

NIH Public Access

Author Manuscript

Int Rev Res Ment Retard. Author manuscript; available in PMC 2011 January 1

Published in final edited form as:

Int Rev Res Ment Retard. 2010; 39(C): 107–126. doi:10.1016/S0074-7750(10)39004-5.

Health conditions associated with aging and end of life of adults with Down syndrome

Anna J. Esbensen, PhD

Cincinnati Children's Hospital Medical Center

Abstract

Expectations for the life course of individuals with Down syndrome (DS) have changed, with life expectancy estimates increasing from 12 in 1949 to nearly 60 years of age today (Bittles & Glasson, 2004; Penrose, 1949). Along with this longer life expectancy comes a larger population of adults with DS who display premature age-related changes in their health. There is thus a need to provide specialized health care to this aging population of adults with DS who are at high risk for some conditions and at lower risk for others. This review focuses on the rates and contributing factors to medical conditions that are common in adults with DS or that show changes with age. The review of medical conditions includes the increased risk for skin and hair changes, early onset menopause, visual and hearing impairments, adult onset seizure disorder, thyroid dysfunction, diabetes, obesity, sleep apnea and musculoskeletal problems. The different pattern of conditions associated with the mortality of adults with DS is also reviewed.

Keywords

Down syndrome; physical health; aging; mortality

A highly significant change in the survival of people with Down syndrome (DS) has occurred during the last two generations. In the 1940s, the average life expectancy for individuals with DS was 12 years (Penrose, 1949). With medical breakthroughs and improvements in services, individuals with DS now enjoy life expectancies into their 60s (Bittles & Glasson, 2004). As a result, we are now witness to the first generation of individuals with DS who have benefited from a revolution during their lifetime of better knowledge, health care, advocacy and services (Yang, Rasmussen & Friedman, 2002). Along with this longer life expectancy comes a larger population of adults with DS who display premature age-related changes in their health. There is thus a need to provide specialized health care to this aging population of adults with DS who are at high risk for some conditions and at lower risk for others. Adults with DS are at age-related increased risk for dementia, skin and hair changes, early onset menopause, visual and hearing impairments, adult onset seizure disorder, thyroid dysfunction, diabetes, obesity, sleep apnea and musculoskeletal problems. Along with these increased risks for some conditions comes a different pattern of conditions associated with the mortality of adults with DS. This review focuses on the rates and contributing factors to medical conditions that are common in adults with DS or that show changes with age.

Skin and hair changes

Adults with DS experience a number of dermatological and autoimmune symptoms characteristic of accelerated aging, including premature graying of the hair, hair loss and wrinkling of the skin (Lott, 1982). Significant differences in the skin and chronological age of the individual have been found in post-mortem examinations of the skin of adults with DS

(Edwards, 1978). Further, sun-exposure may have a greater effect on skin wrinkling for individuals with DS than for the general population, contributing to the appearance of premature skin aging in adults with DS (Brugge, Grove, Clopton, Grove & Piacquadio, 1993).

Alopecia areata (the loss of hair) is estimated to effect between 6% to 18.4% of adults with DS (duVivier & Munro, 1975; Prasher, 1994b). In comparison, only 0.1% of individuals with intellectual disability (ID) and 0.1- 0.2% of the general population are affected by alopecia areata (Safavi, Muller, Suman, Moshell & Melton, 1995; duVivier & Munro, 1975). It is posited that this elevated rate of alopecia areata in adults with DS may be related to immunological deficiency in thymus dependent function (Carter & Jegasothy, 1976).

Other skin conditions common in adults with DS include atopic dermatitis, fungal infections, seborrhoeic dermatitis, and xerosis, affecting 34% to 39% of adults (Kerins, Petrovic, Bruder & Gruman, 2008; Prasher, 1994b; Roizen & Patterson, 2003). These skin conditions are found in higher rates among older than younger adults with DS, and may be due in part to declines in self-care associated with memory loss and dementia that are common in the aging of adults with DS (Kerins et al., 2008).

Several theories have been proposed to account for the premature aging observed in adults with DS. The DNA damage theory of aging focuses on aging as a consequence of unrepaired DNA damage accumulation. The DNA damage theory is supported by lower levels of DNA repair enzymes being found in adults with DS (Madan, Williams & Lear, 2006). An alternate theory focuses on free-radical metabolism which involves a key enzyme, CuZn superoxide dismutase, which is located on chromosome 21 (Druzhyna, Nair, LeDoux & Wilson, 1998). Over-expression of this enzyme leads to the altered structure and function of tissue (Sinha, 2005).

Menopause

Women with DS are found to experience menopause starting at an earlier age than other women with ID and than women in the general population (Carr & Hollins, 1995; Cosgrave, Tyrrell, McCarron, Gill & Lawlor, 1999; Schupf, Zigman, Kapell, Lee, Kline & Levin, 1997). An early report found that 87% of women with DS and 69% of women with ID had stopped menstruating by age 46. All women with DS had stopped menstruating by the age of 51, and all of the women with ID by age 54. An estimate of the median age at menopause for women with DS of 47.1 is two years younger than the estimated median age for women with ID of 49.3 (Schupf et al., 1997). These estimates among women with DS and ID are potentially underestimates as the proportion of women who had never menstruated in the sample was unknown. A recent prospective study using multiple methods of analysis of the age at menopause for women with DS, all of whom had a history of menstruation, reported a median age of 45.8 to 47.1 (Seltzer, Schupf & Wu, 2001). No woman with DS older than 52 was menstruating. In comparison, the age at menopause in the general population is 51.3, with perimenopause starting at 47.5 (McKinlay, Brambilla & Posner, 1992), indicating that women with DS have a median age of menopause that is 4 to 6 years earlier than women in the general population.

The earlier onset of menopause in women with DS has implications for their health as menopause is a risk factor for heart disease, depression, osteoporosis, breast-cancer and dementia in the general population (Harlow & Ephross, 1995), and is associated with cognitive declines and dementia in women with DS (Patel, Seltzer, Wu & Schupf, 2001; Schupf et al., 2003). Some studies have found thyroid deficiency contributing to earlier onset of menopause (Carr & Hollins, 1995), whereas others have not replicated the findings in part due to appropriate thyroid treatment being available to the women sampled (Schupf

et al., 1997; Seltzer et al., 2001). As such, the contribution of thyroid conditions to earlier menopause is still uncertain.

Vision impairments

Visual impairments (44-71%) and eye abnormalities are common among aging adults with DS (Gardiner, 1967; Jacobson, 1988; McCarron, Gill, McCallion & Begley, 2005). The prevalence of visual impairments does not appear to be related to level of intellectual functioning among individuals with DS, and is greater than the prevalence (8-50%) observed in older adults with ID without DS (Gardiner, 1967; Haveman, Maaskant & Sturmans, 1989; Janicki & Jacobson, 1986; Moss, 1991). Comparable to visual acuity in the general population, visual impairment deteriorates among adults with DS, with the prevalence of severe visual impairment increasing from 18% among 30-39 year olds, to 28% among 40-49 year olds and to 45% among 50-59 year olds (Van Buggenhout et al., 1999). Of greater concern than the prevalence of visual impairment are reports of only 53% of cases of impairment being diagnosed, and only 50% of individuals with DS receiving correction for their visual impairment (Jacobson, 1988).

Cataracts (11-33%), strabismus (23-37%), refraction problems (30-34%) and keratoconus (15%) are common ophthalmological problems (Aitchison, Easty & Jancar, 1990; Prasher, 1994b; Van Allen, Fung & Jurenka, 1999; Van Buggenhout et al., 1999). A small study of 19 adults with DS over the age of 40 reported even higher rates of ophthalmological problems, with 55% suffering from strabismus and 75% from refraction problems (Hesmes, Sand & Fostad, 1991). The prevalence of cataracts is greater in adults than in children with DS and is comparable to or higher than the prevalence of 17% found in adults in the general population (Congdon et al., 2004). Higher rates of cataracts among adults with DS have been reported (30-68%), with few warranting surgery (Hesmes et al., 1991; Pueschel, 1990; Van Allen et al., 1999). Even when surgery is performed, visual problems and impairments may persist related to aphakia (absence of the lens of the eye) and to poor use of bifocals (Van Allen et al., 1999). Senile cataracts appear to develop earlier in adults with DS than in the general population and to increase in prevalence with age (Pueschel, 1990; Robb & Marchevsky, 1978; Van Allen et al., 1999). These senile cataracts, characterized by a gradual thickening of the lens, tends to occur at a younger age in DS compared to other individuals with ID, possibly due to the accelerated aging process present in individuals with DS and the increased amounts of free radical reactions (Ellis, 2002).

Keratoconus also increases in prevalence with age, from 11% in middle-age to 20% in the elderly (Van Allen et al., 1999). One small study reported that 37% of adults over the age of 40 had keratoconus (Hesmes et al., 1991).

Hearing Impairments

Age-related hearing loss is more common among adults with DS compared to the general population, and appears to have an earlier age of onset. High frequency sensorineural hearing impairments (such as presbycusis) in adults with DS onsets about 20 to 30 years earlier than in their peers with ID, and about 30 to 40 years earlier than in the general population (Buchanan, 1990). Rates of hearing loss among adults with DS range from 12 to 72% (Howells, 1989; Prasher, 1994b; Van Buggenhout et al., 1999), and may depend on the nature of the hearing assessment. Using detailed audiometric methods, Van Buggenhout and colleagues (1999) found 53% of adults with DS to have moderate hearing loss, 17% to have a severe hearing loss, and 2% to have a profound hearing loss. These rates of hearing loss were reported to increase with age and for the hearing loss to become more severe (Buchanan, 1990; Van Buggenhout et al., 1999). While the rate of hearing loss is not related

to level of ID, it has been found to be higher among adults with co-morbid dementia (McCarron et al., 2005).

Howells (1989) reported that 55% of adults over age 21 may have sensorineural hearing loss. For adults over 35 years of age, 68% of ears tested were reported to have cochlear hearing loss, with conductive hearing loss found in 5% of ears and mixed hearing loss found in 13% of ears (Evenhuis, Van Zanten, Procaar & Roerdinkholder, 1992). Van Buggenhout and colleagues (1999) similarly found a low rate of conductive hearing loss (10%) in their sample of adults with DS, and a comparable number with sensorineural and mixed hearing loss (45% and 44% respectively). However, Evenhuis et al. (1992) argues that we do not know how much the rate and degree of hearing impairment in adults with DS is related to previous middle ear pathology, such as otitis media. With the life expectancy of adults with DS growing longer, it is important to understand how medical conditions common early in the life course may influence the health of the individual later in life.

While hearing impairments are common among adults with DS, few are identified or treated. Of individuals identified with hearing impairments during research testing who did not use hearing devices, 80% of their care providers and general practitioners were unaware of the hearing loss (Van Buggenhout et al., 1999). Additionally, only 41% of individuals with hearing impairments identified during research testing were using hearing devices (Van Buggenhout et al., 1999). Half of this sample had severe to profound ID which may have contributed to a difficulty in using hearing devices.

Seizure disorder

The rate of seizures increases with age for individuals with DS, especially for individuals suffering from comborbid dementia. Early reports of the rate of seizures were significantly lower than more recent prevalence estimates. One early estimate of the rate of seizures was 12.2% for adults with DS over the age of 55 and 15.8% for adults over the age of 60 (Veall, 1974). However, early estimates were consistent with more recent estimates that abnormal readings reflective of seizure activity are high, with 71.4% of adults over 55 showing this abnormal activity (Tangye, 1979). Although these early reports underestimated current prevalence estimates, perhaps consistent with the shorter life expectancy of the time, these studies consistency reported a rise in the rate of seizures with age from adolescents to young adults to later adulthood. This increase in the rate of seizures across the lifespan is supported by other later research. Cohort differences show that 8% of adolescents or young adults with DS suffer from seizures as compared to 24-28% of seniors aged 50 and older (Johannsen, Christensen, Goldstein, Nielsen & Mai, 1996; McDermott, Moran, Platt, Wood, Isaac & Dasari, 2005). McVicker, Shanks and McClelland (1994) also supported a lower rate of seizures among younger individuals (7%) as compared to adults older than 50 (46%). A lifespan study of individuals with DS found that approximately 8% of individuals with DS suffer from seizures, and of these 40% experienced seizures after the age of 20 (Pueschel, Louis & McKnight, 1991). The higher rate of seizures observed in individuals with DS may be related to the gene for myoclonus epilepsy being mapped to chromosome 21, however this form of seizure is more commonly found in children and adolescents (Hattori et al., 2006). Older patients with DS typically have tonic-clonic (formerly known as grand mal), complex partial or simple partial seizures (Pueschel et al., 1991). Alternatively, structural abnormalities and biochemical aberrations of the CNS in adults with DS may in part be responsible for increased seizure frequency (Pueschel et al., 1991).

The increase in seizures related to age parallels the increase in the general population, although the rate of seizures is lower in the general population than among individual with DS (McDermott et al., 2005). However, it should be noted that the rate of seizure activity

among individuals with DS is lower than the reported rate among individuals with ID in general (McDermott et al., 2005). More recent estimates of the rate of seizures among adults with DS range from 9.4% to 26.5%, with a mean onset of seizures over the age of 30, around age 37 (Johannsen et al., 1996; McDermott et al., 2005; McVicker et al., 1994; Puri, Ho & Singh, 2001).

In addition to increasing with age, the rate of epilepsy and seizures is also related to the onset of dementia among adults with DS (Puri et al., 2001; Prasher & Corbett, 1993). In one study, 80% of the adults with seizures also presented with symptoms consistent with a clinical diagnosis of dementia (McVicker et al., 1994). In another study, 53% of individuals with dementia were reported to have seizures and the onset of seizures appeared to presage the onset of cognitive deterioration and symptoms of dementia (Lott & Lai, 1982). Indeed, the onset of seizures has been reported to occur at a younger age for individuals with DS who do not suffer from dementia (age 29) as compared to those who do (age 45). Dementia may be an important risk factor for late-onset seizures in adults with DS, but not for the high rate of seizures among all individuals with DS (Menéndez, 2005).

Thyroid dysfunction

Comparable to how the rate of seizures increases with age in adults with DS, the rate of individuals with DS at risk for thyroid disease also increases with age (Korsager, Chatham & Ostergaard-Kristensen, 1978), although some samples have indicated no increase with age (Murdoch, Ratcliffe, McLarty, Rodger & Ratcliffe, 1977; Šare, Ruvalcaba & Kelley, 1978). Approximately 35-40% of adults with DS are reported to have abnormal thyroid function, although only 7-8% had active hypothyroidism (Dinani & Carpenter, 1990; Prasher, 1994a; Prasher, 1994b). Also comparable to seizure findings, the rate of thyroid disease in adults with DS is greater than that found in the general population (Coleman, 1994).

The high rate of abnormal thyroid function highlights the need for consistent and routine monitoring of thyroid functioning for adults with DS. Routine monitoring is particularly important as some individuals tested with abnormal thyroid functioning were identified with thyroid disease and were receiving too much or too little medication to manage their disease (Prasher, 1994a).

Other Medical Conditions

Diabetes

There are a few reports of an increased risk of Type 1 diabetes among individuals with DS and of increased risk of mortality due to Type 1 diabetes as compared to the general population (Anwar, Walker & Frier, 1998; Hill et al., 2003). The age of onset of Type 1 diabetes appears to be increasing in individuals with DS. Earlier studies of Type 1 diabetes from the 1960s focused on children (Burch & Milunsky, 1969; Farquhar, 1962; Milunsky & Neurath, 1968) and reported that the age of onset peaked at 8 years of age for individuals with DS. However, the life expectancy of individuals with DS in the 1960s was 18 years (Collmann & Stoller, 1963). With increasing life expectancies for individuals with DS, more recent age of onset estimates of 22 years are comparable to the onset of type 1 diabetes in the general population (Anwar et al., 1998) and consistent with more individuals being diagnosed with adult-onset diabetes than juvenile diabetes. However, contrary reports suggest that adults with DS are at lower risk for mortality due to Type 1 diabetes than the general population and than adults with ID due to other causes (Haveman et al., 1989; Yang et al., 2002). Few reports are available regarding Type 2 diabetes in adults with DS, but the rate reported in a preliminary report appears to be lower than that in the general population

(Silverman, 2010). There is a need for more detailed population studies on the rate of Type 1 and Type 2 diabetes in individuals with DS to confirm these findings.

Obesity

A significant proportion of adults with DS are reported to be overweight or obese according to the body mass index (BMI). Between 45-79% of males and between 56-96% of females with DS are reported to be overweight (Bell & Bhate, 1992; Melville, Cooper, McGrother, Thorp & Collacott, 2005; Prasher, 1995; Rubin, Rimmer, Chicoine, Braddock & McGuire, 1998), while the prevalence in the general population that is overweight was reported to be approximately a third during the time period of these studies (Rubin et al., 1998). Contributing factors to the high rate of overweight and obese individuals with DS may include a combination of eating behavior, intake, metabolic rate, hypothyroidism and reduced exercise (Prasher, 1995).

BMIs are found to increase with age in the general population. Conversely, BMIs of cohorts of adults with DS are observed to be smaller with increasing age (Prasher, 1995; Rubin et al., 1998). Contributing factors to the lower BMIs found in older adults with DS are speculative, but may include residential setting, and healthier weights contributing to longevity (Rubin et al., 1998).

Sleep apnea

Obstructive sleep apnea (OSA) is present in approximately 30-55% of children with DS (de Miguel-Díez, Villa-Asensi & Álvarez-Sala, 2003; Stebbens, Dennis, Samuels, Croft & Southall, 1991). The known risk factors for OSA in children include facial (midfacial hypoplasia, mandibular hypoplasia) and other physical features (glossoptosis, an abnormally small upper airway, superficially positioned tonsils, relative tonsillar and adenoidal encroachment, hypotonia of upper airway) (Marcus, Keens, Bautista, von Pechmann & Ward, 1991; Roizen, 2003). Other risk factors have yet to be identified. Adults with DS are at increased risk for OSA as these risk factors observed in children continue into adulthood, and other risk factors become more prevalent. Obesity (reviewed previously) is a risk factor for OSA that put adults with DS at increased risk for developing this disorder. The rate of hypothyroidism (reviewed previously) increases with age in adults with DS, and is associated with OSA. The few studies that have examined the rate of OSA among adults with DS report that up to 94% of adults suffer from the disorder (Trois et al., 2009). Despite the increase in the number of risk factors predisposing adults with DS to OSA, increasing age is found to be the strongest risk factor, particularly when other risk factors are not present (Resta et al., 2003).

Musculoskeletal

Musculoskeletal problems often result from premature degenerative bone and joint disease (Dacre & Huskisson, 1988; Olive, Whitecloud & Bennet, 1988). Osteoporosis is common among adults with DS and adults are at greater risk as they age (Center, Beange & McElduff, 1998). There are several factors that may contribute to this increased risk for osteoporosis in adults with DS, including early menopause, deceased physical activity, low muscle tone and decreased strength. Degenerative osteoarthritis is also common among adults with DS, with osteoarthritis of the spine affecting 22% of middle-age adults and 40% of elderly adults (Van Allen et al., 1999). Typical symptoms include numbness, weakness and pain. It is often difficult to detect these symptoms in individuals with ID, and thus the rate of degenerative osteoarthritis may be underreported. Orthopedic problems, such as flat feet (a congenital condition), are the most common musculoskeletal abnormality observed in adults with DS, affecting approximately 70% of individuals (Prasher, 1994b).

Mitral valve prolapse

Mitral valve prolapse is common among adults with DS, occurring in between 46 to 57% of individuals (Barnhart & Connolly, 2007; Roizen & Patterson, 2003). Even though children with DS have a high risk of congenital heart disease, this previous cardiac pathology is not linked to the high rate of mitral valve prolapse later in life. Early signs of mitral valve prolapse are comparable to those observed in the general population and include fatigue, weight gain, and irritability (Barnhart & Connolly, 2007).

Mortality

Health problems present in adults, reviewed earlier in this chapter such as sensory handicaps, thyroid disorders, and degenerative spine disease, may contribute to the earlier mortality observed in adults with DS (Kapell, Nightingale, Rodriguez, Lee, Zigman & Schupf, 1998; Lantman-de Valk, Haveman, & Crebolder, 1996). However, their direct effect on mortality is not yet well documented. The life expectancy of adults with DS has a similar pattern until the age of 40 as compared to their age peers with other types of ID, and elevated mortality rates thereafter (Haveman, Maaskant & Sturmans, 1989; Maaskant, Gevers & Wierda, 2002; Strauss & Eyman, 1996).

The life expectancy of adults with DS is increasing and now averages around the mid- to late-50s. Still, this life expectancy is substantially below that of the general population and that of their peers with ID (Glasson, Sullivan, Hussain, Petterson, Montgomery & Bittles, 2002; Janicki, Dalton, Henderson & Davidson, 1999). Also, while women with DS are observed to have shorter life expectancies than men with DS, the opposite pattern is seen in the general population and among individuals with other types of ID (Carter & Jancar, 1983; Glasson et al., 2002; Glasson, Sullivan, Hussain, Petterson, Montgomery & Bittles, 2003; Tyrer, Smith & McGrother, 2007). A gender difference in mortality among individuals with DS is still speculative as other studies have not replicated this finding (Day, Strauss, Shavelle & Reynolds, 2005; Janicki et al., 1999). If valid, earlier menopause (discussed earlier) may be a contributing factor to earlier mortality in women with DS as compared to men with DS (Schupf, Zigman, Kapell, Lee, Kline & Levin, 1997).

The evidence is mixed regarding other risk factors found to predict mortality of adults with DS. Some studies have found that functional abilities predict mortality in adults with DS (Chaney & Eyman, 2000; Esbensen, Seltzer & Greenberg, 2007; Eyman, Call & White, 1991; Strauss & Zigman, 1996), comparable to findings in their peers with ID (Bittles, Petterson, Sullivan, Hussain, Glasson & Montgomery, 2002; Strauss & Eyman, 1996). Prior levels of functional abilities and declines in functional abilities were found to predict mortality in a sample of adults with and without DS (Esbensen et al., 2007). However, the relationship between functional abilities and mortality among adults with DS is not always supported (Glasson et al., 2002; Strauss & Eyman, 1996; Strauss & Zigman, 1996). Age has consistently been found to be a predictor of mortality for adults with DS (Esbensen et al., 2007; Eyman, Call & White, 1989; Hayden, 1998), and new research suggests that worsening of behavior problems is another predictor of mortality (Esbensen et al., 2007).

Common causes of death in this population include leukemia, respiratory illness, congenital circulatory defects, diseases of the digestive system, dementia and Alzheimer's disease, and are reported to vary with age (Day et al., 2005; Hermon, Alberman, Beral & Swerdlow, 2001; Hill et al., 2003; Thase, 1982). Although a common cause of death among children with DS is leukemia (behind respiratory illness and congenital heart defects), this risk is found to decrease with age (Hasle, Clemmensen & Mikkelsen, 2000; Yang et al., 2002). In contrast, the risk of mortality due to cancer in adults with DS is equal to or lower than that in the general population or among their peers with ID (Day et al., 2005; Hasle et al., 2000;

Patja, Eero & Iivanainen, 2001b; Sullivan, Hussain, Glasson & Bittles, 2007; Yang et al., 2002). In particular, the risk of mortality due to solid tumors among adults with DS is considerably lower than among their peers and the general population (Hasle et al., 2000; Hill et al., 2003; Sullivan, et al., 2007). In contrast, the risk for dementia was found to increase with age (Yang et al., 2002). Respiratory problems, congenital anomalies (other than congenital heart anomalies) and ischemic heart disease were also found to vary with age in their relation to mortality in individuals with DS. Among older adults with DS, respiratory problems and congenital anomalies are reported to be more common and ischemic heart disease less common than expected (Yang et al., 2002). That cardiovascular and circulatory defects are common causes of death among individuals with DS is not unexpected given the biological phenotype of this syndrome (Roizen, 1996). In comparison, the common causes of mortality found among individuals with ID include cardiovascular diseases, respiratory diseases, and cancers (Patja, Mölsä & Iivanainen, 2001a), and these have been found to be comparable to causes of mortality among a sample of only adults with DS (Esbensen et al., 2007).

Medical Conditions with Low Risk

While adults with DS are at risk for several medical conditions just described, they are also at low risk for other medical conditions. In a review of cancers among individuals with DS, malignant solid tumors were reported to be underrepresented (Satgé, Sommelet, Geneix, Nishi, Malet & Vekemans, 1998). In particular, common epithelial tumors were underrepresented in adults, as are breast, uterine, digestive, genital, skin, bronchial, ear/nose/throat or urinary tract cancers (Hasle, Clemmensen, Haunstrup & Margareta, 2000; Hill et al., 2003; Jancar & Jancar, 1976; Oster, Mikkelsen & Nielsen, 1975; Scholl, Stein & Hansen, 1982). However, a greater risk for testicular cancer has been reported among males with DS as compared to typically developing males (Dieckmann, Rube & Henke, 1997; Hasle et al., 2000).

Possible explanations for the decreased risk of some cancers among adults with DS are that accurate population morbidity studies are rare. It has also been proposed that individuals with DS may be less exposed to environmental contributors to cancer risk (Satgé et al., 1998). Decreased alcohol and tobacco use, early menopause and other lifestyle and environmental factors may contribute to lower cancer risk. However, obesity and the lack of physical activity common in adults with DS would contribute to an increased risk of cancers. The shorter life expectancy of individuals with DS has also been suggested to contribute to lower risk for cancer (Satgé et al., 1998). However, as the life expectancy of individuals with DS has increased dramatically over the last few decades, shorter life expectancy becomes a less probable explanation for the apparent lower risk of solid tumors. Several tumor-suppressor genes have been identified on chromosome 21, potentially contributing to the decreased risks for many solid tumors (Lee, T. Park, S. Park & J. Park, 2003). Copperzinc superoxide dismutase, also located on chromosome 21, and its contribution to the metabolism of oxygen free radicals are further hypothesized to reduce the risk of carcinogens (de la Torre, Casado, Lopez-Fernández, Carrascosa, Ramirez & Saez, 1996).

While the rate of mitral valve prolapse is high, there is a lower risk for cardiovascular and cerebrovascular disease observed in adults with DS as compared to the general population (Marino & Pueschel, 1996) and lower rates of emphysema, fractures, hypercholesterolaemia and heart disease as compared to adults with ID due to other causes (Haveman et al., 1989; Kerins et al., 2008). Further, individuals with DS are found to have lower resting heart rates and lower blood pressure than the general population (Prasher, 1994b; Richards & Enver, 1979). The rise in blood pressure seen with age in the general population is not as great

Esbensen

among individuals with DS, and hypertension is an uncommon problem reported in adults with DS (Kerins et al., 2008; Prasher, 1994b).

While upper respiratory infections are common among adults with DS, significant respiratory problems are not common (Minihan & Dean, 1990; Prasher, 1994b; Wilson & Haire, 1990). Further, as mobility declines with age, recurrent pneumonia with incomplete recovery has been found to occur more often (Van Allen et al., 1999). This is particularly noteworthy as respiratory illness is a common cause of mortality in adults with DS. It may be that chronic respiratory problems contribute to mortality more so than acute respiratory problems.

Health Care

There are excellent guidelines for the health care of individuals with DS across the lifespan, including guidelines specific to adults (Cohen, 2002). They provide recommendations to health care professionals of what conditions to screen for and how frequently. However, little is known about the pattern of screening, health care use and access, or barriers to health care experienced by adults with DS specifically, although efforts are currently being made to explore these questions.

The literature on health care service use by adults with ID indicates that this population experiences significant health disparities in access to health care in comparison to the general population (Horwitz, Kerker, Owens & Zigler, 2000). As an example, few adults with ID receive care from specialists despite a high percentage of individuals, such as individuals with DS, having medical needs that require specialty care. An agenda has been set by the federal government for promoting the health of individuals with ID, improving their quality of and access to health care, and training health care providers to the specific needs of individuals with ID (US Public Health Service, 2001).

Conclusions

As individuals with DS continue to experience longer lives, the need to understand their aging and associated health conditions becomes more critical. The chronic disorders that onset in adults with DS, and the age-related change in other disorders, have important implications for health care management of this aging population. Health care providers need to be informed of the health conditions more common among adults with DS as they age, to be alert for declines earlier than expected in the general population, and the implication that early-life medical conditions may have in the later-life of the individual. For example, chronic and inadequately treated middle ear infections in childhood may have an impact on later hearing loss in adults with DS.

The different pattern of health conditions in aging adults with DS also has implications for family members and support providers. Over 60% of adults with ID co-reside with their families (Fujiura, 1998). As such, families and support providers of adults with DS need to be informed of what symptoms to be alert for in order to better communicate changes in health to medical providers, such as lethargy, irritability and fatigue. The health care provider is then responsible for determining whether these common symptoms are due to hypothyroidism, mitral valve prolapse, symptoms of menopause, pain, poor sleep, or to depression resulting from disorientation due to sensory impairments. Deteriorations in health can also be associated with an increase in behaviors, particularly if the individual with DS has communication difficulties in expressing problems or medical complaints. And finally, adults with DS should be provided with appropriate information to better understand, and counseling to cope with, changes in their own level of ability or health.

Acknowledgments

This manuscript was prepared with support from the National Institute on Child Health and Human Development (R03 HD59848).

References

- Aitchinson C, Easty DL, Jancar J. Eye abnormalities in the mentally handicapped. Journal of Mental Deficiency Research 1990;34:41–48. [PubMed: 2139130]
- Anwar AJ, Walker JD, Frier BM. Type 1 diabetes mellitus and Down's syndrome: Prevalence, management and diabetic complications. Diabetic Medicine 1998;15:160–163. [PubMed: 9507919]
- Barnhart RC, Connolly B. Aging and Down syndrome: Implications for physical therapy. Physical Therapy 2007;87:1399–1406. [PubMed: 17712035]
- Bell AJ, Bhate MS. Prevalence of overweight and obesity in Down syndrome and other mentally handicapped adults living in the community. Journal of Intellectual Disability Research 1982;36:359–364. [PubMed: 1388077]
- Bittles AH, Glasson EJ. Clinical, social, and ethical implications of changing life expectancy in Down syndrome. Developmental Medicine and Child Neurology 2004;46:282–286. [PubMed: 15077706]
- Bittles AH, Petterson BA, Sullivan SG, Hussain R, Glasson EJ, Montgomery PD. The influence of intellectual disability on life expectancy. Journal of Gerontology: Medical Sciences 2002;57A:M470–M472.
- Brugge KL, Grove GL, Clopton P, Grove MJ, Piacquadio DJ. Evidence for accelerated skin wrinkling among developmentally delayed individuals with Down's syndrome. Mechanics of Ageing and Development 1993;70:213–225.
- Buchanan LH. Early onset of presbyacusis in Down syndrome. Scandinavian Audiology 1990;19:103–110. [PubMed: 2142538]
- Burch PRJ, Milunsky A. Early-onset diabetes mellitus in the general and Down's syndrome populations: Genetics, aetiology, and pathogenesis. The Lancet 1969;293:554–558.
- Carr J, Hollins S. Menopause in women with learning disabilities. Journal of Intellectual DisabilityResearch 1995;39:137–139.
- Carter DM, Jegasothy BV. Alopecia areata and Down syndrome. Archives of Dermatology 1976;112:1397–1399. [PubMed: 134671]
- Carter G, Jancar J. Mortality in the mentally handicapped: A 50 year survey at the Stoke Park group of hospitals (1930-1980). Journal of Mental Deficiency Research 1983;27:143–156. [PubMed: 6225874]
- Center J, Beange H, McElduff A. People with mental retardation have an increased prevalence of osteoporosis: a population study. American Journal on Mental Retardation 1998;103:19–28. [PubMed: 9678227]
- Chaney RH, Eyman RK. Patterns in mortality over 60 years among persons with mental retardation in a residential facility. Mental Retardation 2000;38:289–293. [PubMed: 10900936]
- Cohen, WI. Health care guidelines for individuals with Down syndrome 1999 revision. In: Cohen, WI.; Nadel, L.; Madnick, ME., editors. A Vision for the 21st Century: Down Syndrome. Wiley-Liss; New York, NY: 2002. p. 237-245.
- Coleman M. Thyroid dysfunction in Down's syndrome: A review. Down Syndrome Research and Practice 1994;2:112–115.
- Collmann RD, Stoller A. Data on mongolism in Victoria, Australia: Prevalence and life expectation. Journal of Mental Deficiency Research 1963;17:117–122.
- Congdon N, Vingerling JR, Klein BE, West S, Friedman DS, Kempen J, O'Colmain B, Wu SY, Taylor HR. Prevalence of cataract and pseudophakia/aphakia among adults in the United States. Archives of Ophthalmology 2004;122:487–494. [PubMed: 15078665]
- Cosgrave MP, Tyrrell J, McCarron M, Gill M, Lawlor BA. Age at onset of dementia and age of menopause in women with Down's syndrome. Journal of Intellectual Disability Research 1999;43:461–465. [PubMed: 10622361]

- Dacre JE, Huskisson ED. Arthritis in Down syndrome. Annals of Rheumatic Disease 1988;47:254– 255.
- Day SM, Strauss DJ, Shavelle RM, Reynolds RJ. Mortality and causes of death in persons with Down syndrome in California. Developmental Medicine and Child Neurology 2005;47:171–176. [PubMed: 15739721]
- De La Torre R, Casado A, Lopez-Fernández E, Carrascosa D, Ramirez V, Saez J. Overexpression of copper-zinc superoxide dismutase in trisomy 21. Experientia 1996;52:871–873. [PubMed: 8841514]
- Dieckmann KP, Rube C, Henke RP. Association of Down's syndrome and testicular cancer. Journal of Urology 1997;157:1701–1704. [PubMed: 9112509]
- Dinani S, Carpenter S. Down's syndrome and thyroid disorder. Journal of Mental Deficiency Research 1990;34:187–193. [PubMed: 2140417]
- Druzhyna N, Nair RG, LeDoux SP, Wilson GL. Defective repair of oxidative damage in mitochondrial DNA in Down's syndrome. Mutation Research 1998;409:81–89. [PubMed: 9838924]
- Edwards JSH. Skin age in Down's syndrome: A note on the findings of Murdoch and Evans. Journal of Mental Deficiency Research 1978;22:223. [PubMed: 151745]
- Ellis FJ. Management of pediatric cataract and lens opacities. Current Opinion in Pediatrics 2002;13:33–37.
- Esbensen AJ, Seltzer MM, Greenberg JS. Factors predicting mortality in midlife adults with and without Down syndrome living with family. Journal of Intellectual Disability Research 2007;51:1039–1050. [PubMed: 17991011]
- Evenhuis HM, Van Zanten GA, Brocaar MP, Roerdinkholder WHM. Hearing loss in middle-age persons with Down syndrome. American Journal on Mental Retardation 1992;97:47–56. [PubMed: 1386743]
- Eyman RK, Call TL, White JF. Mortality of elderly mentally retarded persons in California. Journal of Applied Gerontology 1989;8:203–215.
- Eyman RK, Call TL, White JF. Life expectancy of persons with Down syndrome. American Journal on Mental Retardation 1991;95:603–612. [PubMed: 1829373]
- Farquhar JW. Diabetic children in Scotland and the need for care. Scottish Medical Journal 1962;7:119–124. [PubMed: 13891676]
- Fujiura GT. Demography of family households. American Journal on Mental Retardation 1998;103:225–235. [PubMed: 9833654]
- Gardiner PA. Visual defects in cases of Down's syndrome and in other mentally handicapped children. British Journal of Ophthalmology 1967;51:469–474. [PubMed: 4226447]
- Glasson EJ, Sullivan SG, Hussain R, Petterson BA, Montgomery PD, Bittles AH. The changing survival profile of people with Down's syndrome: Implications for genetic counselling. Clinical Genetics 2002;62:390–393. [PubMed: 12431254]
- Glasson EJ, Sullivan SG, Hussain R, Petterson BA, Montgomery PD, Bittles AH. Comparative survival advantage of males with Down syndrome. American Journal of Human Biology 2003;15:192–195. [PubMed: 12621607]
- Harlow SD, Ephross SA. Epidemiology of menstruation and its relevance to women's health. Epidemiologic Reviews 1995;17:265–286. [PubMed: 8654511]
- Hasle H, Clemmensen IH, Mikkelsen M. Risks of leukaemia and solid tumors in individuals with Down's syndrome. Lancet 2000;355:165–169. [PubMed: 10675114]
- Hattori M, Fujiyama A, Taylor TD, Watanabe H, Yada T, Park H-S, Toyoda A, Ishii K, Totoki T, Choi D-K, Soeda E, Ohki M, et al. The DNA sequence of human chromosome 21. Nature 2006;405:311–319. [PubMed: 10830953]
- Haveman M, Maaskant MA, Sturmans F. Older Dutch residents of institutions, with and without Down syndrome: Comparisons of mortality and morbidity trends and motor/social functioning. Australia and New Zealand Journal of Development Disabilities 1989;15:241–255.
- Hayden MF. Mortality among people with mental retardation living in the United States: Research review and policy application. Mental Retardation 1998;36:345–359. [PubMed: 9803125]

- Hermon C, Alberman E, Beral V, Swerdlow AJ. Mortality and cancer incidence in persons with Down's syndrome, their parents and siblings. Annals of Human Genetics 2001;65:167–176. [PubMed: 11427176]
- Hesmes A, Sand T, Fostad K. Ocular findings in Down's syndrome. Journal of Mental Deficiency Research 1991;35:194–203. [PubMed: 1833550]
- Hill DA, Gridley G, Cnattingius S, Mellemkjaer L, Linet M, Adami H-O, Olsen JH, Nyren O, Fraumeni JF. Mortality and cancer incidence among individuals with Down syndrome. Archives of Internal Medicine 2003;163:705–711. [PubMed: 12639204]
- Horwitz, SM.; Kerker, BD.; Owens, PL.; Zigler, E. The health status and needs of individuals with mental retardation. Special Olympics; Washington, DC: 2000.
- Howells G. Down's syndrome and the general practitioner. Journal of the Royal College of General Practitioners 1989;39:470–475. [PubMed: 2560050]
- Jacobson L. Ophthalmology in mentally retarded adults. A clinical survey. Acta Ophthalmologica 1988;66:457–462. [PubMed: 3057800]
- Jancar MP, Jancar J. Cancer and mental retardation. Bristol Medico-Chirurgical Journal 1976;92:3–7. [PubMed: 612362]
- Janicki MP, Dalton AJ, Henderson CM, Davidson PW. Mortality and morbidity among older adults with intellectual disability: Health services considerations. Disability and Rehabilitation 1999;21:284–294. [PubMed: 10381241]
- Janicki MP, Jacobson JW. General trends in sensory, physical, and behavioral abilities among older mentally retarded persons. American Journal of Mental Deficiency 1986;90:490–500. [PubMed: 3953681]
- Johannsen P, Christensen JEJ, Goldstein H, Nielsen VK, Mai J. Epilepsy in Down syndrome: Prevalence in three age groups. Seizure 1996;5:121–125. [PubMed: 8795127]
- Kapell D, Nightingale B, Rodriguez A, Lee JH, Zigman WB, Schupf N. Prevalences of chronic medical conditions in adults with mental retardation: Comparison with the general population. Mental Retardation 1998;36:269–279. [PubMed: 9713183]
- Kerins G, Petrovic K, Bruder MB, Gruman C. Medical conditions and medication use in adults with Down syndrome: A descriptive analysis. Down Syndrome Research and Practice 2008;12:141–147.
- Korsager S, Chatham EM, Ostergaard-Kristensen HP. Thyroid function tests in adults with Down's syndrome. Acta Endocrinology 1978;88:48–54.
- Lantman-de Valk HMJ, Haveman MJ, Crebolder HFJM. Comorbidity in people with Down's syndrome: A criteria-based analysis. Journal of Intellectual Disability Research 1996;40:385–399. [PubMed: 8906527]
- Lee EB, Park TI, Park SH, Park JY. Loss of heterozygosity on the long arm of chromosome 21 in nonsmall cell lung cancer. Annals of Thoracic Surgery 2003;75:1597–1600. [PubMed: 12735585]
- Lott IT, Lai F. Dementia in Down's syndrome: Observations from a neurology clinic. Applied Research in Mental Retardation 1982;3:233–239. [PubMed: 6216849]
- Maaskant MA, Gevers JPM, Wierda H. Mortality and life expectancy in Dutch residential centres for individuals with intellectual disability, 1991-1995. Journal of Applied Research in Intellectual Disabilities 2002;15:200–212.
- Madan V, Williams J, Lear JT. Dermatological manifestations of Down's syndrome. Clinical and Experimental Dermatology 2006;31:623–629. [PubMed: 16901300]
- Marcus CL, Keens TG, Bautista DB, von Pechmann WS, Ward SLD. Obstructive sleep apnea in children with Down syndrome. Pediatrics 1991;88:132–139. [PubMed: 1829151]
- Marino, B.; Pueschel, SM. Heart Disease in Persons with Down Syndrome. Paul H. Brooks; Baltimore: 1996.
- McCarron M, Gill M, McCallion P, Begley C. Health co-morbidities in ageing persons with Down syndrome and Alzheimer's dementia. Journal of Intellectual Disability Research 2005;49:560–566. [PubMed: 15966964]
- McDermott S, Moran R, Platt T, Wood H, Isaac T, Dasari S. Prevalence of epilepsy in adults with mental retardation and related disabilities in primary care. American Journal on Mental Retardation 2005;110:48–56. [PubMed: 15568966]

- McKinlay SM, Brambilla DJ, Posner JG. The normal menopause transition. Maturitas 1992;14:103–115. [PubMed: 1565019]
- McVicker RW, Shanks OEP, McClelland RJ. Prevalence and associated features of epilepsy in adults with Down's syndrome. British Journal of Psychiatry 1994;164:528–532. [PubMed: 8038944]
- Melville CA, Cooper S-A, McGrother CW, Thorp CF, Collacott R. Obesity in adults with Down syndrome: A case-control study. Journal of Intellectual Disability Research 2005;49:125–133. [PubMed: 15634321]
- Menéndez M. Down syndrome, Alzheimer's disease and seizures. Brain & Development 2005;27:246–252. [PubMed: 15862185]
- de Miguel-Díez J, Villa-Asensi JR, Álvarez-Sala J. Prevalence of sleep-disordered breathing in children with Down syndrome: Polygraphic findings in 108 children. Sleep 2003;26:1006–1009. [PubMed: 14746382]
- Milunsky A, Neurath PW. Diabetes mellitus in Down's syndrome. Archives of Environmental Health 1968;17:373–376.
- Minihan PM, Dean DH. Meeting the needs for health services of persons with mental retardation living in the community. American Journal of Public Health 1990;80:1043–1048. [PubMed: 2382738]
- Moss SC. Age and functional abilities of people with a mental handicap: evidence from the Wessex mental handicap register. Journal of Mental Deficiency Research 1991;35:430–445. [PubMed: 1837803]
- Murdoch JC, Ratcliffe WA, McLarty DG, Rodger JC, Ratcliffe JG. Thyroid function in adults with Down's syndrome. Journal of Clinical Endocrinology and Metabolism 1977;44:453–458. [PubMed: 138688]
- Olive PM, Whitecloud TS, Bennet JT. Lower cervical spondylosis and myelopathy in adults with Down syndrome. Spine 1988;13:781–784. [PubMed: 2973661]
- Oster J, Mikkelsen M, Nielsen A. Mortality and life-table in Down's syndrome. Acta Paediatrica Scandinavica 1975;64:322–326. [PubMed: 124122]
- Patel BN, Seltzer GB, Wu H-S, Schupf N. Effect of menopause on cognitive performance in women with Down syndrome. Cognitive Neuroscience and Neuropsychology 2001;12:2659–2662.
- Patja K, Eero P, Iivanainen M. Cancer incidence among people with intellectual disability. Journal of Intellectual Disability Research 2001a;45:300–307. [PubMed: 11489051]
- Patja K, Mölsä P, Iivanainen M. Cause-specific mortality of people with intellectual disability in a population-based, 35 year follow-up study. Journal of Intellectual Disability Research 2001b; 45:30–40. [PubMed: 11168774]
- Penrose LS. The incidence of Mongolism in the general population. Journal of Mental Science 1949;95:685–688. [PubMed: 18148788]
- Prasher VP. Prevalence of thyroid dysfunction and autoimmunity in adults with Down syndrome. Down Syndrome Research and Practice 1994a;2:67–70.
- Prasher VP. Screening of medical problems in adults with Down syndrome. Down Syndrome Research and Practice 1994b;2:59–66.
- Prasher VP. Overweight and obesity amongst Down's syndrome adults. Journal of Intellectual Disability Research 1995;39:437–441. [PubMed: 8555720]
- Prasher VP, Corbett JA. Onset of seizures as a poor indicator of longevity in people with Down syndrome and dementia. International Journal of Geriatric Psychiatry 1993;8:923–927.
- Pueschel SM. Clinical aspects of Down syndrome from infancy to adulthood. American Journal of Medical Genetics Supplement 1990;7:52–56. [PubMed: 2149974]
- Pueschel SM, Louis S, McKnight P. Seizure disorders in Down syndrome. Archives of Neurology 1991;48:318–320. [PubMed: 1825777]
- Puri BK, Ho KW, Singh I. Age of seizure onset in adults with Down's syndrome. International Journal of Clinical Practice 2001;55:442–444. [PubMed: 11594252]
- Resta O, Barbaro MPF, Giliberti T, Caratozzolo G, Cagnazzo MG, Scarpelli F, Nocerino MC. Sleep related breathing disorders in adults with Down syndrome. Down Syndrome Research and Practice 2003;8:115–119.

- Richards BW, Enver F. Blood pressure in Down's syndrome. Journal of Mental Deficiency Research 1979;23:123–135. [PubMed: 158658]
- Robb RM, Marchevsky A. Pathology of the lens in Down's syndrome. Archives of Ophthalmology 1978;96:1039–1042. [PubMed: 148880]
- Roizen NJ. Down syndrome and associated medical disorders. Mental Retardation and Developmental Disabilities Research Reviews 1996;2:85–89.
- Roizen NJ, Patterson D. Down's syndrome. Lancet 2003;361:1281-1289. [PubMed: 12699967]
- Rubin SS, Rimmer JH, Chicoine B, Braddock D, McGuire DE. Overweight prevalence in persons with Down syndrome. Mental Retardation 1998;36:175–181. [PubMed: 9638037]
- Safavi KH, Muller SA, Suman VJ, Moshell AN, Melton LJ. Incidence of alopecia areata in Olmsted County, Minnesota, 1975 through 1989. Mayo Clinic Proceedings 1995;70:628–633. [PubMed: 7791384]
- Šare Z, Ruvalcaba RHA, Kelley VC. Prevalence of thyroid disorder in Down syndrome. Clinical Genetics 1978;14:154–158. [PubMed: 151610]
- Satgé D, Sommelet D, Geneix A, Nishi M, Malet P, Vekemans M. A tumor profile in Down syndrome. American Journal of Medical Genetics 1998;78:207–216. [PubMed: 9677053]
- Scholl T, Stein Z, Hansen H. Leukemia and other cancers, anomalies and infections as causes of death in Down's syndrome in the United States during 1976. Developmental Medicine & Child Neurology 1982;24:817–829. [PubMed: 6218002]
- Schupf N, Pang D, Patel BN, Silverman W, Schubert R, Lai F, Kline JK, Stern Y, Ferin M, Tycko B, Mayeux R. Onset of dementia is associated with age at menopause in women with Down's syndrome. Annals of Neurology 2003;54:433–438. [PubMed: 14520653]
- Schupf N, Zigman W, Kapell D, Lee JH, Kline J, Levin B. Early menopause in women with Down's syndrome. Journal of Intellectual Disability Research 1997;41:264–267. [PubMed: 9219076]
- Seltzer GB, Schupf N, Wu H-S. A prospective study of menopause in women with Down's syndrome. Journal of Intellectual Disability Research 2001;45:1–7. [PubMed: 11168771]
- Silverman W. Webinar presented through the American Association on Intellectual and Developmental Disabilities Aging and End of Life Webinar Series. Dementia among adults with Down syndrome: Individual differences in risk and progression. January;2010
- Sinha S. Anti-oxidant gene expression imbalance, aging and Down syndrome. Life Sciences 2005;76:1407–1426. [PubMed: 15670619]
- Stebbens VA, Dennis J, Samuels MP, Croft CB, Southall DP. Sleep related upper airway obstruction in a cohort with Down's syndrome. Archives of Disease in Childhood 1991;66:1333–1338. [PubMed: 1836718]
- Strauss D, Eyman RK. Mortality of people with mental retardation in California with and without Down syndrome, 1986-1991. American Journal on Mental Retardation 1996;100:643–653. [PubMed: 8735577]
- Strauss D, Zigman WB. Behavioral capabilities and mortality risk in adults with and without Down syndrome. American Journal on Mental Retardation 1996;101:269–281. [PubMed: 8933901]
- Sullivan SG, Hussain R, Glasson EJ, Bittles AH. The profile and incidence of cancer in Down syndrome. Journal of Intellectual Disability Research 2007;51:228–231. [PubMed: 17300418]
- Tangye SR. The EEG and incidence of epilepsy in Down's syndrome. Journal of Mental Deficiency Research 1979;23:17–24. [PubMed: 158092]
- Thase ME. Longevity and mortality in Down's syndrome. Journal of Mental Deficiency Research 1982;26:177–192. [PubMed: 6217345]
- Trois MS, Capone GT, Lutz JA, Melendres MC, Schwartz AR, Collop NA, Marcus CL. Obstructive sleep apnea in adults with Down syndrome. Journal of Clinical Sleep Medicine 2009;15:317– 323. [PubMed: 19968008]
- Tyrer F, Smith LK, McGrother CW. Mortality in adults with moderate to profound intellectual disability: A population-based study. Journal of Intellectual Disability Research 2007;51:520– 527. [PubMed: 17537165]

Esbensen

- U.S. Public Health Service. Closing the Gap: A National Blueprint for Improving the Health of Individuals with Mental Retardation. Report of the Surgeon General's Conference on Health Disparities and Mental Retardation. Washington: DC: 2001.
- Van Allen MI, Fung J, Jurenka SB. Health care concerns and guidelines for adults with Down syndrome. American Journal of Medical Genetics 1999;89:100–110. [PubMed: 10559765]
- Van Buggenhout GJCM, Trommelen JCM, Schoenmaker A, de Bal C, Verbeek JJMC, Smeets DFCM, Ropers HH, Devriendt K, Hamel BCJ, Fryns JP. Down syndrome in a population of elderly mentally retarded patients: Genetic-diagnostic survey and implications for medical care. American Journal of Medical Genetics 1999;85:376–384. [PubMed: 10398264]
- Veall RM. The prevalence of epilepsy among Mongols related to age. Journal of Mental Deficiency Research 1974;18:43.
- du Vivier A, Munro DD. Alopecia areata, autoimmunity, and Down's syndrome. British Medical Journal 1975;1:191–192. [PubMed: 122906]
- Wilson DN, Haire A. Health care screening for people with mental handicap living in the community. British Medical Journal 1990;301:1379–1381. [PubMed: 2148703]
- Yang Q, Rasmussen SA, Friedman JM. Mortality associated with Down's syndrome in the USA from 1983 to 1997: A population-based study. Lancet 2002;359:1019–1025. [PubMed: 11937181]