

On 4 June 1921 Sir James Mackenzie defended his thesis, *The Opportunities of the General Practitioner are Essential for the Investigation of Disease and the Progress of Medicine*, in the *British Medical Journal*. Just under a century later, there is still a message for all researchers in primary care which resonates. A short précis of a full commentary from the *International Journal of Epidemiology* is given below.<sup>1</sup>

### INTRODUCTION

Sir James Mackenzie (1852–1925) is known as ‘the father of general practice-based research’.<sup>2</sup> From humble origins in rural Perthshire, Mackenzie overcame early social and educational hurdles to study medicine in Edinburgh, then pursued a career in general practice in Burnley. He initiated the systematic observation of his patients that led to his stellar research career, including an international reputation in cardiology, discovery of novel and important insights into heart rhythms, the use of digitalis, and a knighthood. At the height of his career in London, he returned to establish the Institute for Clinical Research in St Andrews at the age of 64. It was there that Mackenzie brought together all the GPs working in the town, and encouraged the systematic recording of routine observations and the development of record-keeping systems. By working with local colleagues in primary care, he made his real key insight: that systematic observation and recording of symptoms and signs in a whole population could provide essential information on the epidemiology, prognosis, and mechanisms of disease. Common themes and lessons still echo from his paper,<sup>3</sup> highlighting issues that were as important and controversial in 1921 as they are today.

### LESSONS FROM MACKENZIE

#### Primary care research

At the start of Mackenzie’s career in 1879, general practice was seen as, ‘*The lowest place in the [medical] profession*’.<sup>4</sup> Since then, the discipline has grown, and academic general practice in the UK has made substantial contributions to university teaching and research [as described in The Mackenzie Report<sup>5</sup>], matching those of other university disciplines.<sup>6</sup> Mackenzie regretted the compartmentalising of medical research into specialties and

its effect of narrowing the field of vision of the researchers.<sup>7</sup> He saw basic and laboratory science (particularly pathology) as subservient to clinical science, with its main purpose being to identify the biological mechanisms behind clinical observations, rather than to drive clinical practice.<sup>7</sup> This principle drove him to seek the true prognostic nature of signs (such as heart murmurs), resulting in the reversal of the practice of consigning every individual with a heart murmur as an invalid. The strength of an open-minded generalist approach, in collaboration with multiple subject-specific experts, is perhaps the most important lesson for us today.

#### Prevention as the ‘highest aim’ of medical research

While research effort in Mackenzie’s era focused on the management of ‘attributed disease’ (signs presumed to be associated with pathology observed post-mortem), he believed that ‘the prevention of diseases which are common among the people of the country’<sup>3</sup> should be the main focus of research. He was hampered by two main factors: it was unknown which were the common diseases (because population-based research had not been undertaken, and current knowledge was based on information from specialist centres); and the precursors of serious disease were also unknown. The answer to both of these questions could best come from general practice by documenting and following up early signs to establish their prognostic significance. This focus on symptoms rather than established disease was derided in his day. Mackenzie was concerned with his inability to give accurate prognoses to common presentations, and noted that this also hampered good medical care, disease prevention, and knowing whether and when to intervene. Mackenzie’s foresight remains a major pursuit in today’s academic general practice community.<sup>8,9</sup> Without an understanding of which symptoms place

the greatest burden on the health services, irrespective of serious disease, it is impossible to provide adequate resources to deal with them.<sup>10</sup>

#### The importance of observation in medical research

In his 1921 paper, Mackenzie asserted the need to base medical practice in research derived from observation (especially history taking). This is a warning to us in the modern era, where high volumes of clinical data and technologies such as high-throughput genotyping or expensive imaging techniques often predominate (at least as measured by research grant funding). There is little point in working with high quality genotype data if the quality of the phenotype derived from observation is weak.<sup>11</sup> Careful observation remains central to clinical, epidemiological, and translational research. Increasingly, this extends beyond quantification to the use of parallel qualitative methods<sup>12</sup> aimed at applying the results of studies to the individual in the consulting room, who often differ in important ways from those studied in clinical trials, and whose views of an intervention’s relevance and acceptability will be critical to real-world impact.<sup>13–15</sup>

#### The importance of medical records in research

Medical records need to be systematic and consistent, to allow subsequent review and analysis. Mackenzie saw the chief purpose of keeping records as being ‘to lay the basis of prognosis’<sup>3</sup> and to identify, in groups of patients, patterns of signs, symptoms, and other factors associated with eventual outcomes. In modern practice, this has evolved into the amalgamation of large datasets allowing us to generate sample sizes of sufficient power to detect important but rare outcomes, or important but small risks, or extreme phenotype analyses<sup>16,17</sup> with due consideration of the ethical and legal aspects, including data sharing and

---

*“[Mackenzie] believed that ‘the prevention of diseases which are common among the people of the country’ should be the main focus of research.”*

---

“... we should begin our research, as Mackenzie did, by asking what clinical questions need to be answered, rather than what use we can find for the available technology.”

access, and respect for the views and rights of the individual patients who have contributed the data.

### The role of basing research paradigms on current trends

Finally, we can learn from Mackenzie's scepticism of restricting one's view of health and illness to that dictated by current scientific trends or paradigms. In his day he rejected, with some success, theories of disease that were based only on histopathological appearances of organs after death. Current medical research is focused on a molecular understanding of physiology and disease, centring around genomics, proteomics, and other 'omics'.<sup>18</sup> There is undoubtedly much to be gained from an understanding of humans and our diseases at a molecular level but we need to balance this with an integrational perspective, recognising that combinations of conditions have complex effects in individuals.<sup>19</sup>

### CONCLUSION

Through this pioneering approach, Mackenzie demonstrated the importance of epidemiology in non-infectious disease, the role of high-quality routine records in this endeavour, and the importance of the generalist in researching diseases that were (and still are) often considered to be in the domain of the specialist. The generalist approach, so crucial in integrating and implementing findings from diverse scientific sources, remains in danger of being swamped by specialist, single-field studies. Even today, medical research funding bodies often focus their resources on the development of specific interventions, rather than on disease prevention or on understanding how to apply effective interventions in real-world populations with high levels of comorbidity.<sup>20</sup> We have much to learn from Mackenzie's vision and persistence. Perhaps most importantly, we should begin our research, as Mackenzie did, by asking what clinical questions need to be answered, rather than what use we can find for the available technology.

#### Oliver van Hecke,

Clinical Academic Fellow, Medical Research Institute, University of Dundee, Tayside Centre for General Practice, Dundee.

#### Blair H Smith,

Professor of Population Science, Medical Research Institute, University of Dundee, Tayside Centre for General Practice, Dundee.

#### Frank M Sullivan,

Professor of General Practice, Medical Research Institute, University of Dundee, Tayside Centre for General Practice, Dundee.

### REFERENCES

- Smith BH, Guthrie B, Sullivan FM, Morris AD. Commentary: A thesis that still warrants defence and promotion. *Int J Epidemiol* 2012; **41**(6): 1518–1522. DOI: 10.1093/ije/dys178.
- Macnaughton J. The St Andrews Institute for clinical research: an early experiment in collaboration. *Med Hist* 2002; **46**(4): 549–568.
- Mackenzie J. A defence of the thesis that 'The opportunities of the general practitioner are essential for the investigation of disease and the progress of medicine'. *Br Med J* 1921; **1**(3153): 797–804.
- McNair Wilson R. *The beloved physician, Sir James Mackenzie*. London: John Murray, 1926.
- Howie JGR, Hannay DR, Stevenson JSK. The Mackenzie Report: general practice in the medical schools of the UK. *Br Med J* 1986; **292**: 1567–1571.
- Howie JG. Academic general practice: reflections on a 60-year journey. *Br J Gen Pract* 2010; **60**(577): 620–623.
- Mackenzie J. *The future of medicine*. London: Henry Frowde, Hodder and Stoughton, 1919.
- Jones R, Latinovic R, Charlton J, Gulliford MC. Alarm symptoms in early diagnosis of cancer in primary care: cohort study using General Practice Research Database. *BMJ* 2007; **334**(7602): 1040.
- Hippisley-Cox J, Coupland C. Identifying patients with suspected colorectal cancer in primary care: derivation and validation of an algorithm. *Br J Gen Pract* 2012; DOI: 10.3399/bjgp12X616346.
- Elliott AM, McAteer A, Hannaford PC. Revisiting the symptom iceberg in today's primary care: results from a UK population survey. *BMC Fam Pract* 2011; **12**: 16.
- Wong MY, Day NE, Luan JA, et al. The detection of gene-environment interaction for continuous traits: should we deal with measurement error by bigger studies or better measurement? *Int J Epidemiol* 2003; **32**(1): 51–57.
- Medical Research Council. *A framework for the development and evaluation of RCTs for complex interventions to improve health 2000*. London: MRC, 2000. <http://www.mrc.ac.uk/Utilities/Documentrecord/index.htm?d=MRC003372> [accessed 4 Feb 2012].
- Van Spall HGC, Toren A, Kiss A, Fowler RA. Eligibility criteria of randomized controlled trials published in high-impact general medical journals: a systematic sampling review. *JAMA* 2007; **297**(11): 1233–1240.
- Masoudi FA, Havranek EP, Wolfe P, et al. Most hospitalized older persons do not meet the enrollment criteria for clinical trials in heart failure. *Am Heart J* 2003; **146**(2): 250–257.
- Travers J, Marsh S, Caldwell B, et al. External validity of randomized controlled trials in COPD. *Respir Med* 2007; **101**(6): 1313–1320.
- McCarty CA, Chisholm RL, Chute CG, et al. eMERGE Team. The eMERGE Network: A consortium of biorepositories linked to electronic medical records data for conducting genomic studies. *BMC Med Genomics* 2011; **4**: 13.
- Biobanking and Biomolecular Resources Research Infrastructure. <http://www.bbMRI.eu> [accessed 4 Feb 2013].
- Ioannidis JP. Expectations, validity, and reality in omics. *J Clin Epidemiol* 2010; **63**(9): 945–949.
- Tugwell P, Knottnerus JA, Idzerda L. Clinical epidemiologists and EBM proponents need to be able to critically appraise 'Omics,' the fatal flaw of Personalized Medicine. *Clin Epidemiol* 2010; **63**(9): 943–44.
- Barnett K, Mercer S, Norbury M, et al. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. *Lancet* 2012; **380**(9836): 37–43.

### ADDRESS FOR CORRESPONDENCE

#### Blair H Smith

Medical Research Institute, University of Dundee, Tayside Centre for General Practice, Mackenzie Building, Kirsty Semple Way, Dundee, DD2 4BF, UK.

E-mail: b.h.smith@dundee.ac.uk

### Provenance

Freely submitted; not externally peer reviewed.

### Acknowledgement

This article is a shortened version of an article that appeared in the *International Journal of Epidemiology*<sup>1</sup> and is reproduced here with permission from Oxford University Press.

DOI: 10.3399/bjgp13X664423