disease AHA American Heart Association aHUS atypical haemolytic uraemic syndrome AIF apoptosis-inducing factor AIHA autoimmune haemolytic anaemia AIN acute interstitial nephritis AIP autoimmune pancreatitis (also acute interstitial pneumonia) AIS androgen insensitivity syndromes AKI acute kidney injury ALD alcoholic liver disease ALF acute liver failure ALL acute lymphoblastic leukaemia alloSCT allogeneic stem cell transplantation ALP alkaline phosphatase ALS amyotrophic lateral sclerosis ALT alanine aminotransferase AMA antimitochondrial antibody AML acute myeloid leukaemia AMLR autologous mixed lymphocyte reactions AMT Abbreviated Mental Test ANA antinuclear autoantibodies ANC absolute neutrophil count ANCA antineutrophil cytoplasmic antibodies ANP atrial natriuretic peptide AOSD adult-onset Still's disease AP alternative pathway APA aldosterone-producing adenoma APC antigen presenting cell APCM active physiological conservative management APL acute promyelocytic leukaemia APS antiphospholipid syndrome APTT activated partial thromboplastin time AR androgen receptor ara-C cytosine arabinoside ARB angiotensin receptor blocker ARDS adult respiratory distress syndrome ARF acute renal failure ARH autosomal recessive hypercholesterolaemia ARPKD autosomal recessive polycystic kidney disease ART antiretroviral therapy ARVC arrhythmogenic right ventricular cardiomyopathy ARVD atherosclerotic renovascular disease AS ankylosing spondylitis ASAS Assessment of SpondyloArthritis International Society ASCT autologous stem cell transplantation ASD atrial septal defect ASH Action on Smoking and Health ASOT antistreptolysin O titre AST aspartate aminotransferase ATG antithymocyte globulin ATP adenosine triphosphate ATRA all-trans-retinoic acid AV aortic valve AVN arteriovenous nipping

 AVSD atrioventricular septal defect AZA azacitidine BCAA branched-chain amino acid BCC basal cell carcinoma BCG bacillus Calmette–Guérin BEN Balkan endemic

nephropathy BH4 tetrahydrobiopterin BHS British Hypertension Society BICC betaferon in chronic viral cardiomyopathy BKV BK polyomavirus BM bone marrow BMD bone mineral density BMF bone marrow failure BMI body mass index BMP bone morphogenic protein BNF British National Formulary BNP B-type natriuretic peptide BOS bronchiolitis obliterans syndrome BP blood pressure BPG biphosphoglycerate BRAO branch artery occlusion BRVO branch retinal vein occlusion BSEP haemolysis, elevated liver enzymes, and low platelet count BSP bromosulphthalein BTS British Thoracic Society BUN blood urea nitrogen CA carbohydrate antigen CABG coronary artery bypass grafting CAF Comprehensive Assessment for Frailty CAH congenital adrenal hyperplasia CAM Confusion Assessment Method CAMT congenital amegakaryocytic thrombocytopenia CAP community-acquired pneumonia CAPS cryopyrin-associated periodic syndromes CaR calcium-sensing receptor CAT COPD assessment test CBT cognitive behaviour therapy CCB calcium channel blocker CCK cholecystokinin CCP anticyclic citrullinated peptide CCQ Clinical COPD questionnaire CCV clathrin-coated vesicles CCyR complete cytogenetic response CD cluster of differentiation CDA congenital dyserythropoietic anaemia CDC donation after circulatory death CEA carcinoembryonic antigen CETP cholesteryl ester transfer protein CF cystic fibrosis CFA cryptogenic fibrosing alveolitis cfDNA cell-free DNA CFS Clinical Frailty Scale CFTR cystic fibrosis transmembrane regulator CFU colony forming unit CGA comprehensive geriatric assessment CGRP calcitonin gene-related peptide cGVHD chronic graft-versus-host disease CHAD cold haemagglutinin disease CHD coronary heart disease CHF congestive heart failure CHM Commission on Human Medicines CINAC chronic interstitial nephritis in agricultural communities CINCA chronic infantile neurological, cutaneous, and articular syndrome CISN coumarin-induced skin necrosis CK creatine kinase CKD chronic kidney disease CKD-EPI Chronic Kidney Disease Epidemiology Collaboration CLL chronic lymphocytic leukaemia CML chronic myeloid leukaemia CMR cardiac magnetic resonance CMS congenital myasthenic syndrome CMT Charcot–Marie–Tooth disease CMV cytomegalovirus CNI calcineurin inhibitor CNS central nervous system CNSHA congenital non-spherocytic haemolytic anaemia CO cardiac output CoA coenzyme A COPD chronic obstructive pulmonary disease COX cyclooxygenase CPAP continuous positive airway pressure CPM central pontine myelosis CPP central precocious puberty CPPS chronic pelvic pain syndrome CPR cardiopulmonary resuscitation CR complete remission CRDQ Chronic Respiratory Disease Questionnaire CREST calcinosis, Raynaud’s, oesophageal dysmotility, sclerodactyly, telangiectasia CRF chronic renal failure CRH corticotropin-releasing hormone CRIM cross-immunoreactive material CRP C-reactive protein CRT cardiac resynchronization therapy CS continuous smokers CSF cerebrospinal fluid/colony-stimulating factor CT computed tomography CTA computed tomography angiography CTCA computed tomography coronary angiography CTD connective tissue disease CTEPH chronic thromboembolic pulmonary hypertension CTL cytotoxic T-lymphocyte CVD cardiovascular disease CVID common variable immunodeficiency CVS chorionic villus sampling CXR chest radiograph CYP cytochrome P450 CZT cadmium zinc telluride DAEC diffusely adherent Escherichia coli DALY disability-adjusted life year DAMP damage-associated molecular pattern DASH Dietary Approaches to Stop Hypertension DAT direct antiglobulin test

 DBA Diamond–Blackfan anaemia DBD donation after brain death DBP diastolic blood pressure DC dyskeratosis congenita (also dendritic cell) DCA directional coronary atherectomy DCCT Diabetes Control and Complications Trial DCD donation after circulatory death DCI decompression illness dcSSc diffuse cutaneous systemic sclerosis DCT distal convoluted tubule DDAVP 1-deamino-8-d-arginine vasopressin DDD dense deposit disease DECAF dyspnoea, eosinopenia, consolidation, acidosis, and atrial fibrillation DGP deamidated gliadin peptide DHG

dihydroxyglutarate DIC disseminated intravascular coagulation DIC disseminated intravascular coagulation DILI drug-induced liver injury DILV double-inlet left ventricle DIP desquamative interstitial pneumonia DISC death-initiating signalling complex DISH diffuse idiopathic skeletal hyperostosis DLB dementia with Lewy bodies DLBCL diffuse large B-cell lymphoma DMARD disease-modifying antirheumatic drug DMD disease-modifying drugs (can also mean Duchenne muscular dystrophy) DMSA dimercaptosuccinic acid DNACPR do-not-attempt-cardiopulmonary resuscitation DNR do not resuscitate DOAC direct oral anticoagulant DOCA desoxycorticosterone DOPPS Dialysis Outcomes and Practice Patterns Study DORV double-outlet right ventricle DPI dry powder inhalers DRE digital rectal examination DRESS drug reaction with eosinophilia and systemic symptoms dRTA distal renal tubular acidosis DSA donor-specific antibodies DTC direct to consumer DTPA diethylenetriaminepentaacetic acid DVT deep vein thrombosis DXA dual energy X-ray absorptiometry EACTS European Association for Cardio-Thoracic Surgery EAggEC enteroaggregative Escherichia coli EANM European Association of Nuclear Medicine EAPCI European Association of Percutaneous Cardiovascular Interventions EASL European Association for the Study of the Liver EATL enteropathy-associated T-cell lymphoma EBV Epstein–Barr virus ECD extended criteria donor ECF extracellular fluid ECG electrocardiogram ECLAM European community lupus activity measure ECM extracellular matrix ECV extracellular volume EDMD Emery–Dreifuss muscular dystrophy EDRF endothelial-derived relaxing factor EDTA European Dialysis and Transplant Association EDV end-diastolic volume EEG electroencephalography EELV end expiratory lung volume EGF epidermal growth factor eGFR estimated glomerular filtration rate EGPA eosinophilic granulomatosis with polyangiitis EIEC enteroinvasive Escherichia coli EIS endoscopic injection sclerotherapy ELCA excimer laser coronary atherectomy ELISA enzyme-linked immunosorbent assay EM erythema multiforme (also electron microscopy) EMA endomysial antibody EMG electromyography EMS early morning urethral smear ENA extractable nuclear antigens ENaC epithelial sodium channel ENT ear, nose, or throat EOL end of life EoO eosinophilic oesophagitis EPCR endothelial cell protein C receptor EPEC enteropathogenic Escherichia coli EPO erythropoietin ER endoplasmic reticulum ERA European Renal Association ERC endoscopic retrograde cholangiography ERCP endoscopic retrograde cholangiopancreatography ERNV equilibrium radionuclide ventriculography ERS European Respiratory Society ESA erythropoiesis-stimulating agent ESC European Society of Cardiology ESGE European Society of Gastrointestinal Endoscopy ESH European Society of Hypertension ESKD end-stage kidney disease ESR erythrocyte sedimentation rate ESRD end-stage renal disease ESS EULAR sicca score ESWL extracorporeal shock-wave lithotripsy ETEC enterotoxigenic Escherichia coli EUS endoscopic ultrasonography EVLP ex-vivo lung perfusion EVO endoscopic variceal obturation FA Fanconi’s anaemia FACIT fibril-associated collagen with interrupted triple FAK focal adhesion kinase FAP familial adenomatous polyposis FBC full blood count FCAS familial cold autoinflammatory syndrome FCHL familial combined hyperlipidaemia FDA Food and Drug Administration FDG fluorodeoxyglucose FDG-PET fluorodeoxyglucose-positron emission tomography FDP fibrinogen-degradation product FEV forced expiratory volume FEV1 forced expiratory volume in 1 s

 FFR fractional flow reserve FGF fibroblast growth factor FH familial hypercholesterolaemia FISH fluorescent in situ hybridization FL follicular lymphoma FLC free light chain FMF familial Mediterranean fever FMTC familial medullary thyroid carcinoma FNAB fine needle aspiration biopsy FNH focal nodular hyperplasia FOB faecal occult blood FODMAPs fermentable oligosaccharides, disaccharides, monosaccharides, and polyols FRC functional residual capacity FSGS focal segmental glomerulosclerosis FSH follicular stimulating hormone FTD

frontotemporal dementia FVC forced vital capacity FVU first voided urine G6PD glucose-6-phosphate dehydrogenase GABA γ-aminobutyric acid GAD generalized anxiety disorder GALT gut-associated lymphoid tissue GAVE gastric antral vascular ectasia GBD Global Burden of Disease GBM glomerular basement membrane G-CSF granulocyte colony-stimulating factor GCA giant cell arteritis GCS Glasgow Coma Score GDF growth differentiation factors GEP gastroenteropancreatic GFB glomerular filtration barrier GFR glomerular filtration rate GH growth hormone GI gastrointestinal GIB gastrointestinal bleeding GIE glucocorticoid inhibitory element GIP gastric inhibitor peptide GIST gastrointestinal stromal tumour GLP glucagon-like peptide GM-CSF granulocyte–macrophage colony-stimulating factor GM/MS gas chromatography–mass spectrometry GN glomerulonephritis GnRH gonadotropin-releasing hormone GOLD Global Initiative for Obstructive Lung Disease GOMMID glomerulonephritis with organized microtubular monoclonal immunoglobulin deposits GORD gastro-oesophageal reflux disease GOV gastro-oesophageal varices GP glycoprotein (also general practitioner) GPA granulomatosis with polyangiitis GPCR G-protein-coupled-receptors GPI glycosylphosphatidylinositol GRACE Global Registry of Acute Coronary Events GRADE Grading of Recommendations, Assessment, Development and Evaluations GRHPR glyoxylate/hydroxypyruvate reductase GSD glycogen storage disease GSGS focal segmental glomerulosclerosis GSH glutathione GU gonococcal urethritis GUM genitourinary medicine GVHD graft-versus-host disease GVL graft-versus-leukaemia GWAS genome-wide association study H&E haematoxylin and eosin stain HAART highly active antiretroviral therapy HAND HIV-associated neurocognitive disorder HAV hepatitis A virus HBc hepatitis B core HBeAG hepatitis B e antigen HBIg hepatitis B immunoglobulin HBPM home blood pressure measurement HBsAG hepatitis B surface antigen HBV hepatitis B virus HCC hepatocellular carcinoma HCG human chorionic gonadotropin HCV hepatitis C virus HD haemodialysis HDF haemodiafiltration HDL high-density lipoprotein HDL-C high-density lipoprotein cholesterol HDU high-dependency unit HDV hepatitis D virus HE hepatic encephalopathy or hereditary elliptocytosis HELLP haemolysis, elevated liver enzymes and low platelets HES hypereosinophilic syndrome hESC human embryonic stem cell HETE hydroxyeicosatetraenoic acid HEV hepatitis E virus HF haemofiltration HFA Heart Failure Association HFnEF heart failure with a normal ejection fraction HFOV high-frequency oscillatory ventilation HFV high-frequency ventilation HHT hereditary haemorrhagic telangiectasis/ 15-hydroxy-5,8,10-hepatrotrienoic acid HHV human herpesvirus HIF hypoxia-inducible factors HIV human immunodeficiency virus HIV-OL human immunodeficiency virus oral lesion HK high molecular weight kininogen HL hepatic lipase HLA human leucocyte antigen HLH haemophagocytic lymphohistiocytosis HLHS hypoplastic left heart syndrome HMA hypomethylating agent HOGA 4-hydroxy-2-oxoglutarate aldolase HPA hypothalamic-pituitary-adrenal HPG hypothalamic-pituitary-gonadal HPLC high-performance liquid chromatography HPP hereditary pyropoikilocytosis HPRT hypoxanthine-guanine phosphoribosyltransferase HPV human papillomavirus

 HRA high-resolution anoscopy HRCT high-resolution computed tomography HRT hormone replacement therapy HS hereditary spherocytosis HSC haematopoietic stem cell or hepatic stellate cell HSCT haemopoietic stem cell transplantation HSP Henoch–Schönlein purpura HSPC haematopoietic stem and progenitor cell HSV herpes simplex virus HUS haemolytic uraemic syndrome HUV hypocomplementaemic urticarial vasculitis IADL instrumental activities of daily living IAS insulin autoimmune syndrome IBD irritable bowel disease IBS irritable bowel syndrome IBS-C irritable bowel syndrome with constipation IBS-D irritable bowel syndrome with diarrhoea IBS-M irritable bowel syndrome with alternating constipation and diarrhoea IC intercalated cell ICAM intercell adhesion molecules ICD implantable cardioverter-defibrillator ICP

intracranial pressure ICS inhaled oral corticosteroids ICU intensive care unit IDA iminodiacetic acid IDL intermediate-density lipoprotein IEC intestinal epithelial cell IF intrinsic factor IFG impaired fasting glucose IFN interferon Ig immunoglobulin IgAN immunoglobulin A nephropathy IgE immunoglobulin E IGF insulin-like growth factors IgG4-RD immunoglobulin G4-related disease IgG4-SC immunoglobulin G4-related sclerosing cholangitis IGV isolated gastric varices IHD ischaemic heart disease IHME Institute for Health Metrics and Evaluation IIH idiopathic intracranial hypertension IIP idiopathic interstitial pneumonias IL interleukin ILC innate lymphoid cell ILD interstitial lung disease IMA inferior mesenteric artery INR international normalized ratio IPAF interstitial pneumonitis with autoimmune features IPEX immunodysregulation polyendocrinopathy enteropathy X-linked IPF idiopathic pulmonary fibrosis IPI International Prognostic Index iPSC induced pluripotent stem cell IPSID immunoproliferative small intestinal disease IRIDA iron-refractory iron deficiency anaemia IRIS immune reconstitution inflammatory syndrome IRM immunoradiographic assay IRV Inspiratory and expiratory reserve volume ISH International Society of Hypertension ISHLT International Society for Heart and Lung Transplantation ISIS International Study of Infarct Survival ISWT incremental shuttle walking test ITP immune thrombocytopenia ITU intensive care unit IV intravenous IVC inferior vena cava IVF in vitro fertilization IVIG intravenous immunoglobulin IVU intravenous urography JE Japanese encephalitis JIA juvenile idiopathic arthritis JNC Joint National Committee KDIGO Kidney Disease: Improving Global Outcomes LA left atrium LAMA long-acting antimuscarinic agents LBBB left bundle branch block LCAT lecithin–cholesterol acyltransferase LCH Langerhans' cell histiocytosis lcSSc limited cutaneous systemic sclerosis LDH lactate dehydrogenase LDL low-density lipoprotein LDL-C low-density lipoprotein cholesterol LFT liver function test LGE late gadolinium enhancement LGMD limb-girdle muscular dystrophy LGV lymphogranuloma venereum LH luteinizing hormone LIC liver iron content LINQ Lung Information Needs Questionnaire LIP lymphocytic interstitial pneumonia LKM liver–kidney microsomal LMICs low- and middle-income countries LMN lower motor neuron LMWH low molecular weight heparin LMWP low molecular weight protein LOLA l-ornithine l-arginine LP lumbar puncture LPL lipoprotein lipase LPLR lipoprotein lipase receptor LTOT long-term oxygen therapy LV left ventricle LVDD left ventricular diastolic dysfunction LVEF left ventricular ejection fraction LVOT left ventricular outflow tract LVRS lung volume reduction surgery LVSD left ventricular systolic dysfunction MAG3 mercaptoacetyltriglycine MAGIC MAGnesium in Coronaries MAHA microangiopathic haemolytic anaemia MALT mucosa-associated lymphoid tissue MAO monoamine oxidase inhibitor MAP mean arterial pressure MAPK mitogen-activated protein kinase MBD mineral and bone disorder M-CSF macrophage colony-stimulating factor

 MCHC mean cell haemoglobin concentration MCL mantle cell lymphoma MCNS minimal change nephrotic syndrome MCpEF myocarditis with preserved left ventricular ejection fraction MCV mean corpuscular volume MDE myeloma-defining event MDI metered dose inhalers MDRD Modification of Diet in Renal Disease MDS myelodysplastic syndrome MED minimal erythema dose MELD Model for End-Stage Liver Disease MEN multiple endocrine neoplasia MERFF myoclonic epilepsy and ragged red fibres mESC mouse embryonic stem cell MGRS monoclonal gammopathy of renal significance MGUS monoclonal gammopathy of undetermined significance MHC major histocompatibility complex MHRA Medicines and Healthcare Products Regulatory Agency MIC minimum inhibitory concentration MIDD monoclonal immunoglobulin deposition diseases MKD mevalonate kinase deficiency MM malignant melanoma MMA methylmalonic acid MMF mycophenolate mofetil MMP matrix metalloproteinase MMR mismatch repair MN membranous nephropathy MND motor neuron disease MoCA Montreal

Cognitive Assessment MPA microscopic polyangiitis MPO myeloperoxidase MPS mucopolysaccharidosis (also myocardial perfusion scintigraphy) MR magnetic resonance MRA magnetic resonance angiography (can also be medicine regulatory authority) MRC Medical Research Council MRCP magnetic resonance cholangiopancreatography MRI magnetic resonance imaging MRSA methicillin-resistant Staphylococcus aureus MS multiple sclerosis MS/MS tandem mass spectroscopy MSA multiple-system atrophy MSC mesenchymal stromal cell MSH melanocyte-stimulating hormone MSU midstream urine MTC medullary thyroid carcinoma mTOR mammalian target of rapamycin MUS medically unexplained symptoms MWS Muckle–Wells syndrome NAAT nucleic acid amplification testing NABQI N-acetyl-p-benzoquinone imine NADH reduced nicotinamide-adenine dinucleotide NADPH reduced nicotinamide-adenine dinucleotide phosphate NAFLD nonalcoholic fatty liver disease NAIT neonatal alloimmune thrombocytopenia NASH nonalcoholic steatohepatitis NCAM neural-cell adhesion molecule NEP neutral endopeptidase NET neuroendocrine tumour or neutrophil extracellular trap NETT National Emphysema Therapy Trial NEWS National Early Warning Score NGF nerve growth factor NGS next-generation sequencing NHDL-C non-high-density lipoprotein cholesterol NHL non-Hodgkin's lymphoma NHS National Health Service (UK) NICE National Institute for Health and Care Excellence NIPPV non-invasive nasal positive-pressure ventilation NIPT non-invasive prenatal testing NIV non-invasive ventilation NK natural killer NKT natural killer T NLST National Lung Screening Trial NMS neuroleptic malignant syndrome NMSC non-melanoma skin cancer NNH number needed to harm NNT number needed to treat NOTT Nocturnal Oxygen Treatment Trial NREM non-rapid eye movement NRT nicotine replacement therapy NSAID non-steroidal anti-inflammatory drug NSCLC non-small cell lung cancer NSIP non-specific interstitial pneumonia NSTEMI non-ST-elevation myocardial infarction NTD neural tube defect NTM non-tuberculous mycobacterial NT-proBNP N-terminal B-type natriuretic peptide NYHA New York Heart Association OAF osteoclast-activating factor OAPR odds of being affected given a positive result OB obliterative bronchiolitis OCD obsessive–compulsive disorder OCT optical coherence tomography OD once daily OECD Organisation for Economic Cooperation and Development OED other eating disorders OLP oral lichen planus OMIM Online Mendelian Inheritance in Man OMT optimal medical therapy OPAT outpatient parenteral antibiotic therapy OR odds ratio OS overall survival OSA obstructive sleep apnoea OTB oral tuberculosis PA pernicious anaemia (also pulmonary artery) PACAP pituitary adenylate cyclase activating polypeptide PAF platelet activating factor PAH polycyclic aromatic hydrocarbons (can also mean pulmonary hypertension)

 PAOP pulmonary artery occlusion pressure PAS periodic acid–Schiff PASI Psoriasis Area and Severity Index PASP pulmonary artery systolic pressure PBD polyglucosan body disease PBM peripheral blood mononuclear cell PCC prothrombin complex concentrate PCH paroxysmal cold haemoglobinuria (also pulmonary capillary haemangiomatosis) PCI percutaneous coronary intervention PCNSL primary central nervous system lymphoma Pco partial pressure of carbon dioxide PCP Pneumocystis jirovecii pneumonia PCR polymerase chain reaction (also protein:creatinine ratio) PCT proximal convoluted tubule PCV pneumococcal conjugate vaccine PCWP pulmonary capillary wedge pressure PD peritoneal dialysis (also Parkinson's disease) PDA patent ductus arteriosus PDC pyruvate dehydrogenase complex PDD Parkinson's disease dementia PDGF platelet-derived growth factor PE pleural effusion (can also mean pulmonary embolism) PEACH Pelvic Inflammatory Disease Evaluation and Clinical Health PEEP positive end expiratory pressure PEF peak expiratory flow PEG percutaneous endoscopic gastrostomy PET position emission tomography PFO patent foramen ovale PFS progression-free survival PGK

phosphoglycerate kinase PHARC polyneuropathy, hearing loss, ataxia, retinitis pigmentosa, and cataract PICS post-intensive care syndrome PID pelvic inflammatory disease PIGN postinfectious glomerulonephritis PK pyruvate kinase PKD pyruvate kinase deficiency (also polycystic kidney disease) PKU phenylketonuria PLA2R phospholipase A2 receptor PMN polymorphonuclear neutrophil PMR polymyalgia rheumatica PNH paroxysmal nocturnal haemoglobinuria Po2 partial pressure of oxygen POC point of care POMC pro-opiomelanocortin PP polypeptide PPI proton pump inhibitor ppm parts per million PPS Palliative Performance Scale PPV porcine parvovirus PR3 proteinase 3 PRCA pure red cell aplasia PRI population reference intake PRPP phosphoribosyl pyrophosphate PRR pattern-recognition receptor PRrP parathyroid-hormone-related protein PSA prostate-specific antigen PSC primary sclerosing cholangitis PSP primary spontaneous pneumothorax PT prothrombin time PTC percutaneous transhepatic cholangiography PTCA percutaneous transluminal coronary angioplasty PTH parathyroid hormone PTHrP PTH/PTH-related peptide PTLD post-transplant lymphoproliferative disorder PTP post-transfusion purpura PTSD post-traumatic stress disorder PUVA psoralen ultraviolet A PV pemphigus vulgaris (also plasmas viscosity test) PVE prosthetic valve endocarditis PVOD pulmonary veno-occlusive disease PVR pulmonary vascular resistance PYY peptide tyrosine-tyrosine QALY quality-adjusted life year RA rheumatoid arthritis (can also mean right atrium) RAAS renin–angiotensin–aldosterone system RAS renin–angiotensin system (also renal artery stenosis or restrictive allograft syndrome RAVV right atrioventricular valve RBBB right bundle branch block RBF rat bite fevers RCA right coronary artery RCC renal cell carcinoma RCDP rhizomelic chondrodysplasia punctata RCT randomized controlled trial RDA recommended dietary allowance REM rapid eye movement RF rheumatoid factor RI resistivity index RNA ribonucleic acid RNI reference nutrient intake RNP ribonucleoprotein ROC receiver–operator characteristic RP ribosomal protein RRT renal replacement therapy RTA renal tubular acidosis RV residual volume (also right ventricle) RVOTO right ventricular outflow tract obstruction SA short-axis SABR stereotactic ablative body radiotherapy SBP spontaneous bacterial peritonitis (also systolic blood pressure) SCC squamous cell carcinoma SCD sickle cell disease (also sudden cardiac death) SCI spinal cord injuries SCID severe combined immunodeficiency SCLC small cell lung cancer SCMR Society for Cardiovascular Magnetic Resonance SCN sickle cell nephropathy or severe congenital neutropenia sdLDL small dense low-density lipoprotein SDS Shwachman–Diamond syndrome

 SEER Surveillance, Epidemiology, and End Results SGRQ St George's Respiratory Questionnaire SHBG sex hormone binding globulin SHEC Shiga toxin-producing Escherichia coli SIADH syndrome of inappropriate antidiuretic hormone secretion SIRS systemic inflammatory response syndrome SLB surgical lung biopsy SLE systemic lupus erythematosus SM smouldering myeloma SMA superior mesenteric artery (also smooth muscle antibody) SMC smooth muscle cell sMDRD simplified Modification of Diet in Renal Disease SMR standardized mortality ratio SNGFR single-nephron glomerular filtration rate SNP single nucleotide polymorphism SNS sympathetic nervous system SOD sphincter of Oddi disorder SPC Summary of Product Characteristics SPD storage pool deficiency SPECT single-positron emission computed tomography SPF sun protection factor SSc systemic sclerosis SSD somatic symptom disorder SSFP steady-state free precession SSRI selective serotonin reuptake inhibitor STEMI ST elevation myocardial infarction STI sexually transmitted infection STOPP/START set of inappropriate combinations of medicines and disease (STOPP) and a set of recommended treatments for given conditions (START) suPAR soluble urokinase plasminogen activating receptor SVC superior vena cava SVR systemic vascular resistance TACE transarterial chemoembolization TAE transarterial embolization TALH thick

ascending limb of Henle TAR thrombocytopenia with absent radii TAVI transcatheter aortic valve implantation TB tuberculosis TBLC transbronchial lung cryobiopsy TBM tuberculous meningitis TC total cholesterol TCA tricyclic antidepressant TCPC total cavopulmonary connection TCR T-cell receptor TCT thrombin clotting time TdT terminal deoxyribonucleotidyl transferase TEC transient erythroblastopenia of childhood TEN toxic epidermal necrolysis TF transcription factor (also tissue factor) TFPI tissue factor pathway inhibitor TG triglyceride TGF transforming growth factor TGFα, TGFβ transforming growth factor-α, -β TGN trans Golgi network THR total hip replacement THRIVE Treatment of HDL to Reduce the Incidence of Vascular Events TIA transient ischaemic attack TIBC total iron-binding capacity TIMI thrombolysis in myocardial infarction TINU tubulointerstitial nephritis uveitis TIPS transjugular intrahepatic portosystemic shunt TK tyrosine kinase TKI tyrosine kinase inhibitor TKR total knee replacement TLC total lung capacity TLR Toll-like receptor TMA thrombotic microangiopathy t-MDS therapy-related myelodysplastic syndrome(s) TNF tumour necrosis factor TNFα tumour necrosis factor-α tPA tissue plasminogen activator TPN total parenteral nutrition TPN total parenteral nutrition TRAIL TNF-related apoptosis-inducing ligand TRAPS tumour necrosis factor receptor-associated periodic syndrome Treg regulatory T (cell) TROPHY Trial of Preventing Hypertension TSH thyroid-stimulating hormone TTD thiazide-type diuretic tTG tissue transglutaminase TTIP Transatlantic Trade and Investment Partnership TTKG transtubular potassium concentration gradient TTP thrombotic thrombocytopenic purpura TURBT transurethral resection of bladder tumour TV tricuspid valve UAER urinary albumin excretion rate UCB umbilical cord blood UDCA ursodeoxycholic acid UDP uridine diphosphate UI urinary incontinence UIP usual interstitial pneumonia UKELD United Kingdom Model for End-Stage Liver Disease UKM urea kinetic modelling UKMEC UK Medical Eligibility Criteria UKPDS United Kingdom Prospective Diabetes Study ULN upper limit of normal UMN upper motor neuron UPR unfolded protein response URR urea reduction ratio URTI upper respiratory tract infection UTI urinary tract infection UV ultraviolet UVL ultraviolet light UVR ultraviolet radiation V/Q ventilation/perfusion VARD video-assisted retroperitoneal debridement VATS video-assisted thoracoscopic surgery VC vital capacity vCJD variant Creutzfeldt–Jakob disease

 VDRL Venereal Diseases Research Laboratory VEGF vascular endothelial growth factor VEOIBD very early-onset inflammatory bowel disease VIP vasoactive intestinal peptide VKA vitamin K antagonist VLA vertical long axis VLCFA very long-chain fatty acid VLDL very low-density lipoprotein VSD ventricular septal defect VTE venous thromboembolism VWD von Willebrand's disease VWF von Willebrand factor VZV varicella zoster virus WBC white blood cell WCC white cell count WGS whole genome sequencing WHO World Health Organization WM Waldenström's macroglobulinaemia X-ALD X-linked adrenoleukodystrophy XLH X-linked hypophosphataemia YLDs years lived with disability YLL years of life lost ZASP Z-line associated protein

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Preface

Preface

Preface Changes in medicine The Oxford Textbook of Medicine is published online and has been regularly updated for many years, but the production of a new and very substantially updated edition provides a moment when it is nat- ural and proper to reflect on what has changed in medicine—and what has not—in recent years. In the context of burgeoning social changes and inequality across the world, we have cause to weigh and consider exactly what modern medicine has to offer patients and their doctors. Here we reflect on aspects of Medicine that are chan- ging rapidly and set out a vision for this in the sixth edition of the Oxford Textbook of Medicine. Demand, capacity, magic solutions, and the need for perspective Within all healthcare systems, in rich and poor nations alike, most physicians feel the inexorable rise in demand and are strug- gling to provide adequate ‘capacity’—the term commonly applied by healthcare managers charged with the impossible task of con- straining expenditure while serving political masters who, almost without exception, promise more and more and blame inefficiency and ‘unwarranted variation’ for the failure to deliver. In response to the difficulties, claims are made that some new technological advance, be it sequencing of patients’ genomes, healthcare apps, the application of artificial intelligence or ‘Quality Improvement’ methodology, will provide the solutions. In the Oxford Textbook of Medicine, we do not shy away from these aspects and have several new chapters that consider how rich and ‘resource-poor’ countries might best invest their revenues on health. It is often very hard for practising physicians, who care for patients as individuals, to maintain their bearings within the unfamiliar and depersonalized world of modern healthcare management. Many are left wondering whether those who organize health services ‘live on this planet’, or ‘did any working doctor check out that latest directive from above?’. When clinical outcomes that really matter are diffi- cult to quantify, doctors find themselves and their services judged by spurious measures of ‘productivity’ in the process of healthcare ‘de- livery’. Unrealistic and often clinically irrelevant targets might drive the thinking of the insurers, managers, and politicians, but who can determine the human and clinical value of the care provided? Timeliness of care is important and sometimes crucial for salutary outcomes, but disaster strikes when clock-driven targets are blindly pursued for all patients irrespective of clinical urgency and to the ex- clusion of all else, including patients with greater clinical need. In the morass created by financial constraints and zealous pol- itical control of health services exercised by those without clinical responsibility, it is rare for doctors be able to stand back and perceive genuine improvements. However, it is certainly true that today we have greater potential to prevent and treat disease and to maintain health than ever before. It is our hope that the Oxford Textbook of Medicine will inform doctors about these changes and provide good guidance as to how they can be translated into clinical practice. Advances in biomedical sciences We seek to embody advances in understanding and practice that have arisen through scientific research. In the ten years since publication of the last edition of this book there has been spec- tacular progress in the application of science in medicine, espe- cially the

understanding of genomics and molecular cell biology. These include: in diagnostics, non-invasive prenatal diagnosis of chromosome abnormalities and monogenic disease by sampling maternal plasma for cell-free fetal DNA, a technique which also holds promise for screening and monitoring of cancers; in meta- bolic disease, the introduction of molecular therapies that address the defective chloride transport in cystic fibrosis; in oncology, in- creased understanding of cancer immunity leading to the develop- ment of immunotherapies for cancers. Our authors include the very best in their fields. The founding editor and author in this edition, the late David Weatherall, was a recipient of the Lasker-Koshland Special Achievement Award in Medical Science. Two new authors have received the Nobel Prize recently—Professor Tu Youyou the 2015 prize for Medicine or Physiology, and Sir Greg Winter the 2018 prize for Chemistry. Another new author, Professor Y.M. Dennis Lo, was one of two winners of China's inaugural Future Science Prize in 2016. Beyond scientific development, the introduction of new technolo- gies into practice typically leads to a sequence of events including initial 'hype' from many in the field, with extravagant claims of po- tential benefit. After an interval, these claims are followed by a more realistic assessment of what the technology can—and cannot— provide. Frequently, this familiar pattern is driven by powerful com- mercial influences which can corrupt thinking in a manner that generates a climate in which those with views contrary to the big battalions are inevitably marginalized. In this edition of the Oxford Textbook of Medicine we have strived to bring an authentic perspec- tive and realism to recommendations for treatment. We sense, for in- stance, that the excitement generated by the sequencing of patients' genomes continues to increase, but that this trajectory is flattening and expectations becoming more realistic. For patients very likely to have genetic disorders, diagnoses can be made for a proportion that was unimaginable until recently, but for most patients with the degenerative and/or polygenic diseases that are the greatest burden

Preface viii to health, evidence of clinical benefit from genome sequencing re- mains elusive. Beyond the progress in genomics and cell biology there has been immense interest in bioinformatics and, especially with the enthu- siasm of major biomedical charities such as The Wellcome Trust, for 'big data', and the opportunities that these bring to the practice of medicine. However, while there are plentiful examples of gen- omics and cell biology having been translated productively from the bench to the bedside, with enormous benefit to patients, examples of transforming clinical impact from big data and bioinformatics are sparse. But examples there are, such as in the analysis of out- breaks of the scourges Clostridium difficile and methicillin-resistant Staphylococcus aureus (MRSA). These discoveries give hope for the future as we learn which problems are tractable with this type of approach and which are not. Clinical skill Until recently, it would have been, to paraphrase Thomas Jefferson, regarded as self-evident that the key requirements of a good phys- ician are the ability and will to obtain an informative history, carry out a thorough physical examination, formulate a relevant differ- ential diagnosis, instigate appropriate investigations, advise and administer correct treatment, including best efforts to relieve symp- toms in all cases. These skills, and the commitment to use them, are often forgotten when healthcare is described in the commercial terms of demand and capacity. While advances in biomedical sciences have dramatically im- proved the outcome for some diseases, and Paul Erhlich's century- old magische Kugel (magic bullet) has whetted our appetite for wonder, it is prudent to recall Thomas Szasz: 'Formerly, when reli- gion was strong and science weak, men mistook magic for medicine; now, when science is strong and religion weak, men mistake medi- cine for magic'. The term 'personalized' medicine imputes remark- able and as yet unproven powers, excepting in a very few cases, to gene sequencing and molecular therapies, while the

patient wants to be treated as a person. It is also alarming to us that some medical curricula increasingly focus on process, ‘behaviours’, and ‘communi- cation skills’, to the detriment of medical content or mature guidance and attitudes to lifelong learning. There is a tendency to forget the very essence of being, and how to become, a physician in the time- honoured understanding of the role. In the Oxford Textbook of Medicine we unashamedly emphasize the primacy of history, examination, differential diagnosis, investi- gation, and treatment. Without a firm grasp of these essentials the doctor cannot provide good care for patients, and nor can anyone else. Furthermore, having a firm understanding of clinical context and a well-informed clinical perspective is an essential prerequisite for driving biomedical research into avenues that really matter. The broader context of health and disease The world has become a smaller place. We are now in an era when many regard not having a smartphone as an index of deprivation. An event that has happened on a different continent can, as a re- sult of social media, become known to millions of people within hours—the term ‘viral’ has been rightfully translated from commu- nicable illness to global phenomenon. Narratives transmitted in this way often concern disasters, wars, and disease, and they are typically handled by the media in a sensationalized and superficial manner. One hundred and fifty years ago, Darwin’s 1859 masterpiece on evolution was entitled ‘On the Origin of Species by Means of Natural Selection, or the Preservation of Favoured Races in the Struggle for Life’. The ‘less favoured’ undoubtedly have poorer health outcomes, due largely to the persistent social ill of inequality, in poor as well as ostensibly rich countries. Continuing the tradition of previous edi- tions, we have contributions that discuss the impact of social deter- minants of health, also thoughtful chapters on human disasters (by another Nobel laureate, Prof Amartya Sen), and the practical and critically important aspects of humanitarian medicine. In addition, the modern problems of pollution and climate change are exam- ined. We contend that all doctors would benefit from reading these chapters. Patients and their expectations There are continuing changes in patients’ expectations, particularly those of articulate patients suffering from long-term conditions and residing in countries with a rich provision of healthcare. A paternal- istic medical approach is no longer acceptable, and several patients have contributed greatly to the book by taking the opportunity to tell us how they think doctors should behave towards them and care for them. However, we are very aware that one size does not fit all, and that many patients want a doctor who will give them clear recom- mendations and not keep repeating a bewildering (to the patient) variety of options and ask them to choose. The mature and able physician will be alert and sensitive to those patients who want this and will provide them with clear advice, and we have endeavoured to ensure that the Oxford Textbook of Medicine will assist. Access to medical knowledge The ever-expanding world of the smartphone and tablet device gives patients, families, doctors, and other healthcare professionals ready access to more information about medicine than all but a very few would have thought possible a decade ago. This has many benefits but often leaves users of the internet thoroughly perplexed, and some desperate people vulnerable to online quackery. Those wanting de- tails of particular studies will naturally refer to the original literature. Those wanting in-depth reviews of particular subjects can refer to diverse resources: these are typically good at apprising the reader of plentiful options for investigation, diagnosis, or management, but often leave them uncertain of what a clinically experienced expert in the field would actually recommend. In the sections that form the bulk of the Oxford Textbook of Medicine, we have selected experts with specific clinical experience and given them this task, and we contend that they have met the challenge. Acknowledgements The Oxford Textbook of Medicine is a large undertaking: this edition, the most substantial so far, comprises 647 chapters and covers 6654 printed pages, and its production has required an extraordinary co- ordination of

effort from many quarters. In darker moments the edi- tors feared that the process would never end, but as we have read and edited the chapters along the way, we have experienced the joy of learning a huge amount of medicine, often in fields far removed from our own. For this we are very grateful to our contributors, including those whose submissions were delayed!

Preface ix We wish to make particular acknowledgement of our friend and senior colleague, David Warrell, an editor from the first edition of this textbook, senior editor of the fourth and fifth editions, and au- thor in this edition. We and our readers, notably those seeking in- formation on tropical diseases and especially any who have been bitten by snakes, about which his knowledge is truly prodigious, owe him a great debt. We thank Helen Liepman, with whom we remain good friends: she has overseen and directed matters at Oxford University Press and coped in a steadfastly pleasant and professional way with expres- sions of editorial frustration caused by our failure to understand a publishing process that at times seemed to be Byzantine in its com- plexity, as might perhaps be expected in an ancient university. We also thank Anna Kirton, Jamie Oates, and Jess White at Oxford University Press for their considerable efforts on behalf of the book. Finally, we record that the editors' personal lives have remained calm, and we are very grateful to Helen, Jenny, and Sue for their in- dulgence of our bizarre editorial pursuit. John D. Firth Christopher P. Conlon Timothy M. Cox

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