The Art and Science of Personalising Care with Older People with Diabetes

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Foreword

I have known Professor Trisha Dunning for more than 20 years but met face to face with her for the first time in Vancouver at an International Diabetes Federation (IDF) meeting. We were sharing the platform for a symposium on the very substance of this book, *diabetes in older people*! It was then that I appreciated how compassionate an individual she is about wishing to improve the lot of this often vulnerable and neglected population of people with diabetes. She introduced the idea that we, as a caring group of professionals, must listen more to what our patients are saying, take a greater interest in each of their life histories, and try to 'personalise' care at every opportunity. Her use of case histories was memorable. Her talk not surprisingly was received best out of all three speakers! I realised we shared similar concerns about the inadequacies and inequity of diabetes care of older people and since then we have been actively collaborating—which has been a privilege and honour for me!

There are few people in the world of diabetes care who have won the admiration and respect afforded to Trisha. She has been an inspirational leader for nearly two decades, always pushing the agenda for change and improvement in care in those highly important and challenging areas that still receive less attention than they warrant such as care home diabetes, end of life diabetes care, and pharmacovigilance.

Trisha is already an accomplished academic, researcher, and writer of textbooks, and so you might think that the development of this new book might have seemed straightforward for her. This thought was never in her mind, however, because she knew it had to be different from other books available in this area, as well as thought provoking, being able to motivate health professionals and others to go out there and make a difference to the lives of their patients, and of real clinical utility—this book accomplishes all of these aims.

The book comprises ten chapters, half of which are written by Trisha and the other five written by accomplished writers and scientists, most of whom are active locally and therefore on the same wavelength for creating this exciting new book. The term 'personalised care' is often taken for granted and may be considered 'stereotyped'! However, this book unlocks the real meaning of this term and how it should be applied to modern diabetes care of older people in our society. The book explains what the key aims of care should be, how shared decision-making and holistic care are fundamental to achieve meaningful outcomes, and how clinical guidelines can assist in personalising care but at the same time stressing how this

concept must be an essential part of future guideline developments. With chapters on technology, life transitions, nutritional therapy, the challenges of dementia, and future research directions, the book is complete and still remarkably concise. As the title of the book implies, both artistic merit and scientific rigour underpin the principal drive that this book has required.

You should read this book if you want to enhance your own clinical experience in managing the aged individual with diabetes as the process of 'personalisation' will reveal how complex an illness it can be and how routine care has its major shortcomings. It will also stimulate your interest to recognise that many older people do indeed have unique life experiences that will affect their attitudes and responses to your treatment plans. By reading the book, you will be able to motivate others, perhaps members of your interdisciplinary team, to take on board the principles embodied in this short treatise that define and justify the importance of personalised care.

Birmingham, UK Alan Sinclair, M.Sc., M.D., F.R.C.P.

Preface

The wisdom and experience of older people is a resource of inestimable worth. Recognising and treasuring the contributions of older people is essential to the long term flourishing of any society.

Daisaku Ikeda (2007)

A colleague asked: *Where did this book come from?,* which caused me to reflect on where and how did originate—besides the fact I am an older person with a vested interest in advocating for the care of older people with diabetes.

My respect for older people and love of stories began in my early childhood. We lived on an isolated bush property when I was very young. There was no electricity, street lights, telephones, or close neighbours. Dad grew most of our fruit and vegetables and we made a long trek into town for groceries and other necessities once a month. When I turned five I went to live with my Grandma and Pop so I could go to school. Grandma and Pop moved to town from their farm a few years before. Pop developed dementia shortly after they moved and often wandered down the street and stood beneath the street lights quietly watching the 'fairies' (insects) and rainbows around the light. It was my job to bring him home.

Grandma was a stoical, hardworking, no nonsense woman who had some great sayings that influenced who I am: for example *A whistling woman is good to neither God nor man.* I never had the courage to ask her what a whistling woman *was* good for! She was adamant that ladies *do not wear dangling earrings—other kinds of women, like gypsies, do that.* I cannot whistle, and I have never worn dangling earrings. I am not sure what that makes me good for, or whether I am a lady!

One day Grandma was ill and unable to care for me for a few weeks. I went to live with her sister, my Great Aunt Lizzie and my Great Grandma (Nana) in Aunt Lizzie's wonderful house and cottage garden. Aunt Lizzie taught me to cook and enhanced my love of gardening. Both women inadvertently introduced me to the fact that old people die.

Nana was bitten by a snake while she was picking thistles for her canaries. Aunt Lizzie found her several hours later 'dozing in the sun'. Nana often dosed in the sun so I did not realise she died, until much later—she was dozing and was taken away. Aunt Lizzie died in hospital 2 years later. My father would not let me visit her because it would upset me to '*see her like that'*. I still do not know '*what like that'* actually meant, and I still carry unresolved grief at not being able to say goodbye to

her. These old ladies and my Mum shared their accumulated wisdom and taught me compassion and respect.

When I started nursing I encountered vulnerable older people reliant on care to survive. I nursed older people with dementia who were often violent or verbally abusive—a stark contrast to the self-caring, independent women in my family and my docile Pop with dementia. There were no aged care homes or supported accommodation in the town, so dependent older people lived in the hospital if their families were not able to care for them.

Diabetes was rare in those days, or perhaps unrecognised: some people with cardiovascular disease and stroke probably also had diabetes. We had few medicines to treat diabetes apart from Metformin, Glibenclamide, and animal insulins that were administered using large glass syringes and long needles that had to be sharpened and sterilised after each use. There were no blood glucose meters. Initially we tested urine for glucose using Fehling's solution and eventually Clinitest tablets. There was no test for ketones, except the smell of new mown hay. Diabetes self-care was unheard of.

I learned a lot about diabetes and witnessed many advances in diabetes care over the years that improved outcomes, quality of life, and life expectancy for people with diabetes. These changes improved diabetes care and led to diabetes self-management programmes. They also increased self-care and treatment burdens that added to the disease and medicine burden for older people with functional and cognitive changes that lower their resilience to stressors.

Most of my research over the past 10 years concerned care of older people with diabetes and was undertaken *with* advisory groups of older people with diabetes and their families, whose wisdom and life and diabetes experience, which they so generously share, enhance my research and the applicability of the findings to diabetes clinical practice.

These factors are the impetus for and origin of my belief in person-centred care: the core concept underpinning the book. The idea for the book emerged following a conversation with Nathalie Lhorset-Poulain from Springer, after a workshop I delivered with colleagues at the 2015 International Diabetes Federation Congress in Vancouver. I am very grateful to her for her interest and support.

The Preface is not the ramblings of a garrulous old woman. There are important messages in the snippets of my story shared in this Preface. The story is an important reminder that all older people were once young. They are highly individual. They all have stories. They all have explanatory models for many things, including diabetes. We can only truly understand the *person* and plan care *with* them if we look beyond their age and their diabetes and see the person. We can only see the person if we are prepared to hear their stories.

Reading literature forces readers to *fill in gaps and search for meanings among a spectrum of possible meanings* (Bruner 1986). One reason Drs. Cookson and Holmes insisted we read literary stories as well as nursing/medical texts was to enhance our capacity to relate to the people we cared for and their social situation.

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Geelong, Australia Trisha Dunning

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Many people inspired and contributed to this book. I acknowledge two general practitioners, Dr. Charles Cookson and Dr. Charles Holmes, who were mentors and tutors over the 4 years of my nursing training. They taught at teachable moments and not strictly according to the order of curriculum. They took us on home visits and to post-mortems; they insisted we read novels as well as nursing and medical texts. Their supportive teaching style that incorporated art and science was ahead of its time and much of what I learned is reflected in the book.

More recently, colleagues from Barwon Health and Deakin University, Dr. Mark Kennedy who often acts as a sounding board for my ideas, and international colleagues, especially Professor Alan Sinclair, colleague and friend for over 10 years, influenced this book—although they might not know it!

I am grateful to my co-authors, Bodil, Mark, Sital, David, and Natalie, for agreeing to contribute to the book and for writing such great chapters. Their expertise adds depth and value to the book.

Most of all, I acknowledge the many people with diabetes who taught me so much about living with diabetes by sharing their experiences, stories, and explanatory models over the years. I love working with advisory groups of people with diabetes on my research projects; their advice is invaluable.

I am grateful to the Publisher, Springer, especially Nathalie Lhorset-Poulain, who initiated the book, and Abha Krishnan, who monitored the book production.

I owe a very big thank you to Professor Alan Sinclair for writing the foreword to this book and for his friendship and advice.

I acknowledge Indigenous Cultures whose knowledge was largely transmitted orally as stories/songlines. Indigenous people were able to commit a vast amount of information about their culture, practices, and the land to memory. Survival depended on knowing where food and water could be obtained as well as custodianship of the land. Australian Indigenous songlines, stored in memory and passed from generation-to-generation, extend across the country. The method of remembering, recently daubed 'the memory code', is being adopted by teachers in some Australian schools. I particularly acknowledge the Wauthaurang people, on whose land most of this book was written.

My very special thanks go to my husband, John, for his unfailing support—he is the wind beneath my wings. I received a great deal of 'help' from our two beautiful West Highland White Terriers, Flora Weadora and MacBeth MacDunning. I could

not have written the book without Flora's help with word processing, her cuddles, and her attentive listening (Like a Dog) as I read the book out loud. MacBeth, a frail old man who slept a lot and kept my feet warm during the writing process, died 2 weeks before the book was submitted to the publisher. He taught me a lot about cherishing and caring for older people.

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[A volunteer in an aged care home for veterans] spent two hours listening to one of the ladies on the lawn talk about working for Ziegfeld. Afterward the woman apologized profoundly for 'boring you with my stories.' Vivian could have listened for two more hours and not realized time going by. These people were not just old veterans. They were living history books dismissed by almost everyone stupid enough to think they were not worth reading.

(Callahan 2015)

Key Points

- Older people are individuals: they are not defined by their age or their diabetes.
- Ageing is unique to every individual. Chronological age is not a good indicator of health status or care needs.
- Health status in older age is influenced by genetics and lifestyle behaviours in younger age.
- Increasing age is a risk factor for diabetes. Most older people have type 2 diabetes but people with type 1 diabetes survive to older age and type 1 can be first diagnosed in older age.
- It is essential to personalise care *with* the individual and to use a proactive, risk identification and minimise approach.

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1.1 Introduction

This chapter outlines older age and diabetes to set the context for the other chapters in the book. Detailed information about diabetes pathophysiology and management can be found in the guidelines, position statements and reference texts listed in the recommended reading at the end of the chapter.

The global population is ageing and the post-World War 2 generation, the 'Baby Boomers', have very different expectations, preferences and values about their older age than previous generations. The Australian Centre for Social Innovation (tacsi) (2016) identified the following 'big themes' from interviews with baby boomers. They:

- Believe they need to keep working to pay the bills.
- Want to stay in their own homes and grow old where they are known and where their connections are.
- Have very different expectations of health services, including aged care services.
- Feel it is important to 'keep young in the mind'.
- Do not want 'currently available' aged care services, especially ending up in an aged care home, but realise they may need help when they can no longer self-care.

These are not particularly new findings. Lansky identified similar themes/concerns in 1998 in the USA. These were to:

- Be treated with respect.
- Understand what they are told.
- Have access to the health services and providers they need.
- Stay healthy as long as possible, which included having access to education, preventative services and early diagnosis of disease.
- Recover from illnesses and regain normal functioning.
- Live with their illness if they have a chronic disease.
- Be able to cope with changing needs and death and disability in their family by treating pain and suffering.

These findings suggest older people have a basically realistic but positive attitude to their ageing, which differs from the National Ageing Research Institute (NARI) report (2017). The NARI report suggested many countries use a 'doom and gloom', pervasively negative ageing narratives and suggested the language should be changed to positive, inclusive language because if people are consistently given negative messages about older age they begin to believe they have no value. NARI indicate positive messages are particularly important to the 'new middle age' (50–75 years) who have increasing life expectancy, the rapidly changing global social and economic climates.

Many countries have adopted various 'ageing' strategies/frameworks to support people as they grow older and help them 'age in place' in their own homes or in the community for as long as possible. These frameworks include:

- Active ageing
- Healthy ageing
- Successful ageing
- Reablement/restorative care

Most ageing frameworks and strategies are based on the need to support physical and cognitive function as well as economic imperatives, social needs, and the person's capacity to engage with life and other people. New technology such as the five good friends app, Facebook and Skype help older people remain connected (see Chap. 9).

It is difficult to define 'successful ageing'. One size does not fit every older person. Therefore, it is important to ask the individual what 'successful ageing' means to them; or better still, not use the term, given the alternative, 'failed ageing', is very negative!

Older people develop creative ways to remain independent and preserve their dignity; for example, friends living independently on the same site with some shared facilities such as gardens. Despite these positive initiatives, the demand for formal home care, aged care home services is increasing in most countries due to the ageing population and societal changes such as family structure and lifestyle that affect family caregiving capacity (Weng and Landes 2017). Thus, care is often provided by lay 'health aids'.

In addition, many countries are culturally and linguistically diverse, which can lead to communication, engagement and connection issues. Different individuals and cultures have different explanatory models for health, care, ageing and diabetes. These diverse similarities and differences lead to the question: who are older people?

1.2 Older People

'Older' age is commonly defined as older than age 65 (World Health Organisation (WHO) 2002, 2017). Some older people, including older health professionals, indicate 'the older one gets, the older old is', and state 'you are only as old as you feel', as the following anecdote shows:

I am going to my writing group, now.
OK. Who will be there?
Mostly older people—retired teachers.
So, one more older person will join them—you!!

Chronological age is not a good indicator of personhood, health status or function and it is not a useful basis on which to plan care. Older people are highly individual; therefore it is essential to consider each person's physical, mental and spiritual, functional status and life expectancy when planning care (Dunning et al. 2013; IDF 2013; Sinclair et al. 2014). Spirituality is an important life dimension and is concerned with finding meaning and purpose in life and the events people encounter throughout their lives (see Chap. 7). Key dimensions of spirituality include relationships with self and others. It may or may not include religion.

Each older person is an individual and has unique life experiences, inherited characteristics and social circumstances. Older people have sexual health needs, which are often not addressed. Some develop sexually transmitted disease, some are homeless, some are abused, and some are alcoholics. Some travel a lot. Most have a significant body of accumulated wisdom and learned patterns associated with their life, their diabetes and self-care that help them cope with their diabetes, life and other health problems in older age.

However, changed circumstances and uncertainty can cause stress and increase cognitive load, which affect self-care, pattern recognition, problem-solving and self-confidence, especially during illnesses. Importantly, older individual's unique values, preferences, life goals and their opinions must be identified as part of comprehensive assessments and respected; otherwise it is impossible to develop personalised care plans.

It is essential to tailor care to suit the individual (personalised care). In order to personalise care, professionals must understand ageing, diabetes and their cumulative effects on physical and cognitive function, and have impeccable communication skills and cultivate the art of eliciting older people's stories to collaboratively develop care plans *with* the older individual, and sometimes their family carers (see Chaps. 2 and 3). Personalised care must encompass general health and social care as well as diabetes care and be regularly reviewed. People's stories need to be viewed in the context of their whole life.

1.3 Ageism and Stereotyping

Ageist attitudes and stereotypical, discriminatory language is common in the general population, the media and in health care. Ageism refers to discrimination because of older age. The focus is often on the negative aspects of ageing, less often on the positive aspects such as wisdom and patience. Stereotyping occurs when characteristics associated with age are applied to all older people (Butler 1969, 1980). NARI (2017) highlighted the need to use positive rather than negative 'old age' language.

Negative ageism is disrespectful to the individual and their family and has negative effects on older people's self-esteem and health outcomes (Richeson and Shelton 2006). Significantly, it is not consistent with personalised care or shared decision-making. Research shows 'elderspeak' leads to cognitively impaired older people adopting resistive behaviours during care provision. Elderspeak refers to babytake and using words such as 'darl', 'lovey' and other depersonalising and demeaning language. When elderspeak was modified to more respectful language, resistive behaviour was significantly reduced (REF).

1.4 What Is 'Old Age?'

> *Old age is not a status we choose to become; it is a status that we inherit simply by the virtue of living, not dying.* (Holstein 2006)

As indicated, 'old age' generally refers to people older than age 65 (WHO 2002, 2017). Chronological age refers to the linear passage of time from birth onwards and is understood as *chronos* time. *Chronos* time is quantitative and refers to duration of time (Mc Fadden and Thibault 2001). It is useful to maintain schedules, understand disease progression and plan for future care. However, chronological age does not necessarily reflect an individual's biological age, their functional capacity or their perceived age, and is not the best indicator of their care needs or their potential lifespan.

Another time dimension, *kairos* time, refers to opportunity or a suitable time to take action (Mc Fadden and Thibault 2001). That is, 'in the moment time' and 'decision time' (*seize the day*). *Kairos* time is qualitative and is experienced in the moment when people are engaged in immediate experiences, often when decisive action is needed. *Kairos* timed is meaningful for individuals and their connections (Mc Fadden and Thibault 2001). There are many *kairos* moments in an individual's life journey besides those associated with diabetes.

An individual's life journey moves through both dimensions of time. Older people are often focused on maintaining meaning and purpose in their life, being connected and maintaining hope. They are important to quality of life and survival, in combination with 'a healthy lifestyle'.

Many older people, including those with diabetes, are self-caring and live in the community. Some require various degrees of support to undertake Activities of Daily Living (ADL) and/or Instrumental Activities of Daily Living (IADL). A great deal of support is provided by family members. Between 25 and 30% of older people living in care homes have diabetes (Sinclair et al. 2001; Anderson 2014) and a further 25% are undiagnosed but at risk of diabetes (Dunning et al. 2013; Anderson 2014) and may not receive adequate treatment, which could affect well-being, comfort and quality of life.

The combination of diabetes, comorbidities and dementia lead to the individual needing increasingly complex care. Carers need to be able to recognise and manage changes such as hypo- and hyperglycaemia and their effects on well-being, cognition and self-care capacity.

1.5 Factors That Influence Longevity

Life expectancy has increased due to environmental improvements in food and water, control of communicable disease, and technological advances in medical care that enable a range of life-limiting illnesses, including cardiovascular disease and cancer, to be effectively managed for long periods of time. Conversely, technology also contributed to the increase in obesity-related diseases that reduce life expectancy, e.g. by reducing the amount of physical activity needed to catch and prepare food.

Box 1.1 outlines the recommendations for healthy living proposed by ancient healers and philosophers. These recommendations still apply today. Interestingly, Aretaeus, who practised medicine in 120 AD, wrote,

The condition [diabetes] *is fortunately rare but short will be the life of the man in whom the disease is fully developed.* (King et al. 1999)

Box 1.1: Recommendations About Old Age in Ancient Cultures

Modern ageing research largely supports the following recommendations of ancient philosopher and healers such as Cicero, Plato, Solon, and Hippocrates (Dunning 2017). Their recommendations still make common and 'clinical' sense today.

- Growing older is normal and inevitable: not a disease.
- Individuals age at different rates and the speed at which an individual and their individual tissues and organs age depends on humours. These 'humours', hot, cold, dry and wet, influence body function. If the humours became unbalanced, ill health occurs. Modern genomics, epigenetics and other 'nomics' may be a modern way to explain ancient 'balance theories'.
- Older people were encouraged to plan for their older age while they were 'young', including planning for their end of life. Age 50 was old, until relatively recently and is still old in some underprivileged societies. 'Old age' as now defines as older than 65 years (WHO 2002). Many older people do not regard themselves as old (Richeson and Shelton 2006).
- A healthy diet and regular exercise contribute to a healthy old age.
- Learning something new every day throughout life is essential to brain health.
- People were expected to contribute to society. Today many older people contribute to society and the economy through paid and volunteer work, including caring for older family members.
- Society has a collective and individual responsibility to care for its older people.

Diabetes is extremely common today, despite primary prevention strategies and knowledge about the associated devastating complications. Consequently, the second statement is as true today as it was in 120 AD. Most people with diabetes develop complications that reduce life expectancy. Type 2 diabetes is a progressive, incurable disease and complications are present in up to 50% of people with type 2 diabetes, even at the time of diagnosis (King et al. 1999).

Ageing is a gradual process. Age is the biggest risk factor for some of the most debilitating diseases known and feared today such as neurodegenerative diseases, Alzheimer's disease, cardiovascular disease, and inflammatory and metabolic diseases such as diabetes and cancer. Most of these comorbidities are associated with diabetes. Older people often have 3–5 coexisting comorbidities that need to be co-managed. Some studies focus on understanding and preventing/curing ageing as a

way to reverse the pathogenesis of several diseases: for example, identifying the predictors of physiological age and developing new medicines to that target the physiological processes associated with ageing.

Ageing and longevity are moderated by genetic and non-genetic factors and many biological and biochemical mechanisms. Genetic factors account for 25% of the variation in longevity (Passarino et al. 2016). Studies into the genetic and molecular basis of ageing identified several genes associated with maintaining cells and basic cell metabolism that affect individual variation in the ageing phenotype.

Some genes are protective and confer greater functional reserves. Genes involved in lipoprotein metabolism, especially APOE, cardiovascular homeostasis, immunity and inflammation play a role in ageing, age-related disorders and longevity (Schachtner et al. 1994). Ageing is also associated with mitochondrial dysfunction and changes in metabolic function (Lopez-Otin et al. 2013; Petersen et al. 2004).

Alzheimer's disease is one of the most feared diseases associated with old age. People with T2DM are at risk of cognitive impairment, structural changes in the brain and brain atrophy (Rizzo et al. 2010; Launer et al. 2011).The pathogenesis of Alzheimer's disease commences decades before the onset of symptoms present. People who carry the APOE E4 allele are at increased risk of Alzheimer's disease while the E2 allele has a protective effect (Sun et al. 2012). Recently, HealthWatch, a nutritional genomics company that studies gene-diet disease interactions, launched HealthWatch 360 (www.gbhealthwatch.com/healthwatch360-app/) to provide nutrition advice to help people manage their Alzheimer's risk.

HealthWatch 360 also offers people the opportunity of finding out their genetic risk of Alzheimer's based on their APOE genotype. APOE e4 has high sensitivity and high positive predictive value for the diagnosis of Alzheimer's disease but a low negative predictive value and specificity. APOE genotyping may help diagnose the condition, especially when people have atypical signs or early age onset of dementia (Sun et al. 2012). Chapter 8 discusses caring for older people with cognitive impairment and dementia in more detail.

Imagine how Alice, a 50-year-old Harvard linguistics professor recently diagnosed with early onset Alzheimer's disease, felt when she said:

> *I can see the words hanging in front of me and I can't reach them, and I don't know who I am, and I don't know what I'm going to lose next.* (Genova 2009)

Chronic inflammation has a negative impact on tissues and organs and is a consequence of glucose variability as well as chronic hyperglycaemia (Kovalchev and Cobelli 2016). Glucose variability refers to excursions/fluctuations between high and low blood glucose. Fluctuations can be measure by time and by amplitude. The mean amplitude of the glucose excursions (MAGE) is an important determinant of overall metabolic status and risk of complications.

MAGE is significantly associated Mini Mental State Examination (MMSE) scores and composite scores of cognition, independently of age, gender, Body Mass

Index (BMI), waist-hip ratio, medicines and physical activity, which highlights the need to consider MAGE as well as HbA1c when deciding management strategies. Continuous glucose monitoring enables glucose variations to be measured in real time and is becoming used more frequently in diabetes self-care and in acute care settings such as intensive care units.

Low grade inflammation, after age, is the most important determinant of capability, cognition and survival (Ari et al. 2015). Recent research suggests preventing hyperglycaemia is important in older people. It is not a benign condition. The challenge is to balance the adverse consequences of hyperglycaemia with the devastating effects of hypoglycaemia, which includes falls and mortality risk.

Studies show genes associated with the pathways involved in nutrient signalling and regulating transcription factors such as IGF-1/insulin axis and TOR modulate longevity (Junnila et al. 2013). Animal studies show that molecules that modulate these pathways prevent a range of age-related diseases such as cancer, cardiovascular disease, osteoporosis and T2DM. Research is underway to determine whether medicines can modulate these pathways and slow human ageing, in particular, activating a key sirtuin, SIRTI (Hubbard and Sinclair 2014). Sirtuin is one of the silent information regulator genes that promote longevity in many species and mediate the beneficial effects of restricting calories.

More recently, epigenetic studies show that epigenetic changes modulated by genetic inheritance and lifestyle are sensitive to ageing and could be a biomarker of ageing or influence the ageing and/or rate and quality of the ageing process. Horvath et al. formulated a mathematical model to predict an individual's chronological age from the methylation levels of several body cells and tissues based on their work on the Epigenome-wide Association Studies.

The so-called epigenetic clock or Horvath's clock may be an accurate biomarker of age, superior to estimates based on telomere length and can predict all-cause mortality after adjusting for traditional risk factors (Horvath 2013). Interestingly, studies in supercentenarians show the brain and muscle are the youngest body tissues in these individuals (Wagner 2017). It is not clear how widely the epigenetic clock is applied to prognostication outside research and its relevance to clinical care or palliative and end of life care planning is unclear.

Genes and small molecules involved in maintaining DNA repair (Debrabant et al. 2014), conserving telomeres (Sorensen et al. 2012), the heat shock response, and managing free radical levels (Raule et al. 2016) influence longevity. Function is reduced if these processes are not maintained and cellular ageing is accelerated through DNA methylation. Three main pathways control lifespan in mammals: insulin/IGF-1, TSCn/TOR and sirtuins (Hubbard and Sinclair 2014). The latter are central to the body's response to diet and exercise. These three pathways possibly control the response to adversity and cellular stress that contributes to DNA damage and hypoxia. Many of the biomarkers that drive ageing and the functional and pathological changes that result can be measured as shown in Box 1.2.