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**The triple challenges associated with age-related comorbidities  
in Down syndrome**

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### Survival trends in Down syndrome

Down syndrome has a population prevalence of 1/650 to 1/1,000 live births<sup>[1,2]</sup>. Despite a high uptake of prenatal testing and elective termination of affected pregnancies the birth prevalence of Down syndrome has remained stable or even increased during the last two decades in a number of countries<sup>[1,3]</sup>. The principal reason for this phenomenon is the positive association between Down syndrome conceptions and advanced maternal age<sup>[4]</sup>, coupled with the continuing trend of women delaying child-bearing to later ages<sup>[3]</sup>.

In developed countries over 90% of children born with Down syndrome now live to 10 years of age and median life expectancy at birth has increased to approximately 60 years, up from just 12 years of age in the 1950s<sup>[5,6]</sup>. Survival estimates have improved significantly through by early correction of congenital heart defects<sup>[7-9]</sup> as well as more focused treatment of infections, better enhanced nutrition, and improved general health care.

### Comorbidities in Down syndrome

Down syndrome is associated with a wide range of comorbidities across different life phases<sup>[1]</sup>. Early childhood disorders have been well described, for example, congenital heart defects<sup>[10]</sup>, reduced immunological function<sup>[11]</sup>, and a predisposition to acute lymphocytic leukaemia<sup>[12]</sup> which can continue to pose serious concerns throughout the lifespan. However, other major comorbidities develop during and after childhood with some disease states only diagnosed at advanced ages<sup>[13]</sup>. In addition, Down syndrome is associated with premature ageing, becoming apparent around 40 years of age, i.e. some 20 years earlier than in members of the general population. Therefore with a median life expectancy of approximately 60 years individuals may be at risk of a range of age-related diseases over an extended period of their lives<sup>[1,14]</sup>.

To examine these issues data were collated from studies which observed five common comorbidities affecting adults with Down syndrome, visual and hearing defects, epilepsy, thyroid disorders, and Alzheimer disease, at specific age intervals<sup>[15-22]</sup>. Only studies with data reported per decade of life were included. Figure 1 depicts how the prevalence of most of these conditions increases sharply after 40 years of age, and how at this age people with Down syndrome are subject to a high risk of significant multiple morbidities and a consequent need for ongoing specialist care. Secondary conditions such as osteoporosis, obesity, diabetes and poor dentition are also expected to develop with advancing age<sup>[13]</sup>, with their ill-effects exacerbated by long-term medication, polypharmacy, immobility, and general inactivity.

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### Challenges in the delivery of health care to people with Down syndrome

Three main questions relating to the delivery of health care can be identified:

## 1. Are comorbidities being detected in a timely manner~~adequately~~?

Relatively few published studies have included sufficient numbers of adult cases to demonstrate the specific age-related disease patterns that emerge in Down syndrome. Besides small sample sizes, inappropriate descriptors such as ‘above 18 years’ or ‘under 50 years vs over 50 years’ are often applied. Analyses of this nature are insufficiently ~~robust or~~ precise to identify the important decadal changes in health that commonly arise in people with Down syndrome. The paucity of available data implies that health professionals may be inadequately informed about the timing and nature of Down syndrome comorbidities, thus precluding the adoption of appropriate screening schedules.

Sets of health guidelines for adults with Down syndrome have nevertheless been published to encourage primary health care providers to perform regular health checks<sup>[23]</sup>. However ~~t~~the guidelines are, ~~however~~, generally broad in nature, they occasionally vary in the advice proffered, and they usually are compiled without consideration of the timing of symptom onset or possible interactions between comorbid conditions. It is generally recommended that annual medical appointments are arranged to review medications, screen for expected comorbidities, and consider the emergence of prospective illnesses<sup>[24]</sup>. But European studies have shown that many adults with Down syndrome fail to receive regular medical appointments and therefore health checks are not applied<sup>[25,26]</sup>. Of greater concern, an Australian survey of children and adolescents with Down syndrome indicated a decreasing mean number of regular general practitioner visits even by late childhood<sup>[27]</sup>.

In the absence of formally implemented strategies for adult health care it is likely that: i) many people with Down syndrome are not regularly screened; ii) interventions are only introduced when problems have become clinically apparent, with the onset of treatments delayed; iii) different conditions are treated in isolation; and iv) untreated health problems may result in additional disadvantageous complications. Communication difficulties frequently prevent individuals with the disorder from conveying symptoms ~~adequately~~ and providing descriptive information, with awareness of illness initially noticed via behavioural changes that require interpretation by a vigilant carer or clinician. It therefore is important for carers and physicians to be aware of appropriate regimens to maintain health with regular screening for emerging health issues<sup>[28]</sup>, particularly as people with intellectual disability are seldom targeted in community health promotion programmes<sup>[29]</sup>.

## 2. Is the clinical progression of Down syndrome adequately understood?

The combination of age-related comorbidities and positive improvements in survival statistics over the last half-century necessitates a more detailed investigation into the natural progression and

~~longitudinal patterns of comorbidities of the life course in of~~ Down syndrome, ~~especially since~~. As the phenomenon of old age in ~~people with the disorder Down syndrome~~ is relatively recent, ~~detailed investigation into the natural progression of the disorder and longitudinal patterns of comorbidities is needed~~. Although certain comorbidities have been identified ~~that and~~ are common to ~~mostany~~ people with Down syndrome, ~~many cases not all people~~ exhibit ~~dissimilar health the same health~~ histories, suggesting particular health trajectories within Down syndrome itself. Isolating and ascribing these patterns ~~of disease~~ to particular subgroups will increase our understanding of their predetermined health outcomes and the requirement for more personalised care schedules.

~~An individual's The~~ birth cohort should be considered as an important variable in longitudinal analyses, ~~as since people individuals~~ born in more recent decades predictably would have experienced different care protocols which in turn would impact on their overall health status. A prime example of this transition in care is the highly significant ~~positive~~ impact of early surgical intervention on the survival of the estimated 40-50% of infants with Down syndrome diagnosed with a congenital heart defect<sup>[30,318,30]</sup>.

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### 3. Who is responsible for the provision of care?

According to normalisation principles people with Down syndrome are encouraged to live in mainstream society<sup>[31]</sup>, with their wellbeing largely dependent on caregivers at home or in community placements. An inadvertent adverse effect of normalisation has been a reduction in the number of appropriately trained and experienced health professionals<sup>[32,33]</sup>, resulting in increased workloads for general practitioners and greater burdens on families and carers. The development of additional illnesses in the fourth to sixth decades ensures that a lengthy period of specialist care will be required during the remaining years of life, now potentially spanning more than 30 years. However, the management of health care for people after 18 years of age is ill-defined, with continuity of care often fragmented, reluctance from both families and paediatric practitioners to initiate the transition to adult-based services<sup>[34]</sup>, and in some cases a preference to remain linked to paediatric services<sup>[35]</sup>.

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In a US cohort study of people with Down syndrome (median age ~~of~~ 28 years), half of the individuals ~~investigated~~ continued to utilize child-focused providers in some capacity<sup>[20]</sup>. This blurring of the transition to adulthood creates the incongruity that adults with Down syndrome are encouraged to be independent members of society, yet their health care regimes remain largely unmapped. ~~Controversy also Questions~~ remains with respect to the ~~surrounding which~~ medical specialities ~~that~~ can most appropriately deliver ~~their~~ health care ~~for people with Down syndrome~~ in adulthood and old age, and whether community-based practitioners are sufficiently knowledgeable or experienced to administer the levels of advice and support needed.

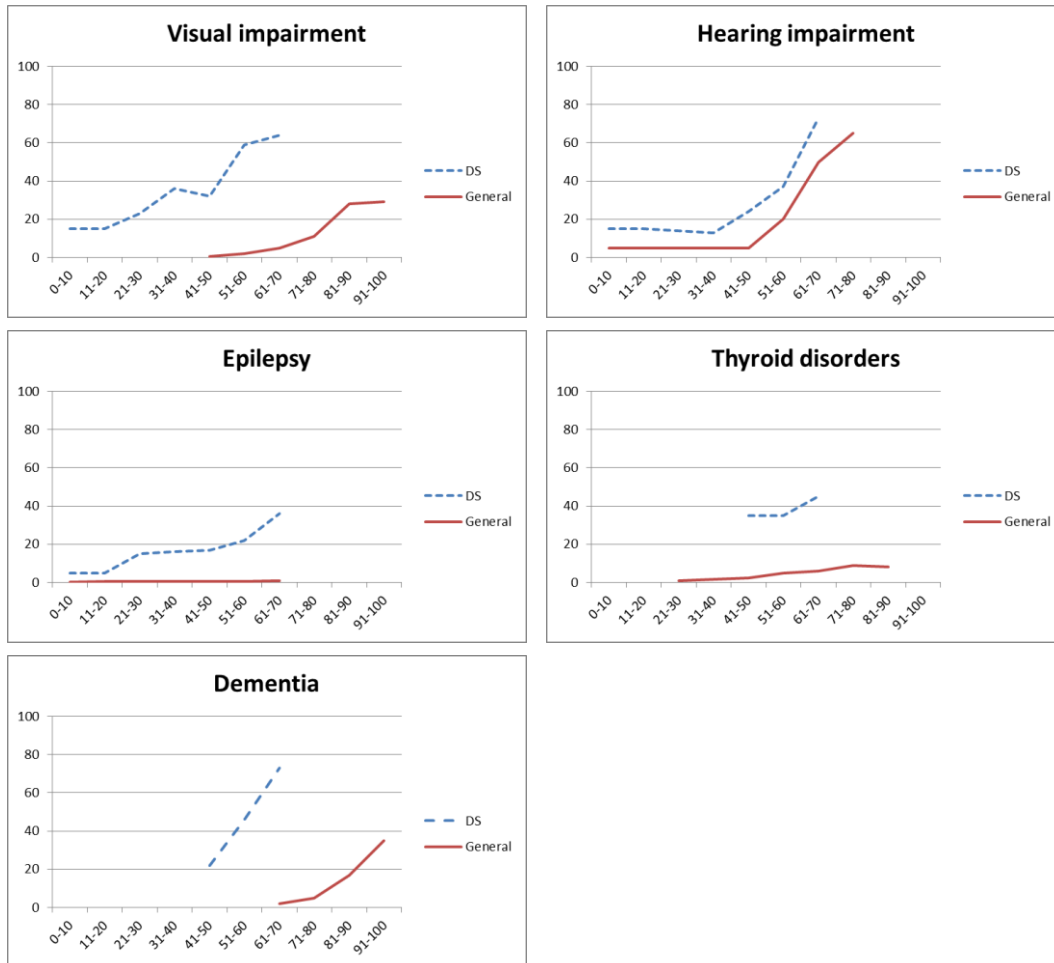
## Conclusion

The triple challenges identified exist because of the significant increase in the life expectancy of people with Down syndrome in recent decades, equating to almost one additional year of survival for every year passed<sup>[5]</sup>. [Detailed research into ~~related changes in~~ their age-related health profiles is therefore essential](#), both for people with the disorder and their families, [is essential if progress towards health and social equality for people with Down syndrome is to continue](#).

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**Figure 1 legend:**

—Probability of developing five common disease states per decade of life for people with Down syndrome compared to the general population: a) Visual impairment <sup>[16,22]</sup>; b) Hearing impairment <sup>[15,22]</sup>; c) Epilepsy <sup>[18,22]</sup>; d) Thyroid disorders <sup>[19,22]</sup>; e) Dementia <sup>[17,21]</sup>.



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Possible additional ref (see attached abstract):

*Pace, J.E., Shin, M. and Rasmussen, S.A. Understanding physicians' attitudes toward people with Down syndrome. American Journal of Medical Genetics A, 2011. 155A(6): 1258-1263.*

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