ARTICLE

Another argument for values-based medicine

Miles Little MD MS FRACS[a], Wendy Lipworth MBBS MSc PhD[b], Jill Gordon MBBS MA PhD FRACGP FACPsychMed[c] and Pippa Markham BA (Hons)[d]

a Emeritus Professor, Centre for Values, Ethics and the Law in Medicine, University of Sydney, Sydney, NSW Australia
b Post-doctoral Research Fellow, Centre for Values, Ethics and the Law in Medicine, University of Sydney, Sydney, NSW and Australian Institute of Health Innovation, University of New South Wales, NSW, Australia
c Associate Professor, Centre for Values, Ethics and the Law in Medicine, University of Sydney, Sydney, NSW Australia
d Research Assistant, Centre for Values, Ethics and the Law in Medicine, University of Sydney, Sydney, NSW Australia

Abstract

There is a contemporary dialectic concerning the status of evidence-based medicine, criticising it for being 'scientistic', epistemologically inconsistent, rigid and dismissive of non-numerical sources of knowledge. A host of alternative frameworks has been proposed, including values-based medicine, narrative medicine, patient-centered care and person-centered medicine. Person-centered medicine is amongst the most persuasive and well-argued models. Miles and Mezzich [1] have argued in a major article that person-centered medicine employs theories of personhood to elaborate and justify its epistemology and praxis. At the same time, they claim that person-centered medicine is an 'emergent' concept that needs no base or foundation to justify it. We believe, however, that without some foundational values to underpin the status claimed for personhood, the arguments for person-centered medicine are incomplete. We therefore propose a set of foundational values – survival, security and flourishing – that underpin individual and social functioning transculturally. While these values are the same in all cultures, their expressions differ from culture to culture. Importantly, our notion of values is only modestly foundational. Modest foundationalism recognises that foundational propositions are only 'warrantable assertions' that may very well change in time and place. Foundational values in this sense are pragmatic and heuristic in kind and not normative. We enter a plea for their recognition in the form of the values-based medicine we describe.

Correspondence address

Emeritus Professor Miles Little, Centre for Values, Ethics and the Law in Medicine, University of Sydney, Sydney, NSW 2006, Australia. E-mail: miles.little@sydney.edu.au

Justification in Medicine

The problem with evidence "based" medicine

There is a strand of criticism applied to evidence-based medicine (EBM) that has grown stronger and more compelling in the 21st century. EBM has been criticised for being "scientistic", morally narrow, dehumanising and productive of 'cookbook' and 'defensive' medicine [2-11]. Despite the vigour and intensity of the critiques of evidence-based medicine (EBM) on epistemological and ethical grounds, it retains much contemporary support and generates considerable heat when taken literally and used to dismiss technologies or treatments whose effectiveness, cost-benefits and relative risks remain unproven. The recent dispute about the use of recombinant activated Factor VII (rFVIIa) is typical of the problem, which is the challenge of providing the most up-to-date and effective treatment when all the evidence for and against the treatment has not yet been fully accounted for.

rFVIIa is a clotting factor indicated for the treatment of haemorrhage in patients with rare haematological

disorders, but is also used for major haemorrhage in people who do not have these disorders (e.g. in surgery and post-partum haemorrhage) [12-16]**.** While this off-label use seems logical, is supported by some systematic evidence [15,17] and has been observed by clinicians to "work" by slowing bleeding, recent systematic reviews have suggested that such uses of rFVIIa have no effect on overall mortality [18-20] and might be harmful [18]**.** A vigorous debate has since emerged, with opponents of these extended uses of rFVIIa raising the possibility of legal action against "physicians who persist in such use in the face of clear evidence of inutility and harm (and who) could be subject to civil action by the affected patients or their heirs" [21] and those in favour of extended prescribing countering that clinical demands and impressions would (and should) trump the evidence offered and that clinicians would (and should) continue to use rFVIIa for off-label indications [22, 23].

The drift in this discourse from epistemological issues to ethical concerns and then to hints of legal sanction raises questions about the validity of EBM as an adequate '*base*' for medicine [24-28]. To *base* a discipline, its knowledge and its praxis, on an abstract category is to claim that the base is un-inferred and provides the justification for the epistemology and practice of the discipline. It is to make a 'foundational' claim for the base, a claim that the discipline can be built from the base by repeated inference and deduction, supported by empirical confirmation when appropriate. There is certainly a case to be made for medical *practice* to be justified, whenever possible, by evidence. There should surely be a supporting reason to defend any particular medical intervention - some demonstrable effect, or outcome that can be agreed upon and approved by practitioners and patients alike. But judging the 'goodness' or 'badness' of these outcomes requires a standpoint *outside* the evidence. It requires the application of implicit or explicit standards against which to judge the outcome. The very nature of evidence places it *within* that evaluative framework.

Alternatives to evidence-based medicine

Values-based medicine (VBM) [29-32], narrative medicine [33,34], patient-centered medicine [35-37], humanistic medicine [38-41], person-centered medicine [1,24-28,30,42] and a host of other competitors have been proposed as alternatives to redress the 'scientistic' bias that EBM seems to have produced in medical thinking. We propose, in this essay, to deal largely with VBM and person-centered medicine.

Person-centered medicine is the latest and perhaps the most intellectually satisfying, alternative. Its lineage can be traced through Hippocrates to the School of Salerno and to William Osler, as well as through Peabody and Tournier. Miles and Mezzich have persuasively outlined the framework and justifications for encouraging person-centered medicine [1]. They ground their arguments in theories of personhood and they show how these theories

can extend to a person-centered public health in addition to the dyadic interactions of conventional medical practice. It is very difficult to object to their ideals of achieving a medical practice that would provide affordable biomedical and technologically advanced care within a humanistic framework and that exhibits respect for the patient as individual within the context of each person's capabilities, attributes and acquisitions.

Importantly, however, they deny that person-centered medicine provides a foundational *base* for medical practice. Indeed, following Upshur [43], they deny that medicine needs a base at all and they present a case for person-centered medicine as 'a dynamic emergent framework', rather than something in need of 'a single, solid foundation' [1]. While we agree to some extent with this claim, we believe that person-centered medicine too must appeal to foundations – in this case, to theories of personhood that are not without problems [44].

The nexus between personhood and moral status has been acknowledged for centuries [45,46], but logical priority of one over the other remains contested [44]. Miles and Mezzich have chosen Eric Cassel's definition of 'a person as an "embodied, purposeful, thinking, feeling, emotional, reflective, relational, human individual always in action, responsive to meaning and whose life in all spheres points both outward and inward"…' [1]. We may be able to define and understand these adjectives and gerunds within Western Anglophone communities. But what does 'relational' mean to a Bosnian Muslim or 'emotional, reflective' to a refugee from Sierra Leone if we are to join patient-centered medicine with 'international' medicine, as Miles and Mezzich do [1]? Definitions and understandings of personhood differ widely from place to place and from time to time. Person-centered medicine still has to answer why we should bother to respect persons. [47-51]

We propose a form of values-based medicine (VBM) that is modestly foundational and that may strengthen the claims of person-centered medicine (and any other alternatives to EBM). VBM has been construed as an economic, cost-benefit approach to medical practice [52], or as a qualitative concept reflecting on the one hand a sensitive attention to patient preferences [29,30,32] and on the other a justification for healthcare based on foundational human needs [31]. In the remainder of this essay we argue for the latter version of VBM and we argue that, unlike evidence-based medicine, this provides an adequate foundation for medical practice. To do so, we need to confront the threats and promises of foundationalism, the range of philosophical positions that accept that spheres of knowledge can be based on un-inferred propositions, particularly those generated by experience. In particular, we need to distinguish between radical and modest foundationalism.

Foundationalism

Foundationalism of a naïve or radical kind in ethics is hard to defend. We take this kind of foundationalism to mean 'deriving a true normative system out of one or several *first norms*' [53]. The bioethics that Gert, Culver and Clouser elaborated in 1997 is of this kind. It defines 10 'moral rules' as its first norms, including such apparently uncontroversial items as 'Do not kill', 'Do not cause pain', 'Do not disable' and 'Do not deprive of freedom' [54]. Yet each of these 'rules' may have to be modified by circumstances and by beliefs – abortion can be justified under certain circumstances, euthanasia can be practised in some parts of the world, surgery frequently causes disability and is usually painful and a mental health restraint act (community order) can be invoked to deprive some people of their freedom. The problem becomes one of validating the first norms universally, leading either to an endless regress or to circularity. This problem has led some writers to champion 'anti-foundationalism' on the grounds that it frees thinkers and agents from the need to stick to a Cartesian chain of reasoning from one truth to another, in order to address propositions that may be contestable [43,53]. On the other hand, without some sort of foundation it is difficult to build any sort of system [1,43], nor is it easy to provide justifications for spheres of thought and practice. Modest foundationalism, by contrast, takes 'the foundations to be only *prima facie* adequately grounded by experience, adequately grounded provided that *prima facie* status is not overridden by things the subject knows or has adequately grounded beliefs about' [55]. As with empirical science, it takes all knowledge to be provisional. As Alston points out:

> *Any reasonable epistemology will have to allow some forms of inference that go from adequately grounded beliefs to other adequately grounded beliefs and therefore will have to find some acceptable way of deciding which to allow* [55].

Alston also suggests that there is no real epistemological alternative to 'accepting what we feel confident of at the moment, subject to revision should it be called for' [55]. In this form, foundational beliefs have a pragmatic function. They are heuristics by which we can proceed to reason and to judge, provided we also accept that they may be subject to revision in the light of new experiences, perceptions and discoveries.

If there are psychological and logical reasons to find foundations, points of inquiry beyond which we cannot fruitfully go, what might these non-inferential propositions look like? We contend that these must be propositions about *values* and that there are some values that, at a very deep level, most people and cultures share. In order to define these foundations, we can proceed, as Alston suggests [55], by iteratively examining the likely explanations for the social systems that distinguish all cultures, including our own. Why do all cultures have health systems of some kind? Perhaps to save life, to preserve or restore function in the face of trauma or disease, to provide access to skills for those with health needs. But why do these things matter? Perhaps because people want to go on living without suffering, want to realise or extend their capabilities, want help when illness threatens or reduces their quality or quantity of life. In short, humans value survival, security and the capacity to flourish. These values seem to be primal. There seems to be nowhere to go beyond them. They take us to the point where there is apparently nothing more to say than that all the communities we know or can imagine are like that. Ernst Junger, for example, imagined a masterly society that would emerge if its members could be inured to pain – a society that ended in the disintegration of the Wehrmacht and chaos for Germany [56]. Without some implicit allegiances to foundational concepts as facts – not norms – mankind would probably have perished. These allegiances exist in individuals and because humans are essentially social they are expressed by the social will in such entities as health and medical services. We each try to ensure survival, to find security and flourishing within societies that both enhance and limit their expression. But what do we mean by each of these terms? They are imperfect semantic labels for extremely complex concepts and the best we can do is to point in the direction of their meanings.

Survival is not too hard to define and understand. In this context it means the continuation of a life, the preservation of life which seems to be instinctively sought. Drowning people struggle to survive. Security is best understood by examining situations of insecurity. Jean Améry, reflecting on his experiences of Auschwitz and exile, writes "One feels secure … where no chance occurrence is to be expected, nothing completely strange to be feared" [57]. We need to know that, in our community, everyone will drive on a particular side of the road and will stop at red lights; that passers-by will respect our space and not assault us; that some kind of health system will be available in our time of illness. Security derives from order and predictability.

Flourishing is more complex, because there are so many ways for individuals to flourish. Broadly, it refers to the increase and expression of capabilities [58] and the opportunities that individuals within a culture or a society have to transcend their quotidian lives, whether this may involve sport, art, literature, film, friendship, religion or any of the other countless commitments and relaxations that can enrich individual experience and development. Each of these foundational values has its opposite – death or the threat of early death, insecurity and threat of danger and loss of the autonomous and agentic capacity to flourish. Practically everyone lives somewhere on the continuum between the ends of each scale and everyone moves their position on the scale from context to context. We thus propose the following:

[I] all human beings desire their own (and perhaps others') survival, security and flourishing and
[II] all cultures are expressions of the dominant members' beliefs about the route to survival, security and flourishing.

In an ideal society, as we would envisage it, all members support the concept of individual autonomy and agency with respect to survival, security and flourishing.

Importantly, unlike the rules proposed by Gert, Culver and Clouser, our notion of values is descriptive [I] and explanatory [II], rather than normative or justificatory. It tells us why things are as they are and not whether they are good or bad. In making these claims we have thus extended our inquiry beyond the bounds of the naturalistic argument, the is-ought distinction, into the domain of axiology [59-61]. As Flanagan and colleagues write:

With regard to the alleged is-ought problem, the smart naturalist makes no claims to establish demonstratively moral norms. He points to certain practices, values, virtues and principles as reasonably based on inductive and abductive reasoning [62].

The question then becomes: Do we have to be extreme moral relativists if we view cultures and systems in this way? Does our capacity to understand all cultures and systems as expressions of survival, security and flourishing mean that we have to condone whatever we find? The answer to this question is a definite "no". To say that we can understand (and perhaps even sympathise with) a particular cultural expression of the need for survival, security and flourishing is *not* to say that any expression of these foundational values is as good as any other. In any culture, those with power might very well be expressing their own foundational values at the expense of those with less power.

Argument about the rights and wrongs of cultural practices is inevitable. All cultures, sub-cultures and discourse communities bring beliefs that have a pragmatic truth about them, a 'warranted assertibility' [63,64]. Even though each group expresses some notion of group or individual attachment to survival, security and flourishing, some groups will inevitably disagree with others on the particular expressions they endorse for each foundational value. Tradition, cultural habits, myths, religious convictions, experiences, environments, contexts, individual differences and so on make sure that modes of expression (such as class or gender discrimination, provision of public health services) will be conceptually contested in any forum that crosses discursive and cultural boundaries [65-69]. Those who defend any form of genital mutilation, for example, may appeal to protection of health (survival), the stability and security of cultural tradition and the flourishing that accompanies initiation into a culture. Those who oppose it point to inherent risks, potential damage to psychological health and sexual

pleasure. Both sides appeal to the same foundational values, but their claims are 'essentially contested'.

In Western liberal countries, we adhere to notions of personal freedom, autonomy, the realisation of capabilities and so on and we use such criteria as norms against which to measure the choices and behaviours of other cultures and societies. Those others judge our choices and behaviours in the same way. We may agree that all seek the same ends, but the ways in which we enact the pursuit of these ends are filtered by cultural intuitions and differences. There may be wide cross-cultural agreement that certain crimes should be punished, for example, but radical disagreement about the death penalty or punitive amputation. All parties to the argument will point to their own approach as a logical and morally appropriate way to protect the security of their people. It is the reasoning and the belief systems behind the local practices that cause essential contestability, not the foundational values that provide the ultimate justifications for undertaking the construction of social systems.

There is similarity between our reasoning and that of Martha Nussbaum in her work on virtues. She has identified non-relative virtues that respond to 'grounding experiences' and has confronted problems with relativism [70]. She argues for common features of humanity, common needs, values and experiences from which to construct a common discourse. She lists mortality, embodiment, pleasure and pain, cognitive capability, practical reason, early infant development, affiliation and humour as categories for debate. She comments that from these categories 'We do not have a bedrock of completely uninterpreted "given" data, but we do have nuclei of experience around which the constructions of different societies proceed' [70]. We suggest that Nussbaum's categories can be subsumed within our own; that 'survival' includes mortality and early infant development at least; that 'security' includes pain, practical reason, early infant development and affiliation and that 'flourishing' includes embodiment, pleasure, cognitive capability, affiliation and humour. Our categories also cover shelter, welfare, justice, transport and other public services like health.

In dealing with the issue of all-embracing relativism, her approach, like ours, does not endorse an 'anything-goes' approach to the practices that express foundational values. She writes:

But the relativist has, so far, shown no reason why we could not at the end of the day, say that certain ways of conceptualizing death are more in keeping with the totality of our evidence and the totality of our wishes for flourishing life than others; that certain ways of experiencing appetitive desire are for similar reasons more promising than others.(p.261).

Nussbaum's reference to 'the totality of our wishes' raises the issue of globalisation. Abuses of human rights are drawn into global discourses. Critiques of honour killings, genital mutilation, detention without trial, the

health consequences of poverty, and so on, are now issues for the media and its participants. They become harder and harder for politicians and public intellectuals to set aside. Changes may be painfully slow – indeed they may never come – but the forces for change have new ways to move and new institutions to back them up. Groups like Amnesty International (www.amnesty.org/) and Transparency International (www.transparency.org/) now contribute increasingly to international discourse on human rights.

Television, radio, computers, newspapers and mobile telephones are disseminative technologies of extraordinary power. Their roles in the recent riots in Britain and the Arab uprisings reinforce what Nussbaum wrote in 1988 [71]:

...it is necessary to stress that hardly any cultural group today is as focussed upon its own internal traditions and as isolated from other cultures as the relativist argument presupposes. Cross-cultural communication and debate are ubiquitous facts of contemporary life.

Modest foundationalism does not equate to extreme relativism. Nor does it equate to normative ethics. Modest foundationalism is descriptive, not prescriptive. The understanding that can be derived from viewing cultures as expressions of foundational values does not justify whatever we find. Rather, it provides a focus for critical reflection on our own culture and for discursive and dialectical engagements with cultures unlike our own. It represents one component of the wide reflective equilibrium [72-74] that is necessary for fully formulated ethical reasoning about medicine or any other social practice.

Values-based medicine

So how does this play out in medicine? First, our conception provides us with a way of understanding why we have health systems at all. We have health systems to save life, to preserve or restore function in the face of trauma or disease, to provide access to skills for those with health needs. In this way, values-based medicine provides us with an abductively-derived "base" for medicine that other systems, such as evidence-based medicine, simply cannot provide. Second, our conception explains why particular health systems have evolved in particular ways and why health systems might differ in different settings. The Texas Heart Center has a quite different philosophy to Médecins sans Frontières. One is a business that depends on capitalistic theories of enterprise, selling survival, security and flourishing at superb level and high price; the other a charitable enterprise that tries to deliver survival, security and the capability to flourish to some of the most vulnerable people in the world, without profit. Both owe their continuing existence to individual and cultural values,

however differently they may be expressed in different socio-economic contexts. Their translation into action in different ways has produced the societies and cultures we know. Other foundations might have produced better ones, but that is to enter the domain of speculative ethics, to recross the naturalistic barrier into a realm of thought experiment.

This kind of modest foundationalism thus develops into a form of values-based medicine (VBM) with broad implications, where the word 'based' is used deliberately to recognise that all healthcare is justified by 'basic' values. It subsumes EBM, narrative-based medicine, patient-centered care, person-centered medicine and public health. It respects cultural differences, preferences and ethonomics, the increasingly important intersection between ethics and economics [75,76]. By recognising their deep, implicit presence we offer practitioners and students a direction for the exercise of wide reflective equilibrium, the process whereby formative experience, moral theory, moral reasoning and moral knowledge are brought to bear on an ethical quandary [72-74].

This leads to the third use of our conception. Understanding why particular health systems have evolved as they have provides the basis for a critique of these systems at all levels, to include their patients, bureaucrats, healthcare workers, researchers and so on. Our capacity to understand (and empathise) provides us with one component of the wide reflective equilibrium according to which we can judge our own healthcare practices and those of others. We can understand, for example, some of the heat engendered by the dispute about the use of Factor VII mentioned early in this article, because it arises in the tension between individual and communitarian conceptions of survival, security and flourishing. Those who practise dyadic medicine must deal with the immediate threat of blood loss, whose consequences are disability or death for their patients, suffering and loss for families. Their sense of security and flourishing depend on the survival of the patient. Surely all measures that may limit blood loss are justified to achieve that end here and now while the bleeding is happening? Those who fund health services, or make policy or who follow EBM's central precepts must take a different view and focus on measurable outcomes such as survival and the risks of complications. In the absence of overwhelming evidence of benefit or harm, dyadic practitioners appeal to potential to secure survival for individual patients and to insure their own sense of purpose and hence the security and flourishing that comes from being able to say "I did all I could." From a communitarian standpoint, the individual episode is less important than the epidemiological outcomes. If there is no clear evidence that survival is increased and a utilitarian calculus of security and flourishing produces equivocal results, then uncertainty must rule out the use of a treatment that remains 'Not Proven'. Both sides may agree on the importance of survival, security and flourishing, while remaining divided on the significance of a 'Not Proven' verdict.

Conclusion

VBM, thus conceived, places foundational values (survival, security and flourishing) at the heart of medical education, training and practice. It goes beyond equating values with preferences [29,30,32]; it tries to find the reasons behind preferences and to stress their commonality. It does not seek (on its own) to alter the content of healthcare or its curriculum, but to remind us of the real justifications for the medical endeavour. VBM will not ensure that the WHO model of health ('Health is a state of complete physical, mental and social wellbeing and not merely the absence of disease or infirmity' (see https://apps.who.int/aboutwho/en/definition.html) will be guaranteed in a society that represses its citizens, robs them of their autonomy, dignity or freedom and in which those in power are concerned only with their *own* survival, security and flourishing. VBM can help those who work in health to keep in mind what justifies the existence of the health system in which they work and justifies the enormous expense of money, effort and emotion involved. It can encourage them to compare their attitudes, practices and desirable outcomes with other systems in other cultures. VBM asks that its practitioners bear in mind the commonality of justification for what they do and look beyond the cultural and individual differences that so often threaten to divide communities of practice [77-79] from one another.

VBM, couched in these terms, provides no cut-and-dried answers to the perennial problems of bioethics. What it might do, however, is provide a conceptual framework and a heuristic for understanding, reflection, discourse and dialectic when there appear to be irreconcilable differences between practices. VBM incorporates EBM, patient-centered care, public health, bench-top research and person-centered medicine. It has some claims to be the basis for medical education at all levels, for establishing standards of practice and for reflection on ethical quandaries at individual and population levels. In no way does it compete with person-centered medicine for rhetorical priority, but it may offer a further justification for value-laden theorising in medical epistemology and practice. Some may even prefer to use the concept in the dialectic of revision between the 'scientistic' and the 'humanistic' extremes of healthcare theory.

Acknowledgements

References

[1] Miles, A. & Mezzich, J.E. (2011). The care of the patient and the soul of the clinic: person centered medicine as an emergent model of modern clinical practice. *International Journal of Person Centered Medicine* 1 (2), 207-222.

[2] Goldenberg, M.J. (2006). On evidence and evidence-based medicine: Lessons from the philosophy of science. *Social Science & Medicine* 62, 2621-2632.

[3] Grossman, J. (2008). A Couple of the Nasties Lurking in Evidence-Based Medicine. *Social Epistemology: A Journal of Knowledge, Culture and Policy* 22 (4), 333 - 352.

[4] Kerridge, I., Lowe, M. & Henry, D. (1998). Personal paper: Ethics and evidence based medicine. *British Medical Journal* 316 (7138), 1151-1153.

[5] La Caze, A. (2008). Evidence-Based Medicine Can't Be.... *Social Epistemology: A Journal of Knowledge, Culture and Policy* 22 (4), 353-370.

[6] Lipworth, W., Carter, S. & Kerridge, I. (2008). The "EBM movement": where did it come from, where is it going, and why does it matter? *Social Epistemology: A Journal of Knowledge, Culture, and Policy* 22, 425-431.

[7] Miles, A. & Loughlin, M. (2011). Models in the balance: evidence-based medicine versus evidence-informed individualized care. *Journal of Evaluation in Clinical Practice* 17, 531-536.

[8] Timmermans, S. & Angell, A. (2001). Evidence-Based Medicine, Clinical Uncertainty, and Learning to Doctor. *Journal of Health and Social Behavior* 42 (4), 342-359.

[9] Timmermans, S. & Kolker, E.S. (2004). Evidence-Based Medicine and the Reconfiguration of Medical Knowledge. *Journal of Health and Social Behavior* 45, 177-193.

[10] Tonelli, M.R. (2006). Integrating evidence into clinical practice: an alternative to evidence-based approaches. *Journal of Evaluation in Clinical Practice* 12 (3), 248-256.

[11] Worrall, J. (2002). What Evidence in Evidence-Based Medicine? *Philosophy of Science* 69 (3), S316-S330.

[12] Kalina, M., Tinkoff, G. & Fulda, G. (2011). Massive postpartum hemorrhage: recombinant factor VIIa use is safe but not effective. *Delaware Medical Journal* 83 (4), 109-113.

[13] DeLaughery, E.P., Lenfesty, B. & DeLoughery, T.G. (2011). A retrospective case contro study of recombinant factor VIIa in patients with intracranial haemorrhage caused by trauma. *British Journal of Haematology* 152 (5), 667-669.

[14] Chapman, A.J., Blount, A.L., Davis, A.T. & Hooker, R.L. (2011). Recombinant factor VIIa (NovoSeven RT) use in high risk cardiac surgery. *European Journal of Cardiothoracic Surgery* Epub ahead of print.

[15] Friederich, P.W., Henny, C.P., Messelink, E.J., Geerdink, M.G., Keller, T., Kurth, K.H., Büller, H.R. &

Levi, M. (2003). Effect of recombinant factor VII on perioperative blood loss in patients undergoing retropubic prostatectomy: a double-blind placebo-controlled randomised trial. *Lancet* 361, 201-205.

[16] Dutton, R.P., Parr, M., Tortella, B.J., Champion, H.R., Bernard, G.R., Boffard, K., Bouillon, B., Croce, M.A., Dimsits, J., Holcomb, J.B. Leppaniemi, A., Vincent, J.L., Hauser, C.J. & CONTROL Study Group. (2011). Recombinant activated Factor VII safety in trauma patients: Results from the CONTROL trial. *Journal of Trauma* 71 (1), 12-19.

[17] Ilyas, C., Beyer, G.M., Dutton, R.P., Scalea, T.M. & Hess, J.R. (2008). Recombinant Factor VIIa for warfarin-associated intracranial bleeding. *Journal of Clinical Anesthesiology* 20, 276-279.

[18] Yank, V., Tuohy, C.V., Logan, A.C., Bravata, D.M., Staudenmayer, K., Eisenhut, R., Sundaram, V., McMahon, D., Olkim, I., McDonald, K.M., Owens, D.K. & Stafford, R.S. (2011). Systematic review: Benefits and harms of in-hospital use of recombinant factor VIIa for off-label indications. *Annals of Internal Medicine* 154, 529-540.

[19] Yank, V., Tuohy, C.V., Logan, A.C., Bravata, D.M., Staudenmayer, K., Eisenhut, R., Sundaram, V., McMahon, D., Olkim, I., McDonald, K.M., Owens, D.K. & Stafford, R.S. (2011). Systematic review: benefits and harms of in-hospital use of recombinant Factor VIIa for off-label indications. *Annals of Internal Medicine* 154, 529-540.

[20] Logan, A.C., Yank, V. & Stafford, R.S. (2011). Off-label use of recombinant factor VII in U.S. hospitals: Analysis of hospital records. *Annals of Internal Medicine* 154, 516-522.

[21] Avorn, J. & Kesselheim, A. (2011). Editorial: A hemorrhage of off-label use. *Annals of Internal Medicine* 154, 566-567.

[22] Karkouti, K. & Levy, J.H. (2011). Comment: The off-label use of recombinant activated factor VII. *Annals of Internal Medicine* [cited 2011 18 August 2011]; Available from: www.annals.org/content/154/8/566/reply.

[23] Hayanga, A.J. (2011). Replies: Trends in the use of Factor VII in cardiac surgery. *Annals of Internal Medicine* [cited 2011 18 August 2011]; Available from: www.annals.org/content/154/8/516.

[24] Miller, C.G. & Miller, D.W. (2011). The Real World Failure of Evidence-Based Medicine. *International Journal of Person Centered Medicine* 1 (2), 295-300.

[25] Penston, J. (2011). The irrelevance of statistics-based research to individual patients. *International Journal of Person Centered Medicine* 1 (2), 240-249.

[26] Raman, R. (2011). Evidence-based Medicine and Patient-centered Care: Cross-Disciplinary Challenges and Healthcare Information Technology-enabled Solutions. *International Journal of Person Centered Medicine* 1 (2), 279-294.

[27] Walsh, B. & Gillett, G. (2011). A post-structuralist view of evidence-based medicine (EBM): what EBM contributes to philosophy. *International Journal of Person Centered Medicine* 1 (2), 223-231.

[28] Walsh, B. & Gillett, G. (2011). Is Evidence-based Medicine positivist? *International Journal of Person Centered Medicine* 1 (2), 232-239.

[29] Fulford, K.W.M. (2007). Values-based medicine: delusion and religious experience as a case study in the limits of medical-scientific reduction. In: The Science of Morality, (Ed. G. Walker) London: Royal College of Physicians.

[30] Fulford, K.W.M. (2010). Bringing together values-based and evidence-based medicine: UK Department of Health Initiatives in the 'Personalization' of Care. *Journal of Evaluation in Clinical Practice* 17 (2), 341-343.

[31] Little, M. (2002). Humanistic medicine or values-based medicine? What's in a name? *Medical Journal of Australia* 177 (6), 319-321.

[32] Petrova, M., Dale, J. & Fulford, K.W.M. (2006). Values-based practice in primary care: easing the tensions between individual values, ethical principles and best evidence. *British Journal of General Practice* 56 (530), 703-709.

[33] Charon, R. (2001). Narrative Medicine: A Model for Empathy, Reflection, Profession, and Trust. *Journal of the American Medical Association* 286 (15), 1897-1902.

[34] Greenhalgh, T. & Hurwitz, B. (eds). (1998). Narrative Based Medicine: Dialogue and Discourse in Clinical Practice. London: BMJ Books.

[35] Cassell, E.J. (1997). Why should doctors read medical books? *Annals of Internal Medicine* 127 (7), 576-578.

[36] Laine, C. & Davidoff, F. (1996). Patient-centred medicine: A professional evolution. *Journal of the American Medical Association* 275 (2), 152-156.

[37] Montgomery, K. & Little, M. (2011). Enriching patient-centered care in serious illness: a focus on patients' experiences of agency. *Milbank Quarterly* 89 (3), 381-398.

[38] Engel, G.L. (1962). The nature of disease and the care of the patient: the challenge of humanism and science in medicine. *Rhode Island Medical Journal* 45, 245-251.

[39] Engel, G.L. (1977). The care of the patient: art or science? *Johns Hopkins Medical Journal* 140 (5), 222-232.

[40] Engel, G.L. (1978). The biopsychosocial model and the education of health professionals. *Annals of the New York Academy of Sciences* 310, 169-187.

[41] Little, M. (1995). Humane Medicine, Cambridge: Cambridge University Press.

[42] Henry, S.G., Zaner, R.M. & Dittus, R.S. (2007). Viewpoint: Moving beyond evidence-based medicine. *Academic Medicine* 82 (3), 292-297.

[43] Upshur, R. (2002). If not evidence, then what? Or does medicine really need a base? *Journal of Evaluation in Clinical Practice* 2, 113-119.

[44] Warren, M.A. (1997). Moral Status: Obligations to Persons and Other Living Things, Oxford: Oxford University Press.

[45] Locke, J.(1689). An Essay Concerning Human Understanding. Oxford: Clarendon Press. (1957).

[46] Kant, I. (1797). The Metaphysics of Morals. Cambridge: Cambridge University Press. (1996).

[47] Michaels, M.D. (1989). The Chaos Paradigm. *Organization Development Journal* 7 (2), 31-35.

[48] Marks-Tarlow, T. (1995). The fractal geometry of human nature. In: Chaos Theory in Psychology and the Life Sciences,(Eds. R. Robertson & A. Combs), pp. 275-283. Lawrence Erlbaum Associates: Mahwah, NJ.

[49] Bourdieu, P. (1984). Distinction: A Social Critique of the Judgement of Taste, Cambridge, Mass: Harvard University Press.

[50] Bourdieu, P. (2008). Outline of a Theory of Practice, Cambridge: Cambridge University Press.

[51] Olafson, F.A. (1995). What is a Human Being? - A Heideggerian View, New York: Cambridge University Press.

[52] Webb, D.J. (2011). Value-based medicine pricing: NICE work? *Lancet* 377 (9777), 1552-1553.

[53] Quintelier, K., Van Speybroeck, L. & Braeckman, J. (2010). Normative Ethics Does Not Need a Foundation: It Needs More Science. *Acta Biotheoretica* 59 (1), 29-51.

[54] Gert, B., Culver, C.M. & Clouser, K.D. (1997). Bioethics: A Return to Fundamentals, New York: Oxford University Press.

[55] Alston, W.P. (2006). Beyond "Justification": Dimensions of Epistemic Evaluation, Ithaca, NY: Cornell University Press.

[56] Junger, E. (1934). On Pain, New York: Telos Press. (2008).

[57] Améry, J. (1980). At the Mind's Limits: Contemplations by a Survivor on Auschwitz and its Realities, Bloomington and Indianapolis: Indiana University Press.

[58] Sen, A. (1993). Capability and well-being. In: The Quality of Life, (Eds. M. Nussbaum & A. Sen), pp. 30-53. Oxford: Clarendon Press.

[59] Hart, S.L. (1971). Axiology--theory of values. *Philosophy and Phenomenological Research* 32 (1), 29-41.

[60] Rescher, N. (2010). Axiogenesis: An Essay in Metaphysical Optimalism, Lanham, Maryland: Lexington Books.

[61] Sagoff, M. (1986). Values and Preferences. *Ethics* 96 (2), 301-316.

[62] Flanagan, O., Sarkissian, H. & Wong, D. (2008). Naturalizing ethics. The evolution of morality: adaptations and innateness. In: Moral Psychology (Vol 1), (Ed. W. Sinnott-Armstrong), pp. 1-25. Cambridge, Mass: MIT Press.

[63] Dewey, J. (1948). Reconstruction in Philosophy. Boston: Beacon Press.

[64] Dewey, J. (1941). Propositions, Warranted Assertibility, and Truth. *The Journal of Philosophy* 38 (7), 169-186.

[65] Connolly, W.E. (1974). Terms of Political Discourse. Lexington, Mass.: D C Heath.

[66] Gallie, W.B. (1956). Essentially Contested Concepts. *Proceedings of the Aristotelian Society* 56, 167-198.

[67] Gallie, W.B. (1956). Art as an Essentially Contested Concept. *The Philosophical Quarterly* 6 (23), 97-114.

[68] Gray, J. (1978). On Liberty, Liberalism and Essential Contestability. *British Journal of Political Science* 8 (4), 385-402.

[69] MacIntyre, A. (1973). The Essential Contestability of Some Social Concepts. *Ethics* 84 (1), 1-9.

[70] Nussbaum, M. (1995). Non-relative virtues: An Aristotelian approach. In: The Quality of Life, (Eds. M. Nussbaum & A. Sen), pp. 242-269. Oxford: Clarendon Press.

[71] Nussbaum, M.C. (1988). Non-Relative Virtues: An Aristotelian Approach. *Midwest Studies In Philosophy* 13 (1), 32-53.

[72] Daniels, N. (1980). Reflective equilibrium and Archimedian points. *Canadian Journal of Philosophy* 10, 83-103.

[73] Daniels, N. (1996). Justice and Justification: Reflective Equilibrium in Theory and Practice. Cambridge: Cambridge University Press.

[74] DePaul, M.R. (2001). Balance and Refinement: Beyond Coherence Methods of Moral Inquiry. London: Routledge.

[75] Little, M. (2000). Ethonomics - the ethics of the unaffordable. *Archives of Surgery* 135, 17-21.

[76] Mann, G.G. (1988). Ethonomics: An Enquiry into the Nature and Causes of the Wealth of Individuals. Ascot, Berkshire: Springwood Books.

[77] Alison, F., Hodkinson, H., Hodkinson, P. & Unwin, L. (2005). Learning as Peripheral Participation in Communities of Practice: A Reassessment of Key Concepts in Workplace Learning. *British Educational Research Journal* 31 (1), 49-68.

[78] Gabbay, J., le May, A., Jefferson, H., Web, D., Lovelock, R., Powell, J. & Lathlean, J. (2003). A case study of knowledge-management in multi-agency consumer-informed 'communities of practice': implications for evidence-based policy development in health and social services. *Health* 7 (3), 283-310.

[79] Wenger, E. (1998). Communities of Practice: Learning, Meaning and Identity. Cambridge: Cambridge University Press.